## Critical Reviews in Toxicology

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**REVIEW ARTICLE** 

### Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/carcinogenicity rodent studies

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#### Abstract

Glyphosate, an herbicidal derivative of the amino acid glycine, was introduced to agriculture in the 1970s. Glyphosate targets and blocks a plant metabolic pathway not found in animals, the shikimate pathway, required for the synthesis of aromatic amino acids in plants. After almost forty years of commercial use, and multiple regulatory approvals including toxicology evaluations, literature reviews, and numerous human health risk assessments, the clear and consistent conclusions are that glyphosate is of low toxicological concern, and no concerns exist with respect to glyphosate use and cancer in humans. This manuscript discusses the basis for these conclusions. Most toxicological studies informing regulatory evaluations are of commercial interest and are proprietary in nature. Given the widespread attention to this molecule, the authors gained access to carcinogenicity data submitted to regulatory agencies and present overviews of each study, followed by a weight of evidence evaluation of tumor incidence data. Fourteen carcinogenicity studies (nine rat and five mouse) are evaluated for their individual reliability, and select neoplasms are identified for further evaluation across the data base. The original tumor incidence data from study reports are presented in the online data supplement. There was no evidence of a carcinogenic effect related to glyphosate treatment. The lack of a plausible mechanism, along with published epidemiology studies, which fail to demonstrate clear, statistically significant, unbiased and non-confounded associations between glyphosate and cancer of any single etiology, and a compelling weight of evidence, support the conclusion that glyphosate does not present concern with respect to carcinogenic potential in humans.

#### Keywords

amino acid, carcinogenicity, epidemiology, glyphosate, herbicide, mouse, neoplasm, phosphonomethylglycine, Roundup, rat, regulatory, tumor

healthcare

#### History

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#### Introduction

Glyphosate (Figure 1), an aminophosphonic analog of the natural amino acid glycine, is widely used as an herbicide for the control of annual and perennial grasses and broadleaved weeds. Glyphosate inhibits 5-enolpyruvateshikimate-3-phosphate synthase (EPSPS), an enzyme of the aromatic acid biosynthesis pathway, which is not present in the animal kingdom. Glyphosate-based herbicide formulations (GBFs) were introduced in 1974 and are formulated with

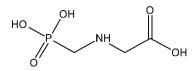


Figure 1. Structure of glyphosate acid.

sodium-, potassium-, ammonium- and isopropyl ammoniumsalt forms of the active ingredient. The bulk-manufactured active herbicide glyphosate has the synonyms glyphosate technical acid, technical grade glyphosate and glyphosate acid.

The economic importance of glyphosate for growers is high. It has been estimated that a hypothetical ban of glyphosate would lead to decreases in the production of wheat, fodder, maize and oilseeds, by 4.3–7.1%, with the result of an estimated annual welfare loss of 1.4 billion USD to society in the European Union alone (Schmitz and Harvert 2012). Furthermore, glyphosate plays an important role in integrated pest management strategies, and affords the environmental benefit of substantially reduced soil erosion resulting from of no-till and reduced-till agriculture.

The long-term toxicity and carcinogenicity of glyphosate has been investigated by multiple entities including academia, registrants, and regulatory authorities, and the data generated have been evaluated in support of herbicide regulatory approvals in many world regions including the USA (US EPA 1993) and the European Union (EC 2002), and several scheduled reevaluations are currently ongoing in the USA, Canada, Japan and Europe (Germany Rapporteur Member State 2015a), with imminent conclusions.

Studies of appropriate scientific quality are the basis for regulatory decision making. Mandatory testing guidelines (TGs) exist for toxicological studies submitted for regulatory review of active substances for plant protection in many regions of the world. Such TGs have been released, inter alia, by the United States Environmental Protection Agency (US EPA 2012), the European Union (EU 2008), the Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF 2000), and the Organization of Economic Co-operation and Development (OECD 2012b). These TGs set quality standards for each type of study by giving guidance regarding test species, strains, and number of animals to be used, the choice of dosing, exposure duration, and parameters to be measured and observed, as well as for the reporting of results. Due to the lack of effective legal and regulatory provisions for the sharing of vertebrate study data in the past, and to guarantee the safety of technical glyphosate obtained from different processes of synthesis, several manufacturers of glyphosate had to initiate toxicological testing programs of their own. Occasionally, regulatory studies had to be repeated to reflect major changes in the underlying TG. In the case of glyphosate, this has given rise to a multitude of studies for the same toxicological endpoints, leading to the availability of an extraordinarily robust scientific study database that can be considered unique among pesticides, industrial chemicals, and pharmaceuticals. Such a remarkable volume of studies addressing the same endpoints, conducted over the last 40 years by several independent companies and laboratories while toxicology test guidelines have evolved, warrants investigation for consistency, reliability, and application to their intended purpose: identifying potential human health hazards and setting appropriate endpoints for human health risk assessment. Studies conducted with equivalent test substances using the same TG are readily comparable and can be evaluated by regulators following standardized schemes. Minor differences in the findings reported by such repetitive studies are attributable to statistical chance, natural biological variability, type of basal diet, rate of feed consumption, animal strain differences, choice of dose levels, inter-strain genetic drift over time due to varying vendor breeding practices, changes in animal care and husbandry practices across laboratories over the years, inter-laboratory variations in clinical measurements, and differences between individual pathologist evaluation and interpretation of tissue specimens.

Glyphosate is under significant political pressure due to its widespread use, particularly in association with use on genetically modified crops. One focus area of contention has been the human safety of glyphosate, which has been repeatedly challenged by interest groups via the media, as well as select research publications in the scientific literature (Antoniou et al. 2012, Aris and Leblanc 2011, Aris and Paris 2010, Benachour and Seralini 2009, Gasnier et al. 2010, Paganelli et al. 2010, Romano et al. 2012, Romano et al. 2010). To that end, one specific publication by Seralini et al. (2012, retracted) drew significant criticism from both the toxicology and broader scientific communities (Barale-Thomas 2013, Berry 2013, de Souza and Oda 2013, Grunewald and Bury 2013, Hammond et al. 2013, Langridge 2013, Le Tien and Le Huy 2013, Ollivier 2013, Panchin 2013, Sanders et al. 2013, Schorsch 2013, Tester 2013, Trewavas 2013, Tribe 2013). After a special review of the investigators' raw data by a mutually agreed-upon expert panel, the manuscript was retracted by Food and Chemical Toxicology (FCT), for reasons of inconclusive data and unreliable conclusions (Hayes 2014). The Editor of the International Journal of Toxicology highlighted this manuscript as an example of possible failure of the peer review process in a well-respected toxicology journal with an editorial board of well-known and respected toxicologists (Brock 2014). The manuscript was later republished without peer-review in an open access journal (Seralini et al. 2014), but will not be addressed in this data evaluation due to the inappropriate study design, insufficient reporting of tumor incidence data, and the lack of a data supplementary to the manuscript.

The chronic/carcinogenicity studies discussed in this paper have been submitted to and evaluated by a variety of agencies over time, including the World Health Organization (WHO/ FAO 2004b, WHO/FAO 2004a), the United States Environmental Protection Agency (US EPA 1993), the European Rapporteur Member State Germany for the initial glyphosate Annex I listing (EC 2002) and the recent European reevaluation (Germany Rapporteur Member State 2015a), as well as the ongoing reevaluations in the USA, Canada and Japan. These regulatory bodies, drawing upon internal and/or external expertise, have consistently concluded that glyphosate is devoid of carcinogenic risk to humans.

The purpose of this article is to provide the broader scientific community with insight into this large body of carcinogenicity data on glyphosate, originally generated for

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regulatory purposes. Each study discussed in this review has been assigned a reliability score in Tables 3-19, following the Klimisch scoring system (Klimisch et al. 1997). In this system, a score of 1 is assigned to studies that are fully reliable based on compliance with Good Laboratory Practice (GLP) and adherence to appropriate study guidelines. A score of 2 is appropriate if some guideline requirements are not met, but if these deficiencies do not negatively affect the validity of the study for its regulatory purpose. Studies with a reliability of 3 employ a test design that is not fit for the scientific purpose of the study, due to significant scientific flaws, or the objective of the study not covering the regulatory endpoints, or both. Such studies can provide supplemental information but do not allow a stand-alone appraisal of a regulatory endpoint. No studies were assigned a reliability of 4, since each report contained sufficient information to judge the validity of the study.

This manuscript presents the robust glyphosate carcinogenicity data generated by industry. Study summaries will focus on carcinogenicity evaluation, to allow third parties the opportunity to independently evaluate the carcinogenicity data presented alongside other relevant data on carcinogenicity, i.e. genotoxicity testing and epidemiology, and facilitate a multidisciplinary carcinogenicity assessment as proposed in the literature, by recognized experts in the fields of toxicology and human health risk assessment (Adami et al. 2011).

## Absorption, distribution, metabolism and excretion of glyphosate

A number of absorption, distribution, metabolism, and excretion studies (ADME) have been conducted on glyphosate for evaluation in regulatory submissions (EC 2002, US EPA 1993, WHO/FAO 2004a) and also by academic institutions (Anadon et al. 2009). Glyphosate consistently demonstrates low gastrointestinal absorption (20–40%). Its metabolism is very limited, whereby only small quantities of a single metabolite, aminomethylphosphonic acid (AMPA), are eliminated in feces. AMPA is likely produced by the limited metabolism of glyphosate by the gastrointestinal microflora, rather than via mammalian metabolism. Glyphosate is structurally akin to a phase II metabolite, a glycine-conjugate of methyl phosphonate, and thus avails itself to rapid urinary excretion. Systemic elimination is biphasic, with alpha-phase half-lives in the range of 6–14 h (Anadon et al. 2009, WHO/FAO 2004a).

#### **Toxicological properties of glyphosate**

Table 1 contains a short overview of toxicological endpoints of glyphosate that have been published in the List of Endpoints identified for glyphosate by the Rapporteur in the European Union under Regulation 1107/2009 (Germany Rapporteur Member State 2015c). Glyphosate is of low acute toxicity via all routes of exposure. Glyphosate's active ingredient, an organic acid, has an irritating effect on mucosa which is evidenced by eye irritation and effects on oral and gastrointestinal mucosa; final formulated products contain more neutral pH salt forms, as reflected in the tabulated eye irritation data reported in Table 11, on page 109 of the 2004 JMPR Toxicological Evaluation (WHO/FAO 2004a). Glyphosate is not mutagenic, not neurotoxic, and has no effect on pre-natal development and fertility at doses not exceeding the maximum tolerated dose (MTD).

#### Genotoxicity

Very recently, a review of the vast body of genotoxicity studies on glyphosate and GBFs has been published (Kier and Kirkland 2013), including an online data supplement presenting detailed data from 66 separate in vitro and in vivo genotoxicity assays. The authors incorporated these studies and published genotoxicity data into a weight-of-evidence analysis. The vast majority (over 98%) of the available bacterial reversion and in vivo mammalian micronucleus and chromosomal aberration assays were negative. Negative results for in vitro gene mutation and a large majority of negative results for clastogenic effect assays in mammalian cells support the conclusion that glyphosate is not genotoxic for these endpoints in mammalian test systems. DNA damage effects are reported in some instances for glyphosate at high or toxic dose levels. The compelling weight of evidence is that glyphosate and typical GBFs are negative in core assays, indicating that the reported high-dose effects are secondary to toxicity and are not due to DNA-reactive mechanisms. Mixed results were observed for micronucleus assays in non-mammalian systems and DNA damage assays of GBFs. These effects of GBFs may also be associated with surfactants present in the formulated products. Kier and Kirkland conclude that glyphosate and its typical formulations do not present significant genotoxic risk under normal conditions of human or environmental exposures.

#### Epidemiology

Available epidemiological studies of glyphosate and cancer endpoints were recently reviewed (Mink et al. 2012). Seven cohort studies and fourteen case-control studies examining a potential association between glyphosate and one or more cancer outcomes were subjected to a qualitative analysis. The review found no consistent pattern of positive associations between total cancer (in adults or children) or any site-specific cancer, and exposure to glyphosate. A recent review article (Alavanja et al. 2013) cites one epidemiology study associating glyphosate use with non-Hodgkin's lymphoma (NHL), and accepts the study findings prima facie. However, Alavanja et al. (2013) did not highlight six other published epidemiology studies which evaluated glyphosate use and NHL, noting that any association between NHL and glyphosate use was null or not statistically significant. All seven studies were scrutinized by Mink et al. (2012). NHL is not a specific disease, as mentioned in both the epidemiology review publications above, but is rather multiple presentations of lymphoma which are simplistically classified as not being Hodgkin's lymphoma (HL). This dichotomous classification of HL/NHL was rejected by the World Health Organization in 2001, whereby 43 different lymphomas of various etiologies were precisely characterized (Berry 2010). The Bradford Hill criteria are often applied in efforts to determine whether an association between a health effect and human exposure may be deemed causal. However, an important premise often overlooked from Sir Austin Bradford Hill's famous speech of 1965, is that before applying these criteria, the observations should "reveal an association between two variables, perfectly clear-cut and beyond what we care to attribute to the play of chance" (Bradford Hill 1965). This predicate of the association being "perfectly clear-cut"

Table 1. Summary of toxicological endpoints for glyphosate (Germany Rapporteur Member State 2015c).

Endpoint	Value	Remark		
Oral absorption Dermal absorption	ca 20%	Rat, <i>in vivo</i> Human, <i>in vitro</i> ,		
Dermai absorption	<1%	0.015 g glyphosate/L		
Rat LD50 oral	> 2000 mg/kg bw	0000		
Rat LD50 dermal	>2000  mg/kg bw			
Rat LC50 inhalation	>5  mg/L	4-h exposure		
Skin irritation	Not irritating	-		
Eye irritation	Acid: moderately to severely irritating			
-	Salts: slight or non-irritating			
Skin sensitization	Not sensitizing			
	(LLNA, Magnusson-Kligmant, and Buehler test)			
Genotoxicity	Not genotoxic (in vitro and in vivo)			
Chronic toxicity	BW gain, liver (organ weight ↑, clinical chemistry, histology); salivary glands (organ weight ↑, histology); stomach mucosa and bladder epithelium(histology); eye (cataracts), caecum (distention, organ weight ↑)	Critical study used for ADI setting		
Reproductive toxicity	NOAEL = $100 \text{ mg/kg bw/day}$ (2-yr rat) Reduced pup weight at parentally toxic doses.			
Reproductive toxicity	NOAEL = $300 \text{ mg/kg bw/day}$			
Developmental toxicity	Post-implantation loss, fetal BW & ossification $\downarrow$ ; effects confined to			
Developmentar toxicity	maternally toxic doses			
	Rat NOAEL: 300 mg/kg bw/day			
	Rabbit NOAEL: 50 mg/kg bw/day			
Delayed neurotoxicity	No relevant effects, NOAEL: 2000 mg/kg bw/day			
Acceptable Daily Intake (ADI)	0.5  mg/kg bw/day	Safety factor 100		
	Based on developmental toxicity in rabbits			
Acceptable Operator Exposure	0.1 mg/kg bw/day	Safety factor 100		
Level (AOEL)	Based on maternal toxicity in rabbit teratogenicity study	Corrected for oral absorption of 20%		

was recently highlighted as requiring statistical significance, wherein the confidence interval of a relative risk ratio is bracketed above 1.0, as well as concluding that the association may not be attributable to bias, confounding or sampling error (Woodside and Davis 2013). According to Bradford Hill, should an epidemiology study be considered to demonstrate a "perfectly clear-cut" association between glyphosate exposure and a human health outcome, only then should the Bradford Hill criteria be investigated to determine whether there is causality. To date, no such "perfectly clear-cut" association between glyphosate exposure and any cancer exists. However, investigative toxicology is an important discipline to evaluate chemicals before any human exposure occurs, and these data may inform subsequent considerations of whether associations are attributable to causality. One Bradford Hill criterion in establishing disease causality is plausibility, based on known disease etiologies. In the case of lymphoma, there are numerous etiologies for the numerous and different lymphoma diseases, and as such, each lymphoma type should be investigated for a plausible mechanism to determine whether causality may be attributed an appropriately qualified association. Another Bradford Hill criterion is identification of a biological gradient, or dose-response, which is a key consideration in the following data evaluation.

#### **Chronic toxicity studies**

Several one-year chronic studies have been undertaken in dogs and one in rats, in addition to the many chronic/carcinogenicity studies with one-year interim sacrifice groups. Current Test Guidelines (OECD, EPA, EU and JMAFF) for long-term studies clearly state that the highest dose tested should either be at the maximum tolerated dose (MTD), conventionally interpreted as a dose causing non-lethal toxicity, often noted as reduced body weight gain of 10% or more (IUPAC 1997). For test substances with low toxicity, a top dose not exceeding 1000 mg/kg bw/day may apply, except when human exposure indicates the need for a higher dose level to be used (OECD 2012a). All human exposure estimates are well below 1 mg/kg bw/day (see Discussion section), so that 1000 mg/kg bw/day is a practical limit dose for glyphosate in carcinogenicity studies. In the original pre-guideline chronic/carcinogenicity study, rats were dosed well below the MTD (Monsanto 1981), but in many subsequent studies, they were dosed well in excess of today's standard practice of not exceeding the dose limit.

#### **Dog chronic studies**

Five one-year oral toxicity studies have been conducted in Beagle dogs (Table 2). Studies in dogs are not designed to detect neoplastic effects; these studies are therefore not discussed in detail. Nonetheless, the histopathological investigations that are part of one-year dog studies according to OECD TG 452 did not identify (pre) neoplastic lesions related to the administration of glyphosate.

Treatment-related effects in dog studies with glyphosate were restricted to non-specific findings like small retardations in body weight gain and soft stools, which are common findings in this test species. The lowest relevant NOAEL (i.e. highest NOAEL below the lowest LOAEL) in dogs on a daily treatment regimen for one year was 500 mg/kg bw/day. These studies demonstrate that glyphosate is of very low toxicity following repeat exposures in dogs.

#### **Rat chronic studies**

The chronic toxicity potential of glyphosate acid was assessed in a 12-month feeding study (conducted in 1995 and 1996) in

Table 2. Summary of one-year toxicity studies with glyphosate.

Authors:	Monsanto (1985)
Reliability/Justification	2 Study performed according to GLP and OECD guideline requirements, with the following deviation: MTD not
	reached by highest dose
Substance:	Glyphosate (96.1% pure)
Species/Strain:	Dog/Beagle, groups of 6 $\eth$ and 6 $\heartsuit$
Administration route: Doses:	Oral, capsule
Duration:	0, 20, 100, 500 mg/kg bw/day 1 year
Findings:	$\geq 500 \text{ mg/kg bw/day: NOAEL } (\mathcal{J} + \mathcal{Q}) \text{ no treatment-related effects}$
Authors:	Cheminova (1990)
Reliability/Justification	1 Study performed according to GLP and OECD guideline requirements, with no deviations.
Substance:	Glyphosate (98.6–99.5% pure)
Species/Strain	Dog/Beagle, groups of 4 $\Im$ and 4 $\Im$
Administration route:	Oral, capsule
Doses:	0, 30, 300, 1000 mg/kg bw/day
Duration:	1 year
Findings:	$300 \text{ mg/kg bw/day: NOAEL } (\mathcal{J} + \mathcal{D})$
	1000 mg/kg bw/day: soft, liquid stools (attributable to capsule administration); equivocal impact on body weight gain
Authors:	Nufarm (2007)
Reliability/Justification	2 Study performed according to GLP and OECD guideline requirements, with the following deviation: MTD not
0.1.	reached by highest dose
Substance:	Glyphosate (95.7% pure)
Species/Strain	Dog/Beagle, groups of 4 $\eth$ and 4 $\heartsuit$
Administration route:	Oral, capsule
Doses: Duration:	0, 30, 125, 500 mg/kg bw/day
Findings:	1  year
r indings.	≥ 500 mg/kg bw/day: NOAEL (♂ + ♀) No treatment-related effects
Authors:	Arysta Life Sciences (1997c)
Reliability/Justification	2 Study performed according to GLP and OECD guideline requirements, with the following deviation: MTD not
	reached by highest dose
Substance:	Glyphosate (94.6% pure)
Species/Strain	Dog/Beagle, groups of 4 $\Im$ and 4 $\Im$
Administration route:	Oral, diet
Concentration:	0, 1600, 8000, 50 000 ppm diet (3 about 34.1, 182, 1203 mg/kg bw/day; 9 about 37.1, 184, 1259 mg/kg bw/day)
Duration:	l year
Findings:	182/184 mg/kg bw/day: NOAEL (♂/♀)
	At high dose: loose stool, non-statistically significant retarded body weight gain, decreased urinary pH, slight and non-statistically significant feed another statistical characteristic dependence of $Cl \uparrow clburrin = R + (0)$
Authors:	non-statistically significant focal pneumonia ( $\mathfrak{Q}$ ), minor clinical chemistry changes of Cl $\uparrow$ , albumin $\downarrow$ , P $\downarrow$ ( $\mathfrak{Q}$ ) Syngenta (1996a)
Reliability/Justification	1 Study performed according to GLP and OECD guideline requirements, with no deviations.
Substance:	Glyphosate (95.6% pure)
Species/Strain	Dog/Beagle, groups of 4 $\sigma$ and 4 $\varphi$
Administration route:	Oral, diet
Concentration:	0, 3000, 15 000, 30 000 ppm diet (♂ about 90.9, 440, 907 mg/kg bw/day; ♀ about 92.1, 448, 926 mg/kg bw/day)
Duration:	l vear
Findings:	15000  ppm diet: NOAEL (Q)
e	$\geq$ 30 000 ppm diet: NOAEL (3): No treatment-related effects
	30 000 ppm diet: slight body weight reduction (\$)
Authors:	Syngenta (1996b)
Reliability/Justification	1 Study performed according to GLP and OECD guideline requirements, with no deviations.
Substance:	Glyphosate (95.6% pure)
Species/Strain	Rat/Wistar Alpk: AP <sub>f</sub> SD, groups of 24 3 and 24 9
Administration route:	Oral, diet
Concentration:	0, 2000, 8000, 20 000 ppm diet (♂ about 141, 560, 1409 mg/kg bw/day; ♀ about 167, 671, 1664 mg/kg bw/day)
Duration:	1 year
Findings:	8000 ppm diet: NOAEL $(\mathcal{J}+\mathcal{Q})$
	20 000 ppm diet: parotid salivary glands (focal basophilia of the acinar cells considered non-adverse adaptive
	response, $\delta$ : 13/24, Q: 15/24), body weight reduction

24 male and female Wistar rats per group, dosed at 0, 2000, 8000 and 20 000 ppm (Syngenta 1996). The mean achieved dose levels were 0, 141, 560 and 1409 mg/kg bw/day for males, and 0, 167, 671 and 1664 mg/kg bw/day for females. Spastically significant reductions in bodyweight were evident in animals receiving 20 000 ppm glyphosate acid, together with a marginal reduction in bodyweight in rats receiving 8000 ppm, but food consumption relative to controls was lower for these dose groups, suggesting reduced palatability of the diets containing these doses of glyphosate. There were no toxicologically significant or treatment-related effects on hematology, blood and urine clinical chemistry, or organ weights (Table 2).

The treatment-related pathological finding, that is increased incidence of mild focal basophilia, and a hypertrophy of the acinar cells of the parotid salivary gland in both sexes which had received 20 000 ppm glyphosate acid, is considered an adaptive response due to oral irritation from the ingestion of glyphosate, an organic acid, in the diet. This was verified by

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mode of action investigations and studies with dietary administration of citric acid, a non-toxic organic acid with irritation properties and pH dilution curve similar to those of glyphosate (Saltmiras et al. 2011), which elicited the same response in the acinar cells of the parotid salivary glands.

In conclusion, the 12-month NOAEL in rats for glyphosate acid, as determined from this study, is 8000 ppm (corresponding to 560 mg/kg bw/day in males and 671 mg/kg bw/day in females). This study does not cover neoplastic endpoints. These were addressed in a subsequent study by the same sponsor (Syngenta 2001). Consistent with the findings observed in dogs, this study demonstrates that glyphosate is of very low toxicological concern following long-term daily exposures.

Similarly, most of the following 2-year rat carcinogenicity studies included additional groups for 1-year interim sacrifice to evaluate chronic toxicity. These studies did not elucidate significant toxicological concerns for chronic dietary exposures to glyphosate in rats in multiple expert reviews by governmental agencies and several technical branches of the World Health Organization including the Joint Meeting on Pesticide Residues Toxicological Evaluations (WHO/FAO 2004a).

#### **Carcinogenicity studies**

Chronic/carcinogenicity tests are designed to simulate lifetime exposures to an individual chemical and represent the most robust in vivo assay to evaluate the effects of chronic exposure including carcinogenicity. These models are biological systems with natural background variability due to tumor formation as a natural consequence of aging. Glyphosate was found to have no carcinogenic potential, which is reflected in the data showing only background noise of spontaneous tumors across the wide range of doses. Normal biological variability should display various tumor types across all dose groups without an apparent dose-response. The study summaries discuss "select neoplasms", identified by the authors as having an elevated incidence above concurrent controls across one or more dose groups, most of which lacked statistical significance and/or dose-response within an individual study. These tumors are then evaluated in the context of the whole data set, to provide a robust weight of evidence overview for the doses spanning several orders of magnitude. While not all studies have select neoplasms identified in the individual study summary tables, select neoplasms for all studies are reported in Tables 20-23. Summary tables of the select neoplasms footnote the strain tested for each dose, to allow consideration of strain differences in spontaneous tumor susceptibility (Tables 20-23). In addition, complete tumor incidence summary tables have been extracted from the original eight rat (the published rat study, Study 9, is not included) and five mouse study reports or study files, and posted in their original format, as a comprehensive online data supplement to this manuscript.

#### **Rat carcinogenicity**

A total of nine chronic/carcinogenicity studies in the rat, including one peer-reviewed published study, were available for review. This duplication of large-scale studies in the same animal model using the same test substance is not consistent with today's broader appreciation for animal welfare and the reduction of unnecessary animal testing. However, these studies offer the opportunity for a critical discussion of findings in individual studies in the context of the larger body of data. Wistar and Sprague Dawley were the strains used for the bioassays in rats. Seven studies were conducted under conditions of GLP, and two studies were not under GLP (Study 1, conducted before the introduction of GLP; Study 9, non-GLP). Most studies in rats were designed as combined chronic toxicity/ carcinogenicity studies, with interim sacrifices after 12 months of treatment for the assessment of non-neoplastic chronic toxicity. Statistical methods are noted in the manuscript tables where statistical significance was attained. Statistical differences in neoplasm incidence summary tables are reported in the online data supplements. Chronic endpoints and NOAEL values are captured in each study summary table; however, the following study reviews focus on carcinogenicity.

#### Study 1 (Monsanto 1981)

An early study into the long-term effects of orally administered glyphosate in the rat was conducted between 1978 and 1980 (Monsanto 1981), prior to the adoption of international test guidelines and GLP standards (Tables 3–6). Nonetheless, the test protocol was broadly compliant with OECD TG 453 (1981). However, an MTD was not reached and the high dose was well below an acceptable dose limit of 1000 mg/kg bw/ day. Therefore, this study is rated Klimisch 3 for reliability, and is considered inadequate for carcinogenicity evaluation from a regulatory perspective.

Groups of 50 male and 50 female Sprague Dawley rats were administered glyphosate acid in the diet, at concentrations of 0, 30, 100 and 300 ppm, for up to least 26 months. The mean doses achieved were 0 (control), 3, 10, and 31 mg/kg bw/day for the males, and 0 (control), 3, 11, and 34 mg/kg bw/day for the females. Study results are summarized in Table 3.

In general, the incidences of all neoplasms observed in the treated and control animals were similar, or occurred at low incidence, such that a treatment-related association could not be made. The most common tumors found were common spontaneous neoplasms, as reported in the literature relating to rat (Johnson and Gad 2008), in the pituitary glands of both control and treated animals (Table 4). In the females, mammary gland tumors were the next most common neoplasm across control and dose groups (see data Supplementary Study 1 to be found online at http://informahealthcare.com/doi/abs/1 0.3109/10408444.2014.1003423).

Table 3. Study 1–26-month feeding study of glyphosate in rats (Monsanto 1981).

Study owner:	Monsanto (1981)
Reliability/Justification:	3 Study not performed under GLP.
	High-dose well below MTD. Does not
	conform to modern testing standards.
Substance:	Glyphosate (98.7% pure)
Species/Strain:	Rat/Sprague-Dawley, groups of 50 3 and 50 9
Administration route:	Diet
Concentration:	0, 30, 100, 300 ppm diet (3 about 0, 3,
	10, 31 mg/kg bw/day; 9 about 0, 3, 11,
	34 mg/kg bw/day)
Duration:	26 months
Findings:	$\geq$ 300 ppm diet: NOAEL ( $\mathcal{J} + \mathcal{Q}$ )
÷	No treatment-related effects
Select neoplasms:	Pituitary adenoma, Testes interstitial cell

Table 4.	Study	1 –	Pituitary	tumor	findings.

	Dose group (mg/kg bw/day)							
	Males					Fen	ales	
Tumors	0	3.05	10.3	31.49	0	3.37	11.22	34.02
Pituitary tumors		Number of animals/total number examined (% per group)						
Adenomas - B	16/48 (33)	19/49 (39)	20/48 (42)	18/47 (38)	34/48 (70)	29/48 (60)	31/50 (62)	26/49 (53)
Carcinomas - M	3/48 (6)	2/49 (4)	3/48 (6)	1/47 (2)	8/48 (17)	7/48 (14)	5/48 (19)	12/49 (24)
Combined	19/48 (40)	21/49 (43)	23/48 (48)	19/47 (40)	42/48 (88)	36/48 (75)	36/50 (72)	38/49 (78)

B benign, M malignant

The incidence of interstitial cell tumors of the testes in male rats in both the scheduled terminal sacrifice animals, as well as for all animals, suggested a possible treatment-related finding, and was presented along with contemporary historical control data for comparison (Tables 5 and 6). It was noted that at 12 months, the incidence of interstitial tumors was near zero; however, in animals aged 24-29 months at necropsy, the incidence increased to approximately 10%. The historical control data for chronic toxicity and carcinogenicity from 5 studies terminated at 24-29 months showed background levels of interstitial cell tumors comparable to those found at the highest dose in the study. Furthermore, the reported incidences in all dose groups reflect the normal range of interstitial cell tumors in rat testes, reported in the Registry of Industrial Toxicology Animal Data (Nolte et al. 2011). The incidence of interstitial cell hyperplasia did not provide evidence of a pre-neoplastic lesion. The investigators noted that at terminal sacrifice, the incidence of interstitial cell tumor was 15.4% (4/26), while the range in control animals from 5 contemporary studies (historical controls) was 6.2% (4/65) to 27.3% (3/11), with an overall mean value of 9.6% (16/166). When all animals on test are included, the incidence for the high-dose males was 12% (6/50), compared to a contemporary historical control range of 3.4% (4/116) to 6.7% (5/75), with a mean of 4.5% (24/535). The concurrent control incidence of interstitial cell tumors (0%) was not representative of the normal background incidence noted in contemporary historical control data. Therefore, the data suggest that the incidence in treated rats is within the normal biological variation observed for interstitial cell tumors at this site in this strain of rat. When evaluated in the context of the full data set for male rats (Table 20), a dose-response is clearly absent for the 25 doses evaluated in rats, ranging from 3 to 1290 mg/kg bw/day, which demonstrates that this tumor is clearly not a consequence of glyphosate exposure.

In conclusion, glyphosate was not considered carcinogenic in Sprague Dawley rats following continuous dietary exposure of upto 300 ppm, corresponding to 31 and 34 mg/kg bw/day in males and females, respectively, which is consistent with evaluations by the US EPA (US EPA 1993), the original Annex I listing in Europe (EC 2002), and WHO/FAO (WHO/FAO 2004a). Based on the low doses tested in Study 1, Monsanto was obliged to conduct a second chronic/carcinogenicity study in rats (Study 2, discussed below) in accordance with OECD TG 453 (1981), which had been developed and instituted after this initial study was conducted.

#### Study 2 (Monsanto 1990)

In response to evolving regulatory requirements, this study was conducted in accordance with the contemporary version of OECD TG 453 (Monsanto 1990). The chronic toxicity and carcinogenic potential of glyphosate were assessed in a 24-month feeding study in 50 male and 50 female Sprague Dawley rats, dosed with 0, 2000, 8000 and 20 000 ppm (equivalent to mean achieved dose levels of 0, 89, 362 and 940 mg/ kg bw/day for males and 0, 113, 457 and 1183 mg/kg bw/day for females (Table 7). In addition, 10 rats per sex per dose were included for interim sacrifice after 12 months. Observations covered clinical signs, ophthalmic examinations, body weight, food consumption, hematology, clinical chemistry and urinal-ysis, as well as organ weights, necropsy, and histopathological examination. This study was rated Klimisch 1 for reliability.

Treatment-related findings in this study were significantly reduced body weight in high-dose females, as well as increased liver weight in high-dose males and females, and a slight increase in incidence of cataract lens changes in high-dose males, which was not statistically significant for eye lesions confirmed by histopathology (Table 7). The body weight changes confirm that the MTD was achieved in the highest dose group. Benign thyroid C-cell adenomas were statistically higher than controls in the mid-dose terminally sacrificed males, but when pooled with unscheduled deaths, no statistically significant increase was noted. Benign pancreas islet cell adenomas were not statistically higher for the unscheduled or scheduled deaths, but when combined, were statistically higher than controls in the low and high dose males. In both cases, the benign tumors did not exhibit a dose-response, and did not progress to carcinomas, and thus the US EPA concluded that these tumors were not related to the administration

Table 5. Study 1	- Interstitial cell	tumor findings in	the testes.
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		Dose (mg/kg	bw/day)			
Tumors	0	3.05	10.3	31.49		
Interstitial cell tumor – B	Number of	Number of animals/total number examined (% per group)				
Terminal sacrifice	0/15 (0)	2/26 (7.7)	1/16 (6.3)	4/26 (15.4)		
All Animals	0/50 (0)	3/50 (6)	1/50 (2)	6/50(12)		
Interstitial cell hyperplasia		Number of animals	(% per group)			
Terminal sacrifice	1/15 (6.7)	1/26 (3.8)	0/16(0)	0/26(0)		
All Animals	1/50 (2)	1/50 (2)	1/50 (2)	0/50 (0)		

B benign, M malignant

Table 6. Study 1 – Summary of the contemporary historical control data for interstitial cell tumors in the testes of rats in chronic toxicity studies.

	Study 1	Study 2	Study 3	Study 4	Study 5	
	Number of	of control anim	als/total number	r examined (% p	er study)	Range
Terminal sacrifice All animals	4/65 (6.2) 4/116 (3.4)	3/11 (27.3) 5/75 (6.7)	3/26 (11.5) 4/113 (3.5)	3/24 (12.5) 6/113 (5.3)	3/40 (7.5) 5/118 (4.2)	6.2–27.3% 3.4–6.7%

of glyphosate (US EPA 1993). These neoplasms, in addition to skin keratoacanthoma in males, a common rat tumor, were selected for further weight of evidence evaluation (Tables 20 and 21). No evidence of a glyphosate-induced carcinogenic effect was noted in either sex (see data Supplementary Study 2 to be found online at http://informahealthcare.com/doi/abs/ 10.3109/10408444.2014.1003423).

In conclusion, glyphosate was not carcinogenic in Sprague Dawley rats following continuous dietary exposure of up to 20000 ppm for 24 months, corresponding to 940 and 1183 mg/kg bw/day in males and females, respectively, which is consistent with evaluations by the US EPA (US EPA 1993), European Authorities (EC 2002), and WHO/FAO (WHO/ FAO 2004a).

#### Study 3 (Cheminova 1993a)

The chronic toxicity and carcinogenic potential of glyphosate technical acid were assessed in a 104-week feeding study in

male and female Sprague Dawley rats (Cheminova 1993a). The study was conducted between 1990 and 1992. Groups of 50 rats per sex received daily dietary doses of 0, 10, 100, 300, or 1000 mg/kg bw/day of glyphosate technical acid for 24 months (Table 8). Five additional groups of 35 rats per sex, receiving daily dietary doses of, 0, 10, 100, 300 or 1000 mg/kg bw/day, were included for interim sacrifice at the 12th month for evaluation of chronic toxicity. The dietary glyphosate levels were adjusted weekly to ensure that animals were receiving the intended dose levels at all times. This study was rated Klimisch 1 for reliability.

At 1000 mg/kg bw/day, female mean liver weights were decreased, while males and females had statistically significant reductions in body weight throughout the study, confirming that the MTD was achieved (Table 8). Neoplasms were noted in control and treated groups, but dose-responses were not evident, and no statistically significant increases versus controls were noted for any tumor type (p < 0.05). No treatment-related neoplastic lesions were observed at termination,

Table 7. Study 2 - Two-year feeding study of glyphosate in rats (Monsanto 1990).

Study owner:	Monsanto (1990)						
Reliability/Justification:	1 Study performed acco	1 Study performed according to GLP and OECD guideline requirements, with no					
	deviations.						
Substance:	Glyphosate (96.5% pure)						
Species/Strain:	Rat/Sprague-Dawley, gr	Rat/Sprague-Dawley, groups of 50 $\sigma$ and 50 $Q$ (10 rats per sex per dose were					
	included for interim sac	rifice after 12 m	onths).				
Administration route:	Diet						
Concentration:	0, 2000, 8000, 20 000 p		t 0, 89, 362, 9	40 mg/kg bw/da	ay; ♀ about 0,		
	113, 457, 1183 mg/kg b	w/day)					
Duration:	2 years						
Findings:	8000 ppm diet: NOAEL						
	20 000 ppm diet: catara	cts (♂), >20% r	educed cumul	ative body weig	ht gain		
	through months 18–20 (	(Q), 13% increas	ed liver weigh	t (ð). Local effe	ects:		
	inflammation of gastric	mucosa					
Select neoplasms:	Pancreatic islet cell ader	noma, skin kerat	oacanthoma (i	males), thyroid	C cell		
	adenoma						
Tumor				g/kg bw/day)			
Males		0	89	362	940		
Findings for dead and mor							
Pancreas: Islet call adenoma – B		1/34 (3%)	4/28 (14%)	2/33 (6%)	4/32 (13%)		
Skin: Keratoacanthon		0/36	1/31 (3%)	2/33 (6%)	1/32 (3%)		
Thyroid: C cell adeno		0/36	2/29 (7%)	1/31 (3%)	1/33 (3%)		
Thyroid: C cell carcin		0/36	1/29 (3%)	2/31 (6%)	1/33 (3%)		
Findings for animals sacrif		0.44.4					
Pancreas: Islet call ad		0/14	4/19 (21%)	3/17 (6%)	3/17 (6%)		
Skin: Keratoacanthon		0/13	2/19 (11%)	2/17 (12%)	2/17 (12%)		
Thyroid: C cell adeno		0/14	2/19 (11%)	*7/17 (41%)	4/17 (24%)		
Thyroid: C cell carcin	oma – M	0/14	0/19	0/17	0/17		
Females		0	113	457	1183		
Findings for dead and mor		2/29 (110)	0/20	2/22/000	0/21		
Pancreas: Islet call ad		3/28 (11%)	0/28	3/33 (9%)	0/31		
Thyroid: C cell adenoma – B		0/28	0/28	1/33 (3%)	2/32 (6%)		
Thyroid: C cell carcin		0/28	0/28	1/33 (3%)	0/32		
Findings for animals sacrif		2/22 (0%)	1/22 (507)	1/17 (60)	0/18		
Pancreas: Islet call ad		2/22 (9%)	1/22 (5%)	1/17 (6%)			
Thyroid: C cell adeno Thyroid: C cell carcin		2/22 (9%) 0/22	2/22 (9%) 0/22	5/17 (29%) 0/17	4/18 (22%) 0/18		
ritytotu. C celi carcili	$O \Pi a = W I$	0/22	0/22	0/17	0/10		

B benign, M malignant

\*Statistically higher than controls (p < 0.05, Fisher's Exact Test with the Bonferroni Inequality).

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Table 8. Study 3 – Two-year feeding study of glyphosate in rats (Cheminova 1993a).

	·
Study owner:	Cheminova (1993a)
Reliability/	1 Study performed according to GLP and OECD
Justification:	guideline requirements, with no deviations.
Substance:	Glyphosate (98.7–98.9% pure)
Species/Strain:	Rat/Sprague-Dawley, groups of 50 ♂ and 50 ♀
	(additional groups of 35 $\sigma$ and 35 $Q$ per dose were
	included for 1-year interim sacrifice)
Administration rou	te: Diet
Achieved dose:	♂+♀: 0, 10, 100, 300, 1000 mg/kg bw/day
	(weekly adjustment of dietary concentration for
	the first 13 weeks and 4-weekly thereafter)
Duration:	2 years
Findings:	300 mg/kg bw/day: NOAEL (♂+♀)
-	1000 mg/kg bw/day: body weights ↓, urinary pH
	$\downarrow$ , salivary glands (histopathology, organ weight
	↑); evidence of weak liver toxicity (alkaline
	phosphatase $\uparrow$ , $\varphi$ : organ weight $\downarrow$ )
Select neoplasms:	No neoplasms from this study were identified for
1	further consideration.

and no select neoplasms were identified in this study for further consideration (see data Supplementary Study 3 to be found online at http://informahealthcare.com/doi/abs/10.3109/10408 444.2014.1003423). Glyphosate was not considered carcinogenic in male and female Sprague Dawley rats following 104 weeks of continuous dietary exposure of up to 1000 mg/kg bw/day, the limit dose, which is consistent with evaluations by the European Authorities (EC 2002, Germany Rapporteur Member State 2015b) and WHO/FAO (WHO/FAO 2004a).

#### Study 4 (Feinchemie Schwebda 1996)

A 2-year bioassay in the Wistar rat used dietary glyphosate levels of 0, 100, 1000, and 10 000 ppm (Feinchemie Schwebda 1996). Groups of 50 rats per sex were fed for 24 months. The mean achieved dose levels were 0, 7.4,

73.9, and 740.6 mg/kg bw/day (Table 9). This study was rated Klimisch 1 for reliability.

In addition, one vehicle control with ten rats per sex and one high dose (10 000 ppm) group with 20 rats per sex were included for interim sacrifice after one year of treatment, to study non-neoplastic histopathological changes. The mean achieved dose level in the treated group was 764.8 mg/kg bw/day. Observations covered clinical signs, body weight, food consumption, hematology, clinical chemistry, and urinalysis, as well as organ weights, necropsy, and histopathological examination.

There were no treatment-related deaths or clinical signs in any of the dose-groups. Moreover, there were no treatmentrelated effects on body weight gain or food consumption noted. This suggests that the MTD may not have been reached by the applied dosing regimen.

There was some background variation in the incidences of benign tumors (e.g. reduced tumor incidence in low and middose males, increased tumor incidence in middose females), which was considered incidental in absence of a dose-response relationship (see data Supplementary Study 4 to be found online at http://informahealthcare.com/doi/abs/10.3109/1040 8444.2014.1003423).

The different liver tumors observed in the dead and moribund sacrificed and terminally sacrificed rats included hepatocellular adenoma, intrahepatic bile duct adenomas, cholangiocarcinoma, hepatocellular carcinoma, histiocytic sarcoma, fibrosarcoma, and lymphosarcoma. Among these, hepatocellular adenomas and carcinomas occurred more frequently, as often observed in aging rats (Thoolen et al. 2010). These tumors appeared to be incidental and not compoundrelated, as their frequency of occurrence was not dependent on dose. Hepatocellular adenomas and carcinomas were considered select neoplasms (Table 9), based on increased incidence above controls for total animals, albeit non-dose

Table 9. Study 4 - Two-year feeding study of glyphosate in rats (Feinchemie Schwebda 1996).

Study owner:		Feinchemie Sc	hwebda (1996)	)			
Reliability/Justification:	1 Study performed accordi	ng to GLP and C	DECD guidelin	e requirements	s, with no		
	deviations.						
Substance:	Glyphosate (96.0–96.8% p	ure)					
Species/Strain:	Rat/Wistar, groups of 50 $\Im$ and 50 $\Im$						
Administration route:	Diet						
Concentration:	0, 100, 1000, 10 000 ppm diet (♂ about 0, 6.3, 59.4, 595 mg/kg bw/day; ♀ about 0, 8.6, 88.5, 886 mg/kg bw/day)						
Duration:	2 years	•					
Findings:	10 000 ppm diet: $\geq$ NOAE	L(3+9)					
-	Only mild effects on clinic		er enzymes), w	vithout histopa	thological		
	changes.	5 <	5 //	1	0		
Select neoplasms:	Hepatocellular adenoma, h	epatocellular car	rcinoma				
Tumor	1	Dose (mg/kg bw/day)					
Males		0	7.4	73.9	741		
Findings for dead and mo	oribund sacrificed animals						
Hepatocellular adenom	1a – B	9/30 (30%)	9/30 (30%)	6/32 (19%)	6/21 (29%)		
Hepatocellular carcino	ma – M	12/30 (40%)	12/30 (40%)	9/32 (28%)	5/21 (24%)		
Findings for animals sa	acrificed at termination	. ,	. ,	. ,	. ,		
Hepatocellular adenom		15/20 (75%)	13/20 (65%)	4/16 (25%)	15/20 (75%)		
Hepatocellular carcino	ma – M	9/20 (45%)	16/20 (80%)	9/16 (56%)	19/29 (66%)		
-		Dose (mg/kg bw/day)					
Females		0	7.4	73.9	741		
Findings for dead and mo	oribund sacrificed animals						
Hepatocellular adenom	1a – B	2/26 (8%)	8/23 (3%)	3/17 (18%)	5/29 (17%)		
Hepatocellular carcino	ma – M	4/26 (15%)	4/23 (17%)	2/17 (12%)	5/29 (17%)		
Findings for animals sacr	ificed at termination						
Hepatocellular adenom	1a – B	16/24 (67%)	10/25 (40%)	16/32 (50%)	8/21 (38%)		
Hepatocellular carcino	ma – M	6/24 (25%)	11/25 (44%)	12/32 (38%)	4/21 (19%)		

B benign, M malignant

responsive, for adenoma in mid-dose females, carcinoma in low- and high-dose males, and carcinoma in low- and mid-dose females. These liver neoplasms are considered in the weight of evidence evaluation (Tables 20 and 21).

The study report concluded that glyphosate technical acid was not carcinogenic in Wistar rats following continuous dietary exposure of up to 595 and 886 mg/kg bw/day in males and females, respectively, for 24 months, which is consistent with evaluations by the European Authorities (EC 2002, Germany Rapporteur Member State 2015b).

#### Study 5 (Excel 1997)

A 2-year feeding study in the Sprague Dawley rats (Excel 1997) featured dietary concentrations of 0, 3000, 15 000, and 25 000 ppm glyphosate technical acid. Groups of 50 rats per sex were fed for 24 months, and mean dose levels of 0, 150, 780 and 1290 mg/kg bw/day (males) and 0, 210, 1060 and 1740 mg/kg bw/day (females) were achieved (Table 10).

In addition, 20 rats/sex/group were included for interim sacrifice at week-52, to study non-neoplastic histopathological changes with a different high-dose level of 30 000 ppm. The dietary doses correspond to 180, 920 and 1920 mg/kg bw/day (males) and 240, 1130 and 2540 mg/kg bw/day (females), for 3000, 15 000 and 30 000 ppm, respectively. Thus, a limit dose above 1000 mg/kg bw/day was achieved.

The study report notes that glyphosate technical acid was not carcinogenic in Sprague Dawley rats following continuous dietary exposure to up to 1290 mg/kg bw/day, and 1740 mg/kg bw/day for males and females, respectively, for 24 months. However, this study was rated Klimisch 3 for reliability (Germany Rapporteur Member State 2015b), and therefore, is considered unreliable for carcinogenicity evaluation based on lower than expected background tumor incidences (see data Supplementary Study 5 to be found online at http://informahealthcare.com/ doi/abs/10.3109/10408444.2014.1003423). In addition, the test substance was not adequately characterized, and several deviations from the OECD Test Guideline 453 were noted.

#### Study 6 (Arysta Life Sciences 1997b)

A combined chronic toxicity/carcinogenicity study in Sprague Dawley rats (Arysta Life Sciences 1997b) was conducted between December 1994 and December 1996. The rats were fed 0, 3000, 10 000, and 30 000 ppm glyphosate for two years (equivalent to 0, 104, 354 and 1127 mg/kg bw/day for males and 0, 115, 393 and 1247 mg/kg bw/day for females (Table 11). Thus, a limit dose was achieved, and the MTD was noted at the high dose in males and females with decreased body weight, increased cecum weight, distention of the cecum, loose stool and skin lesions. In addition, 30 rats/sex/group were included for interim sacrifice at 26, 52 and 78 weeks, to study nonneoplastic histopathological changes. Observations covered clinical signs, body weight, food consumption, hematology, clinical chemistry, and urinalysis, as well as organ weights, necropsy, and histopathological examination. This study was rated Klimisch 1 for reliability.

Non-statistically significant increases versus controls (p < 0.05) were noted for pituitary adenomas, skin keratoacanthoma in high-dose males, and mammary gland fibroadenoma in low and mid-dose females (Table 11). These neoplasms were considered for the weight of evidence evaluation (Tables 20 and 21), and the full tumor summary data are available online (see data Supplementary Study 6 to be found online at http://informahealthcare.com/doi/abs/ 10.3109/10408444.2014.1003423). As mentioned under Study 1, pituitary and mammary tumors are common spontaneous neoplasms in aging rats (Johnson and Gad 2008), and skin keratoacanthoma is noted as one of the most common spontaneous benign neoplasms in male Sprague Dawley rats (Chandra et al. 1992). The study report concluded that glyphosate was not carcinogenic in Sprague Dawley rats following continuous dietary exposure to up to 30 000 ppm for 24 months, corresponding to 1127 mg/kg bw/day and 1247 mg/kg bw/day for males and females, respectively, which is consistent with the recent evaluation in Europe under the Annex I Renewal of glyphosate (Germany Rapporteur Member State 2015b).

Table 10. Study 5 – Two-year feeding study of glyphosate in rats (Excel 1997).

Study owner:	Excel (1997)					
Reliability/Justification:	3 Test substance not characterized and other deviations from OECD 453, lower than expected background tumor incidence					
Substance:	Glyphosate (no purity reported)					
Species/Strain:	Rat/Sprague-Dawley, groups of 50 $\mathcal{J}$ and 50 $\mathcal{Q}$ , additional groups of 20 rats per sex and group were included for interim sacrifice after 52 weeks					
Administration route:	Diet					
Concentration:	2-year group: 0, 3000, 15 000, 25 000 ppm diet (σ about 0, 150, 780, 1290 mg/kg bw/ day; Q about 0, 210, 1060, 1740 mg/kg bw/day)					
	1-year group: 0, 3000, 15 000, 30 000 ppm diet (♂ about 0, 180, 920, 1920 mg/kg bw/ day; ♀ about 0, 240, 1130, 2540 mg/kg bw/day)					
Duration:	2 years					
Findings:	$\geq$ 25 000 ppm diet: NOAEL ( $\delta$ + $\varphi$ )					
	Only mild toxic effects, such as clinic without correlating histopathologic		ble relevance	in aged rats,		
Select neoplasms:	No neoplasms from this study were identified for further consideration. Low background tumor incidence indicates low study reliability with no relevant increases in the incidence of tumors.					
Males		se (mg/kg bw/day)				
	0	150	740.6	1290		
Mortality	16/50 (32%)	17/50 (34%)	18/50 (36%)	23/50 (46%)		
Females	Do	se (mg/kg bw/day)	. ,			
	0	210	1060	1740		
Mortality	19/50 (38%)	20/50 (40%)	20/50 (40%)	25/50 (50%)		

Table 11. Study 6 - Two-year feeding study of glyphosate in rats (Arysta Life Sciences 1997b).

Study owner:	Arysta Life Sciences (1997b)			•			
Reliability/Justification:	1 Study performed according to GLP and OECD g	uideline requiremen	its, with no deviat	ions.			
Substance:	Glyphosate (94.6–97.6% pure)	11.4 6.20	120.06				
Species/Strain:	Rat/Sprague-Dawley, groups of 50 ♂ and 50 ♀; sate	ellite groups of 30 d	s and 30 Q for inte	rim investigations			
Administration route:	Diet						
Concentration:		0, 3000, 10 000, 30 000 ppm diet (3 about 0, 104, 354, 1127 mg/kg bw/day; 9 about 0, 115, 393, 1247 mg/kg bw/day)					
Duration:	2 years						
Findings:	3000 ppm diet: NOAEL ( $\mathcal{J}+\mathcal{Q}$ )						
	10 000 ppm diet: cecum weight $\uparrow$ , distension of cec abscess of the skin, body weight $\downarrow$	um, loose stool, foll	icular hyperkerat	osis and/or folliculi	itis/follicular		
Select neoplasms:	Pituitary adenoma, skin keratoacanthoma (males),	mammary gland fib	roadenoma (fema	les)			
Tumor	•		Dose (m	g/kg bw/day)			
Males		0	104	354	1127		
Findings for dead and me	oribund sacrificed animals (Table 25–10)						
Pituitary anterior aden	oma – B	22/32 (69%)	21/30 (70%)	*14/32 (44%)	18/21 (86%)		
Skin keratoacanthoma		2/32 (6%)	1/30 (3%)	0/32	1/21 (5%)		
Findings for animals sac	rificed at termination (after 104 weeks, Table 25-8)	. ,					
Lung adenoma – B		0/18	2/20 (10%)	1/18 (6%)	3/29 (10%)		
Pituitary anterior aden	ioma – B	13/18 (72%)	14/20 (70%)	13/18 (72%)	21/29 (72%)		
Pituitary adenoma in i		0/18	1/20 (5%)	0/18	0/29 (0%)		
Skin keratoacanthoma		1/18 (6%)	2/20 (10%)	0/18	6/29 (21%)		
Tumor			Dose (m	g/kg bw/day)			
Females		0	115	393	1247		
Findings for dead and me	oribund sacrificed animals						
Pituitary anterior aden		34/35 (97%)	29/31 (94%)	28/33 (82%)	31/36 (86%)		
Thyroid follicular ade	noma – B	0/35	2/31 (6%)	0/32	0/36		
Mammary gland fibro		13/35 (37%)	14/31 (45%)	12/34 (35%)	20/36 (56%)		
	acrificed at termination						
Pituitary anterior aden		12/15 (80%)	19/19 (100%)	12/16 (75%)	13/14 (93%)		
Mammary gland fibro	10/15 (67%)	13/19 (68%)	12/16 (75%)	10/14 (71%)			

B benign, M malignant

\*Statistically lower than controls (p < 0.05).

#### Study 7 (Syngenta 2001)

The same rat model that was used in the previously discussed 12-month chronic rat study (Syngenta 1996b) was also employed in a 2-year feeding study (Syngenta 2001). A group of 52 male and 52 female Wistar rats received 0, 2000, 6000 or 20 000 ppm via feed (Table 12). The mean achieved dose levels were 0, 121, 361 and 1214 mg/kg bw/day for males, and 0, 145, 437 and 1498 mg/kg bw/day for females. Thus, a limit dose was achieved. In addition, three satellite groups with 12 rats per sex each were included for interim sacrifice after 12 months of treatment, to investigate potential non-neoplastic histopathological changes. Observations covered clinical signs, body weight, food consumption, hematology, clinical chemistry, and urinalysis, as well as organ weights, necropsy, and histopathological examination. This study was rated Klimisch 1 for reliability.

Treatment-related findings in this study were found in the liver and kidney, and were confined to animals (predominantly males) fed 20 000 ppm glyphosate acid. There were a number of changes in males and females fed 20 000 ppm glyphosate acid, notably renal papillary necrosis, prostatitis, periodontal inflammation, urinary acidosis, and hematuria, which may be attributed to the acidity of the test substance. Slight increases in proliferative cholangitis and hepatitis were noted in males at 20 000 ppm. Despite the findings at 20 000 ppm, survival was better in males fed 20 000 ppm than in the controls and lower dose groups. This improved survival was associated with a decreased severity of renal glomerular nephropathy and a 5% reduction in body weight (see data Supplementary Study 7 to be found online at http:// informahealthcare.com/doi/abs/10.3109/10408444.2014. 1003423, for neoplastic and non-neoplastic findings).

A small increase in the incidence of hepatocellular adenoma was observed in males fed 20 000 ppm glyphosate acid. While not statistically significant using the Fisher's exact test, the difference was statistically significant for total male rats using the Peto Test for trend. However, there was no evidence of pre-neoplastic foci, no evidence of progression to adenocarcinomas, and no dose-response. In addition, the incidence was within the laboratory's historical control range for tumors of this type in the liver (Table 12). Therefore, the increased incidence was considered not to be related to treatment, yet these were considered select neoplasms (Table 12) and evaluated in context of the complete data set (Tables 20 and 21).

The study report concluded that glyphosate acid was not carcinogenic in the Wistar rats following continuous dietary exposure to up to 20 000 ppm for 24 months, at 1214 and 1498 mg/kg bw/day in males and females, respectively, which is consistent with the WHO/FAO review (WHO/FAO 2004a) and the recent evaluation in Europe under the Annex I Renewal of glyphosate (Germany Rapporteur Member State 2015b).

#### Study 8 (Nufarm 2009b)

The most recent study in this series of regulatory studies investigating the potential carcinogenicity of glyphosate in rats was conducted from September 2005 through March 2008 (Nufarm 2009b). The study was conducted by feeding dietary concentrations of 0, 1500, 5000 and 15 000 ppm glyphosate to groups of 51 Wistar rats per sex. To ensure that a received limit dose of 1000 mg/kg bw/day overall was achieved, the highest dose level was progressively increased to 24 000 ppm.

Table 12. Study 7 – Two-year feeding study of glyphosate in rats (Syngenta 2001).

Study owner:	Syngenta (200	1)					
Reliability/Justification	1 Study perfor	med according to GLF	and OECD guideli	ine requirements, with no deviations.			
Substance:	Glyphosate (97						
Species/Strain	Rat/Wistar Alp	ok: AP <sub>f</sub> SD, groups of $\pounds$	52 ♂ and 52 ♀ (addi	tional 12 animals per sex and dose for			
	1-year interi	m sacrifice)					
Administration route:	Diet	Diet					
Concentration:	0, 2000, 6000,	20 000 ppm diet (3 ał	oout 0, 121, 361, 12	14 mg/kg bw/day; Q about 0, 145, 437,			
	1498 mg/kg	bw/day)					
Duration:	2 years	•					
Findings:	6000 ppm diet	NOAEL (♂+♀)					
	20 000 ppm di	et: Kidney and liver fir	ndings. Increased su	rvival due to reduction in CPN,			
		eriodontal inflammation					
Select neoplasms:	Hepatocellular	adenoma (males), not	a statistically signi	ficant increase for the high dose using			
1		exact test, but statistic					
			g/kg bw/day)	6 5			
Males	0	121	361	1214			
Liver							
Hepatocyte fat vacuolation	6	7	11	11			
Hepatitis	3	4	2	5			
Kidney							
-		Dose (m	g/kg bw/day)				
Females	0	145	437	1498			
Liver							
Hepatocyte fat vacuolation	7	5	6	6			
Hepatitis	6	5	4	4			
Tumors:		Dose (m	g/kg bw/day)				
Males	0	121	361	1214			
Findings for dead and moribund sacrificed a							
*Hepatocellular adenoma – B	0/37	2/36 (6%)	0/35	3/26 (12%)			
Hepatocellular carcinoma – M	0/37	0/36	0/35	0/26			
Findings for animals sacrificed at termination							
*Hepatocellular adenoma – B	0/16	0/17	0/18	2/26 (8%)			
Hepatocellular carcinoma – M	0/16	0/17	0/18	0/26			

B benign, M malignant

\*Historical Control Range: 0-11.5% total males with hepatocellular adenoma, 26 studies, 1984-2003

Mean dose levels of 86/105, 285/349, and 1077/1382 mg glyphosate/kg bw/day (males/females) were achieved (Table 13). This study was rated Klimisch 1 for reliability.

Non-neoplastic findings included transient liver enzyme activity for mid-dose males and high-dose males and females, and equivocal nephrocalcinosis depositions at the high-dose. Histopathology noted a statistically significant increase in adipose infiltration of the bone marrow in high-dose males compared to controls, suggestive of myeloid hypoplasia, which may be considered a stress response (Everds et al. 2013).

Skin keratoacanthoma in males and mammary gland adenocarcinoma in females (Table 13) were considered for evaluation in the context of the weight of evidence for rat tumor incidence (Tables 20 and 21), wherein dose-

Study owner:	Nufarm (2009a)						
Reliability/Justification:	1 Study performed according to G	LP and OECD	guideline requ	irements, with no deviations			
Substance:	Glyphosate (95.7% pure)						
Species/Strain:	Rat/Wistar, groups of 51 & and 51	Ŷ					
Administration route:	Diet						
Concentration:	0, 3000, 10 000, 15 000 ppm diet, about 0, 84, 285, 1077 mg/kg by				ppm diet by Week-40 (ð		
Duration:	2 years						
Findings:	$\geq$ 1077/1382 mg/kg bw/day: NOA	EL(3/2)					
8	Transient liver enzyme activity for mid-dose males and high-dose males and females; equivocal nephrocalcinosis						
Select neoplasms:	depositions at the high-dose ma Skin keratoacanthoma (males), ma	les and females	s; increased adi	pose infiltration of the bone			
1	depositions at the high-dose ma	les and females	s; increased adi	pose infiltration of the bone a			
Tumor	depositions at the high-dose ma	les and females ammary gland	s; increased adi adenocarcinom	pose infiltration of the bone a Dose (mg/kg bw/day)	marrow in high-dose males		
Tumor Males	depositions at the high-dose ma	les and females	s; increased adi	pose infiltration of the bone a			
Tumor Males Findings for all animals	depositions at the high-dose ma	les and females ammary gland a 0	s; increased adi adenocarcinom 84	pose infiltration of the bone a Dose (mg/kg bw/day) 285	marrow in high-dose males 1077		
Tumor Males	depositions at the high-dose ma	les and females ammary gland	s; increased adi adenocarcinom	Dose (mg/kg bw/day) 285 0/51	marrow in high-dose males		
Tumor Males Findings for all animals Skin keratoacanthoma – B	depositions at the high-dose ma	les and females ammary gland a 0 2/51 (4%)	s; increased adi adenocarcinom 84 3/51 (6%)	Dose (mg/kg bw/day) 285 0/51 Dose (mg/kg bw/day)	marrow in high-dose males 1077 6/51 (12%)		
Tumor Males Findings for all animals Skin keratoacanthoma – B Females	depositions at the high-dose ma	les and females ammary gland a 0	s; increased adi adenocarcinom 84	Dose (mg/kg bw/day) 285 0/51	marrow in high-dose males 1077		
Tumor Males Findings for all animals Skin keratoacanthoma – B	depositions at the high-dose ma	les and females ammary gland a 0 2/51 (4%)	s; increased adi adenocarcinom 84 3/51 (6%)	Dose (mg/kg bw/day) 285 0/51 Dose (mg/kg bw/day)	marrow in high-dose males 1077 6/51 (12%)		

B benign, M malignant

responses were not evident. Tumor incidence summary data have been tabulated (see data Supplementary Study 8 to be found online at http://informahealthcare.com/doi/abs/10.3109/ 10408444.2014.1003423). Microscopic evaluation of tissues did not reveal any indications of neoplastic lesions caused by glyphosate treatment. The study report concluded that glyphosate acid was not carcinogenic in Wistar rats following continuous dietary exposure to up to 24 000 ppm for 24 months, at 1077 and 1382 mg/kg bw/day in males and females, respectively, which is consistent with the recent evaluation in Europe under the Annex I Renewal of glyphosate (Germany Rapporteur Member State 2015b).

#### Study 9 Publication (Chruscielska et al. 2000a)

A two-year combined chronic toxicity and carcinogenicity study in Wistar rats was published by academic researchers from Warsaw, Poland. The study was conducted as a drinkingwater study in Wistar-RIZ rats according to OECD TG 453. The test material was a 13.85% aqueous formulation of glyphosate as its ammonium salt (equivalent to 12.6% glyphosate acid). However, the ammonium salt of glyphosate tested is not commercially available, and the concentration of active ingredient suggests that a glyphosate-formulated product was tested; this is supported by a concurrent genotoxicity publication by the same lead author (Chruscielska et al. 2000b), previously reviewed by Kier and Kirkland (Kier and Kirkland 2013), in which a glyphosate formulation, Perzocyd, was tested. Deficiencies noted with respect to OECD TG 453 include insufficient dosing to elicit toxic effects, inadequate test material characterization, no reporting of water/feed consumption, body weights and diet composition, and no individual animal data. Although the manuscript reporting deficiencies may have been included in the study, they were not reported in the manuscript, and could warrant a Klimisch reliability score of 4 (not assignable), but the low doses employed in this study justify a Klimisch reliability score of 3.

The test material was administered in water at glyphosate salt concentrations of 0, 300, 900, and 2700 mg/L. Each dose group consisted of 85 animals per sex. Ten animals per sex and dose were sacrificed after 6, 12, and 18 months of exposure, for evaluation of general toxicity. The remaining 55 animals per sex and dose were scheduled for sacrifice after 2 years of exposure.

Water consumption was claimed to have been measured, but these data have not been reported. To estimate the glyphosate doses received via drinking water, the assumed default water consumptions were 50 and 57 mL/kg bw/day by male and female rats, respectively (Gold et al. 1984). Using these standard figures and the glyphosate content of the tested formulation (12.6%), daily doses are estimated at 0, 1.9, 5.7, and 17 mg of glyphosate/kg bw/day for males and 0, 2.2, 6.5, and 19 mg of glyphosate/kg bw/day for females. As this study appears to have tested a formulated product, data were not included in the weight of evidence review (Tables 20 and 21), but given the very low glyphosate doses and reported low tumor incidence, these were of no consequence to the overall data review.

Exposure to glyphosate ammonium salt had no effect on body weight, appearance and behavior, and hematological parameters, which is consistent with glyphosate chronic toxicity data regulatory reviews. Even though there seems to be a trend towards higher 2-year mortality in treated females (Table 14), this difference had no statistical significance according to the authors. There were sporadic alterations of clinical-chemical and urinalysis parameters, but not in a consistent fashion over time and without dose-dependence. These alterations were not interpreted as treatment-related. There was no effect of glyphosate on the incidence of neoplastic lesions (Table 14). Thus, the NOAEL for chronic toxicity and carcinogenicity in this study was greater than or equal to 17 and 19 mg glyphosate/kg bw/day, in males and females, respectively.

Due to the lack of systemic effects in the highest dose group, the MTD was not reached by this study. Judging from other rat studies reviewed here, the MTD is likely to be greater than 1000 mg/kg bw/day. Thus, the top glyphosate dose of an estimated 19 mg/kg bw/day in this study is too low to satisfy regulatory validity criteria for a carcinogenicity study.

#### Mouse carcinogenicity

There are a total of five carcinogenicity studies with glyphosate in mice, that have been submitted to support glyphosate Annex I renewal in the European Union. All but the oldest study (Study 10) were considered reliable without restriction, and were performed under conditions of GLP following OECD TGs. Most studies were conducted in the CD-1 strain. Each study was sponsored by a different manufacturer. In each case, technical grade glyphosate was administered via diet for at least 18 months. Select neoplasms, mostly lymphoreticular, liver and lung, are summarized for all mouse chronic studies in Tables 22 and 23. These neoplasms are widely recognized as occurring spontaneously in aging mice (Gad et al. 2008, Son and Gopinath 2004). Lymphomas have been recognized for many years as one of the most common, if not the most common category of spontaneous neoplastic lesions in aging mice (Brayton et al. 2012, Gad et al. 2008, Son and Gopinath 2004). The subclassification of malignant lymphomas is not a typical diagnostic feature in rodent studies, likely due to either expense and/or feasibility. It is, however, important to recognize that lymphomas are not a single type of neoplasm, rather they are a grouping of different neoplasms arising from different pathogeneses, and should be considered as different diseases (Bradley et al. 2012). As is the case for NHL in humans, these different immune system neoplasms are clustered together based on manifestation in lymphocytes, despite their very different etiologies; for example, the most common subset of NHL lymphomas clustered together as "diffuse large B cell lymphomas", have for many years been considered multiple clinical-pathologic entities (Armitage 1997), and therefore may be considered attributable to different modes of action. Chronic endpoints and NOAEL values are captured in each study summary table; however, the following study reviews focus on carcinogenicity.

#### Study 10 (Monsanto 1983)

The first chronic-carcinogenicity mouse study with glyphosate was conducted between March 1980 and March 1982 (Monsanto 1983), prior to the institution of GLP (Table 15). The study design was essentially in compliance with OECD TG 451 for carcinogenicity studies, adopted in 1981, when

Table 14. Publication, Study 9 – Two-year drink	ng water study in rats with 13.85% glyphosate ammonium sal	(Chruscielska et al. 2000a).

Authors:	Chruscielska et al. (20	00a)						
Reliability/Justification:	3 Study not performed according to GLP, but according to OECD TG 453, with the following deficiencies: Reporting deficits (water and feed consumption, body weights, diet composition, individual							
						et composi	ition, indiv	idual
	animal data, substan Highest dose did not e		on, purity,	, and stabil	iity)			
Substance:	Ammonium salt of gly	phosate, 13.8	5% soluti	on				
Species/Strain:	Rat/Wistar -RIZ outbred, 85 & and 85 & per dose group. 10 & and 10 & each were sacrificed after							ficed after
	6, 12, and 18 months of exposure.							
Administration route:	Drinking water 0, 300, 900, and 2700 mg/L							
Concentration:	Estimated glyphosate i	mg/L intoleo: 1:0-1	0.57.01	d 17 ma/b	a hu/dou	0.0.22	65 and 10	) ma/ka
	bw/day, based on as 1984)							
Duration:	2 years							
Findings:	17/19 mg glyphosate/k		DAEL (ð/	Q)				
	No treatment-related e							
Tumors reported for 85 rats/sex/dose:	No increase in the inci					administra	tion	
	0	Est		ose (mg/kg )/2.2		//6.5	1	7/19
	ð	Ŷ	1.9 රී	η2.2 Q	ਤ.1 ਹੈ	70.5 Q	ı گ	ν19 Ω
Two-year mortality	42%	38%	42%	45%	54%	53%	44%	60%
Lungs								
Lymphoma	2	_	2	-	1	_	3	1
Histiocytoma	-	-	-	-	-	-	-	1
Adenocarcinoma	1	_	-	-	-	-	-	-
Histiocytoma, malignant	_	1	-	—	1	—	- 1	-
Spleen, leukemia Kidneys, Fibrous histiocytoma	0	_	2	_	0	_	1 1	-
Pituitary gland	—	—	—	-	-	_	Т	-
Adenoma	4	10	4	6	2	8	0	3
Adenoma, malignant (assumed to be carcinoma)	0	1	0	3	1	$\overline{2}$	1	5
Carcinoma	0	_	0	-	1	_	0	-
Thyroid								
Adenoma	1	1	1	2	0	0	3	3
Carcinoma	0	-	1	-	0	-	0	- 1
Uterus, cervix carcinoma Uterus, body, histiocytoma	_	0 3	_	$\begin{array}{c} 0 \\ 1 \end{array}$	_	0 0	_	$\frac{1}{1}$
Mammary gland	—	5	—	T	-	0	_	1
Fibroma	_	0	_	0	_	0	_	0
Fibroadenoma	_	3	_	2	_	3	_	3
Adrenal medulla, adenoma	1	2	2	2	1	2	0	2
Thymus, lymphoma	0		0		0		1	
Testis, Leydigoma	-		3		6		1	
Subcutaneous tissue	0		1				2	
Fibroma	0		1		1		3	1
Lipoma Cystadenoma	_	_ 1	_	_	_	_	_	1
Lymph nodes	—	1	_	_	_	_	_	_
Lymphoma	0		0		0		1	
Lymphoma, malignant	_	1	_	_	_	_	_	_
Skin, carcinoma	2	-	_	_	-	_	-	_
Prostate, adenoma	1	-	-	-	-	_	_	-

the study was already ongoing. Groups of 50 male and female CD-1 mice received glyphosate at dietary levels of 1000, 5000, and 30 000 ppm, over a period of nearly two years. The mean achieved doses were 157/190, 814/955, and 4841/5874 mg/kg bw/day in males and females, respectively, exceeding the limit dose. Based on this study predating both GLP and OECD TG 451, a reliability score of Klimisch 2 has been assigned.

In addition to post-mortem pathological examinations after terminal sacrifice, hematological investigations were performed on 10 mice per sex and dose at months 12 and 18, and on 12 male animals/group, as well as all surviving females at scheduled termination.

Two non-neoplastic histological changes affecting the liver and urinary bladder were assumed to be treatment-related. There was a higher incidence of centrilobular hepatocyte hypertrophy in high-dose males, and a more frequent occurrence of slight-to-mild bladder epithelial hyperplasia in the mid and high dose; however, a clear dose-response was lacking. Tumor incidences, which did not significantly increase with dose, were mostly bronchiolar-alveolar, hepatocellular, or lymphoreticular, all of which are commonly noted spontaneously occurring tumors in aging mice (Table 15). Lymphoreticular tumors combined for males and females totaled 7, 12, 10 and 12 for control, low, mid- and high-dose groups respectively, and were not considered as being related to test substance.

A more frequent occurrence of slight-to-mild bladder epithelial hyperplasia was observed in the mid and high-dose groups; however, clear dose-response was lacking (Table 15) and no urinary bladder neoplasms were noted at these doses (see data Supplementary Study 10 to be found online at http://

Table 15. Study 10 - Two-year feeding study with glyphosate in mice (Monsanto 1983).

Study owner:	Monsanto (1983)							
Reliability/Justification	2 Study was performed	d prior to institution of C	LP and OECD	guideline requirem	ents			
Substance:	Glyphosate (99.7% pu	Glyphosate (99.7% pure)						
Species/Strain:	Mouse/CD-1, groups of	Mouse/CD-1, groups of 50 $\Im$ and 50 $\Im$						
Administration route:	Diet	Diet						
Concentration:	0, 1000, 5000, 10 000 mg/kg bw/day)	0, 1000, 5000, 10 000 ppm diet (♂ about 0, 157, 814, 4841 mg/kg bw/day; ♀ about 0, 190, 955, 587 mg/kg bw/day)						
Duration:	24 months							
Findings:	1000 ppm diet: NOAE	L(3+9)						
	epithelial hyperplas	veight $\downarrow$ , histological chains in males at mid and hi	igh doses)		slight to mild			
Select neoplasms:	Lymphoreticular neop	Lymphoreticular neoplasms, bronchiolar-alveolar adenocarcinoma						
			Dose (	(mg/kg bw/day)				
Males		0	157	814	4841			
Lymphoreticular system								
Lymphoblastic lymphosarcoma wi	th leukemia – M	1/48 (2%)	4/49 (8%)	3/50 (6%)	2/49 (4%)			
Lymphoblastic lymphosarcoma wi	thout leukemia – M	0/48	1/49 (2%)	0/50 (0%)	0/49			
Composite lymphosarcoma – M		1/48 (2%)	0/49	1/50 (2%)	0/49			
Histiocytic sarcoma – M		0/48	1/49 (2%)	0/50	0/49			
Total lymphoreticular neoplasms#		2/48 (4%)	6/49 (12%)	4/50 (8%)	2/49 (4%)			
		Dose (mg/kg bw/day)						
Females		0	190	955	5873			
Lymphoreticular system								
Lymphoblastic lymphosarcoma wi	th leukemia – M	1/50 (2%)	4/48 (8%)	5/49 (10%)	1/49 (2%)			
Lymphoblastic lymphosarcoma wi		0/50 (0%)	1/48 (2%)	0/49 (0%)	3/49 (6%)			
Composite lymphosarcoma – M		4/50 (8%)	1/48 (2%)	1/49 (2%)	6/49 (12%)			
Histiocytic sarcoma – M		0/50 (0%)	0/48 (0%)	0/49 (0%)	0/49 (0%)			
<sup>#</sup> Total lymphoreticular neoplasms		5/50 (10%)	6/48 (13%)	6/49 (12%)	10/49 (20%)			

<sup>#</sup>Sum of lymphoblastic lymphosarcoma, composite lymphosarcoma, and histiocytic sarcoma.

M malignant

informahealthcare.com/doi/abs/10.3109/10408444.2014.100 3423). Benign renal tubule adenomas were noted in mid- and high-dose males at incidences of 1/50 and 3/50 respectively. These neoplasms were not observed in females, lacked statistical significance, and were considered spontaneous and unrelated to glyphosate administration by the study pathologists; this neoplasm, while not seen in the concurrent control group, had previously been noted in control male CD-1 mice of comparable age by the author of the study. As an additional measure of diligence, a Pathology Working Group was convened, and it concluded that the absence of any pre-neoplastic kidney lesion in all male animals provided sufficient evidence that this finding was spurious and not related to glyphosate administration. This is reflected in the US EPA review of glyphosate (US EPA 1993). This neoplasm was not observed in the other four mouse carcinogenicity studies discussed.

The author of the study also reported a trend towards a nonstatistically significant increased occurrence of lymphoreticular neoplasia in treated female mice (Table 15). However, these consisted of three different categories of lymphoreticular neoplasms. Regulatory reviews confirmed that there is no apparent dose-dependence for these endpoints (EC 2002, US EPA 1993, WHO/FAO 2004a). Summary tables of incidence of neoplastic findings are available (see data Supplementary Study 10 to be found online at http://informahealthcare.com/ doi/abs/10.3109/10408444.2014.1003423).

Glyphosate was reported as not carcinogenic in CD-1 mice up to doses well in excess of the limit dose for carcinogenicity testing, which is consistent with evaluations by the US EPA (US EPA 1993), European Commission (EC 2002), recent EU Annex I Renewal evaluation by the Rapporteur (Germany Rapporteur Member State 2015b), and WHO/FAO (WHO/ FAO 2004a).

#### Study 11 (Cheminova 1993b)

Another carcinogenicity bioassay in mice was conducted between December 1989 and December 1991 (Table 16) (Cheminova 1993b). In this assay, 50 male and 50 female CD-1 mice per dose group received glyphosate via their diet over a period of approximately two years. This treatment period is 6 months longer than the 18 months stipulated for mice by OECD TG 451 (1981 version). The dietary levels were adjusted regularly to achieve constant dose levels of 0, 100, 300 and 1000 mg/kg bw/day, achieving the limit dose. This study was rated Klimisch 1 for reliability.

Slight non-statistically significant increases in bronchiolar-alveolar adenomas were noted for all male dose groups above controls in a non-dose-responsive manner. Bronchiolar-alveolar neoplasms are evaluated in the context of the full data set (Tables 22 and 23), demonstrating a lack of dose-response across doses ranging from approximately 15 mg/kg bw/day to 5000 mg/kg bw/day. Although the number of pituitary adenomas were low and considered incidental, they were conservatively included in the select neoplasms, based on being slightly higher in high dose females than concurrent controls (Table 16). The data summary of all histological findings, including tumor incidence, is available (see data Supplementary Study 11 to be found online at http://informahealthcare.com/doi/abs/10.3109/10408444. 2014.1003423).

There were no statistically significant increases in the occurrence of any tumor type in this study. The observed variations did not show a dose relationship, and were within the range of historical control data. Glyphosate was determined to be not carcinogenic to CD-1 mice at up to 1000 mg/kg bw/day, which is consistent with evaluations by the European Commission (EC 2002) and WHO/FAO (WHO/FAO 2004a).

Table 16. Stud	v 11 – Two-year	r feeding study w	ith glyphosate in n	nice (Cheminova 1993b).

Study owner:	Cheminova (1993b)	Cheminova (1993b)					
Reliability/Justification:		1 Study performed according to GLP and OECD guideline requirements					
Substance:	Glyphosate (98.6%)	Glyphosate (98.6% pure)					
Species/Strain:	Mouse/CD-1, group	Mouse/CD-1, groups of 50 $\Im$ and 50 $\Im$					
Administration route:	Diet	Diet					
Concentration:	♂+9:0, 100, 300, 1 concentration)	$\mathcal{F}$ + $\mathcal{P}$ : 0, 100, 300, 1000 mg/kg bw/day (regular adjustment of dietary concentration)					
Duration:	24 months						
Findings:	$\geq$ 1000 mg/kg bw/d	ay: NOAEL (♂+♀)					
	no treatment-related	leffects					
Select neoplasms:	Bronchiolar-alveola	r adenoma, bronchiola	r-alveolar carc	inoma, pituita	ry adenoma		
-	(females)				-		
	. ,	Dose (mg/kg bw/day)					
Males		0	10	300	1000		
Bronchiolar-alveolar ade	noma – B	9/50 (18%)	15/50 (30%)	11/50 (22%)	13/50 (26%)		
Bronchiolar-alveolar card	cinoma – M	10/50 (20%)	7/50 (14%)	8/50 (16%)	9/50 (18%)		
			Dose (mg/kg bw/day)				
Females		0	100	300	1000		
Bronchiolar-alveolar ade	noma – B	7/50 (14%)	3/50 (6%)	3/50 (6%)	6/50 (12%)		
Bronchiolar-alveolar card	cinoma – M	3/50 (6%)	2/50 (4%)	1/50 (2%)	5/50 (10%)		
Pituitary adenoma – B		1/41 (2%)	0/32	0/23	3/43 (6%)		

*B* benign, *M* malignant

#### Study 12 (Arysta Life Sciences 1997a)

An 18-month feeding study in ICR-CD-1 mice, conducted between February 1995 and September 1996, investigated higher doses by admixing 1600, 8000, or 40 000 ppm glyphosate into the diet fed to groups of 50 male and 50 female mice per dose (Arysta Life Sciences 1997a). The calculated test substance intake was 165/153, 838/787, and 4348/4116 mg/kg bw/day (males/females, Table 17), exceeding the limit dose. This study was rated Klimisch 1 for reliability.

Histopathological examinations did not show statistically significant increases for any type of neoplastic lesion in all treatment groups of both sexes (see data Supplementary Study 12 to be found online at http://informahealthcare.com/ doi/abs/10.3109/10408444.2014.1003423). Select neoplasms evaluated across the data set with some nonstatistically significant increases above concurrent controls included lymphoma and lung tumors, all of which lacked a clear dose-response. Glyphosate was considered not carcinogenic in CD-1 mice up to doses well in excess of the limit dose for carcinogenicity testing, which is consistent with the recent evaluation in Europe under the Annex I Renewal of glyphosate (Germany Rapporteur Member State 2015b).

#### Study 13 (Feinchemie Schwebda 2001)

An 18-month feeding study in Swiss albino mice (Feinchemie Schwebda 2001), conducted between December 1997 and June 1999, featured treatment groups, each with 50 animals per sex, receiving 100, 1000, and 10 000 ppm technical grade glyphosate

Table 17. Study 12 – Two-year feeding study with glyphosate in mice (Arysta Life Sciences 1997a).

-		• 1			-			
Study owner:	Arysta Life Sciences (1997)	))						
Reliability/	1 Study performed accordin	g to GLP and	OECD guidelin	ne requirements	, with no			
Justification:	deviations.							
Substance:	Glyphosate (94.6-97.6% pu	ilyphosate (94.6–97.6% pure)						
Species/Strain	Iouse/CD-1, groups of 50 $\Im$ and 50 $\Im$							
Administration route:	Diet	Diet						
Concentration:	0, 1600, 8000, or 40 000 ppm diet (♂ about 0, 165, 838, 4348 mg/kg bw/day; ♀ about 0, 153, 787, 4116 mg/kg bw/day)							
Duration:	18 months	18 months						
Findings:	8000/1600 ppm diet: NOAE	L (ð/q)						
	8000 ppm diet (Q): retarded	growth						
	40 000 ppm diet: pale-color	ed skin 3, loos	se stool, retarde	d growth, redu	ced food			
	consumption and food eff							
	relative cecum weight, wi	thout histopat	hological findi	igs of increased	incidence of			
	anal prolapse, consistent							
Select neoplasms:	Lung adenoma, lung adenoc	arcinoma, lyn	iphoma					
I.	0	•	Dose (m	g/kg bw/day)				
Males		0	165	838	4348			
Lung adenoma – B		8/50 (16%)	14/50 (28%)	13/50 (26%)	11/50 (11%)			
Lung adenocarcinoma	– M	1/50 (2%)	1/50 (2%)	6/50 (12%)	4/50 (8%)			
Lymphoma – M		2/50 (4%)	2/50 (4%)	0/50	6/50 (12%)			
v 1			Dose (mg/kg bw/day)					
Females		0	153	787	4116			
Lung adenoma – B		8/50 (16%)	5/50 (10%)	12/50 (24%)	5/50 (10%)			
Lung adenocarcinoma	– M	1/50 (2%)	2/50 (4%)	3/50 (6%)	1/50 (2%)			
Lymphoma – M		6/50 (12%)	4/50 (8%)	8/50 (16%)	7/50 (14%)			

*B* benign, *M* malignant

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Table 18. Study 13-18-	3-Month feeding study v	with glyphosate in mice	(Feinchemie Schwebda 2001).
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Study owner:	Feinchemie Schwe	ebda (2001)				
Reliability/Justification				requirements, with n	o deviations, but p	ossible viral
Substance:	Glyphosate (>95)	ave confounded inter	rpretation of results			
Species/Strain		no, groups of 50 3 a	nd 50 0			
Administration route:	Diet	no, groups or 50 0 a	na 50 ‡			
Concentration:		0 ppm diet (& about	0, 14.5, 150, 1454 mg	g/kg bw/day; ♀ about	0, 15.0, 151, 1467 r	ng/kg bw/day)
Duration:	18 months		-,,,	5	-,,,	
Findings:	1000 ppm diet: No	DAEL $(3+9)$				
C		(3+Q): increased mo	rtality			
Select neoplasms:		lar adenoma, lympho				
	Historica	l controls		Dose (mg/kg	bw/day)	
			0	14.5	150	1454
Males	· · · · · · · · · · · · · · · · · · ·					
Mortality	<sup>§</sup> 11/50–27/50		+22/50 (6)	20/50 (6)	22/50 (8)	27/50 (8)
Findings for dead and moribund	sacrificed animals	06 76 10 111	0/00 (41.00)			12/27 (40.00)
Lymphoma – M	#20/75	26.7% [0-44]	9/22 (41.0%)	*12/20 (60.0%)	*13/22 (59.0%)	13/27 (48.0%)
Findings in animals sacrificed at		14.000 50.043	1/20 (2 (21)	2/20 (10.0%)	0.00 (10 70)	
Lymphoma – M	26/175	14.9% [8–24]	1/28 (3.6%)	3/30 (10.0%)	3/28 (10.7%)	*6/23 (26.1%)
Total animals	461250	19 407 17 201	10/50 (20.00)	15/50 (20.007)	1(150 (22.00))	******
Lymphoma – M	46/250	18.4% [6–30]	10/50 (20.0%)	15/50 (30.0%)	16/50 (32.0%)	*19/50 (38.0%)
	Historica	I controls	0	Dose (mg/kg		1467
Females			0	15.0	151	1407
Mortality	12/50-20/50		16/50 (7)	16/50(7)	20/50 (2)	20/50 (3)
Findings for dead and moribund			10/50(7)	10/30(7)	20750(2)	20/30 (3)
Bronchiolar/alveolar	_	_	0/16	0/16	1/20 (5%)	2/20 (10%)
adenoma – B					(/-)	
Lymphoma – M	49/77	63.6% [0-100]	9/16 (56.0%)	10/16 (63.0%)	13/20 (65.0%)	12/20 (60.0%)
Findings in animals sacrificed			. ,	. ,	. ,	
at termination						
Bronchiolar/alveolar adenoma			1/34 (3%)	0/0	1/1 (100%)	1/30 (3%)
-B						
Lymphoma – M	50/175	28.9% [2043]	9/34 (26.5%)	10/30 (29.4%)	6/30 (20.0%)	*13/28 (43.3%)
Total animals						
Bronchiolar/alveolar adenoma			1/50 (2%)	0/16	2/21 (10%)	3/50 (6%)
-B	00/050	20 69 51 652	10/50 (07.000)	00/50 /10 020	10/50 (00.0%)	
Lymphoma – M	99/250	39.6% [1458]	18/50 (36.0%)	20/50 (40.0%)	19/50 (38.0%)	*25/50 (50.0%)

B benign, M malignant.

<sup>§</sup>Nine studies, performed by the same laboratory in the timeframe encompassing the study summarized here.

<sup>+</sup>(Number of animals killed in extremis).

<sup>#</sup>Five studies, conducted in the same laboratory between 1996 and 1999.

\*Statistically higher than concurrent controls (p < 0.05).

in the diet. Control mice received a plain diet. The calculated test substance intake was 14.5/15.0, 150/151, 1454/1467 mg/ kg bw/day (males/females, Table 18), exceeding the limit dose, as reflected in elevated mortality in the high dose groups. This study was rated Klimisch 2 for reliability, based on speculation of a viral infection within the colony, discussed below.

Based on the slightly higher mortality and lower survival rates in the high dose groups, the NOAEL was considered 1000 ppm (151 mg/kg bw/day). There were no treatment-related effects on clinical signs, behavior, eyes, body weight, body weight gain, food consumption, and differential white blood cell counts in both sexes. Gross pathology, organ weight data, and histopathological examination demonstrated no treatment-related effects. An increase in the number of malignant lymphomas, the most common spontaneously occurring tumor category in the mouse, was statistically significant in the high-dose groups compared to controls (Table 18). The Germany Rapporteur Member State concluded that the malignant lymphoma increase in high-dose males was inconclusive but unrelated to treatment in the context of similar higher dosed studies (Germany Rapporteur Member State 2015b), and considered this endpoint irrelevant to carcinogenic risk in humans (Germany Rapporteur Member State 2015a). Whether or not a viral component (Taddesse-Heath et al. 2000) may have contributed to this endpoint, the finding was considered incidental background variation based on historical control data, and in agreement with the study director. As in Study 11, bronchiolar-alveolar adenoma was also considered a select neoplasm for evaluation in the broader data set (Tables 22 and 23), and as previously discussed, demonstrates a lack of dose-response across doses ranging from approximately 15 mg/kg bw/ day to 5000 mg/kg bw/day. Summary tables of all histopathological neoplastic findings are available (see data Supplementary Study 13 to be found online at http://informahealthcare.com/doi/abs/10.3109/10408444.2014.1003423).

Technical grade glyphosate was reported as not carcinogenic in Swiss albino mice, following continuous dietary exposure of up to 1460 mg/kg bw/day (average for both sexes) for 18 months. The NOAEL for general chronic toxicity was 151 mg/kg bw/day for both sexes combined.

#### Study 14 (Nufarm 2009a)

The most recent mouse carcinogenicity assay was conducted between October 2005 and November 2007 (Nufarm 2009a).

Table 19. Study 14-18-Month feeding study with glyphosate in mice (Nufarm 2009a).

Study owner:	Nufarm (2009b)			
Reliability/Justification:	1 Study performed accord	ing to GLP and OECD gu	ideline requirements,	with no deviations
Substance:	Glyphosate (94.6–97.6% p	oure)		
Species/Strain:	mouse/CD-1, groups of 51	∂ and 51 ♀		
Administration route:	Diet			
Concentration:	0, 500, 1500, and 5000 pp	m diet (3 about 0, 0, 71.4,	234, 810 mg/kg bw/d	lay; Q about 0, 97.9,
	300, 1081 mg/kg bw/da			<b>3</b> , ,
Duration:	18 months			
Findings:	$\geq$ 5000 ppm diet: NOAEL	. ( <i>3</i> /♀)		
-	No treatment-related effec	ts		
Select neoplasms:	Bronchiolar-alveolar aden	oma, Bronchiolar-alveolar	adenocarcinoma, hep	atocellular adenoma
	(males), hepatocellular	carcinoma (males), lymph	oma, pituitary adenon	na (females)
		Dose (mg/kg by	· 1 ·	· · · ·
Males	0	157	814	4841
Bronchiolar-alveolar adenoma – B	9/51 (18%)	7/51 (14%)	9/51 (18%)	4/51 (8%)
Bronchiolar-alveolar adenocarcinoma – M	5/51 (10%)	5/51 (10%)	7/51 (14%)	11/51 (22%)
Hepatocellular adenoma – B	1/51 (2%)	1/51 (2%)	4/51 (8%)	2/51 (4%)
Hepatocellular carcinoma – M	6/51 (12%)	11/51 (22%)	7/51 (14%)	4/51 (8%)
Lymphoma – M	0/51	1/50 (2%)	2/51 (4%)	5/51 (10%)
• •		Dose (mg/kg by	w/day)	
Females	0	190	955	5873
Bronchiolar-alveolar adenoma – B	2/51 (4%)	4/51 (8%)	2/51 (4%)	2/51 (4%)

5/51 (10%)

11/51 (22%)

0/51

Pituitary adenoma - B B benign, M malignant

Lymphoma - M

Bronchiolar-alveolar adenocarcinoma - M

Groups of 51 CD-1 mice per sex received daily dietary doses of 0, 500, 1500, and 5000 ppm technical grade glyphosate (equivalent to an average intake of 85, 267 and 946 mg/kg bw/day, Table 19). The MTD was apparently not reached in the high-dose group, which is more indicative of low general toxicity of the test substance rather than a flaw in the study design. The NOAEL for chronic toxicity was 810 mg/kg bw/ day for male mice and 1081 mg/kg bw/day for female mice, the highest dosage tested. Despite not quite achieving a limit dose in males, this study was arguably rated Klimisch 1 for reliability.

Several increases in common spontaneous mouse neoplasms in male mice were noted. Non-dose-response increases were noted for hepatocellular adenoma and carcinoma in males, and dose-responses were noted for bronchiolar-alveolar adenocarcinoma and malignant lymphoma in males, but not females. Pituitary adenoma incidences were low, and considered incidental in low and high-dose females, although they were slightly higher than controls (Table 19). These neoplasms were all evaluated in context of the broader data set (Tables 22 and 23). The summary of neoplastic findings is available (see data Supplementary Study 14 to be found online at http://informahealthcare.com/doi/abs/10.3109/10408444. 2014.1003423).

Glyphosate was considered not carcinogenic in the CD-1 mice, following continuous average dietary exposure for males and females, to quantities up to 945.6 mg/kg bw/day for 18 months, which is consistent with the recent evaluation in Europe under the Annex I Renewal of glyphosate (Germany Rapporteur Member State 2015b).

#### Discussion

An extraordinarily large volume of animal data has been compiled to evaluate the carcinogenic potential of glyphosate.

The expected normal biological variability for spontaneous tumor formation is reflected across this extensive data set (Tables 20-23). However, no specific neoplasm stands out as a consequence of glyphosate exposures. While some individual studies may note an increase in a specific neoplasm at the high dose, the pooled data fail to identify any consistent pattern of neoplasm formation, demonstrating that the effect is not reproducible and not treatment-related. The lack of a dose-response across the several orders of magnitude suggests that no individual tumor of single etiology is attributable to glyphosate administration.

2/51 (4%)

10/51 (20%)

0/51

2/51 (4%)

8/51 (16)

1/50(2%)

Glyphosate has undergone repeated and extensive review by the United States Environmental Protection Agency (US EPA 1993), the European Union (EC 2002, Germany Rapporteur Member State 2015b) and the World Health Organization/Food and Agriculture Organization of the United Nations (WHO/FAO 2004b, WHO/FAO 2004a). With regard to potential carcinogenic effects of glyphosate, the unanimous outcome of these reviews has been that the data provide sufficient evidence to conclude that glyphosate should not be considered a carcinogen. Genotoxicity studies with glyphosate, conducted under conditions stipulated by internationally accepted testing guidelines and GLP, as reviewed in 2000 (Williams et al. 2000) and recently updated (Kier and Kirkland 2013), indicate that glyphosate clearly does not exhibit the properties of a DNAreactive genotoxic carcinogen. This lack of mutagenicity rules out an important concern for carcinogenicity.

Mink et al. published a review of the available epidemiological studies that investigated possible associations between glyphosate and cancer diagnosed in humans (Mink et al. 2012). No evidence was found for a statistically significant positive association between cancer and exposure to glyphosate. While one Agricultural Health Study (AHS) publication mentions a "suggested association" between glyphosate use and multiple myeloma (De Roos et al. 2005), a later summary of AHS

3/51 (6%)

11/51 (22%)

2/51 (4%)

#### Table 20. Summary of select neoplasms in male rats (Studies 1-8).

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		Tume	or Incic	lence/nı	imber of	fanimal	s examin	ied, by o	dose (n	1g/kg b	w/day)			
	Controls – 0													
Select neoplasm	[% range for studies]			<sup>a</sup> 3	<sup>d</sup> 7.4	<sup>a</sup> 10	°10	<sup>a</sup> 31	<sup>d</sup> 73.9	<sup>h</sup> 86	<sup>b</sup> 89	°100	<sup>f</sup> 104	<sup>g</sup> 121
Pancreas islet cell adenoma	20/397 [0-14]			5/49	0/30	2/50	1/24	2/50	0/32	1/51	8/57	2/17	1/75	2/64
Pituitary adenoma	153/398 [6–57]			19/49	4/30	20/48	12/24	18/47	3/31	11/51	32/58	8/19	41/75	17/63
Pituitary carcinoma	4/98 [2–6]			2/49	NF	3/48	1/24	1/47	NF	NF	NF	0/19	NF	NF
Testes interstitial cell (Leydig)	14/447 [0–8]			3/50	0/37	1/50	1/25	6/50	2/32	3/51	0/60	0/19	2/75	2/63
Thyroid C cell adenoma	35/391 [4–18]			1/49	0/26	0/49	1/21	2/49	1/29	#1/51	5/58	1/17	10/74	#1/63
Hepatocellular adenoma	30/351 [0-48]			NF	22/50	NF	1/50	NF	10/48	2/51	2/60	1/49	0/75	2/64
Hepatocellular carcinoma	22/384 [0-42]			0/50	28/50	1/50	1/50	2/50	18/48	0/51	2/60	1/49	1/75	NF
Benign keratoacanthoma (skin)	8/250 [2-5]			NF	NF	NF	NF	NF	NF	3/51	3/60	NF	3/75	0/64
		Tume	r Incid	lence/nı	imber of	fanimal	s examin	ed, by	dose (n	1g/kg b	w/day)			
Select neoplasm	e150	<sup>h</sup> 285	°300	<sup>f</sup> 354	<sup>g</sup> 361	<sup>b</sup> 362	<sup>d</sup> 740.6	<sup>e</sup> 780	<sup>b</sup> 940	°1000	<sup>h</sup> 1077	f1127	<sup>g</sup> 1214	e1290
Pancreas islet cell adenoma	NF	2/51	2/21	1/80	0/64	5/60	1/49	NF	7/59	1/49	1/51	1/78	1/64	NF
Pituitary adenoma	NF	10/51	7/21	33/80	18/64	34/58	5/49	NF	32/59	17/50	20/51	42/78	19/63	NF
Pituitary carcinoma	NF	NF	1/21	NF	NF	NF	NF	NF	NF	0/50	NF	NF	NF	NF
Testes interstitial cell (Leydig)	1/49	1/51	0/21	0/80	2/63	3/60	3/50	2/49	2/60	2/50	1/51	2/78	2/64	0/47
Thyroid C cell adenoma	NF	#0/51	2/21	5/79	#1/63	8/58	1/50	NF	7/60	8/49	#3/51	6/78	#0/64	NF
Hepatocellular adenoma	NF	0/51	2/50	2/80	0/64	3/60	21/50	NF	8/60	2/50	1/51	1/78	5/64	NF
Hepatocellular carcinoma	1/49	0/51	0/50	2/80	NF	1/60	24/50	0/49	2/60	0/50	0/51	1/78	NF	0/47
Benign keratoacanthoma (skin)	NF	0/51	NF	0/80	1/64	4/60	NF	NF	5/59	NF	6/51	7/78	1/63	NF

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<sup>a</sup>Study 1 (Monsanto) (CD) SD rats, rated unreliable for carcinogenicity evaluation.

<sup>b</sup>Study 2 (Monsanto) (CD) SD rats, including interim sacrifice groups.

<sup>c</sup>Study 3 (Cheminova) SD rats.

<sup>d</sup>Study 4 (Feinchemic Schwebda) Wistar rats.

<sup>e</sup>Study 5 (Excel) SD rats, rated unreliable for carcinogenicity evaluation.

fStudy 6 (Arysta Life Sciences) Crj:CD SD rats, including interim sacrifice groups.

<sup>g</sup> Study 7 (Syngenta) Alpk:AP<sub>f</sub>SD Wistar rats, including interim sacrifice groups.

<sup>h</sup> Study 8 (Nufarm) Wistar Han Crl:WI rats.

\*Recorded as parafollicular adenoma.

NF not found/not reported

Table 21. Summary of select neoplasms in female rats (Studies 1-8).

		Tui	nor Inc	idence/1	number	of anima	ls exan	ined, b	y dose	(mg/kg	bw/day)			
	Controls – 0													
Select neoplasm	[% range for studies]			<sup>a</sup> 3	<sup>d</sup> 7.4	°10	<sup>a</sup> 11	<sup>a</sup> 34	<sup>d</sup> 73.9	°100	<sup>h</sup> 105	<sup>b</sup> 113	<sup>f</sup> 115	<sup>g</sup> 145
Pancreas islet cell adenoma	11/397 [0–9]			1/50	0/23	2/27	1/50	0/49	0/16	2/29	0/51	1/60	2/79	0/63
Pituitary adenoma	246/397 [14–78]			29/48	13/33	19/28		26/49	7/23	19/29	23/51	48/60	54/79	44/63
Pituitary carcinoma	16/155 [2–17]			7/48	NF	5/28	5/50		NF	5/28	NF	0/60	NF	NF
Thyroid C cell adenoma	25/302 [3% – 16%]			3/49	0/24	1/27	6/50	3/47	1/17	1/29	# 1/51	2/60	7/78	# 0/63
Hepatocellular adenoma	22/302 [0–36]			NF	18/48	1/50	NF	NF	19/49	3/50	0/51	2/60	1/79	0/64
Hepatocellular carcinoma	14/210 [0-20]			0/50	15/48	0/50	0/50	2/50	14/49	0/50	0/51	0/60	NF	NF
Mammary gland	113/384 [6–58]			16/46	NF	12/28	20/48	16/44	NF	17/29	9/51	<sup>\$</sup> 24/54	30/79	4/63
fibroadenoma														
Mammary gland	40/334 [2-22]			6/46	0/30	NF	5/48	8/44	0/33	NF	3/51	~10/54	8/79	0/63
adenocarcinoma														
		Tui	nor Inc	idence/1	number	of anima	ls exan	ined, b	y dose	(mg/kg	bw/day)			
Select neoplasm	e210	°300	<sup>h</sup> 349	f393	<sup>g</sup> 437	<sup>b</sup> 457	<sup>d</sup> 740.6	°1000	e1060	<sup>b</sup> 1183	<sup>f</sup> 1247	<sup>h</sup> 1382	<sup>g</sup> 1498	e1740
Pancreas islet cell adenoma	NF	2/29	0/51	1/78	1/64	4/60	1/49	1/49	NF	0/59	1/78	0/51	0/64	NF
Pituitary adenoma	NF	25/30	16/51	47/77	46/63	46/60	6/50	34/49	NF	34/59	52/78	32/51	49/64	NF
Pituitary carcinoma	NF	2/30	NF	NF	NF	0/60	NF	7/49	NF	1/59	NF	NF	NF	NF
Thyroid C cell adenoma	NF	2/29	#1/50	8/76	#0/64	6/60	1/47	7/49	NF	6/60	4/78	# 0/51	# 2/64	NF
Hepatocellular adenoma	NF	1/50	1/51	0/78	1/64	6/60	13/50	2/50	NF	1/60	0/78	1/51	0/64	NF
Hepatocellular carcinoma	NF	0/50	1/51	NF	NF	1/60	9/50	0/50	NF	2/60	NF	0/51	NF	NF
Mammary gland	1/22	19/30	7/51	27/77	6/64	\$27/59	NF	29/50	5/22	<sup>\$</sup> 28/57	30/78	5/51	5/64	5/50
fibroadenoma														
Mammary gland	0/22	NF	1/51	11/77	0/64	~14/59	0/48	NF	0/22	~9/57	8/78	6/51	2/64	0/50
adenocarcinoma														

<sup>a</sup>Study 1 (Monsanto) (CD) SD rats, rated unreliable for carcinogenicity evaluation.

<sup>b</sup>Study 2 (Monsanto) (CD) SD rats, including interim sacrifice groups.

<sup>c</sup>Study 3 (Cheminova) SD rats.

<sup>d</sup>Study 4 (Feinchemic Schwebda) Wistar rats.

eStudy 5 (Excel) SD rats, rated unreliable for carcinogenicity evaluation.

fStudy 6 (Arysta Life Sciences) Crj:CD SD rats, including interim sacrifice groups.

<sup>g</sup>Study 7 (Syngenta) Alpk:AP<sub>f</sub>SD Wistar rats, including interim sacrifice groups.

<sup>h</sup>Study 8 (Nufarm) Wistar Han Crl:WI rats.

<sup>\$</sup>Recorded as adenoma/adenofibroma/fibroma.

~Recorded as carcinoma/adenocarcinoma.

NF not found/not reported.

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Table 22. Summary of select neoplasms in male mice (Studies 10-14).

	Tumo	r Incidence/1	number of ani	mals examin	ned, by dos	e (mg/kg b	w/day)	
	Controls – 0							
Select neoplasm	[% range for studies]	<sup>d</sup> 14.5	°85	<sup>b</sup> 100	ď150	<sup>a</sup> 157	°165	<sup>e</sup> 267
Bronchiolar-alveolar adenoma	31/249 [10-18]	2/22	<sup>\$</sup> 7/51	15/50	0/22	9/50	<sup>§</sup> 14/50	<sup>\$</sup> 9/51
Bronchiolar-alveolar adenocarcinoma	10/149 [2–10]	NF	<sup>\$</sup> 5/51	NF	NF	3/50	<sup>\$</sup> 1/50	<sup>\$</sup> 7/51
Bronchiolar-alveolar carcinoma	10/100 [0-20]	0/22	NF	7/50	0/22	NF	NF	NF
Hepatocellular adenoma	27/250 [0–28]	5/25	1/51	12/50	3/28	0/50	15/50	4/51
Hepatocellular carcinoma	15/250 [0–16]	0/25	11/51	5/50	0/28	0/50	1/50	7/51
Malignant lymphoma	16/205 [0-100]	15/50	1/51	2/4	16/50	#5/50	2/50	2/51
Myeloid leukemia	3/101 [0-6]	1/50	1/51	NF	1/50	NF	NF	0/51
	Tumo	r Incidence/1	number of ani	mals examin	ned, by dos	e (mg/kg b	w/day)	
Select neoplasm	<sup>b</sup> 300	<sup>a</sup> 814	°838	°946	<sup>b</sup> 1000	<sup>d</sup> 1454	°4348	<sup>a</sup> 4841
Bronchiolar-alveolar adenoma	11/50	9/50	<sup>\$</sup> 13/50	<sup>§</sup> 4/51	13/50	1/50	<sup>§</sup> 11/50	9/50
Bronchiolar-alveolar adenocarcinoma	NF	2/50	<sup>§</sup> 6/50	<sup>\$</sup> 11/51	NF	NF	<sup>\$</sup> 4/50	1/50
Bronchiolar-alveolar carcinoma	8/50	NF	NF	NF	9/50	1/50	NF	NF
Hepatocellular adenoma	11/50	1/50	15/50	2/51	9/50	3/50	7/50	0/50
Hepatocellular carcinoma	6/50	0/50	3/50	4/51	7/50	2/50	1/50	2/50
Malignant lymphoma	1/1	#4/50	0/50	5/51	6/8	19/50	6/50	#2/50
Myeloid leukemia	NF	NF	NF	0/51	NF	1/50	NF	NF

<sup>a</sup>Study 10 (Monsanto) CD-1 mice.

<sup>b</sup>Study 11 (Cheminova) CD-1 mice.

<sup>c</sup>Study 12 (Arysta Life Science) CD-1 mice.

<sup>d</sup>Study 13 (Feinchemic Schwebda) Swiss albino mice.

<sup>e</sup>Study 14 (Nufarm) CD-1 mice.

<sup>§</sup>Recorded as lung rather than bronchiolar-alveolar.

<sup>#</sup>Recorded as sum of malignant lymphoblastic lymphosarcoma with leukemia, lymphoblastic lymphosarcoma without leukemia and composite lymphosarcoma.

<sup>\$</sup>Recorded as lymphoblastic lymphosarcoma with leukemia.

NF not found/not reported.

results note that there were no associations between glyphosate use and a number of cancers, including lymphohematopoietic cancers, leukemia, NHL, and multiple myeloma (Weichenthal et al. 2010). A subsequent reanalysis of AHS data obtained under the Freedom of Information Act notes no suggestion of an association between glyphosate use and multiple myeloma, with a relative risk of 1.1 and 95% and a confidence interval of 0.5–2.9 (Sorahan 2012). A recent review paper (Alavanja et al. 2013) cites another epidemiology study claiming an association between glyphosate use and NHL (Eriksson et al. 2008), but this research is strongly criticized in the recent Reevaluation Assessment Report for glyphosate Annex I Renewal in Europe (Germany Rapporteur Member State 2015b), highlighting potential referral bias, selection bias, uncontrolled confounding, limited data usage contrary to claims of including all new cases (living cases only, rather than living

Table 23. Summary of select neoplasms in female mice (Studies 10-14).

	Tumo	r incidence/n	umber of an	imals exam	ined, by dos	e (mg/kg bv	v/day)	
Select neoplasm	Controls – 0 [% range for studies]	<sup>d</sup> 15.0	°85	<sup>b</sup> 100	<sup>d</sup> 151	°153	<sup>a</sup> 190	°267
Bronchiolar-alveolar adenoma Bronchiolar-alveolar adenocarcinoma	28/250 [2–20] 2/99 [2]	0/16 NF	\$4/51 \$2/51	3/49 NF 2/40	2/21 NF	\$5/50 \$2/50	9/50 3/50	<sup>\$</sup> 2/51 <sup>\$</sup> 2/51
Bronchiolar-alveolar carcinoma Malignant lymphoma Myeloid leukemia	9/151 [2–10] 54/215 [10–100] 2/156 [0–4]	0/16 20/50 1/50	NF 8/51 0/51	2/49 12/15 NF	0/20 19/50 2/50	NF 4/50 0/50	NF #6/50 NF	NF 10/51 1/51
Pituitary adenoma	1/232 [0–2] Tumo	0/16 r incidence/n	1/51 umber of an	0/32 iimals exam	0/17 iined, by dos	1/50 se (mg/kg by	0/21 v/day)	0/51
Select neoplasm	<sup>b</sup> 300	۶87°	°946	<sup>a</sup> 955	<sup>b</sup> 1000	<sup>d</sup> 1467	°4116	<sup>a</sup> 5874
Bronchiolar-alveolar adenoma Bronchiolar-alveolar adenocarcinoma Bronchiolar-alveolar carcinoma Malignant lymphoma Myeloid leukemia Pituitary adenoma	3/50 NF 1/50 9/12 NF 0/23	<sup>\$</sup> 12/50 <sup>\$</sup> 3/50 NF 8/50 0/50 0/50	<sup>§</sup> 2/51 <sup>§</sup> 3/51 NF 11/51 0/51 2/51	10/49 4/49 NF #6/50 NF 0/44	6/50 NF 5/50 13/14 NF ~3/50	3/50 NF 0/50 25/50 1/50 1/48	<sup>§</sup> 5/50 <sup>§</sup> 1/50 NF 7/50 1/50 0/50	1/50 4/50 NF #10/50 NF 0/37

<sup>a</sup>Study 10 (Monsanto) CD-1 mice.

<sup>b</sup>Study 11 (Cheminova) CD-1 mice.

<sup>c</sup>Study 12 (Arysta Life Science) CD-1 mice.

<sup>d</sup>Study 13 (Feinchemic Schwebda) Swiss albino mice.

eStudy 14 (Nufarm) CD-1 mice.

<sup>§</sup>Recorded as lung rather than bronchiolar-alveolar.

\*Recorded as sum of lymphoblastic lymphosarcoma with leukemia, lymphoblastic lymphosarcoma without leukemia and composite lymphosarcoma. ~2 animals in anterior lobe, 1 animal in intermediate lobe.

NF not found/not reported.

plus dead), and questionable definition/interpretation of doseresponse. It is important to note that the Eriksson et al. study did detect statistically significant positive associations for small lymphocytic lymphoma/chronic lymphocytic leukemia and "unspecified NHL", while the following lymphomas were not statistically significantly associated with glyphosate use: B-cell lymphomas, grade I-III follicular lymphoma, diffuse large B-cell lymphoma, other specified B-cell lymphomas, unspecified B cell lymphomas, and T-cell lymphomas (Eriksson et al. 2008). As previously discussed, statistically significant associations need to be evaluated further for study bias, confounders and sampling error, before expending resources and energy on further evaluation of potential causality.

Epidemiological investigations face the difficulty of reliably determining the magnitude of exposure to the chemical in question, while ruling out confounders like co-exposure to other chemicals, and environmental and lifestyle factors. In contrast, carcinogenicity studies in experimental animals, when conducted according to appropriate testing guidelines, are designed in a fashion that allows a direct association between observed effects and substance exposure, yet the relevance of observed findings to humans is an important consideration. This manuscript collectively presents the scientific community with carcinogenicity results from a remarkably large body of data from fourteen long-term carcinogenicity studies on glyphosate.

Glyphosate is of very low acute toxicity with an oral  $LD_{50}$ in the rat in excess of 5000 mg/kg of body weight.. The subchronic NOAEL is 400 mg/kg bw/day, and is based on effects that do not impair long-term survival (WHO/FAO 2004b, WHO/FAO 2004a). This allows administration of very high glyphosate doses to rodents for a prolonged time. Dietary levels of up to 30 000 and 40 000 milligrams of glyphosate per kilogram of diet have been administered to rats and mice, respectively, in chronic feeding studies covering their expected lifespan without apparent effects on longevity.

One of the most critical aspects of designing a carcinogenicity study is the choice of dose levels, especially the top dose, at either the limit dose or MTD. The relevant OECD TGs 451 and 453 for carcinogenicity studies propose a body weight depression of approximately 10% as evidence for systemic toxicity. This is equivalent to the concept of the MTD, which is discussed in a supporting OECD guidance document (OECD 2012b). For chemicals which are well tolerated by the experimental animal, where no dose-limiting toxicity is observed, the respective OECD guidance suggests 1000 mg/ kg bw/day as the highest dose level (OECD 2012a). Many of the carcinogenicity studies performed in rats and mice with glyphosate have been conducted with the high dose group receiving levels of glyphosate at, or in excess of the limit dose because of its very low toxicity following repeat exposure. Following this extensive testing, even at very high exposure levels, there was no evidence of a carcinogenic effect related to glyphosate treatment. The select neoplasms highlighted in Tables 20-23 show normal biological background levels of spontaneous neoplasms, with lack of dose-response across the data sets. The combined studies clearly indicate that glyphosate's carcinogenic potential is extremely low or nonexistent in animal models up to very high doses.

By way of comparison, the worst-case calculated human dietary exposure to glyphosate, the Theoretical Maximum Daily Intake (TMDI) is 0.14 mg/kg bw/day (EFSA 2012). Systemic exposure of operators, as assessed for the EU reapproval of glyphosate, is predicted to be between 0.0034 (German BBA model, tractor-mounted ground-boom sprayer) and 0.226 mg/kg bw/day (UK POEM, hand-held-spraying to low targets, data not shown). The model estimates are supported by human biomonitoring data in farmers showing systemic exposures of 0.004 and 0.0001 mg/kg/day for worst-case and mean acute doses, respectively (Acquavella et al. 2004). The high doses in chronic rodent studies at which no evidence of carcinogenicity is demonstrated are at least hundreds of thousands fold greater than peak human systemic exposure levels. Clearly, there is no scientific basis for concern of carcinogenic risk to humans resulting from glyphosate exposure.

With over 40 years of scientific research on glyphosate, no compelling evidence exists for a mechanism for glyphosate to cause cancer. Mammalian metabolism does not activate glyphosate to a toxic metabolite (Anadon et al. 2009, WHO/FAO 2004a). The lack of glyphosate DNA reactivity supports the

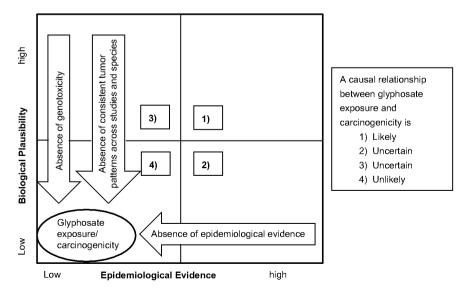


Figure 2. Likelihood of glyphosate carcinogenicity based on experimental and epidemiological data; a causal inference grid as proposed by Adami et al. (2011) to utilize both toxicological and epidemiological data.

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lack of potential for an initiation event for carcinogenesis (Kier and Kirkland 2013). Clearly, there is a lack of potential for glyphosate to induce hormonal oncogenesis, based on both the tumor incidence data presented and the unequivocal evidence that glyphosate is not an endocrine disruptor (Bailey et al. 2013, Levine et al. 2012, Saltmiras and Tobia 2012, Webb et al. 2013, Williams et al. 2012).

The absence of test substance-related neoplastic findings in a total of 14 rodent cancer bioassays with glyphosate is in stark contrast to the recent dramatic media reports, internet postings, and YouTube videos of rat tumors, hypothesized to be caused by treatment with maize containing glyphosate residue or drinking water spiked with a glyphosate formulation (Seralini et al. 2014). Such reports, under the scrutiny of the global scientific community, demand greater data transparency and accountability within the peer review process.

The absence of a glyphosate-related mechanism for carcinogenesis, the huge volume of genotoxicity data studies indicating no likely mutagenic or DNA-reactive potential (Kier and Kirkland 2013), combined with the lack of epidemiological evidence for glyphosate-induced cancer (Mink et al. 2012), and the lack of carcinogenicity in multiple rodent carcinogenicity assays, are depicted in a causal inference grid in Figure 2, as put forth by Adami et al. (Adami et al. 2011). The overwhelming weight of the available evidence, demonstrating a lack of both biological plausibility and epidemiological effects, draws a compelling conclusion that glyphosate's carcinogenic potential is extremely low or non-existent.

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#### **Declaration of interest**

The employment affiliation of the authors is as shown on the cover page. Volker Mostert was an employee of the consulting group, Dr. Knoell Consult GmbH, involved in the preparation of the recent glyphosate Annex I Renewal dossier for the Glyphosate Task Force (GTF; a consortium of European glyphosate registrants http://www.glyphosatetaskforce. org/). Helmut Greim was funded as an independent consultant for his expert contributions to this manuscript. David Saltmiras and Christian Strupp are employed by member companies of the GTF, Monsanto and ADAMA Agriculture B.V. (formerly Feinchemie Schwebda GmbH) respectively. David Saltmiras is also Chair of the Toxicology Technical Working Group of the GTF. Christian Strupp is an expert member of the Toxicology Technical Working Group of the GTF. Monsanto Company was the original producer and marketer of glyphosate formulations. The authors had sole responsibility for the writing and content of the paper and the interpretations and opinions expressed in the paper are those of the authors and may not necessarily be those of the member companies of the Glyphosate Task Force.

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Data Supplementary Study 1–14.

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Supplementary material for Greim H, et al. (2015). Evaluation of carcinogenic potential of the herbicide glyphosate, drawing on tumor incidence data from fourteen chronic/carcinogenicity rodent studies. Critical Reviews in Toxicology, 45: 185–208.

# BIO/DYNAMICS PROJECT NUMBER M-6, 77-2062

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NEOPLASM SUMMARY INCIDENCE TABLES

MALES

CONTAINS TRACE SETTED OF CIDERIN E CONCENTRE NOCEMATION OF MUNSANTO COMPANY

Defendant's Exhibit 2570\_0026

SUMMARY INCIDENCE TABLE NEOPLASM

Ę<sup>r nj</sup>

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice Male Rats

Male Rat	Male Rats		Group I		9	Group II		9	Group III	I	G	Group IV	
		Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
LId	PITUITARY (NO. EXAMINED)	(15)	(33)	(48)	(26)	(23)	(49)	(16)	(32)	(48)	(25)	(22)	(47)
4	Adenoma	8	8	16	14	പ	19	7	13	20	10	ω	18
	Carcinoma*		3	3		2	2	1	~	с			
BRA	BRAIN (NO. EXAMINED)	(15)	(34)	(49)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
<sup>O</sup>	G1 ioma		1	1	2	1	3				1		1
HEA	HEART (NO. EXAMINED)	(15)	(34)	(49)	(25)	(24)	(49)	(16)	(34)	(20)	(26)	(24)	(20)
	Reticulum Cell Sarcoma*								1	1			
LUN	LUNG (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
2	Metastatic Undifferentiated												
	Sarcoma*										1		1
æ	Reticulum Cell Sarcoma*		1	1		1	1		1	1		1	1
2	Malignant Lymphoma*			F-1									
2	Metastatic Osteogenic Sarcoma*												1
2	Metastatic Malignant Mixed Tumor*					1							
	*Malignant Neoplasm					V LINU 1	INS TRV	I ONTAINS TRADE SECRET OF	RET OF				
EPL				<b>'</b> ,	1-55		WILLE C	CONFIGERATION OF MONSANTO	ISANTO				
	Experimental Pathology Laboratories, Inc						NE	5					

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SUMMARY INCIDENCE TABLE Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of

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Rats	
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Male Rats		Group I		5	Group II		9	Group III		6	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	T otal	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
LIVER (NO. EXAMINED)	(15)	(32)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
Reticulum Cell Sarcoma*		1	1		1	<b></b>		2	2			1
Malignant Lymphoma*		1	1						1			
Metastatic Undifferentiated												
Sarcoma*			1									
Neoplastic Nodule	2	1	3	2	1	e		1	-1	2	4	ε
Hepatocellular Carcinoma*							1		-1	2		2
MESENTERIC LYMPH NODE (NO. EXAMINED)	(15)	(33)	(48)	(25)	(23)	(48)	(16)	(27)	(43)	(26)	(23)	(49)
Angioma	1		1		-1	1					1	
Malignant Lymphoma*		1		1								
Reticulum Cell Sarcoma*		1	1								1	1
PANCREAS (NO. EXAMINED)	(15)	(32)	(20)	(26)	(23)	(49)	(16)	(34)	(20)	(26)	(24)	(20)
Islet Cell Adenoma				4	1	5		2	2	1	1	2
Islet Cell Carcinoma*										1		1
Acinar Cell Adenoma										1		r-4
Malignant Lymphoma*		1	<b></b>									
Reticulum Cell Sarcoma* .		1	1					2	2			
*Malignant Neoplasm				T E E	(				po			

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SUMMARY INCIDENCE TABLE NEOPLASM

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice Wale Bars

Male Rats		Group I		Ü	Group II		9	Group III	I	9	Group IV	
	Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrífice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
MANDIBULAR SALIVARY GLAND												Τ
(NO. EXAMINED)	(15)	(34)	(49)	(26)	(23)	(49)	(16)	(33)	(49)	(26)	(23)	(4)
Reticulum Cell Sarcoma*									1			
MEDIASTINAL LYMPH NODE (NO. EXAMINED)	(11)	(28)	(39)	(25)	(14)	(39)	(10)	(22)	(32)	(21)	(14)	(35)
Metastatic Fibrosarcoma*								1	1			
Reticulum Cell Sarcoma*		1	-1					1	1			
SPLEEN (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
Angiosarcoma*		1	1									•
Malignant Lymphoma*		1	-1					1	-1			
Reticulum Cell Sarcoma*								2	2		1	-
STOMACH (NO. EXAMINED)	(15)	(35)	(20)	(26)	(23)	(49)	(15)	(33)	(48)	(25)	(24)	(49)
Squamous Cell Carcinoma, Cardia*										, I		
								}				
JEJUNUM (NO. EXAMINED)	(14)	(32)	(49)	(25)	(21)	(46)	(14)	(34)	(48)	(25)	(24)	(49)
Reticulum Cell Sarcoma*								1			•	
*Malignant Neoplasm												

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NEOPLASM	SUMMARY INCIDENCE TABLE	
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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical) Terminal Sacrifice

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Male Rats		Group I		9	Group II		9	Group III	I	Ġ	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
KIDNEY (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
Tubular Adenoma			-									
Malignant Lymphoma*			-1									
Reticulum Cell Sarcoma*			-4			-4			1			
Lipoma		1	1		<del>ب</del>	-	<b></b> 4					
TESTIS (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
Interstitial Cell Tumor				2	1	S	1		1	4	2	6
PROSTATE (NO. EXAMINED)	(15)	(35)	(20)	(25)	(22)	(47)	(16)	(33)	(49)	(25)	(24)	(49)
Reticulum Cell Sarcoma*												
URINARY BLADDER (NO. EXAMINED)	(15)	(31)	(46)	(23)	(22)	(45)	(14)	(29)	(43)	(23)	(23)	(46)
Papilloma				1		1						
THYROID (NO. EXAMINED)	(15)	(32)	(47)	(26)	(23)	(49)	(16)	(33)	(49)	(26)	(23)	(49)
C-Cell Adenoma	4	1	5	1		1				2		2
C-Cell Carcinoma*							1		1			
Follicular Adenoma	1		1	1	1	2	1	3	4	з	1	4
*Malignant Neoplasm				C L	VINOU	11 S TR	CONTAINS TRADE SECRED OR	REI OR				

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NEOPLASM SUMMARY INCIDENCE TABLE

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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice Male Rats

Male Rats		Group I		9	Group II		9	Group III	1	G	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Mortbund Sacrifice & Deaths	Total
PARATHYROID (NO. EXAMINED)	(11)	(16)	(27)	(15)	(15)	(30)	(2)	(23)	(28)	(13)	(14)	(27)
Adenoma					2	2						
								`				1
ADRENAL (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(34)	(20)	(26)	(24)	(20)
Reticulum Cell Sarcoma*								1	1			
Pheochromocy toma	2	6	8	4	4	8	3	2	5	5	6	11
Cortical Adenoma		2	2	4		4	1		1	1		1
Malignant Lymphoma*		1	1									
SKIN (NO. EXAMINED)	(15)	(34)	(49)	(25)	(23)	(48)	(16)	(33)	(49)	(26)	(23)	(49)
Basosquamous Cell Tumor										1		
Sebaceous Gland Adenoma												1
SKELETAL MUSCLE (NO. EXAMINED)	(15)	(35)	(20)	(26)	(24)	(20)	(16)	(33)	(49)	(25)	(24)	(49)
Reticulum Cell Sarcoma*		1	1									
HARDERIAN GLAND (NO. EXAMINED)	(15)	(32)	(47)	(25)	(24)	(49)	(16)	(33)	(49)	(26)	(24)	(20)
Malignant Lymphoma*		1	1									

\*Malignant Neoplasm

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NEOPLASM SUMMARY INCIDENCE TABLE

> Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice

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Terminal Sacrilice Male Rats		Group I		9	Group II		Ċ	Group III		Ĝ	Group IV	
	Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
BONE MARROW (RIB) (NO. EXAMINED)	(13)	(28)	(41)	(22)	(19)	(41)	(16)	(33)	(49)	(23)	(20)	(43)
Malignant Lymphoma*		1	1					1	1			
Reticulum Cell Sarcoma*					1	1		2	2			
LIP (NO. EXAMINED)	(1)		(1)									
Papilloma	1		1									
HIND FOOT (NO. EXAMINED)	(3)	(1)	(4)	(3)		(3)	(2)	(1)	(3)	(1)		(1)
Os teoma										1		
EAR (NO. EXAMINED)	(1)	(3)	(4)				(1)		(1)			
Fibroma		-	1									
Fibrosarcoma*							Ч		1			
Os teochondroma			1									
TAIL (NO. EXAMINED)	(1)		(1)	(9)	(1)	(1)	(3)	(3)	(9)	(2)	(3)	(2)
Papilloma									1			
Osteoma									1			
*Malignant Neoplasm					CMTA	INS TRA	ADE SEI	CCNTAINS TRADE SECRET OR				

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SUMMARY INCIDENCE TABLE NEOPLASM

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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical) Terminal Sacrifice

Male	Male Rats		Group I		Gı	Group II		6	Group III		Gı	Group IV	
		Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrífice	Moribund Sacrifice & Deaths	Total
ΒE	PERIOCULAR TISSUE (NO. EXAMINED)								(1)	(1)			
	Squamous Cell Carcinoma*								1	-1			
SU	SUBCUTANEOUS TISSUE (NO. EXAMINED)	(4)	(9)	(10)	(6)	(3)	(12)	(9)	(4)	(10)	(3)	(4)	(1)
	Fibrosarcoma*	1	1	2			1	7		2	1	2	ო
	Fibroma				3		3	1		1	1	1	2
	Neurofibrosarcoma*										1		1
	Undifferentiated Sarcoma*										1		1
	Reticulum Cell Sarcoma*		1	7					1	1		1	1
	Lipoma		1		1	1	2						
	Osteogenic Sarcoma*							1		1			
	Malignant Mixed Tumor*												
MEI	MEDIASTINAL TISSUE (NO. EXAMINED)		(1)	(2)		(1)	(1)		(4)	(4)		(2)	(2)
	Reticulum Cell Sarcoma*												1
	Malignant Lymphoma*		-1	-1									
	Metastatic Osteogenic Sarcoma*		1	1									
													r-90)
	*Malignant Neoplasm								0 1203	ų			ľ
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NEOPLASM SUMMARY INCIDENCE TABLE	
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Bio/dynamics Project Number M-6, ' A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice Male Rats

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Male Rats		Group I		G	Group II		9	Group III	I	Gı	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
ABDOMEN (NO. EXAMINED)											(1)	(1)
Lipoma											1	
MESENTERY (NO. EXAMINED)		(5)	(2)	(3)	(1)	(4)		(4)	(4)	(2)	(1)	(3)
Malignant Lymphoma*		1	1									
Reticulum Cell Sarcoma*		1	1					1	-			
Scirrhous Adenocarcinoma*					1	1						
ABDOMINAL CAVITY (NO. EXAMINED)								(1)	(1)			
Reticulum Cell Sarcoma*								1	<b>1</b> 1			
SUBCUTANEOUS LYMPH NODE												
(NO. EXAMINED)		(1)	(1)									
Malignant Lymphoma*		1	1									
BRONCHIAL LYMPH NODE (NO. EXAMINED)		(1)	(1)									
Malignant Lymphoma*		1,	1									
•												
*Malignant Neoplasm												

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SUMMARY INCIDENCE TABLE NEOPLASM

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical) Terminal Sacrifice Male Rats

Male Kats		Group I		9	Group II		9	Group III	I	G	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrìfice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
MANDIBULAR LYMPH NODE (NO. EXAMINED)		(3)	(3)				(1)		(1)		(1)	(1)
Malignant Lymphoma*			1									
LUMBAR LYMPH NODE (NO. EXAMINED)										(1)		(1)
Metastatic Islet Cell Carcinoma*												1
SACRAL LYMPH NODE (NO. EXAMINED)		(1)	(1)	(2)	(1)	(3)	(2)	(1)	(3)	(1)	(2)	(3)
Reticulum Cell Sarcoma*					<del>,</del> 1	1						
										-		
*Malignant Neoplasm		1 										
EPL	5 1 6	٤	i. Ii	I-63	U	ONTAIN: 1. FKWI	S THALK	CONTAINS TRADE SECRET CAR	1 (.42 21			
Experimental Pathology Laboratories, Inc						4FURMA		INFORMATION OF MONSANDO	NIC			
					ر	COMPANY	~					

BIO/DYNAMICS PROJECT NUMBER M-6, 77-2062 NEOPLASM SUMMARY INCIDENCE TABLES FEMALES

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	NEOPLASM	SUMMARY INCIDENCE TABLE
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Bio/dynamics Froject Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice Female Rats

Female Rats		Group I		9	Group II		9	Group III	I	Gı	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total									
PITUITARY (NO. EXAMINED)	(17)	(31)	(48)	(22)	(26)	(48)	(30)	(20)	(20)	(15)	(34)	(49)
Adenoma	13	21	34	15	14	29	20	11	31	6	17	26
Carcinoma*	2	9	ω	2	5	7	_	5	5	4	ω	12
BRAIN (NO. EXAMINED)	(18)	(32)	(20)	(23)	(26)	(49)	(30)	(20)	(20)	(12)	(35)	(20)
Invasive Pituitary Carcinoma*								1	1	I		-
Malignant Lymphoma*											-1	1
G1 ioma											1	-1
CERVICAL SPINAL CORD (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(35)	(20)
Malignant Lymphoma*									-		-1	1
HEART (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(32)	(20)
Malignant Lymphoma*											1	1
Metastatic Fibrosarcoma*			-1									
TRACHEA (NO. EXAMINED)	(18)	(31)	(49)	(23)	(26)	(49)	(30)	(19)	(49)	(15)	(35)	(20)
Metastatic Fibrosarcoma*			1									

\*Malignant Neoplasm

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NEOPLASM	SUMMARY INCIDENCE TABLE
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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical)

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	Sacrifice
1	Terminal

Female Rats		Group I		9	Group II		9	Group III	I	9	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
ESOPHAGUS (NO. EXAMINED)	(18)	(30)	(48)	(21)	(26)	(47)	(30)	(19)	(49)	(15)	(32)	(20)
Metastatic Fibrosarcoma*			1				1					
LUNG (NO. EXAMINED)	(18)	(31)	(49)	(23)	(27)	(20)	(30)	(19)	(49)	(15)	(35)	(20)
Reticulum Cell Sarcoma*	1	1	2		2	2			1		ю	с
Malignant Lymphoma*					1						1	<b>t</b> 1
Metastatic Mammary Gland												
Adenocarcinoma*												
Metastatic Adrenal Cortical												
Carcinoma*								<b>6-4</b>	1			
Metastatic Fibrosarcoma*		1	1									
LIVER (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(35)	(20)
Reticulum Cell Sarcoma*		1	2		2	2			-1		2	2
Malignant Lymphoma*									7			2
Metastatic Fibrosarcoma*		1										
Hepatocellular Carcinoma*		1	1							2		2
Neoplastic Nodule	9	5	11	æ	4	7	5	1	9	2	5	7
*Malignant Neoplasm												
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TABLE

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice

Female Rats		Group I		9	Group II		9	Group III	I	Gı	Group IV	-
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total									
MESENTERIC LYMPH NODE (NO. EXAMINED)	(18)	(24)	(42)	(23)	(16)	(39)	(59)	(19)	(48)	(14)	(33)	(47)
Malignant Lymphoma*											-1	
Reticulum Cell Sarcoma*											2	2
				-								
PANCREAS (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(34)	(49)
Islet Cell Adenoma	1	<b>7-1</b>	2		1	1	1		1			
Islet Cell Carcinoma*						1	1		1		1	1
MANDIBULAR SALIVARY GLAND												
(NO. EXAMINED)	(18)	(30)	(48)	(23)	(27)	(20)	(30)	(19)	(49)	(15)	(34)	(49)
Metastatic Fibrosarcoma*							1		1			
THYMUS (NO. EXAMINED)	(6)	(16)	(25)	(19)	(13)	(32)	(26)	(11)	(37)	(15)	(19)	(34)
Malignant Lymphoma*									-			1
Thymoma									-			
*Malignant Neoplasm						T SMA	אניע געינ	CONTAINS TRADE SECRET OR	~			

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NEOPLASM SUMMARY INCIDENCE TABLE
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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical) Terminal Sacrifice

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i i.

Female Rats		Group I		9	Group II		9	Group III	I	G	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Mortbund Sacrifice & Deaths	Total
MEDIASTINAL LYMPH NODE (NO. EXAMINED)	(14)	(19)	(33)	(13)	(16)	(29)	(24)	(13)	(37)	(10)	(20)	(30)
Metastatic Fibrosarcoma*		1	1									
Reticulum Cell Sarcoma*					1	1					2	2
Malignant Lymphoma*							<del>،</del>		1	<del>ب</del>	1	2
SPLEEN (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(35)	(20)
Malignant Lymphoma*								1	1	1	1	2
Reticulum Cell Sarcoma*	7	<b></b>	2		2	2					5	പ
STOMACH (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(15)	(32)	( 20 )
Malignant Lymphoma*											1	1
Reticulum Cell Sarcoma*	1		1									
Metastatic Fibrosarcoma*	-	1	1									
JEJUNUM (NO. EXAMINED)	(18)	(32)	(20)	(23)	(25)	(48)	(29)	(20)	(49)	(15)	(34)	(49)
Leiomyosarcoma*				1		1						
ILEUM (NO. EXAMINED)	(16)	(31)	(47)	(22)	(27)	(49)	(29)	(20)	(49)	(14)	(34)	(48)
Reticulum Cell Sarcoma* .											1	1
*Malignant Neoplasm				; ,		2141 × 714 × 4	AND TER RECRET	18 198	AC 7			

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CONTAINS TRADE SECRET OR GTHERVILE CONTROLLING REORMANON OF MOREANIO COMPANY

SUMMARY INCIDENCE TABLE NEOPLASM

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical)

1		
	Terminal Sacrifice	Female Rats

Female Rats		Group I		G	Group II		9	Group III	I	9	Group IV	
	Scheduled Sacrifice	Morlbund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrífice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
COLON (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(19)	(49)	(14)	(34)	(48)
Reticulum Cell Sarcoma*											1	1
									-			
KIDNEY (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(12)	(32)	(20)
Malignant Lymphoma*											F.	
Reticulum Cell Sarcoma*						1					2	2
Transitional Cell Carcinoma*							1		1			
URINARY BLADDER (NO. EXAMINED)	(18)	(32)	(20)	(23)	(25)	(48)	(28)	(20)	(48)	(14)	(30)	(44)
Transitional Cell Carcinoma*											<b></b> 1	
OVARY (NO. EXAMINED)	(18)	(31)	(49)	(23)	(27)	(20)	(30)	(18)	(48)	(13)	(32)	(45)
Granulosa Cell Tumor	ю	5	ω	4	4	ω	ى ک		6	2	4	6
Theca-Granulosa Cell Tumor										. 1	,,	
*Malignant Neoplasm EPL	I	، ابو		I-68	C C	ONTAIN 11 L. V.	IS TRACH	CONTAINS TRADE SECRET OR				÷

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Experimental Pathology Laboratories, Inc.

NEOPLASM SUMMARY INCIDENCE TABLE

> Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical)

1

	Sacrifice
くつかいつけんですが	Terminal

Female Rats		Group I		9	Group II		G	Group III	I	6	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total									
UTERUS (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(29)	(20)	(49)	(15)	(34)	(49)
Squamous Cell Carcinoma*											1	
Endometrial Sarcoma*												ç
Adenoma							2		2		1	]
Polyp	4	1	5	1	1	2	3	2	5	2	I	ε
Reticulum Cell Sarcoma*	1		1		1	1						
THYROID (NO. EXAMINED)	(18)	(29)	(47)	(23)	(26)	(49)	(30)	(20)	(20)	(14)	(33)	(47)
C-Cell Adenoma	2	3	5	2	-1	3	4	2	9	,,	2	ю
C-Cell Carcinoma*	1		-1				Τ	1	2	2	4	6
Follicular Adenoma		3	3	1	1	2	1		1			
Metastatic Fibrosarcoma*							1		1			

\*Malignant Neoplasm

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(23)

(18)

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(25)

(12)

(13)

(25)

(13)

(12)

(23)

(11)

(12)

PARATHYROID (NO. EXAMINED)

Adenoma

SUMMARY INCIDENCE TABLE NEOPLASM

Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUP® Technical) Terminal Sacrifice

Female Rats

	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Totał	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Totaf	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
ADRENAL (NO. EXAMINED)	(18)	(32)	(20)	(23)	(27)	(20)	(30)	(20)	(20)	(12)	(34)	(49)
Reticulum Cell Sarcoma*		1	۳٦		<b></b> 4	<b>,</b> ,		1			ю	3
Pheochromocy toma			1	1	1	2	2		2	1	1	2
Cortical Adenoma	3	2	5	4	9	10	9		6		4	4
Cortical Carcinoma*		1	1						1	1		1
Malignant Lymphoma*									-	1		1
									-			
MAMMARY GLAND (NO. EXAMINED)	(17)	(30)	(47)	(22)	(24)	(46)	(28)	(20)	(48)	(15)	(29)	(44)
Adenoma <sup>a</sup>	2/2	2/2	4/4	4/4	3/3	7/7	7/5	3/3	10/8	3/3	2/2	5/5
Fibroadenoma <sup>a</sup>	9/6	24/18	33/24	13/9	15/7	28/16	15/11	12/9	27/20	6/4	16/12	22/16
Adenocarcinoma <sup>a</sup> *	4/4	7/6	11/10	3/1	5/5	8/6	3/3	3/2	6/5	3/2	6/6	9/8
Reticulum Cell Sarcoma*			1									
EYE (NO. EXAMINED)	(18)	(31)	(49)	(21)	(27)	(48)	(30)	(20)	(20)	(15)	(32)	(47)
Periocular Fibrosarcoma*							Г		1			
HARDERIAN GLAND (NO. EXAMINED)	(17)	(30)	(47)	(20)	(25)	(45)	(28)	(19)	(47)	(15)	(29)	(44)
Malignant Lymphoma*											1	1
Invasive Fibrosarcoma*							1		1			
*Malignant Neoplasm Ept <sup>a</sup> Number of Animals with Lesion	nals with	1 Lesion	-	. 0 <b>/-</b> I	I-70 CTT NEE TRAFF. DECRET OR	1.]⊽.41 ÷	CEURE	( or	-			

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NEOPLASM SUMMARY INCIDENCE TABLE	
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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice

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Female Rats		Group I		-	Group II		9	Group III		0	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
BONE MARROW (RIB) (NO. EXAMINED)	(18)	(28)	(46)	(21)	(23)	(44)	(28)	(18)	(46)	(14)	(31)	(45)
Malignant Lymphoma*								-1	1		1	-1
Reticulum Cell Sarcoma*		1	1						1		ε	с
EAR (NO. EXAMINED)		(2)	(2)								(1)	(1)
Chondroma		1	1									
Os teochondroma		1	1									
SUBCUTANEOUS TISSUE (NO. EXAMINED)	(2)	(2)	(4)	(3)	(3)	(9)	(1)		(1)	(1)	(1)	(2)
Lipoma												2
Fibrosarcoma*					-1	-1						8
Reticulum Cell Sarcoma*					2	2						
Fibroma				1		П						
MEDIASTINAL TISSUE (NO. EXAMINED)		(2)	(2)		(1)	(1)	(1)	(1)	(2)		(2)	(2)
Fibrosarcoma*		1										
Reticulum Cell Sarcoma*					1							
*Malignant Neoplasm	CONTAINS TRADE SECRET OR 1-71	TRADE	SFC RF1	GR 1-7								
		-	<b>T</b> 's !	1								

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NEOPLASM SUMMARY INCIDENCE TABLE

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Bio/dynamics Project Number M-6, 77-2062 A Lifetime Feeding Study of Glyphosate (ROUNDUF® Technical) Terminal Sacrifice

Female Rats		Group I		9	Group II		9	Group III		9	Group IV	
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
MESENTERY (NO. EXAMINED)	(1)	(4)	(2)	(4)	(1)	(2)	(1)	(1)	(2)	(1)	(9)	(2)
Reticulum Cell Sarcoma*											2	2
Metastatic Adrenal Cortical												
Carcinoma*		1	1									
SKULL (NO. EXAMINED)									-		(1)	(1)
Fibroma												-
		i										
URETER (NO. EXAMINED)							(1)		(1)		(1)	(1)
Transitional Cell Carcinoma*							-1		1			
MANDIBULAR LYMPH NODE (NO. EXAMINED)	(2)		(2)	(1)	(2)	(3)	(9)		(9)	(3)	(3)	(9)
Malignant Lymphoma*												-
*Malignant Neoplasm						ť.	1. T.A.IN L.S.	12 A. 1261	L REY	E		
EPL				I-72		(		Toto in the second seco	101111	ţ		
Experimental Pathology Laboratories, Inc						1	ILLE URN TH	HUERANT IN OF MURICANIO COMPANY	UNDAN	5		

Defendant's Exhibit 2570\_0045

NO: 87122	P+++ MONSANTO ENVIRONMENTAL HEALTH P A T H O L O G Y S E C T I		LAB	PAGE: 1
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: QLY	HOSATE			PRINTED: 13-JUL-90
ection criteria: Scheduled gagaifices	DENCE OF HISTOP	HOLOGIC	T-AUG-1	*** 89:15*AUG-1989
	ANIMAL SEX : N U DOSAGE GROUP: MN MI NO. IN GROUP: 14 19	3	BER0 MALES M2 M3 17 17	OTANIKALS ATTECTED
ADREMAL (S) -88 - CORTICAL ADENOMA -88 - PHEOCHNOMOCYTOMA -84 - PHEOCHNOMOCYTOMA	689			
BRAIN				
BONE	ï	:	(16)	
SP.CORD,CERVICAL -AM - GLIONA	•	1	e e	
CECUM				
DUODENUM				
EYE(S) - <b>A</b> M - Neurofibrosarcoma (Schwannowa)	•	•	ч. •	
KIDNEY(S) -#B - LIPOMA -#M - LIPOSARCOMA -#B - TUBULAR ADENOMA	~ 9 9	0 Q -1	000 0-0	
LIVER -88 - Hepatocellular Adenoma -84 - Hepatocellular Carcinoma	~~~		<b>* 8</b>	
LUNG				
MAMMARY GLAND -#8 - Adenoma/Adenofibroma/Fibroma -#M - Carcinoma/Adenocarcinoma		(13) (13) (13)		
LY.NODE,MESENT. -4B - HEMANGIONA	•	(18) (18)		CONTAINS RA
MESENTERY/OW'TUM	(8)	) (1 )	2) (2)	CONFICTION CONFICTION
NOSE/TURBINATES			(16)	OF MONSANTO CCARPANT

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STUDY ND: 87122 HONSA	••••• MONSANTO ENVIRONMENTAL HEALTH LAB ••••• P a t h n i n g y s f t t n n	TAL HEA		AB +++++	PAGE: 2
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYP	GLYPHOSATE	ר ע ס	-	E	PRINTED: 13-JUL-00
TION CRITERIA: SCHEDULED SACRIFICES		OPATHOL	DQIC	NEOPLASMS +++ 7-AUG-1989:10-AUG-1989	
	ANTMAL SEX : Dosage group : No. In group :		334	3 E R O F A N I M A L E S	ALS AFFECTED
NOSE/TURBINATES - <b>8</b> - Papillary Adenoma		•	•	(16) 1	
PANCREAS ' -#B - ISLET CELL ADENOMA -#M - ISLET CELL CARCINOMA		<b>0</b>	~ <b>2</b>	~ •	
PAWS/FEET	J	5) (9)	<b>6) (</b> 2)	(8) (	
PITUITARY - <b>4</b> 8 - Adenoma, Pars distalis	·	13 15	<b>1</b>	16	
PROSTATE				į	
PARATHYROID(S)				(01)	
SKIN -#8 - KERATOACANTHOMA -#M - SQUAMOUS CELL CARCINOMA -#8 - SQUAMOUS PAPILLOMA -#8 - SQUAMOUS PAPILLOMA -#8 - SEBACEDUS QLAND ADENOMA			<b>8000</b> 0 N <b>DQ</b> N	****	
SPLEEN					
SP.CORD,THORACIC	•				
TESTIS(ES) - <b>Åb - Inters</b> titial cell tumor		-		8	
THYROID(S) -48 - C CELL ADENOWA -48 - Follicular Adenowa/Cystadenowa -44 - Follicular Adenowa/Cystadenowa			0 7 7 0	• •	Help y ha
THYMUS -AM - LYMPHOMA / LYMPHOSARCOMA Urinary Bladder	-	(8) (15) 8 8		(1) (1)	NUL COMPANY

PAGE 231 EHL 87122

ATA: SCHEMLED BACARTACIOS: SUMMAY INCIDENCE OF HISTORTHAUGGET WERLASSS S WITH FINDINGS WARE GENER:	STUDY NO: 07122 Study type: Ch Species: Rat	•••••       MONSANTO ENVIRONMENTAL HEALTH LAB       •••••         P       T       H       L       0       G       Y       S       E       C       I       0       N       PR         SUBSTANCE:       GLYPHOSATE       PR	PAGE: 13-J
TTH FINDINGS MINLER	SELECTION CRITERIA: SCHEDULED SAK	••• SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS •••         ••• SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ••• <th></th>	
	TISSUES WITH FI	L L L L L L L L L L L L L L L L L L L	E D
	SUBCUTIS SUBCUTIS -#B - FIBROSARCOMA -#B - LIPOWA	5 <b>6</b> 1) (	-
<text></text>	ORAL CAVITY	<b>(</b>	
		CONTAINIS TRALIF CKEI OR OTHERWYILL CONFICENTIAL INFORMATION OF MONSANIO COMPANY	
			•

PRINTED: 13-JU		I CES PERIODS: ANIMAL SEX : NO. IN GROUP: NO. IN GROUP:	STUDY TYPE: CH SPECIES: RAT SUBS SELECTION CRITERIA: SCHEDULED AACRIFICES SELECTION CRITERIA: SCHEDULED AACRIFICES TI S S U E S W I T H F I N D I N G T I S S U E S W I T H F I N D I N G ADRENAL (S) ADRENAL (ANDENOMA EYE (S) ADRENAL CECUM CCCUM ADD - CONCLULAR ADENOMA - CONCLULAR ADENOMA - CONCLULAR ADENOMA - CONCHOALVEOLAR ADENOMA - CONCHOALVEOLAR ADENOMA - CONCHOALVEOLAR ADENOMA - CONCHOALVEOLAR ADENOMA
CONTAINS READE ALCOLO OR OTHERVAL	-		MANMARY GLAND -46 - Adenoma/Adenofibroma/Fibroma -4m - Carcinoma/Adenocarcinoma 
CONTAINS PRACE	16 16		
	•		
			- HEPATOCELLULAR - CHOLANGIONA
			HEPATOCELLULAR
	-		KIDNEY(S) - <b>86 -</b> L <b>IPONA</b>
			EYE (S)
			DUODENUM
			CECUM
			SP. CORD, CERVICAL
			BONE
			nt na
-			ADREVAL (S) -#B - CORTICAL ADENOMA -#B - PHEOCHROMOCYTOMA -#M - PHEOCHROMOCYTOMA -#M - CORTICAL CARCINOMA
IMALS AFFECTED	U M B E R O F A 1 F2 F3 2 17 18	ANIMAL SEX : ANIMAL SEX : DOSAGE GROUP : MO. IN GROUP :	I SSUES WITH F
	T-AUG-1989:10	ICES PERIODS:	TION CRITERIA: SCHEDULED
PRINTED: 13-JU		*** SUMMARY INCIDENCE OF HIST	TYPE: CH SPECIES:

	POOP MONSANTO ENVIRONMENTAL P A T H O L O G Y S I	NTAL H	LHEALTH		••••• PAGE: 6
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLY	GL YPHOSATE		- )		PRINTED: 13-JUL-90
RIA: SCHEDULED GACRIFICES	INMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS Periods: 7-AUG-106	TOPATH	OLOGIC	NEOPL	EOPLASMS +++ 7-AUG-1989:18-AUG-1989
TISSUES WITH FINDINGS D	ANIMAL SEX : DOSAGE GROUP: NO. IN GROUP:	L LN LN	N U M F F E M 22 J F	B E R B A L E F2 F3 17 18	OF ANIMALS AFFECTED
NOSE/TUNBINATES					
OVARY(IES) - <b>48 - Granulosa</b> Cell Tu <b>ndr</b>		•	F	6 (17) 6 (17)	
PANCREAS ►∦0 - ISLET CELL ADENOMA		8	-	-	
PAWS/FEET		( 2) (	2) (	2) (7	2)
PITUITARY - <b>4</b> 8 - Ademona, Pars distalis		19	19 1	16 11	1
PARATHYROID (S) - #B - ADENOMA		•	1	-	
SKIN -#M - Squamous Cell Carcinoma -#B - Clitoral Gland Adendma	_	<b>Q</b> =			
SPLEEN					
SP. CORD, THORACIC		;	•		
THYROID(S) -AB - C CELL ADENOUA -AB - FOLLICULAR ADENOMA/CYSTADENOMA -AM - FOLLICULAR CELL CARCINOMA		<b>0</b> 1→●	~~		
THVAUS -EM - LYMPHOMA / LYMPHOSARCOMA		(1 2 2 2 2	) (10) 3		
URINARY BLADDER		•	(21) (1 <b>9</b>	(16) (17) 1 9	
UTERUS UTERUS -#8 - POLYP -#8 - ADENOMA, ENDOMETRIAL -#8 - LEIOMYOUA					CONTAINS TRA OR OTHERVIE CONFICENTIAL INFORMANTICAL

STUDY NO: 87122	••••• MONSANTO ENVIRONMENTAL HEALTH LAB •••••	PAGE: 6
: CH S	FATHUCE: OLYPHOSATE	PRINTED: 13-JUL-96
SELECTION CRITERIA: SCHEDULED SACR	*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS *** *** PERIODS: : :	)   
	INDINGS DOSAGE GROUP: 22 22 17 18	F E C T E D
UTERUS	(17)	
VAGINA - <b>46 - Fibrowa</b>	( Ø) ( Ø) ( 3) 1	
- SUBCUTIS -4M - FIBROUS HISTIOCYTOMA -48 - FIBROWA -49 - LIPOMA		
NOTE: A NUMBER IN PARENTHESES OPPOSITE A T WHEN LESS THAN THE NUMBER OF ANIMALS	DSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED	
<ul> <li>SIGNIFICANTLY DIFFERENT [P LESS THAN WITH THE BOWEERRONI INEQUALITY.</li> <li>SIGNIFICANTLY DIFFERENT [P LESS THAN WITH THE BOWEERRONI INEQUALITY.</li> </ul>	SS THAN OR EQUAL TO <b>G.05] FROM</b> CONTROL USING FISHER'S EXACT TEST Ty Ess than or equal to, <b>g.01] From</b> control using fisher's exact test Ty.	
	OR OTHERWISE CONFIDENTIAL INFORMATION	
	OF MONSANTO COMPANY	

Appendix 1

	ANTO ENVIRONMENTAL HEA	LTH LAE	3 ***** PAGE: 1
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLY	TANCE: GLYPHOSATE	-	PRINTED: 13-JUL-98
<pre>election criteria: UNSCHEDULED DEATHS</pre>	· ا	OGIC N	
ようしょうからしいししようるような道仏を自然が没たるとなるときまたできますのであるであるできる。		2	
TISSUES WITH FINDINGS	ANIMAL SEX :	A U U M W M W	1 333 F
ENAL (S)	(53)		
-#B - CORTICAL ADENDWA -#B - PHEDCHROWDCYTOMA	<b>6</b> 10 1	- 01	- 10 1
-#W - PHEOCHROMOCYTOMA -#W - Ganglioneurona/Pheochromocytoma		- 0	5 6
BRAIN -#M - Astrocytoma	6	1	1
BONE - BM - OSTEOSARCOMA	(36) 8 8	ہ آء	1
011	88	6 (32) 1 6	(32) 8 8
CECUN	(31) (21)	(29)	(26)
PERITONEAL CAV. -#W - MALIGNANT FIBROUS HISTIOCYTOWA	(@) (@)	(e) (e	( 1) 1
	(34) (26) 1 8	8) (32) 8	(32) 8
EYE (S)			
KIDNEY(S) -48 - LIPOMA -44 - LIPOSARCOMA -44 - Mesenchymal Tumor -48 - Tubular Adenoma	- <b>6 6 6</b>	8	0000
LIVER -#B - HEPATOCELLULAR ADENDWA -#W - HEPATOCELLULAR CARCINOMA -#W - HISTIOCYTIC SARCOMA -#W - NEOPLASW, UMDETERWINED ORIGIN	N N <b>B B</b>	0-0 <b>0</b>	DE MONS ANT COMBACT
TONO			

STUDY NO: 87122		ENTAL HE	ALTH L	AB	PAGE: 2
STUDY TYPE: CH SPECIES: RAT SUBSTANCE	SUBSTANCE: GLYPHOSATE		-	z	PRINTED: 13-JUL-90
SELECTION CRITERIA: UNSCHEDULED DEATHS	SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS	STOPATHO	LOGIC	NEOPLASMS +++	_
			!≊.		
TISSUES WITH FINDINGS	DOSAGE GROUP: NO. IN GROUP:	NN	M1 M2 31 33		
744		(24) 8 8	(14) (24) 8 8 8 8	4) (20) 8 1 8 1	
8		(33)	(3:	(32) (29)	
MESENTERY/OW'TUM -4M - MESOTHELIOMA		) କ୍ଷ )	2) (5) 1 Ø	5) (4) Ø 1	
		) (ø)	(0) (0)	() () () ()	
NOSE/TURBINATES		Ű	(38)		
PANCREAS -#B - Islet cell adenoma		(34) (5 1	(28)	(32) 2 4	
PAWS/FEET -BM - SARCOMA, UNDETERMINED CELL TYPE		) (9) )	२ २	1 (3)	
PITUITARY -#8 - Adenowa, Pars Distalis -#8 - Adenowa, Pars Intermedia		0.0	(29) (3 15 1 8	(31) (32) 19 19 6 1	
PROSTATE - AMENOCARCINOMA		1		6	
PARATHYROID(S) - <b>#</b> B - Ademoma		- -	(29) (3 1	(32) 6 2 (32)	
SKIN -#B - KERATOACANTHOWA -#W - SQUAMOUS CELL CARCINOMA -#W - CARCINOMA/ADENOCARCINOMA, ZYMBAL'S GLAND -#W - FIBROUS HISTIOCYTOMA -#W - FIBROUS HISTIOCYTOMA -#B - ADENOMA, ZYMBAL'S GLAND -#B - ADENOMA, ZYMBAL'S GLAND	9	のこうのののこ	~ \$ \$ \$ \$ \$ \$ \$ \$	,	OR DEFINITION OF AND
		Ŭ	(38)		CUMPAINIC CUMPANY

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	MUNSANIO ENVIRUNMENIAL HEALIH LABI 40000 P A T H O L O G Y S E C T I O N	PAGE: 3
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE	HOSATE	PRINTED: 13-JUL-90
LECTION CRITERIA: UNSCHEDULED DEATHS	IDENCE OF HISTOPATHOLOGIC NEOPLASMS +++	!   .   .
TISSUES WITH FINDINGS	ANIMAL SEX :NUWBEROFANIMALSAF Dosage Group: Man Man Les	FFECTED
SPLEEN .	(38)	
TAIL -#B- INTRACUTANEOUS CORNIFYING EPITHELIOMA	(1) (8) (8) (8) 1	
SP.CORD,THORACIC - Astrocytoma	8	
TESTIS(ES) -#B - INTERSTITIAL CELL TUMOR	1 6 2 0	
THYROID(S) -#B - C CELL ADENOMA -#M - C CELL CARCINOMA -#B- FOLLICULAR ADENOMA/CYSTADENOMA	(29) (31) (29) (31) (2 1 1 (3 2 6 1 (3 1 2 1 (3 1 2 1)	
THYMUS -#M - LYMPHOMA / LYMPHOSARCOMA	(22) (14) (17) (20) 1 8 8 8	
URINARY BLADDER	(36)	
SUBCUTIS -#W - FIBROUS HISTIOCYTOMA -#B - FIBROMA -#W - FIBROSARCOMA -#W - LIPOMA -#W - SQUAMOUS CELL CARCINOMA		
G I TRACT - BM - MUCINOUS ADENOCARCINOMA	( 1) ( 0) ( 0) ( 0) 1	
-#00TH -#0 = DDDNTOGENIC TUMOR -#8 = DDDNTOGENIC TUMOR		184
	(1) (1) (0) (0) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1	A CONFRACT COMPANY

STUDY ND: 87122 .	MONSANTO ENVIRONMEN	ATAL HE	EALTH	LAB	PAGE: 4	
STUDY TYPE: CH SPECIES: RAT SUBSTANCE.	PATHOLOGY SECTION SUBSTANCE: GLYPHOSATE	S Б	1 1 0	Z		_
ELECTION CRITERÍA: UNSCHEDULED DEATH	●●● SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS	TOPATHO	DLDGIC	NEOPLASMS ***		!
TISSUES WITH FINDINGS	ANIMAL SEX : DOSAGE GROUP: ND. IN GROUP:		N U M B F E M / 28 33	LERDFANI LESTANI 53 32	MALS AFFECTED	!!!
ADRENAL(S) -#B - CORTICAL ADENOMA -#B - PHEDCHROMOCYTOMA		00	6	96		
BRAIN -fb - Granular Cell Tumor		•		6		
BONE						
SP. CORD, CERVICAL	-			(11)		
CECUM -#W - NEUROFIBROSARCOMA		(23) (: Ø	(24) (32) Ø 1	2) (27) 1 Ø		
PERITONEAL CAV. - AM - NEURO-ENDOCRINE TUMOR, GASTRIN SECRETING		) (@ )	( Ø) ( 1) 1	1) (Ø) 1		
DUDDENUK		Ű	(21) (32)	2) (29)		
EYE (S)				(31)		
KIDNEY(S) -#M - Tubular Carcinoma -#B - Hemangioma		6-		00		
LIVER -#B - HEPATOCELLULAR ADENOMA -#M - HEPATOCELLULAR CARCINOMA -#W - HISTIOCYTIC SARCOMA -#W - HEMANGIOSARCOMA				~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
FUNG						Er
MAMMARY GLAND -#8 - Adenowa/Adenofibroma/Fibroma -#M - Carcinoma/Adenocarcinoma -#M - Carcinosarcoma			(24) (32) 9 11 6 6 6 (27) (32)	(30) 14 1 1	S IN OTHER	L 87122
LY.NODE,MESENT.		-			THE TO COVIDANY	

TISSUESWITHFINDINGS MESENTERY/ON'TUM NOSE/TURBINATES OVARY(TES) -#B - GRAMULOSA CELL TUMOR -#B - GRAMULOSA CELL TUMOR -#B - THECA CELL TUMOR -#A - TSI FI CELL ADENOMA	ANIMAL SEX : DOSAGE GROUP: NO. IN GROUP:	STUDY TYPE: CH SPECIES: RAT       SUBSTANCE: GLYPHOSATE         SELECTION CRITERIA: UNSCHEDULED DEATHS       SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS         SELECTION CRITERIA: UNSCHEDULED DEATHS       SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS         SELECTION CRITERIA: UNSCHEDULED DEATHS       SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS         T I S S U E S W I T H F I N D I N G S       ANIMAL SEX         MESENTERY/OW'TUM       N U M B E R O F         MOSE/TURBINATES       NO IN GROUP: 28 28 33 32         OVARY (IES)       OR OR OF         PANCRES       OR OF         PANCREAS       TSIET CELL TUMOR	PATH 0 L 0 G Y S E C T I 0 N TANCE: GLYPHOSATE SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEL SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEL SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEL SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEL SUMMARY INCIDENCOMARY INTO NEL SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEL	0 N NEOPLASW B E R 1 A L E S 2 F3 3 32 3 (31) 3 (31)	ASMS *** ASMS *** D F A N I M A L S A F F E C T E D 2 9) 1)
PITUITARY PITUITARY -#B - ADENOMA, PARS DISTALIS -#M - CARCINOMA, PARS DISTALIS -#M - CARCINOMA, PARS DISTALIS -#B - ADENOMA, ZYMBAL'S GLAND -#B - BASAL CELL TUMOR		(8) 22 88 (2, 2) (2, 2) (2, 2)	(1) (2 (2) (2) (2) (2) (2) (2) (2) (2) (2) (2)	0) (1) 26 (31) 0 1 1 0 1 (36) 1 330) 1 0 1 (330)	1. 1. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.
SPLEEN -M - LYWPHOMA / LYMPHOSARCOMA -M - LYWPHOMA / LYMPHOSARCOMA -M - HEMANGIOSARCOMA SP.CORD,THORACIC THYROID(S) -M - C CELL CARCINOMA -M - C CELL CARCINOMA -M - C CELL CARCINOMA -M - C CELL CARCINOMA -M - LYWPHOMA / LYMPHOSARCOMA URINARY BLADDER URINARY BLADDER		ng <b>ass 138</b>	(27) (; (27) (;	5 5 5 6 7 7 6 6 6 6 6 6 6 6 6 6 6 6 6 6	CONTAINS TRAFE SECURE OR OTHERVATE COMENTIAL INFORMATION OF MODIFICATION OF MODIFICATION

STUDY NO: 87122	*** MONSANTO ENVIRONMENTAL HEALTH LAB *****
Y TYPE: CH SPECIES: RAT SUBSTA	UL 0 G Y S E C I I D N ATE PRINTED: 13-JUL-90
ECTION CRITERIA: UNSCHEDULED DEATHS	MMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS +++
TISSUESWITH FINDINGS DOSAGE NO. IN	L SEX :
UTERUS -#8 - POLYP -#8 -VSCULAR HAMARTOMA -#M - STROMAL SARCOMA -#8 - FIBROMA	-056 -07 -07 -07 -07 -07 -07 -07 -07 -07 -07
VAGINA	(1) (0) (2) (0)
SUBCUTIS -#M - FIBROUS HISTIOCYTOMA -#B - FIBROMA -#M - FIBROSARCOMA	(3) (0) (2) (3) 6 2 1 1 0 2 6 0
ORAL CAVITY -#B - SQUAMOUS PAPILLOMA, PALATE -#B - CHONDROMA, ALVEOLUS -#M - GRANULAR CELL TUMOR	( 0) ( 1) ( 1) ( 1) 0 1 0 0 0 1 0 0 1 0
TOOTH	(8) (1) (8) (8)
NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME I WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROU	IN THE GROUP.
<ul> <li>E SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQUAL TO 0.06) FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.</li> <li>SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQUAL TO 0.01) FROM CONTROL USING FISHER'S EXACT TEST</li> <li>WITH THE BONFERRONI INEQUALITY.</li> </ul>	3.065] FROM CONTROL USING FISHER'S EXACT TEST 9.01] FROM CONTROL USING FISHER'S EXACT TEST
	CONTAINS TRAFF GECRET OR OTHERVISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY

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Table 21

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THIS REPORT GENERATED FROM DATA LOCKED THRU 12-JUN-90

Appendix 1 PAGE 241 EHL 87122

STUDY NO: 87122 +++++ MONSANTO ENVIRON	MENTAL F	IEAL TH	-AB *****	PAGE: 1
FATHOLOGY SECTION Study type: CH Species: Rat Substance: Glyphosate	S ×	C 1 1 (	z	PRINTED: 12-JUL
LECTION CRITERIA: ALL DEATHS REPORTE	IISTOPATH	IDL DGTC	NEOPLASN	
TISSUES WITH FINDINGS ANIMAL SEX TISSUES WITH FINDINGS DOSAGE GROUP: NO. IN GROUP:	29		M A L R D M A L R D M2 M3 66 66	F ANIMALS AFFECTED
ADRENAL(S) -#B - CORTICAL ADENOMA -#B - PHEOCHROMOCYTOMA -#M - PHEOCHROMOCYTOMA -#M - GANGLIONEUROMA/PHEOCHROMOCYTOMA	<u>ខ</u> លស្ត	<b>8</b> 73 <b>8</b> 73		
BRAIN -fim - Astrocytoma	8	-	1 1	
BONE -#M - OSTEOSARCOMA	•	(59) Ø	e (58)	
SP.CORD,CERVICAL -#M - Astrocytoma -#M - Glioma	56	(59) (59) 2 (59)	9) (59) 1 (6 8 (8	
CECUM	(22)	(56) (55)	6) (63)	
PERITONEAL CAV. -#W - WALIGNANT FIBROUS HISTIOCYTOWA	(0)	(0) (0)	Ø) (1)	
DUODENUM -#W - Adenocarcinoma	(58) 1	(55) (59) Ø	9) (59) Ø	
EYE(S) -#M - Neurofibrosarcoma (Schwannoma)	6	5	9	
KIDNEY(S) -#8 - LIPOMA -#M - LIPOSARCOMA -#M - MESENCHYMAL TUMOR -#8 - TUBULAR ADENOWA	0 <b>0 0</b> 0	8 N	0~00 00000	
LIVER -#B - HEPATOCELLULAR ADENOMA -#W - HEPATOCELLULAR CARCINOMA -#W - HISTIDCYTIC SARCOMA -#W - NEOPLASM, UNDETERWINED ORIGIN	n n 8 8	~~~	8 6 m 7 8	CONTAINS TRADE SECRET OR OTHERVULE CONFINENTIAL INFORMATION OF MONICENTIC COMPANY
FLING				

	****	PATHOLSANTO ENVIRONMENTAL HEALTH LAB	ENTAL H	EALTH	BV V	•••••	
TUDY TYPE: CH SPECIES:	SUBSTANCE:	GLYPHOSATE	- -	ן - ע		PRINTED: 12-JUL-90	_
L DEATHS	NEPORTED	••• SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS	STOPATH	010010	NEOF	6 6 8 8 8 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7	•
	у у 2	ANIMAL SEX : Dosage Group : No. In Group :	D 190 Z ¥0 NW	12 1	K B K B 60 A F C 0 A	R OF ANIWALS AFFECTED ES M3 60	. I
1033			6 - 6 ( )	(31) (3 0 0 0 1 0 1 (7		(37) 1 9 1	
LY.NODE,MESENT. -#B - HEMANGIOMA			(57) 8	(63) (1	(58) (1	(66) 1	
Wesentery/ow/tum -#W - Mesotheliowa			ි හ )	( 3) ( 1	) (- 8	( 8 ) 1	
NERVE, UNDESIG. -#B - NEUROFIBROMA (SCHWANNOMA)			(a)	) (ø )	) (ø )	(1)	
NOSE/TURBINATES -#8 - PAPILLARY ADENDMA			•	(69) 8	ت ه	(68) 1	
PANCREAS -#B - ISLET CELL ADENOWA -#M - ISLET CELL CARCINOMA			(68) 1 1	(67) 8 8	ت دە دە	(59) 7 8	
/FEET - SARCOMA, UNDETERWINED CELL	TYPE		(12) Ø	(15) ( 8	(12) (	(11) 8	
PITUITARY -#B - ADENOMA, PARS DISTALIS -#B - ADENOMA, PARS INTERMEDIA			4 8 M	32 32 32	(68) 34 34	(69) 31 1	
PROSTATE			-	•	•	8	
PARATHYROID (S)			1	(68) ( 1	(68) (	(67) 2	спı
ANTHDWA S CELL CARCINDWA AA/ADENOCARCINDWA, HISTIOCYTOWA	ZYMBAL'S GLAND		(69) 1 8 9	n 9 8 9	-00-	CONTAINS TRADE SECRET CONTAINS TRADE SECRET CONFIDENTIAL INFORMATION CONFIDENTIAL INFORMATION OF MOREANTO COMPANY	01122

Defendant's Exhibit 2570\_0059

Table 22 Appendix 1

THIS REPORT GENERATED FROM DATA LOCKED THRU 12-JUN-90

PAGE 243 EHL 87122

THOLOGIC NEOPLASMS ****       PRINTED: 12-JUL         NU W B E R       0 F       A N I W A L S       A F F E C T E D         NU W B E R       0 F       A N I W A L S       A F F E C T E D         NU W B E R       0 F       A N I W A L S       A F F E C T E D         NU W B E R       0 F       A N I W A L S       A F F E C T E D         NU W B E R       0 F       0 F       A N I W A L S       A F F E C T E D         NU W B E R       0 F       0 F       0 F C T E D       D         NU W B E R       0 F MOHS TRANE       CONTAINS TRANE       LEB         1       0       1       0       CONTAINS TRANE       LEB         1       0       0       CONTAINS TRANE       LEB       LEB         1       0       0       CONTAINS TRANE       L	STUDY NO: 87122	••••• MONSANTO ENVIRONMENTAL HEALTH LAB ••••• P a t h 0 i 0 c v s f c t 1 n N	***** PAGE: 3
ELIONA       IN CIDENCE OF HISTORYTOLOGIC MEDICANS         1 N G S       MINULES       N U M B E R OF AN I UALLS AFFECTED         1 N G S       MINULES       N U M B E R OF AN I UALLS AFFECTED         1 N G S       MINULES       N U M B E R OF AN I UALLS AFFECTED         1 N G S       MINULES       N U M B E R OF AN I UALLS AFFECTED         1 N G S       MINULES       N I UALLS AFFECTED         1 0 N OF NOT AN OF OUT AN OF	TYPE: CH SPECIES: RAT SUBS		PRINTED:
INGS       MIML SEX NO. IN GROP: NO. IN GROP: NO. IN GROP: E       N U W B E R NO. IN GROP: E       O F AN I WALES A F F E C T E D NO. IN GROP: E         (59)       0       0       0       0       0       0         (59)       1       0       0       0       0       0         (59)       1       0       0       0       0       0         (59)       (59)       (59)       (60)       0       0       0         (59)       (59)       (60)       (70)       0       0       0         (59)       (59)       (60)       1       0       0       0       0         (60)       (30)       (30)       (43)       (43)       0       0       0       0         (60)       (30)       (43)       (43)       (43)       0       0       0       0         (60)       (70)       (70)       (70)       (70)       0 <th>CRITERIA: ALL DEATHS REPORT</th> <th>INCIDENCE OF HISTOPATHOLOGIC NEO</th> <th></th>	CRITERIA: ALL DEATHS REPORT	INCIDENCE OF HISTOPATHOLOGIC NEO	
(56)     (56)     (59)       (11)     (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)       (11)     (11)     (11)	ISSUES WITH FINDING	SEX : N U M B E SEX : N U M B E GROUP : NN M1 M2 GROUP : 66 66 66	OFANIMALS AFFECTED
1       0       0       0       0         (50)       (50)       (50)       (7)       0         (1)       0       0       1       0       0       0         (1)       0       0       1       0       0       0       0         (1)       0       0       1       0       0       1       0         (1)       0       0       1       0       0       1       0         (2)       (30)       (30)       (30)       (40)       (5)       1         (2)       0       1       0       0       1       0       1         (2)       (30)       (30)       (4)       (5)       1       0       1         (1)       0       0       0       0       0       1       0       1         (1)       0       (1)       (1)       (1)       (1)       (1)       (1)	- ADENOMA, 3 - BASAL CFLI - SQUARDUS	(59) 68 8 1 1 6 1 1 1 6 1 1 1 6 1 1 1 1	68) 1 1
(1)       (0)       (0)       (0)       (0) $0$ $1$ $0$ $2$ $0$ $1$ $0$ $2$ $0$ $1$ $0$ $2$ $0$ $1$ $0$ $2$ $0$ $0$ $1$ $0$ $0$ $1$ $0$ $2$ $0$	- JEBROMA	8 (59)	
8       1       8         2       8       3       2         2       68       68       7         2       4       8       7         2       4       8       7         2       4       8       7         2       4       8       7         2       1       9       36       1         3       3       38       36       43         1       9       38       36       43         1       9       38       1       3         2       8       1       3       1         1       9       38       1       3         2       8       1       3       1         1       1       1       2       3         2       8       1       2       3         1       1       1       2       1         1       1       2       1       3         1       1       2       1       1         1       1       1       1       1       1         1       1       1	TAIL -#8- Intracutanegus cornifying epithelioma	1) ( <b>6</b> ) ( 1	( @ )
2       8       3       2         2       (58)       (58)       7         2       1       8       7         2       1       3       2       1         2       1       3       2       1         2       1       3       3       2         3       3       3       3       3       2         3       3       3       3       3       2         3       3       3       3       3       3         3       3       3       3       4       5         6       1       1       2       3       3       3         1       1       1       2       3       3       3       3         1       1       1       2       3	SP.CORD,THORACIC -#M - ASTROCYTOMA	8	8
2       4       8       7         2       3       3       3       3       1         3       3       3       3       3       3       2         3       3       3       3       3       3       3       3         3	TESTIS(ES) - AB - INTERSTITIAL CELL TUMOR	5	2
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	THYROID(S) -#B - C CELL ADENOMA -#M - C CELL CARCINOMA -#B- FOLLICULAR ADENOMA/CYSTADENOMA -#M - FOLLICULAR CELL CARCINOMA	(58) (58) 4 8 2 8 1 3 8 8	22
VARY BLADDER       (59)         CUTIS       (6) (3) (4) (5)         - FIBROUS HISTIOCYTOMA       2       9       9         - FIBROWA       2       9       1       3         - FIBROWA       2       9       1       3         - FIBROWA       2       9       1       3         - FIBROSARCOMA       1       1       2       6       1         - LIPPOMA       1       1       2       6       1       1         - LIPPOMA       1       1       2       6       1       1       2       6       1         - LIPPOMA       1       1       2       6       1       1       2       6       1       1         - SQUAMOUS CELL CARCINOMA       1       1       2       6       1       1       2       6       1       1       2       6       1 <td>THYMUS - AM - LYMPHOMA / LYMPHOSARCOMA</td> <td>(38) (36) 8 8</td> <td>(43) 1</td>	THYMUS - AM - LYMPHOMA / LYMPHOSARCOMA	(38) (36) 8 8	(43) 1
CUTIS       (4) (5)         - FIBROUS HISTIOCYTOMA       2         - FIBRONA       2         - FIBROSARCOMA       2         - LIPOWA       1         - LIPOWA       0         - SQUAMOUS CELL CARCINOMA       0         - NUCINOUS ADENOCARCINOMA       0         - MUCINOUS ADENOCARCINOMA       0         - MUCINOUS ADENOCARCINOMA       0         - MUCINOUS ADENOCARCINOMA       0         - MUCINOUS ADENOCARCINOMA       0	URINARY BLADDER	(63)	
TRACT (1) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0	CUTIS - FIBROUS HISTIC - FIBRONA - FIBROSARCONA - LIPONA - SQUAMOUS CELL	) (n a a a - a )	CONTAINS TRADE
. CAVITY (0) (0) (0) (1)	TRACT - MUCINDUS	(g) (g)	
		() () () ()	

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STUDY ND: 87122	B A T NONSANTO ENVIRONMENTAL HEALTH LAB +++++	PAGE: 4
STUDY TYPE: CH SPECIES: RAT		PRINTED: 12-JUL-90
CRITERIA:	• SUMMARY INCIDENCE OF HIS	 F F - - - - - - - - - - - - -
TISSUES WITH FINDIN	IGS DOSAGE GROUP: MUMBER OFANIMALS ANIMALSEX: MALES MALES DOSAGE GROUP: MN MI M2 M3 NO. IN GROUP: 60 60 50 60	AFFECTED
DRAL CAVITY	(1)(0)(0)	
TOOTH - #M - ODONTOGENIC TUMOR - #B - ODONTOGENIC TUMOR	(1)(1)(0)(0) 1 60 1	
MULTIPLE TISSUES -#M - FIBROUS HISTIOCYTOMA -#M - LYMPHOMA/LYMPHOSARCOMA	(1) (1) (0) (0) 1 0 0 1	
	C C MINS TRANKEL OR OTHERV	
	OF MONSANTO COMPANY	

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ND: 87122	••••• MONSANTO ENVIRONMENTAL HEALTH LAB ••••• P A T H D L D G Y S F C T T D N	PAGE: 5
STUDY TYPE: CH SPECIES: RAT SUBSTANCE:	•	PRINTED: 12-JUL-90
CTION CRITERIA: ALL DEATHS REPORTED	INCIDENCE OF HISTOPAT	;
TISSUES WITH FINDINGS	AL SEX : N U M B E R O F A N I M GE GROUP: FN F1 F2 F3 IN GROUP: 60 60 60 60	ALS AFFECTED
ADRENAL(S) -#B - CORTICAL ADENOMA -#B - PHEOCHROMOCYTOMA -#M - PHEOCHROMOCYTOMA -#M - CORTICAL CARCINDMA	900 7 7 900 7 7 900 7 7	
BRAIN - <b>HB</b> - Granular Cell Tumor	8	
BONE		
SP.CORD,CERVICAL	(63)	
CECUM ~∰M ~ NEUROFIBROSARCOMA	(55) (58) (59) (56) 8 8 1 8	
PERITONEAL CAV. - AM - NEURO-ENDOCRINE TUMOR, GASTRIN SECRETING	(0) (0) (1) (0) 1	
DUODENUM	(59) (59) (57)	
EVE (S)	(63)	
KIDNEY(S) -{B - LIPOMA -{B - TUBULAR CARCINOMA -{B - HEWAVVGIOMA	000 001 001 000 000	
LIVER -48 - HEPATOCELLULAR ADENOMA -4M - HEPATOCELLULAR CARCINDMA -4M - HISTIOCYTIC SARCOMA -4M - HEMANGIOSARCOMA -48 - CHOLANGIOMA	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
LY.NDDE,UNDESIG.		CONFERENTIAL AND
LUNG - #B - Bronchdalveolar Adendma	1 69 69 C-F-X-	OF MONSALLIC CCAIPAINY
•		•

122	NMENTAL HI	ALTH L	LAB	PAGE: 8
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE		> •	:	PRINTED: 12-JUL-90
CTION CRITERIA: ALL DEATHS REPORTED	HISTOPATH	DLDGIC	NEOPLASN	
ちちそそそうとしとしてした。「しってもってもで、そうでも思して思いません。「「「「」」」」」」」」」」」」」」」」」」」」」」」」」」」」」」」」」	, , , , , , , , , , , , ,		ц Ш Ш	FANIMALS AFFECTED
TISSUES WITH FINDINGS DOSAGE GROUP:	FN	F E M	ч Т Ш	
NO. IN GROUP	66			
		24) (63)	(22)	
-#B - ADENDMA/ADENDFLBRUMMA/FIBRUMMA -#M - CARCINDMA/ADENOCARCINDMA -#M - CARCINDSARCINDMA	2 E F	24 10 14 0		
	C	(63) (63)	~	
WESENTERY/DW'TUW	) (ø )	3) (2) 1 Ø	(ø) (	
NOSE/TURBINATES -#M - Squamous cell carcinoma, nasolacrimal duct	8	1 6	0	
OVARY(IES) -#B - GRANULOSA CELL TUMOR -#B - THECA CELL TUMOR	Q ~	6 6 6	(69) Ø	
PANCREAS -#B - ISLET CELL ADENOMA	م	4	8 9	
PAWS/FEET	( 2) (	3) (2)	(8) (	
PITUITARY -#B - Adenoma, Pars Distalis -#W - Carcinoma, Pars Distalis	40	48 48 48 69	(69) 34 1	
PARATHYROID (S) - <b>4</b> B - Adendia	(59) 2 1	(67) (69) 1 2		
SKIN -#M - Squamous Cell Carcinoma -#B - Adenoma, Zymbal's Gland -#B - Basal Cell Tumor -#B - Clitoral Gland Adendma	(69) 68 1 1 1	(56) 66 66 7 6 7 7 6 7 6 8 7 6 8 7 6 8 7 6 8 7 8 7	) (68) 88 88	CONTAINS TRADE SI CRET
SPLEEN -#M - LYWPHOMA / LYWPHOSARCOMA -#B - HEMANGIOMA -#M - HEMANGIOSARCOMA	8 9 <b>-</b> -	000 000		COMPANY COMPANY TON

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STUDY NO: 87122	• MONSANTO ENVIRONMENTAL HEALTH LAB •••••	
STUDY TYPE: CH SPECIES: RAT SUBSTANCE	PATHOLOGY SECTION : GLYPHOSATE	PRINTED: 12-JUL-90
ORTED	RY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***	
TISSUES WIT	ANIMAL SEX :NUMBEROFANIMALSAFFECTE Dosage Group: FN F1 F2 F3 NO, IN Group: 60 60 60 60	E D
SP.CORD,THORACIC	(69)	
THYROID(S) -#B - C CELL ADENOMA -#M - C CELL CARCINOMA -#B- FOLLICULAR ADENOMA/CYSTADENOMA -#M - FOLLICULAR CELL CARCINOMA	6670 6770 6770 6770 6770 7770 7770 777	
THYMUS - <b>E</b> M - LYMPHOMA / LYMPHOSARCOMA	(43) (61) (39) (44) 6 3 2 1	
URINARY BLADDER -#8 - POLYP/PAPILLOMA	(59) (59) (59) 0 0 1 0	
UTERUS -#8 - POLYP -#8-VASCULAR HAWARTOWA -#8 - STROMAL SARCOMA -#8 - ADENOWA, ENDOMETRIAL -#8 - LEIOMYOMA -#8 - FIBROMA	1 6 6 6 6 6 7 7 7 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7	
VAGINA - <b>fb</b> - fibroma	(1)(8)(2)(3) 6 8 1	
SUBCUTIS -#W - FIBROUS HISTIOCYTOMA -#B - FIBROWA -#W - FIBROSARCOMA -#B - LIPOMA	(4) (1) (4) (6) 1 1 6 2 1 8 1 2 2 8 8 8 8 8 2 1 2	
ORAL CAVITY -#B - Squamous Papilloma, Palate -#B - Chondroma, alveolus -#M - Granular Cell Tumor	( e) ( 1) ( 1) ( 1) ( e) 1 CONTAINS TRADE SECRET ( ) THATE SECRET ( ) THATE SECRET ( ) THATE SECRET	
T00TH	( 0) ( 1) ( 0) ( 0) OF MONSANTO COMPANY	Z

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PAGE: 8 PRINTED: 12-JUL-90				Table	22	Appendix	1	PAGE 249 EHL 87122
***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** P A T H O L O G Y S E C T I O N SUBSTANCE: GLYPHOSATE	SUMMAR	A NAMBER IN PARENTHESES OPTOSITE A 1155UE NAME INDICATES THE TOTAL NUMBER EXAMINED When Less than the NAMBER of Animals in the Group. Significantly different (P Less than or equal to 0.05) from control using fisher's exact test with the bowferroni inequality. Significantly different (P Less than or equal to 0.01) from control using fisher's exact test	D. CONTAINS TRADE SECRET	CONFIDENTIAL INFORMATION OF MONSANTU COMPANY				•
STUDY ND: 87122 STUDY TYPE: CH SPECIES: RAT		NOTE: A NUMBER IN PARENTHESES OPTOSITE A TISSUE WHEN LESS THAN THE NUMBER OF ANIMALS IN TH * = SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQU ** = SIGNIFICANTLY DIFFERENT (P LESS THAN OR EQU	WITH THE BOWFERRONI INEQUALI					

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THIS REPORT GENERATED FROM DATA LOCKED THRU 12-JUN-90

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TABLE 51

## Glyphosate 104 Week Combined Chronic Feeding/Oncogenicity Study in Rats With 52 Week Interim Kill Incidence of Histological Findings : Males and Females Oncogenicity Study

		-								
FIKDINGS	REATMENT Grp 1 0 /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
ABDOMEN:		£				£	 		(2)	(2)
Vasculitis Focal chronic inflammation Fat necrosis						0 - 0		·	0 0 N	-0-
ACCESSORY SEX GLAND(S):							5		Ĵ	£
CliTORAL GLAND: cystic duct(s) CliTORAL GLAND: abscess(es)							<del>-</del> 0		0	-0
ADRENALS:	(67)	(22)	(12)	(21)	(67)	(48)	(36)	(2)	(30)	(67)
No abnormality detected Unilateral focal corticat hyperplasia Focal cortical hyperplasia Unilateral CORTICAL CARCINOMA [M] Metastasising CORTICAL CARCINOMA [M]	~~~~~~	20-00		<sup>2</sup> N000		~~~~~~	14 N O O O O	w-000		v-000
Unilateral CORIJCAL ADEROMA (BJ Unilateral focal medullary hyperplasia Rilateral focal medullary hyperplasia				⊃ <i></i>	⊃ ~ r	- M -		⊃ <del>-</del> -		
Focal medullary hyperplasia Unilateral PHAEOCHROMOCYTOMA [M]				- 0 0	10 <del>.</del>			- 0 0		
	~	-	-	-	80	'n	0	•	-	*

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TABLE 51 (continued)

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TABLE 51 (continued)

FINDINGS		Grp 2 10 mg/kg	Grp 3 100 mg/kg		Grp 5 1000 mg/kg	Grp 1 0 mg/kg		Grp 3 100 mg/kg		Grp 5 1000 mg/kg
ADRENALS:	(49)	/ day (25)	(17)	/day (21)	/ day (49)	/day (48)	/day (26)	(29)	(30)	(49)
Angiectasis Autolysed, diagnosis difficult Extra section(s) examined		0 ~ 0	0 M O	- MO		0 N O	<b>0</b> ⊷0	0 1 0	0 1 0	0 M O
AORTA:	(50)	(22)	(19)	(12)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected Medial mineralisation Autolysed, diagnosis difficult	<u> </u>	0 0 52	÷	050		000 000	0058	005	800	
BRAIN:	(50)	(22)	(19)	(12)	(05)	(4)	(28)	(29)	(30)	(02)
No abnormality detected GRANULAR CELL TUMOUR [M] Meningeal infiltration by histiocytic cells	800 	<b>6</b> 00	<del>,</del> 000	200	115	*000	200	005	200	<u>Моо</u>
Compression by pituitary	10	5	m 	4	5	0	12	0	12	
Infiltration by lymphoma cells	-	0	<u> </u>		0	<u> </u>	•	0	•	0
Focal curonic meningitis Focal dinais				- -	о с —	-			- c	
GLIOMA [M]		)	> 0 	> 0		0	> <del>-</del>		>	10
Autolysed, diagnosis difficult	-	0	-	0	0	0	0	0	0	~

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TABLE 51 (continued)

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		. ,	-								
F I ND I NGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
BRAIN:		(50)	(25)	(19)	(21)	(50)	(67)	(28)	(29)	(30)	(50)
n by pituitar ot available	y tumour for histological	- 0	- 0	00	-0	0 10	vo m	40	-0	N 0	<b>00</b>
examination Cerebetium not examined histologically	gically	•	0	0	•	0	-	0	•	0	-
CAECUM:		(42)	(8)	(9)	(12)	(43)	(43)	(53)	(23)	(26)	(27)
No abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells Autolysed, diagnosis difficult	s	4000 4		••••	1005	000 <del>7</del>	<u></u>	N000			1005
CERVIX:							Ð			-	
No abnormatity detected							-				
COLON:		(43)	(11)	(2)	(13)	(44)	(97)	(25)	(56)	(27)	(44)
No abnormality detected Infiltration by histiocytic cells Perivasculitis	s	¥00	÷00	900 	٥ o d	4	<b>9</b> 00	×00	20 0 	22 0 0	¥00
Hypertrophy in muscle layer		0	0	-	0	0	0	0	0	0	0

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TABLE 51 (continued)

				MALES							
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
COLON:		(43)	<del>1</del>	6	(13)	(44)	(97)	(25)	(26)	(27)	(44)
Dilatation Autolysed, diagnosis difficult						~ <del>~</del>	0 N	00	0 N		0 N
DUODENUM:		(42)	(12)	(10)	(14)	(95)	(42)	(32)	(22)	(29)	(46)
No abnormality detected CARCINOMA [M] Infiltration by histiccytic cells Serosal perivasculitis Autolysed, diagnosis difficult	a	40064	× 0 0 0 7	2000m	2000N	4000N	40-0W	90000 50005	10005	00005	00 - t¢
EYES:		(3)			Û	(2)		£	£		
No abnormality detected Panophthalmitis Keratitis Haemorrhage Autolysed, diagnosis difficult					000-0	N0000		0-000	000-0		
HEART:		(50)	(54)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(67)
No abnormality detected		12	7	5	9	13	32	20	21	21	31

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TABLE 51 (continued)

							_				
			Σ	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
HEART:		(50)	(24)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(67)
Infiltration by Mistiocytic cells		0	0	0	0	0	-	<b>.</b>	0	0	-
Infiltration by Jeukaemic cells					0	•	c	· C	0	0	0
Infitration by tymphoma cells		• •	0	0	0				0	0	0
Cardiomyopathy(mineralised) Cardiomyopathy		-	<del>~-</del>	0		•	•	•	•	0	•
(Grade	(-/+	M	<u>م</u>	-	-	9	'n	Ś	<u>ب</u>	-4	4
		18	80	~	1	21	Ð	~	2	4	12
(Grade ++)	Ŧ	5	m	Ś	м	7	0	0	0	0	0
(Grade +++)	(Ŧ	-	0	0	0	0	0	0	0	0	0
Total incidence for score expanded finding	ē	37	16	t.	71	34	13	~	2	₽0 	16
Metastasis from primary in adrena	_	0	0	0	0	0	0	0	0		0
		0	-	-	0	0	0	0	0	0	-
Myocarditis		0	0	-	0	m	m	-	2	-	•
Vascular mineralisation		0	0	-	0	0	0	0	0	0	0
Focus(i) of mast-cell infiltration	Ē	0	0	0	0	0	-	0	0	0	•
Endocarditis		0	0	0	0	-	-	0	0	0	•
Autolysed, diagnosis difficult		0	0	0	•	0	-	0	0	•	•
1 LEUM:		(75)	(8)	2	(12)	(12)	(45)	(23)	(22)	(22)	(42)
No abnormality detected		42	80	7	12	43	44	23	55	25	42

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TABLE 51 (continued)

			-•	INCIDENCE		SIONS (I	OF LESIONS (NUMERIC)	~		1
		Ξ	MALES			   		FEMALES		
FINDINGS	ENT Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
1LEUM:	(42)	(8)	(2)	(12)	(43)	(45)	(23)	(25)	(22)	(42)
Infiltration by lymphoma cells Autolysed, diagnosis difficult	00	<u> </u>	o -	00	00	- o	00	0-	o-	o-
JEJUNUM :	(£7)	6)	(8)	(15)	(45)	(42)	(52)	(26)	(28)	(77)
Xo abnormality detected Mucosa damaged Autolysed, diagnosis difficult	0 - 1 4	000	80 <del>.</del>	<u>то</u> м	1042	42 42	005	1056	80+-	40+
KIDNEYS:	(05)	(50)	(50)	(50)	(50)	(05)	(47)	(05)	(67)	(50)
ko abnormality detected Mesenchymal TUMOUR [M] Unilateral TUBULAR ADENOMA [B] Metestasision unothalial CADFTUOMA FW1	N0-0	2000	2000	1000 <del>-</del>		0-0C	2000	4000	°••••	<u>6000</u>
					0 N O	o-o			o-o 	o-a
(Grade +/-) (Grade +/-)		c	0 ~ 0	0 14 0	010	~~~	м <del>Г</del> м	мо.		+* • • • •
Total incidence for score expanded finding	- M	• ~ ·	⇒ ~ <b>.</b>	л с — — —	2 M	18	n ₽	- <del>[]</del>	- o 	***

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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		£	MALES					FEMALES		
FINDINGS	ENT Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
KIONEYS:	(50)	(50)	(50)	(50)	(50)	(50)	(49)	(50)	(67)	(50)
Nephropathy										
(Grade +/-) (Grade +)	50	13	16	50 50	<u>15</u>	44	12	°.≓	19*	7 <del>1</del> 3
(Grade ++) (Grade +++)	<u>~ ~</u>	€ -3	6'2	~~	<del>ہ</del> ہ	~ 0	~ 0	00	-0	- e
Total incidence for score expanded finding	40	37	33	37	34	52	21	15	26	27
Infiltration by lymphoma cells	0	0	0	~	•	0	0	0	•	0
Basophilic tubules	• I	•••		- 1	- <b>t</b> -	<del>-</del> (	<del>.</del> .	0,	• •	0 .
Tubular dilatation	N <del>-</del>			א רי 	∍ -		4 0	<u>.</u>	∽ -	t <del>-</del>
Petvic ditatation Papillary necrosis		• •	- 0	י ר- 		00	, o	- 0	- 0	- 0
Cortical tubular hyaline inclusions	0	-	0	ò	~	<b>~</b> ~	-	0	0	-
Mineral deposit(s)	0	0	~	0		0	0	0	0	0
Cortical brown pigment deposit(s)	0	0	0	~	-	<b></b> -	0	rî -	~ ·	0
Lymphocytic infiltration	-	0	0	0				۔ 		0
Cortical tubular vacuolation	0	0	0	0	0	-	0	-	0	8
Pyelonephritis	0	•	-		0	0	0	0	0	0
Pyelitis	0	0	0	2	~	0	~	-	<b>.</b>	0
Perivasculitis	0	0	0	0	0	0	0	0	•	-
Glomerular nephropathy	0	0	-	-	0	0	0	0	0	0
Tubular necrosis	0	0	0	0	0	ru	-	0	-	-

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

TABLE 51 (continued)

			Ξ	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300  mg/kg /day	Grp 5 1000 mg/kg /day
KIDNEYS:		(50)	(50)	(50)	(50)	(50)	(50)	(67)	(50)	(65)	(50)
Inflammatory cell infiltrate Focal inflammation		00	00	<del>ہے</del> ج	00	00	0-	0~	00	00	- 0
Cyst(s) Autolysed, diagnosis difficult Tumour infiltration		~~~	o * o	-00	040	- ~ 0	-~0	<del>- м -</del>	o in o	N 4 0	000
LACRIMAL GLANDS:		6				<u> </u>					
No abnormality detected Focal cellular atypia		- 0				0-		- <u> </u>		•	
LIVER:		(50)	(050)	(67)	(50)	(50)	(50)	(50)	(50)	(50)	(05)
No abnormality detected Haemannioma present			~~ =	-0-	90	c	80	~~~	<u>ہ</u> م	мс 	~ 0
Focal hepatocellular hyperplasia HEPATOCELIULAR CARCINOMA MULTIPLE	[H]	) o c	, o -	C						→	, 
A CM] MULTIPLE		00	00	- 0	0-			0	00		00
HEPATOCELLULAR ADENOMA [B] Infiltration by histiocytic cells		~ 0		- 0		~-	o -	0-	00	•~ N	~ ~

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MALES         FEMALES           FINDINGS         FINDINGS         FEMALES           FINDINGS         FINDINGS         FEMALES           FINDINGS         FINDINGS         FEMALES           FINDINGS         FEMALES           TREATMENT         Grap 3         Grap 3         FEMALES           ILIVER:         Carp 4         Grap 3         FEMALES           Aday         /day					ī	INCIDENCE	E OF LES	SIONS (	OF LESIONS (NUMERIC)	~	:	
INGS         TREATMENT         Grp 1         Grp 2         Grp 3         Grp 4         Grp 5         Grp 1         Grp 2         Grp 3         Grp 4         Grp 7         Grp 2         Grp 3         Grp 3         Grp 3         Grp 3         Grp 3         Grp 3         Grp 4         Grp 2         Grp 3         Grp 3         Grp 4         Grp 2         Grp 4         Grp 3         Grp 4         Grp 2         Grp 3         Grp 4         Grp 3         Grp 4         Grp 4         Grp 2         Grp 4         Grp 4         Grp 2         Grp 4         Grp 4				E	ALES					FEMALES		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day		Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
furcation of median       0       1       0	LIVER :		(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
s       (Grade +/-)       5       1*       5       7       4       5       9         (Grade +/-)       5       1       1       22       1	Foamy hepatocytes (bifurcation o Loba)	of median	_	~	0	0	0	0	0	0	0	0
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Foamy hepatocytes Portal tract sclerosis		80	<del>,</del>	'n	7	4	ι <b>Λ</b>	¢	\$	-	6
core       expanded       18 $\overline{25}$ 16 $\overline{4}$ $\overline{4}$ (Grade +/-)       1       1       1       1       1       1       1       1         (Grade +/-)       1		(-/+ (++	v∩ ⊗0 ư	- 22*		19*	- 5 ~	+- N +-	• M C	mNC	5 M C	ыл <b>м</b> С
17       18       22       17       11       0       1         (Grade +/-)       1       0       1       1       1       0       1         (Grade ++)       8       4       7       5       7       4       3         (Grade ++)       1       3       1       4       5       2       0       1         (Grade ++)       1       3       1       4       5       2       0       0         (Grade ++)       10       7       9       10       14       6       4       3         core       expanded       10       7       9       10       14       6       4         (Grade ++)       9       8       9       3       8       5       5       1         (Grade ++)       2       6       6       1       2       6       4       7	core	led	,≊	35	16	23	16	• • •	<b>7</b>	· ທ	8	80
(Grade +/-)       1       0       1       1       1       0       1         (Grade +)       8       4       7       5       7       4       3       1       1       3       1       1       0       1       0       1       0       1	spongiosis hepatis Clear cell focus(i)		17	18	22	17	11	o	-	-	-	o
(Grade ++)       1       3       1       4       5       2       0         (Grade +++)       0       0       0       0       1       0       0       0         (Grade +++)       10       7       9       10       14       6       4         (Grade +/-)       1       0       0       2       6       1       2       0         (Grade ++)       2       6       6       1       2       1       2       0         (Grade ++)       2       6       6       1       2       1       2       0       0       0         (Grade ++)       0		(-/+ (-/+	<b>-</b> 00	04	~ <b>~</b>	- v		64	<del>с</del> м	• •	<u> </u>	о'n
score expanded 10 7 9 10 14 6 4 (Grade +/-) 1 0 0 2 0 1 (Grade +) 9 8 9 3 8 5 5 5 (Grade ++) 2 6 6 1 2 1 2 1 2 (Grade ++) 0 0 0 0 0 2 0 0	(Grade (Grade	(++	- 0	m 0	- 0	40	<u>س</u>	~ 0	00	00	00	
(Grade +/-) 1 0 0 2 0 0 1 (Grade +) 2 6 6 1 2 1 2 1 2 1 2 (Grade ++) 0 0 0 0 0 2 0 0 0 0 0 2 2 3 3 2 3 3 3 3	score	led	10	~	δ	10	2	S	4	*0	μ.	м
		(-/+	~- o	0 «	00	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0 a	οv	- v		- >	0 4
	Grade (Grade	÷.	0 10	500	~~00	0	งผณ	) <del></del> 0	0 10			) <del></del>
				•		,	!			,	,	,

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

MALES 2 Grb 3 Gr 4 100 30 7 /day /d 0) (49) ( 15 4		Grp 1 0 mg/kg /day		FEMALES			
INGS INGS INGS INGS INGS INGS ING ING/E							
l incidence for score expanded 12 14 15 ing philic focus(i) (50) (49) (	<u> </u>		Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	
12 14 15	0 12	(50)	(05)	(02)	(05)	(05)	
(Grada + /_) 1 1 2 1 1	0	<b>v</b> 0	ø	7	<u>س</u>	μ.	
2 2	Σ	-=	0.0	<u></u> ء	35		
(Grade ++) 0 0 2 0 2 0 0 2 0 0 0 2 0	м с 	~ ~	e -	2,	- ·-	~ ~	
10 4 8	, ao	22	15	56	54	 	
tion by leukaemic cells 0 0 0		0	0	0	0	0	
Infiltration by lymphoma cells 0 0 0 1 Dilated sinusoids 5 1 1 0 0 Bile duct hyperplasia	00	0	- 0	00	00	~ 0	- -
(Grade +/-) 4 1		0	m	-	0	m	Ĵ.
15 13 15		4	ŝ	ŝ	JUN I	m	Ľ
	- C	~ ~	~	0	~ 1	ر. س	
n7 - 57 -	* <u>~</u>	٥	<u>د</u> ا	 א	~	1	- 
ullary haemopoiesis		-7	~	0	-	س	•
0	-	0	0	0	0	0	•
0 0 0	0	0		0	0	0	
18	5	13	16	18	16	∑u≺ ₽	

FINDINGS         TREATMENT         GP         1         G         100         300         100         100         100         1											
csis       csis       (50)					Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
osis         osis         osis         ammatory cell infiltrate         0         2         2         1         0         3         4         0         4         3         2         4         0	Lîver:	(50			(50)	(20)	(50)	(50)	(50)	(50)	(05)
ammatory cell infiltrate $2$ $3$ $2$ $3$ $5$ $5$ $6$ $3$ $2$ I inflammation100100000I inflammation10001000I inflammation10001000I inflammation10000000I inflammation000000000rilobular hypertrophy000000000apsular fibrosis0000000000apsular fibrosis00000000000apsular fibrosis00000000000use degeneration00000000000use degeneration00000000000det cyst(s)000000000000det cyst(s)000000000000estion000000000000estion0 </td <td>Necrosis</td> <td></td> <td></td> <td>2</td> <td></td> <td>0</td> <td>M</td> <td>4</td> <td>0</td> <td>4</td> <td>л</td>	Necrosis			2		0	M	4	0	4	л
nic periportal inflammation       0       0       0       1       0 <th< td=""><td>tory cell infil</td><td>2</td><td>м</td><td>2</td><td>m</td><td>ŝ</td><td>~</td><td>9</td><td>m</td><td>~</td><td>~</td></th<>	tory cell infil	2	м	2	m	ŝ	~	9	m	~	~
I inflammation       1       0       4       5       4       1       0       0       1         portal hypertrophy       1       0       0       1       1       0	Chronic periportal inflammation	-	-	0	0	-	0	0	0	0	0
portal hypertrophy         0         0         1         1         1         0	Focal inflammation	-		4	5	4	-	0	0	-	2
rilobular hypertrophy0100100apsular fibrosisapsular fibrosisapsular fibrosisapsular fibrosisapsular fibrosisapsular fibrosisapsular fibrosisapsular fibrosisause degenerationuse degenerationduct cyst(s)duct cyst(s)ause degenerationause difficultbased mitoric ratea section(s) examineda section(s) examinedb o 0a section(s) examinedb o 0b o 0c o 0 <td>Periportal hypertrophy</td> <td>0</td> <td></td> <td>0</td> <td>0</td> <td>0</td> <td>-</td> <td>-</td> <td>0</td> <td>o</td> <td>•</td>	Periportal hypertrophy	0		0	0	0	-	-	0	o	•
apsular fibrosis       3       0	Centrilobular hypertrophy	0		-	0	0	-	-	0	0	0
use degeneration       0       1       1       0	Subcapsular fibrosis	m 	-	0	0 	0	0	0	0	0	0
duct cyst(s)       0       1       1       1       0       2       0       2       12       12       13       15       22       10       12       12       12       13       15       22       10       12       2       4       2       2       4       2       4       2       2       4       2       2       4       2       2       4       12       10	Diffuse degeneration	-		•	0	0	0	0	0	0	0
(s)       (s)       (s)       0       0       1       0<	Bile duct cyst(s)	0			-	0	~	0	2	~	~
estion       5       0       0       0       3       1       0 </td <td>Cyst(s)</td> <td>-</td> <td></td> <td>•</td> <td>0</td> <td>0</td> <td>-</td> <td>0</td> <td><u> </u></td> <td>0</td> <td>0</td>	Cyst(s)	-		•	0	0	-	0	<u> </u>	0	0
ectasis       12       13       15       22       10       12       13       15       22       10       12       12       13       15       22       10       12       12       13       15       22       10       12       12       13       15       22       10       12       12       13       15       22       10       12       12       13       15       22       10       12       12       13       15       22       10       12       12       12       13       12       3<	Congestion	۰۰ ۱	-	0	-	rî.	_	0	0	0	0
Uysed, diagnosis difficult       5       6       9       3       3       7       3       2       4         eased mitoric rate       0       0       1       0       1       0 <td< td=""><td>Angiectasis</td><td>16</td><td></td><td>13</td><td>12</td><td><u>۳</u></td><td><u>ج</u></td><td>52</td><td><b>e</b></td><td>12</td><td>ň</td></td<>	Angiectasis	16		13	12	<u>۳</u>	<u>ج</u>	52	<b>e</b>	12	ň
eased mitotic rate       0       1       0       1       0	Autolysed, diagnosis difficult	<u>~</u>		<u>ہ</u>	<b>m</b>	m	~	m 	~	4	in.
a section(s) examined 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0	Increased mitotic rate	0		-	0		-	<b>-</b>	0	ð	•
UT INTITTATION bhormality detected stasising souramous-cell CARCINOMA 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Extra section(s) examined	0		<u> </u>	00		-	•	00	ب ہ	~ ~
bnormality detected     (50)     (49)     (49)     (49)     (50) <t< td=""><td>lumour infiltration</td><td><b>-</b></td><td></td><td>⊃</td><td>&gt; </td><td>⊃ </td><td>∍</td><td></td><td>&gt;</td><td>&gt; </td><td>&gt;</td></t<>	lumour infiltration	<b>-</b>		⊃	> 	⊃ 	∍		>	> 	>
CELL CARCINOMA 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	LUNGS:	(50	<u> </u>	(4)	(20)	(05)	(50)	(50)	(50)	(02)	(50)
CELL CARCINOMA 0 0 1 0 0 1 0 0 0 0	No abnormality detected	50		20	27	52	25	36*	34	35	54
	CELL			0	•	0	0	0	0	0	•

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FINDINGS	NT Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 1000 /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
LUNGS:	(50)	(67)	(67)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Metastasising ALVEOLAR/BRONCHIOLAR	0	•	0	0	•	0	0	<b>4</b> -4	0	0
CARCINUMA MULIIPLE [M] Alveolar/Bronchiolar Adenoma [b]	~		-	~	。 	-			0	
SARCOMA [M]	0			0	-	, <del>.</del> –	0	0	-	0
Infiltration by histiocytic cells	0	0	0	-	7	0	-	0	2	~
Infiltration by leukaemic cells	-	0	•	0	-	0	0	•	0	0
Infiltration by lymphoma cells	•	•	0	-	•	0		0	-	-
Interstitial pneumonitis	~	4	4	~	۲ 	m	<del>-</del>	~	•	m
Increased alveolar macrophages	0	~	۰۰ 	*	9	m 	~	2	-	m -
Food present	<b>,</b>		•	-:	••	•			00	-
	<u>.</u>	~	91		- 0-	2	<u> </u>	2	<u> </u>	2
	• •	0		0,	-	0		0	0	••
Ē	0	-	o 		0	-		-	0	0
Metastasis from primary in kidney	-	0	-	<del>،</del>	0	0	0	0	0	0
Metastasis from primary in adrenal	-	0	0	0	•	0	0	0		0
	0	<b>-</b> -	-	0	0	-	•	0	0	0
Perivascular lymphocytic infiltration	2	-	0	0	0	0	0	0	0	0
<pre>Grade(++++) granuloma(ta)</pre>	0	•	0	0	0	0	-	•	0	-
Granuloma(ta)	•	м	0	ریا 	-	0	0	0	0	0
Focal chronic pleurisy	-	0		0	0	0	0	o	0	0
Oedema	-	0	m	-	-	0	0	0	0	0
inflammatory cell infiltrate	- c	- c			-	~		0		· ^
	<b>,</b>	, 	-	-	> 	1 	> 	,	-	J

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FINDINGS	TREATMENT Grp 1 0 mg/kg	6rp 2 10 mg/kg /day	6rp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
CUNGS:	(50)	(67)	(67)	(50)	(50)	(50)	(50)	(50)	(50)	(05)
Haemorrhage(s)	-	0	-	0	0	0		0	0	0
Alveolar epithelialisation		<b>ج</b> ر )	01	••	0.	- 4	00	00	00	
Congestion	4 •	ი ი 	ი (	- 0	<u> </u>	> < 		- -	- c	- c
Bronchopneumonia Autoline d'actorie difficulté		⇒ ¤	⊃ M		-	> ~	- ~	2 4	- -	
Autolyseu, diagnosis difiléult Tumour metestesis (primery site unknow	n c 	• -	r	+ C	- c	+ c	. <del>.</del>	+ C		t C
Delv teo lobes available for		• c		) <b>-</b>	• •		- 0		• •	• • •
histological examination		, 	, 		,	,	,		,	-
Only one lobe examined	0	•	0	0	•	•	-	•	0	0
LYMPH NODE(S):	(10)	(9)	(2)	(5)	(15)	(23)	6)	(15)	(21)	(28)
infiltration by histionstic calle		•	-	- -		-	•	-	0	c
Infiltration by leukaemic cells		. 0	0	0	, <del>.</del>	• •	0	. 0	0	0
Infiltration by lymphoma cells	0	0	0	-	0	-	-	0	0	-
findings with n	ю 	m	M	м	<u>م</u>	-15	ñ	10	16	16
detected tymmh moder to mare or with	-	-	c		~	-	ę-	~	~	۲
Find notes version wass of available necrops findings but were not available for histological examination	le	-	, 		1	•			ı 	1
Tumour metastasis	0	•	0	-	0	0	0	٥	-	0

TABLE 51 (continued)

FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
LYMPH NODE(S):		(10)	(9)	(2)	(5)	(15)	(23)	6	(15)	(21)	(28)
Pigmented macrophages Reactive Cyst(s) Congestion Autolysed, diagnosis difficult		0 1 1 0 0	0-0-0	00000		0 M	~~~00	0 10 - 0	040-0	04000	~~~~~
LYMPHORETICULAR/HAEMOPOIETIC TISSUE:	·	(1)	(2)		3	(2)	(7)	(2)	£	(2)	(5)
HISTIOCYTIC SARCOMA [M] LYMPHOMA in thymus only [M] LYMPHOMA [M]		~00	0		кл о -7	M	MO	- 0	-00	000	MON
MAMMARY GLANDS:		(45)	(22)	(17)	(12)	(47)	(50)	(28)	(29)	(30)	(50)
No abnormality detected FIBROADENOMA MULTIPLE [B] FIBROADENOMA [B] CARCINOMA MULTIPLE [M] Metastasising CARCINOMA [M] CARCINOMA [M] ADENOMA [B] ADENOMA [B]		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	20000-00	N0000000	F0000000	00000702	M	N00000	₩₩₩200~M+	- 8 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0	

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FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
MAMMARY GLANDS:		(45)	(25)	(12)	(21)	(47)	(50)	(28)	(29)	(30)	(50)
Infiltration by histiocytic cells	s		•	0	<u>م</u>	0	0	- ì	•	0	
Mammary development	t	20	<u>+</u> -	2 ⊂	2.	ž c	3-	* c	₽.		5
Focus(I) of pigmented matrophages Focal lymphocyfic infiltration	à		0	 -		) <b>-</b>	• •		- 0	> 0	• •
Chronic inflammation		0	0	0	0	0	-	0	2	0	0
Inflammation		0	0	0	0	0	2	0	0	0	0
Abscess(es) Autolysed, diagnosis difficult		00	0	00	00	00	0 +-	00	00	o <del></del>	
MESENTERIC LYMPH NODE:		(12)	(54)	(19)	(12)	(05)	(8)	(28)	(2)	(30)	(4)
No abnormality detected Haemangioma present		-14	- 53	÷00	÷	74 O C	97 0	580	-0%	800	0 42
Inflitration by mistiocytic cell Infiltration by leukaemic cells Infiltration by leukaemic cells	uj.	- 0 0				v c	- o c		- 0 c		
Lymphoid depletion		0	0	) <b>0</b>		• •	- 0	) <b>0</b>	0	00	- 0
Pigmented macrophages		0	c	0	•	0	-	0	-	0	~
Reactive		•	0	0	0	-	0	0	-	0	-
Cyst(s) Condection		- 0	••	00	0-	01	0,-	00	0	<u> </u>	00
Autolysed, diagnosis difficult		~	0	0	. 0	<del>، ب</del>	. 0	0	0	0	0

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TABLE 51 (continued)

			Σ	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 m9/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
MESENTERY:					Ē					·	£
MESOTHELIOMA [B] Abscess(es)					0						-0
DESOPHAGUS:		(67)	(57)	(19)	(21)	(50)	(50)	(28)	(5)	(30)	(50)
No abnormality detected Infiltration by histiocytic cells Infiltration by thyroid tumour		\$00	0055	<u>6</u> 00		000 000	<u> </u>	0 58	005	R00	\$+0
OPTIC NERVE:		£		£	£						
No abnormality detected Autolysed, diagnosis difficult		-0			- 0						
OVARIES:							(50)	(28)	(2)	(62)	(50)
No abnormality detected Unilateral GRANULOSA/THECAL CELL TUMOUR	UMOUR	_					50 2	0 13	<u>ه</u> -	<u>~</u>	0 20
undiltration by histiocytic cells Only one examined Cystic foilicle(s)							 	004	001	~04	000

				-	INCIDENCE		DF LESIONS (NUMERIC)	NUMERIC	~		
			×	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grр 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
OVARIES:							(50)	(28)	(29)	(29)	(02)
Stromal hyperplasia Bursal cyst(s) Atrophy Autolysed, diagnosis difficult Tumour infiltration							04224	N02+		00220	4-5m0
PANCREAS:		(50)	(54)	(17)	(21)	(4)	(67)	(27)	(2)	(29)	(67)
No abnormality detected Islet hyperplasia EXOCRINE CARCINMA [M] EXOCRINE ARROMA [B] EXOCRINE ADENOMA [B] Infiltration by histiocytic cells infiltration by histiocytic cells pilated duct(s) Acinar atrophy Pigment deposit(s) Lymphocytic infiltration Granuloma(ta) Thrombus (canalised) Perivasculitis Interstitial oedema		NNOMN0-400-010	20000-00/0000+	₩00-N00+000000	4 2 2 2 2 2 2 2 2 2 2 2 2 2	***************************************	40-0040000-0	N00000+M00000	000000-0000 	00000700000	8000-0040000N0

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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				-	INCIDENCE	5	LESIONS (NUMERIC)	שחשבאוכ	~		
			I	MALES		1			FEMALES		
F 1 ND 1 NGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
PANCREAS:		(0)	(54)	(17)	(11)	(67)	(67)	(27)	(29)	(29)	(47)
Perivascular inflammatory cell Acinar hypertrophy Ductal hyperplasia Autolysed, diagnosis difficult Extra section(s) examined Infiltration by uterus tumour	ory cell infiltrate ifficult ned tumour	0m4m00		000m00	000000	0moo	000-00	000-0-	0000+0	000000	<b>0</b> 00400
PARATHYROIDS:		(77)	(02)	(17)	(61)	(95)	(95)	( (26)	(23)	(77)	(11)
No abnormality detected Unilateral focal hyperplasia Unilateral ADENOMA [B] Only one examined Fibrosis Haemorrhagic cyst(s) Cyst(s) Autolysed, diagnosis difficult			Noomoooo	Looscoco	°°°°°°°°°°°°°	400 <sup>0</sup> 0000		0004000	N000000	Noonoo+o	8077-007
PITUITARY:		(50)	(54)	(19)	(12)	(50)	(46)	(28)	(2)	(30)	(67)
No abnormatity detected Only anterior lobe examined		5.2		⇔	<u>مہ</u>	54	N0	M 0	<u>ه</u> -	0 0	м с/

			ž	MALES					FENALES		
FIRDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
P[TU]TARY:		(50)	(77)	(19)	(12)	(05)	(4)	(28)	(29)	(30)	(67)
CARCINOMA [M] Adenoma multiple [b]		- 0	- 0	00	0	00	N N	<u>.</u>	-0	NO	4 -1
ADENOMA (B) Focal hyperplasia Intermediate lobe hyperplasia		58 77	0 1 7	8 2 0	~ m o	*/~~0	ñoo	\$ o o	°-00	500	йчо
Damaged Posterior Lobe not examined		-0 M	00	04	0-	- 0	0-	• •	••	00	0 N
histologically Cvst(s)		4	0	2	-	<u>س</u>	-	-	0	2	м
Autolysed, diagnosis difficult Anatomical defect (possibly congenital)	tal)	-0	-0	40	N 0	m ←	NO	-0	N 0	-0	<b>~ 0</b>
PROSTATE:		(05)	(54)	(18)	(11)	(50)					
No abnormality detected CARCINOMA [M]		42	23 0	14	17	1					
ADENOMA [B] Focal lymphocytic infiltration		o <del>-</del>	00	• •	00	-0					
Inflammation Interetital fibrosic		<del>،</del> ٥	c	40	<b>.</b>	<u></u> п с					
Autolysed, diagnosis difficult		- 0	0	2	) <b>0</b>	0					

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

TABLE 51 (continued)

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FLNDINGS	TREATMENT Grp 1 0 mg/kg		Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
RECTUM:	4)	(£7)	(12)	(8)	(13)	(77)	(97)	(26)	(28)	(22)	(643)
No abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells Lymphocytic hyperplasia Dilatation Autolysed, diagnosis difficult		4000F0F	× • • • • • •	80000N	£0000+	₩-00+F	40400M		×0000%	00000	M0000-
SALIVARY GLAND:	(5)	(20)	(46)	(67)	(92)	(4)	(20)	(50)	(02)	(50)	(48)
No abnormality detected PARDT1D: NAD SUBLINGUAL: NAD MANDIBULAR: NAD PARDT1D: not examined histologically SUBLINGUAL: not examined histologically MANDIBULAR: not examined histologically		0 + 0 + 78 22 	001650	007 562 57 50 50 50 50 50 50 50 50 50 50 50 50 50			- n 4 n 0 0 0	-27673	- M 4 W N O C	0 ¢ / 3 0 ×	001-1-2-20 201-1-2-20 *
						000				000	00
PAROTID: infiltration by histiocytic cells WADDIRNIAD: infiltration by histiocutic			c	0 0	o c		o c	о с 			<del>-</del> -
			» •	,	>	-	> 	> 	>	> 	-

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FINDINGS										
	MENT Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
SALIVARY GLAND:	(50)	(97)	(67)	(50)	(65)	(50)	(50)	(50)	(50)	(87)
PAROTID: dilated/cvstic duct(s)	0		0	0	0	0	0	0	-	0
MANDIBULAR; hyperplastic focus(i)	0	D	0	0	-	0	0	0	D	0
PAROTID: (ymphocytic infiltration	-	•	•	0	-	0	0	0	0	0
MAND1BULAR: perivasculitis	0	0	0	0	-	0	0	0	0	0
MANDIBULAR: inf(ammation	0	0	0	0	ö	-	0	Ð	0	-
SUBLINGUAL: acinar hypertrophy	0	0	0	0	0	0	0	0	0	<del>.</del>
PAROTID: ductal hyperplasia	0	0	ð	0	-	-	0	0	0	<b>+</b>
MANDIBULAR: ducta( hyperplasia	-	0	0	o	0	0	0	0	0	•••
MANDIBULAR: hyperplasia	-	0	0	¢	0	0	0	0	0	0
PAROTID: acinar atrophy	~	4	0	0	N	•	-	-	0	m
PAROTID: celtular alteration										
(Grade +/-)	4	4	æ	2		•	2	N	~	<u>س</u>
(Grade +)	ň	<u>بہ</u>	6	21***	-		ŝ	**6	**6	13***
(Grade ++)	0	0	4	***24	-		-	-	*	18***
(Grade +++)	0	0	0	0	0	0	0	0	-	~
Total incidence for score expanded	~	\$	21**	41**	36***	~	ø	12**	21***	38***
	,		•		(			•	,	•
(Grade +/)	_	~ 	10	_		_	•	'n		•
(Grade +)	-	•	12***	_	52***	\$	~	<del>م</del>	15	19*
(Grade ++)	0	0	0	0			0	0	N	-
Total incidence for score expanded	~	ŝ	22***	45***	31***	F	ß	12	18	26**
finding										

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TABLE 51 (continued)

			W	MALES					FENALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
SALIVARY GLAND:		(50)	(97)	(67)	(50)	(67)	(50)	(50)	(50)	(50)	(48)
Autolysed, diagnosis difficult		~	10	9	<u>ь</u>	9	~	м	t-	'n	<u>د</u>
SCIATIC NERVE:		(05)	(22)	(19)	(12)	(50)	(67)	(28)	(2)	(30)	(67)
Wo abnormality detected Infiltration by histiccytic cells Chronic inflammatory cell infiltrate Axonal degeneration Autolysed, diagnosis difficult	Q	40000	5000B	°00m0	<u></u>	40+M0	40000	000 	800-0 Noo-0		40000
SEMINAL VESICLES:		(2)	(2)	(2)	(2)	(2)					
No abnormality detected Serosal inflammation Haemorrhage(s)		0	000	000	- 0	000					
SKELETAL MUSCLE:		(50)	(22)	(19)	(1)	(50)	(05)	(27)	(2)	(30)	(05)
No abnormality detected Infiltration by histiocytic cells Focal lymphocytic infiltration Myositis		0-04	600 <sup>2</sup>	°000		5005	0000	0015	Å000	200%	<b>2</b> 000

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

			ε	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 4 mg/kg /day	Grp 5 1000 mg/kg /day
SKELETAL MUSCLE:		(50)	(25)	(19)	(21)	(50)	(50)	(27)	(29)	(30)	(50)
focal inflammatory cell infiltrate Myofibre degeneration Autolysed, diagnosis difficult	ate	040	000	0	000	- ~ 0	000		000	000	000
skin/subcutis:		(50)	(52)	(19)	(12)	(50)	(05)	(28)	(29)	(30)	(05)
No abnormality detected TRICHOEPITHELIOMA [N] BASAL CELL TUMOUR [N] SEBACEOUS CARCINOMA [N] SEBACEOUS CARCINOMA [N] SYMBAL'S GLAND: CARCINOMA [N] SQUAMOUS-CELL CARCINOMA [N] SARCOMA [N] SARCOMA [N] FIBROMA ANJ FIBROMA [B] FIBROMA [B] Dermal FIBROMA [B] LIPOMA [B] LIPOMA [B]		M0-0-0000-+->0N-			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	N=000=000N=M0N0	4000-0000-000	м 00000-000000000		ñoooooooo-ooo	M 4000000000000000000000000000000000000

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TABLE 51 (continued)

2     Grp 3     Grp 4     Grp 5     Grp 1     Grp 2     Grp 3       kg     mg/kg     mg/kg     mg/kg     mg/kg     mg/kg       y     /day     /day     /day     /day     /day       y     /day     /day     /day     /day     /day       y     /day     /day     /day     /day     /day       y     0     0     0     0       y     0     1     0     0       y     0     0     0     0		1									
US CORNIFYING EPITHELICMA 0 (25) (19) (21) (50) (50) (28) US CORNIFYING EPITHELICMA 0 0 0 1 0 0 0 0 US CORNIFYING EPITHELIOMA [B] 1 2 0 0 0 0 4 1 0 0 0 by histiocytic cells 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
ING EPITHELIOMA     0     0     0     0     0       ING EPITHELIOMA [B]     1     2     0     0     1     0       Cytic cells     0     1     0     0     0     0     0	// SUBCUTIS:	(50)	(25)	(19)	(12)	(50)	(50)	(28)	(29)	(30)	(50)
ING EPITHELIOMA [B] 1 2 0 0 4 1 cytic cells 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	US CORNIFYI	0		0	0	•••	0	0	•	0	0
	US CORNIEVING EPITHEILOMA	•	~	C	c	7		_	0	-	0
	sytic cells	- 0	0		·	0	0	• •	0	0	-
	bcutaneous pedema	0	-	0	0	0	0	•	•	0	0
	ithelial hyperplasia	c	••	00	o c	00	00		- c	0	<u> </u>
	flammation	∍	- 0			> m		0		- -	0
	baceous cyst(s)	0	0	0	0	-	0	0	0	0	0
	rmal cyst(s) cress(sc)			o <del>.</del>	o c	5					
gnosis difficult 0 1 0 0 0 0	gnosis di	• •	, <del>-</del>	- 0	» o	10	。 —	0	- 0	- 0	, o
4 3 2 2 4 4		*	۲۹ 	N	2	4	4	4	-	-	m
SPINAL CORD: (50) (25) (19) (21) (50) (50) (28) (29)	AL CORD:	(05)	(22)	(19)	(12)	(50)	(50)	(28)	(29)	(30)	(05)
25 19 19 46 50 27	) abnormality detected	49	25	19	19	46	50	27	29	29	50
a cells 0 0 0 2 0 0 0	a	0	0	0	2	0	0	0	0	0	•
	emorrhage(s)	0	0	0	-	•	<b>.</b>	<u> </u>	0	0	0
				0,	<b>-</b> -	4 C	-	c		- c	-
		⊃ +-		- 0	00	0	00	00	> 0	- -	c

			Ē	MALES					FEMALES		
FINDIKGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
SPINAL CORD:		(50)	(22)	(19)	(21)	(05)	(50)	(28)	(29)	(30)	(50)
Lumbar not examined		-	-	4	0	ю	0	0	2	9	4
SPLEEN:		(20)	(22)	(19)	(12)	(67)	(67)	(27)	(29)	(30)	(05)
No abnormality detected Haemangiosarcoma present Infiltration by histiocytic cells		\$000	2000		00-0	33	20-0	F000	n0-0	<u>م</u> وبر	°000
Infiltration by lymphoma cells Lymphoid depletion			000		0 0 0	-00	o ← ←	o <i>−</i> o	000	 	⊃ • •-
increased extramedullary haemopoiesis Inflammatory cell infiltrate	sis	50	~ 0	800	o -	00	58 92	• • •	f o	÷	- <del>1</del> 0
Chronic serosal inflammation			00	00	0	0,	00	00	00	0.	00
Small cyst(s)		• 0		0	10		0	0	>0	- 0	00
Congestion		<b>∩</b> 1 •	0	01	0	0	0	01	0	0	Ö
Increased brown pigment Autolvsed, diagnosis difficult		- 4	۳÷	'nνο	0 1	st M	¢ 10	~ -	2 10	v	₩ ₩
Infiltration by uterus tumour		0	0	0	0	0	0	-	0	• •	0

TABLE 51 (continued)

		*	MALES					FEMALES		
FLNDINGS	TREATMENT Grp 1 0 Mg/kg	l Grp 2 10 10 /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
STERNUM:	(20)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected Infiltration by histiccytic cells Infiltration by lymphoma cells Bone marrow hyperplasia Autolysed, diagnosis difficult		00003	60000	<u></u>	\$ <b>-</b> 000	0000 <sup>8</sup>	00775	60000	000-00	
STOMACH:	(50)	(23)	(15)	(18)	(50)	(48)	(27)	(27)	(2)	(47)
<pre>ko abnormality detected Dilated/cystic gland(s) Keratinised cyst(s) Ulceration in glandular region Ulceration in non-glandular region Perivasculitis Submucosal oedema in non-glandular r Mineralisation Inflammation Focal hyperplasia in non-glandular region Autolysed, diagnosis difficult</pre>	region 23 8 4 1 6 0 0 23 8 4 1 6 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	, , , , , , , , , , , , , , , , , , ,		<u>м</u> -00-0оми	8 K 0 0 7 N 0 0 M 0 M 0	M-00-0-0-004		N	<u>"</u> +000000+00N	<u> </u>

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						-					
			£	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
SUBMANDIBULAR LYMPH NODE:		(9)	(3)	(2)	(2)	(3)	(9)	÷	(†)	6	(12)
No abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells Reactive	Ø	0000	N000	-00-		+ <del>-</del>	NOTN		0N	000-	M00N
Congestion TESTES:		(50)	1 (25)	(1)	2 (21)	(20)	0	0	o 	0	N
No abnormality detected Unilateral focal interstitial cell		37 0	51	16 0	18,	35					
nyperplasia Bilateral focal interstitial cell hyperplasia	_	•	0	0		27					
Unitateral INTERSTITIAL-CELL ADENOMA Bilateral INTERSTITIAL-CELL ADENOMA	NOMA [B] OMA [B]	mo	- 0	00	00	0-					
INTERSTITIAL-CELL ADENOMA [B] Infiltration by histiocytic cells	υ		00	<u> </u>	00						
Only one examined		0	-	0	0	0					
Tubular atrophy		6	m	M	-	10					
Sperm granuloma Granuloma(ta)			••	<del>-</del> -	0	00					
Perivasculitis		- ~-	0	0	0	) <del></del>					

TABLE 51 (continued)

FINDINGS TREATMENT		X	MALES					FEMALES		
N N N N N N N N N N N N N N N N N N N					1					
ESTES:	.T Grp 1 0 /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
	(50)	(25)	(19)	(21)	(50)					
Mineralisation Autolysed, diagnosis difficult	0-		- 0	~0						
THORAX:					£					
MESOTHELIOMA [M]					-	- R				
THYMUS:	(48)	(23)	(19)	(18)	(77)	(48)	(27)	(36)	(28)	(97)
Ko abnormality detected THYMOMA EBJ Infiltration by histiocytic cells Infiltration by leukaemic cells Infiltration by lymphoma cells Focal lymphoid hyperplasia Epithelial hyperplasia Haemorrhage(s) Perivascular fibrosis Cyst(s)			£0000000000	°000000-00000	Mon000	<sup>6</sup> 00000000000000	00000000000000000000000000000000000000	°-0000000000		Хасономоо <sup>20</sup>

FINDINGS	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
THYROIDS:	(50)	(21)	(11)	(21)	(47)	(50)	(27)	(29)	(29)	(4)
No abnormality detected	35	19	15	16	33	34	21	18	22	31
Unilateral FOLLICULAR CARCINOMA [M]	0	0	0	-	0	0	0	0	0	0
Unilateral FOLLICULAR ADENOMA [B]	0	0	0	-	2	- -	0	0	0	0
Unilateral focal follicular-cell hyperplasia	0	0	0	<del></del>	0	•	<b>.</b>	•	<b>.</b>	-
	0	0	0	0	•	0	o	0	0	0
Bilatera\ metastasising C-CELL CARCINOMA [M]	0	0	0	<del>-</del>	0	0	0	0	0	<u> </u>
Unilateral C-CELL ADENOMA MULTIPLE [B]	0	0	0	0	0	0	0	0	-	-
<	<u>م</u>	-	<b></b> -	2	~	9	-	-		9
Bilateral C-CELL ADENOMA [B]	0	0	0	0	-	2	0	0	-	_
	0	0	0	Ċ	-	0	<u> </u>		0	0
Unilateral focal c-cell hyperplasia	2	-	0	0	4	<u>ь</u>	4	•	-	5
		0	0	0	-1	-	-	0	-	0
Dilated/cystic follicle(s)	N	0	0	<b>0</b>	~ ~		0	m	4	\$
Only one examined	0	0	0	-	-	0	_		-	0
Diffuse c-cell hyperplasia	-	0	-	0	0	~	0	9	-	Ś
Lymphocytic infiltration	-	0	0	0	0	0	0	0	0	0
Perivasculitis	0	0	0	0	<del></del>	0	0	0	0	0
Bilateral diffuse follicular-cell	0	0	0	0	0	0	0	-	•	•
Autolysed, diagnosis difficult	7	9	~	Ð	'n	м	-	ы	0	<u>ل</u> م

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TABLE 51 (continued)

		   	E	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
THYROIDS:		(50)	(21)	(17)	(21)	(67)	(05)	(27)	(62)	(29)	(67)
Extra section(s) examined		ð	0	0	2	-	<b>.</b>	•	•	•	0
TONGUE:							<b></b>	£			
Epithelial hyperplasia								-			
TRACHEA:		(50)	(23)	(18)	(12)	(50)	(50)	(27)	(29)	(30)	(67)
No abnormality detected Inflammatory cell infiltrate Autolysed, diagnosis difficult Infiltration by thyroid tumour		\$0	0 0 0 5				0000	0005	0-05	M000	4040
URETER:					£						
Infiltration by lymphoma cells					-						
URINARY BLADDER:		(67)	(22)	(19)	(20)	(67)	(50)	(28)	(29)	(30)	(64)
No abnormality detected Urothelial hyperplasia		47	23	5	15	45	20	27	59	30	<b>7</b>
(Grade	Ŷ	0	0	•	Ö	-	0	•	0	0	0

,

TREATMENT         Grp         1         Grp         3         Grp         4         Grp         5         Grp         1         Grp         4         Grp         5         Grp         3         Grp         4         Grp         7												
BLADDER: elial hyperplasia elial hyperplasia (49) (20) (49) (50) (29) (30) (30) incidence for score expanded incidence for score expanded incidence for score expanded ophilic contents ascutitis ascutitis ophilic contents ascutitis ophilic contents ascutitis ophilic contents ascutitis ascutitis ascutitis ophilic contents ascutitis	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
elial hyperplasia       (Grade ++)       0       0       2       1       0       0       0       0         incidence for score expanded       0       0       0       2       1       0	JRINARY BLADDER:		(67)	(22)	(19)	(20)	(46)	(50)	(28)	(29)	(30)	(46)
Incidence for score expanded       0 <td< td=""><td></td><td></td><td>c</td><td>c</td><td>c</td><td>ŗ</td><td>c</td><td></td><td>-</td><td>-</td><td></td><td>C</td></td<>			c	c	c	ŗ	c		-	-		C
tration by lymphoma cells       0       0       1       0       0       0       0         ophilic contents       0       1       3       0<		<b>.</b> –	0	, o	0	5	~	0	0	• •	0	,0
ophilic contents       0       2       0       1       3       0	infiltration by lymphoma cells			0	0	-	0	0	0	0	0	0
ascutitis mmation rrhage(s) ation rrhage(s) ation ysed, diagnosis difficult ysed, diagnosis difficult tration by uterus tumour normality detected AL SARCOMA [M] at sising endometrial CARCINOMA [M] etrial ADENOMA [B] MULTIPLE [B] MULTIPLE [B]	Eosinophilic contents		•	~	0	-	m	0	0	0	0	0
mmation       2       0       1       3       0 </td <td>Perivasculitis</td> <td></td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>-</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td>	Perivasculitis		0	0	0	0	-	0	0	0	0	0
rnhage(s)       ation       0       <	Inflammation		~ ~	•		<b>m</b> ,	0	0	0	0 (	0 0	0 0
attration by uterus tumour       0       8       2       1       0	Haemorrhage(s) vilatotion			<b>-</b> -	⇒ ۲		- c			-	- c	20
tration by uterus tumour       0       0       0       1       0       0         normality detected       0       0       0       1       0       0       0         AL SARCOMA [M]       1       0       0       0       1       0 </td <td>Ultatation Autolveed diagnosis difficult</td> <td></td> <td></td> <td><b>&gt;</b> «</td> <td><u>ה</u> ה</td> <td>- c</td> <td>- c</td> <td>⊃ ~4</td> <td>&gt; -</td> <td>- -</td> <td></td> <td><u> </u></td>	Ultatation Autolveed diagnosis difficult			<b>&gt;</b> «	<u>ה</u> ה	- c	- c	⊃ ~4	> -	- -		<u> </u>
normality detected       (49) (28) (29) (30)         AL SARCOMA [M]       38 26 19 20         AL SARCOMA [M]       0 0 0         tasising endometrial CARCINOMA [M]       0 1         etrial ADENOMA [B]       0 0         MULTIPLE (B]       0 0	Infiltration by uterus tumour		0	, 0	. 0	- 0	0	0		0	0	10
CARCINOMA [M]	JTERUS:							(47)	(28)	(23)	(30)	(67)
CARCINOMA [M]	No abnormality detected							38	26	19	20	39
CARCINOMA [M]								0	0	0	-	0
								0	-	0	0	0
	Endometrial CARCINOMA [M]							0,	• •		2	<u>ه</u>
	Endometrial ADENOMA [8]									-	<b>-</b> -	
	PULIP MULIFIC [0] DAIVO FDI							- ົ		- c	<b>-</b> -	м с

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				-	INCIDENCE OF LESIONS (NUMERIC)	E OF LE	SNO1S	NUMERIC	~		
ı			R	MALES					FEMALES		
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 10 mg/kg /day	Grp 3 100 mg/kg /day	Grp 4 300 mg/kg /day	Grp 5 1000 mg/kg /day
UTERUS:							(67)	(28)	(29)	(30)	(67)
Infiltration by histiocytic cells Dilated/cystic gland(s) Pvometra	S						- 40		0 80 <del>-</del>	- 40	040
Myometrial hypertrophy Dilatation Autolysed, diagnosis difficult							0-m		010	0 m +-	- m -
VAGINA:									3		
No abnormality detected									-		
VASCULAR SYSTEM:		Ē	0	Ð		£			£		
HAEMANGIOMA [B] Haemangiosarcoma [m]		-0	-0	-0		0-			÷0		

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

TABLE 52

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## Glyphosate 104 Week Combined Chronic Feeding/Oncogenicity Study in Rats with 52 Week Interim Kill Incidence of Histological Findings up to Week 52: Males and Females Toxicity Study

		sur	SURVIVORS				DE	DECEDENTS			
FINDINGS	ATMENT Grp 1 0mg kg/day	g Grp 2 g 10mg y kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	
LIVER:	(15)	(15)	(15)	(15)	(15)			(2)		£	
Ko abnormality detected Basenbilic forusti)	2	м 	e	~ ~	m			-		0	
(Grade +/~)	0 	2	2	m	0			0		0	
Total incidence for score expanded finding Pale cell focus(i)	<b>.</b>	5	2	M	0			0		0	182
(Grade +/-) (Grade +++)	-0		₩- <del>-</del>	••	n□			00		00	
SCOP	• <del>-</del>		- N		m			0			
Clear cell focus(1)											
(Grade +/-) (Grade +)	m 0	- 0	~-		-0			00		00	Σ.
Total incidence for score expanded finding	м 	<del>.</del>	m	2	Ļ			0		0	
Periportal hepatocyte hypertrophy	•	0	0	Ģ	0			-		0	Ŀ
Spongiosis hepatis	-	0	0	<b>+</b>	0			0			در.
Focus(i) of anglectasis	-	0	0	0	0			0	·	0	
Focal cellular change with vascular changes	-	<del>.</del>	0	•	0			0		0	· · · ·
Foamy hepatocytes (bifurcation of median lobe)	۳ 	0	0	2	0			0		<b>.</b>	•
					_					÷	

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TABLE 52 (continued)

	1	i İ	SURV	SURVIVORS				DE	DECEDENTS		
FINDINGS	TREATMENT G	Grp 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 5 Grp 1 1000mg 0mg kg/day kg/day		Grp 2 Grp 3 10mg 10mg kg/day kg/day	Grp 4 300mg Kg/day	Grp 5 1000mg kg/day
LIVER:		(15)	(15)	(15)	(15)	(15)			(2)		5
Bile duct hyperplasia Vacuolation Increased Kupffer-cell pigmentation Necrosis Inflammatory change(s) Congestion		400000	~~~~~~	MMFF 0	N-0-40	4M00N0			000-00		
HEART:		(15)				(15)			(2)		Ð
No abnormality detected Cardiomyopathy		312				► 63			<del>-</del> -		-0
KIDNEYS:		(15)	(15)	(15)	(15)	(15)			6		£
No abnormality detected Nephropathy		2		*0	'n	9			0		-
(Grade (Grade (Grade	(-/+ (++		4100	* * - 0 -	*	4			00-		000
Total incidence for score expanded finding Basophilic tubules	ed	12	> <b>h</b>	5***	**	*			- <del>-</del> -	_	
(Grade +/-)	(-/+		ž	4	4	2			0		0

				MALES		SENCE OF	F LESION	: INCIDENCE OF LESIONS (NUMERIC	() III		
			SURV	SURVIVORS				DE	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 Grp 1 Grp 2 000 10000 000 10000 000 10000 000 100000 0000	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 1 Omg kg/day			Grp 4 300mg kg/day	Grp 5 1000mg kg/day
KIDNEYS:		(15)	(15)	(15)	(15)	(15)			Ē		Ê
Total incidence for score expanded finding	ded	-	۲ <b>א</b>	4	4	2			0		0
Tubular dilatation (Grade +/-) Total incidence for score expanded finding	+/-) ded	00		00	••				00		00
Urothelial hyperplasia Mineral deposit(s) Pyelitis Focus(i) of inflammation Cyst(s)		-0400	-00+0	-0000	0000-	N 0 N					
LUNGS:		(15)	(15)	(15)	(15)	(15)			(2)		Ð
No abnormality detected Alveolitis Area(s) of interstitial pneumonitis Focus(i) of increased alveolar	itis	10 N N N	0-00	ec – ω ιν	44-10	1004m			-0-0		-000
macropnages Focal inflammation Lymphoid tissue increase Medial hypertrophy		0-0	000	000	0 1 1	~~~			0-0		000

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and cach treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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	<b></b>		SURV	SURVIVORS				B	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 2 Grp 3 10mg 100mg kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
LUNGS:		(15)	(15)	(15)	(15)	(15)			(2)		6
focal mineral deposit(s) Agonal congestion		- 0	00	- 0	00	00			o <del>-</del>		00
SPLEEN:		(15)				(15)			(2)		Ð
No abnormality detected		5				15			2		-
ADRENALS:	<b></b> . ·	(15)				(15)			(2)		£
	(X	80M-		_		00100			N000		-000
degeneration/vascular dilatation Subcapsular pale cell focus(i) Focal subcapsular cellular change		7 5	-			<u>мо</u>			00		00
THYMUS:		(15)				(13)			Ð		£
No abnormality detected THYMONA(TA) [B] Increased atrophy		20 0 20 0				- - -			0-0		00F

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TABLE

		SUR	SURV I VORS				90	DECEDENTS	6	
FINDINGS	TREATMENT Grp 1 0mg kg/day		Grp 2 Grp 3 10mg 100mg kg/day kg/day	6rp 4 300mg kg/da)	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 2 Grp 3 10mg 100mg kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
TESTES:	(15)				(15)			(2)		:
No abnormality detected Interstitialcell ADENOMA [B] Tubular atrophy	30 <sup>12</sup>				5-1-2			N 0 D		-00
PROSTATE:	(15)			<u> </u>	(15)			(2)		Ð
No abnormality detected Inflammation	15				2 13					-0
SEMINAL VESICLES:										0
Secretion decreased										-
BRAIN:	(12)				(15)			(2)		(1)
No abnormality detected Fore-brain not available for examination	tion 7				15 8			20		-0
SPINAL CORD:	(15)				(15)			(2)	_	3
No abnormality detected	15				15			~		-

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TABLE

						UL LEGIURS		1117		
		SUR	SURVIVORS				DE	DECEDENTS		
FLNDINGS		Grp 1 Grp 2 Grp 3 0 0mg 10mg 100mg kg/day kg/day kg/day	Grp 3 100mg kg/day		Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 1 Grp 2 Grp 3 Dmg 10mg 100mg kg/day kg/day kg/day			srp 4 Grp 5 300mg 1000mg cg/day kg/day
SKELETAL MUSCLE:	(15)				(15)			(2)		£
Ko abnormality detected					15			5		
PANCREAS:	(15)				(15)			(2)		Ð
No abnormality detected Acinar atrophy Focal inflammation Pigment deposit(s)	Смио 				£044			00		-000
SALIVARY GLAND:	(15)	(15)	(15)	(15)	(15)			(2)		£
MANDIBULAR: NAD MANDIBULAR: celluíar alteration	15	15	14	10*	***			~		0
(Grade +) Total incidence for score expanded		00		* * 	12***			00		
PAROTID: NAD	14	15	**9	***£	***0			-		
PAROTID: celluiar alteration (crade +)			844	**8	~			-	_	- -
(Grade ++)	, o 	, -	) <del>.</del> -	, -≄ 	**^			. 0		00
	0	0	0					0		0
Total incidence for score expanded finding	0	•	9***	<u>-</u>	15***			-		0

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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TABLE 52 (continued)

				MALES	MALES : INCIDENCE OF LESIONS (NUMERIC)	ENCE OF	LESION	IS (NUME	RIC)		
			SURV	SURVIVORS				DE	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 1         Grp 2         Grp 3         Grp 4         Grp 5         Grp 7         Grp 3         Grp 4         Grp 5           0mg         10mg         100mg         300mg         1000mg         300mg         100mg         300mg         100mg           kg/day         kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
SALIVARY GLAND:		(15)	(15)	(15)	(15)	(15)			(2)		60
PAROTID: inflammation PAROTID: not examined histologically SUBLINGUAL: NAD SUBLINGUAL: not examined histologically	cally ogically	0-20	0 0 0 0 0	00 <b>~0</b>	4 0 <sup>2</sup> 0 4	0 7 0			OONO		00-0
SUBMANDIBULAR LYMPH NODE:		(1)									
Plasmacytosis		٢									
PITUITARY:		(15)				(15)			60		(1)
No abnormality detected GLIOMA [M] Myperplasia		201				507 <u>3</u>			-00		0-0
skin/subcutis:		(15)				(15)			(2)		(1)
No abnormality detected Area of ulceration with chronic, active inflammation	active	14				15			20		-0

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001</pre>

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	<u>i                                    </u>		SURV	SURVIVORS				B	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 Omg kg/day	Grp 2 Grp 3 10mg 100mg kg/day kg/day		Grp 4 300mg kg/day		Grp 1 0mg kg/day	Grp 5 Grp 1 Grp 2 Grp 3 1000mg 0mg 100mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
MAMMARY GLANDS:		(15)				(15)			(2)		E
No abnormality detected		٦.				15			2		-
URINARY BLADDER:		(15)			_	(15)			(2)		Ĵ
No abnormality detected		15				15			2		-
AORTA:		(15)			_	(15)			(2)		9
No abnormality detected		15				15			57		-
MESENTERIC LYMPH NODE:		(15)				(15)			(2)		£
No abnormality detected Increased macrophage aggregation Contains lymphosarcoma		60 <del>]</del> 5				-04		. <u> </u>	0		-00
THYROIDS:		(15)			_	(15)					£
No abnormatity detected Follicular Adenoma [B] C-Cell Adenoma [B]		0 F N				=0					-00
C-CELL ADENOMA [8] Diffuse c-cell hyperplasia		N -				- N		_			

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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		SUR	SURVIVURS				5	DECEDENIS		
FINDINGS	TREATMENT Grp 1 0mg kg/day	Grp 1         Grp 2         Grp 3         Grp 4         Grp 5         Grp 1         Grp 2         Grp 3         Grp 4         Grp 5           0mg         100mg         300mg         1000mg         1000mg         300mg         1000mg         300mg         1000mg           kg/day         kg/day <th>Grp 2 Grp 3 Grp 4 10mg 100mg 300mg kg/day kg/day kg/day</th> <th>Grp 4 300mg kg/day</th> <th>Grp 4 Grp 5 300mg 1000mg kg/day kg/day</th> <th>Grp 1 Omg kg/day</th> <th>Grp 2 10mg kg/day</th> <th>Grp 3 100mg kg/day</th> <th>Grp 4 300mg kg/day</th> <th>Grp 5 1000mg kg/day</th>	Grp 2 Grp 3 Grp 4 10mg 100mg 300mg kg/day kg/day kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 1 Omg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
THYROIDS:	(15)	   			(15)					÷
Dilated/cystic follicle(s)	2				-					0
PARATHYROIDS:	(14)				(14)			(2)		Ð
No abnormality detected Pale cell focus(i)					14			20		- 0
TRACHEA:	(15)				(15)			(2)		£
No abnormality detected	15				15			2		÷
OE SOPHAGUS :	(15)				(15)			(2)		£
No abnormality detected	15				15			N		
STOMACH:	(15)				(15)			(2)		£
No abnormality detected Dilated/cystic gland(s)	8~				4 11			0 7		00
Ulceration with inflammation/necrosis					0			0		-

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TABLE

			SUR/	SURV1 VORS				DE	DECEDENTS	ú	
FINDINGS	TREATMENT	Grp 1 Omg kg/day	Grp 1 Grp 2 Grp 3 0mg 10mg 100mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 2  Grp 3   10mg 100mg kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day
DUGDENUM:		(15)				(15)			£	. <u>.</u>	Ð
No abnormality detected		15				15			-		
JE JUNUM:		(15)				(15)			_		£
Ko abnormality detected		15				15					-
ILEUM:		(15)				(15)					£
No abnormality detected		15				15					-
CAECUM:		(15)				(15)					£
No abnormality detected		15				15					-
COLON:		(15)				(15)					£
No abnormality detected		15				15					-
RECTUM:		(15)				(15)			£		£
No abnormality detected		- 2				15			-		-

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				MALES	: INCI	MALES : INCIDENCE OF LESIONS (NUMERIC)	: LESION	IS (NUME	(SIC)		
	<u>!</u>		SURV	SURVI VORS		<u></u>		90	DECEDENTS		
FINDINGS	TREATMENT K	rp 1 0mg g/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 1         Grp 2         Grp 3         Grp 4         Grp 5         Grp 1         Grp 2         Grp 4         Grp 5           0mg         10mg         100mg         300mg         1000mg         300mg         1000mg         300mg         1000mg           kg/day         kg/day <th>Grp 1 Omg kg/day</th> <th>Grp 2 10mg kg/day</th> <th>Grp 3 100mg kg/day</th> <th>Grp 4 300mg kg/day</th> <th>Grp 5 1000mg kg/day</th>	Grp 1 Omg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
SCIATIC NERVE:		(15)				(15)			(2)		£
No abnormality detected		15				15			~		-
STERNUM:		(15)				(15)			(2)		£
No abnormality detected Fat vacuolation absent Bone marrow reactive Localised depressed haemopoiesis Contains histiocytic sarcoma		0-1004				000-t			00-0-		-0000
LYMPHORETICULAR/HAEMOPUIETIC TISSUE:						Ξ			£		
Metastasising HISTIOCYTIC SAREOMA(TA) [M] LYMPHOSARCOMA [M]	CHI O					o <del></del>			<del>-</del> 0		

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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TABLE	

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		ļ	SUR	SURVIVUKS				ĥ	DECEDENIS		
F I ND I NGS	TREATMENT	Grp 1 Omg kg/day		Grp 2 Grp 3 10mg 100mg kg/day kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 0mg kg/day		Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
LIVER:		(15)	(15)	(15)	(15)	(15)				(2)	
No abnormality detected		-	-	2	-	M	_		_		
HEPATOCELLULAR ADENOMA [8] Basophilic focusti)		-	0	0	0	0				0	
(Grade	(-/+	\$	~	2	\$	~				0	
(Grade +)		4		m	м	~				0	
(Grade	(++	~	2	0	2	0				0	
(Grade	(+++	-	-	-	0	0				0	
Total incidence for score expanded finding Pale cell focus(i)	pa	13	5	=	5	<u>م</u>		_		0	
(6rade +/-)	+/-)	m	-	~	4	•				0	
Total incidence for score expanded finding Clear cell focus(i)		ñ	-	N	4	~					
(Grade +/-)	(-/+	-	0	0	2			_		0	
Total incidence for score expanded finding	- pa	-	0	0	~					0	
Focal hepatocellular hypertrophy		-	-	-	0	0				0	
Periportal hepatocyte hypertrophy	Y	0	0	0	-	0				0	
Spongiosis hepatis	-	0	0	-	-	0				0	
Subcapsular dilated sinusoids		0	2	•	•	0	_			0	

(continued)
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TABLE

				L EMALE.	561 . 0	ז הבשרבי		FEMALES : INCLUENCE OF RESTONS (NUMERIC)	ובעורל		
			SURV	SURVIVORS				DE	DECEDENTS	5	
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 0mg 100mg 300mg 1000mg 0mg 100mg 700mg 100mg 300mg 100mg kg/day kg/day kg/day kg/day kg/day kg/day kg/day kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 100mg kg/day
LIVER:		(15)	(15)	(15)	(15)	(15)				(2)	
foamy hepatocytes (bifurcation of median	of median	ñ	ñ	4	N	-				0	
lobe) Increased Kupffer-cell pigmentation	ion		00	0 1	00	00				••	
inflammatory change(s) Hepatocytes contain red blood ceils (a	its (a	1.1.1.1	- N O	140	000		_			•	
tew) Diffuse mitotic increase Increased multinucleate giant-cell(s) Focal fibrosis	ll(s)	000	-0-	000	000	0-0				000	
KEART:		(15)				(15)				Ê	
No abnormality detected Cardiomyopathy		20				5 2				0-	
KIDNEYS:		(15)	(15)	(15)	(15)	(15)				£	
No abnormality detected		m	4	ŝ	9	£				-	
Nephilopaulty (Grade +/-) (Grade +)	(-/+	<u>ب</u>	<u>ال</u> ال	50	44	40				00	

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

TABLE 52 (continued)

		_		FEMALES	••	INCIDENCE C	OF LESTO	LESIONS (NUMERIC)	IERIC)		
	·		SURV	SURVIVORS			   	DE	DECEDENTS	5	
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 1 Grp 2 Grp 3 Omg 10mg 100mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 Grp 1 Omg 10mg 100mg 300mg 1000mg 0mg kg/day kg/day kg/day kg/day kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp Z Grp 3 Grp 4 Grp 5 10mg 100mg 300mg 1000mg kg/day kg/day kg/day kg/day	Grp 5 1000mg kg/day
KIDNEYS:		(15)	(15)	(15)	(15)	(15)				£	
Nephropathy (Grade ++) Total incidence for score expanded finding	(† p	00	<u>6</u> 9	οw	οv	*** P=				00	
Basophilic tubules (Grade +/- Total incidence for score expanded finding	(-/- Pi	00	00		2 2	00				••	
Tubular dilatation (Grade +/-) Total incidence for score expanded	(-/- Pi	00			00	00				00	
ringing Urothelial hyperplasia Unilateral pelvic dilatation Mineral deposit(s) Increased tubular pigment deposit(s) Cyst(s)	(s):	87-47	N0400	NONOO	N0-00	* * 000000				00000	
LUKGS:		(15)	(15)	(15)	(15)	(15)				Ē	
No abnormality detected Aiveolitis		80 N	¢0	æ−	~-	÷0				- 0	

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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(continued)
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TABLE

1			SUR	SURVI VORS					DECEDENTS		
FINDINGS	TREATMENT	Grp 1 Grp 2 0mg 10mg kg/day kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 3 Grp 4 Grp 5 100mg 300mg 1000m kg/day kg/day kg/da	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 1 0mg. kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 5 1000mg kg/da)
I'UNGS:		(15)	(15)	(15)	(15)	(15)				(1)	
Area(s) of interstitial pneumonitis Focus(i) of increased alveolar	м	61	-4	<del>ر</del> ا	-~	m <del>-</del>				00	
macropnages Focal inflammation Eccol switholicition		00		• •	c	00				00	
rocat epitheriation Lymphoid fissue increase Medial hypertrophy Focat mineral deposit(s)		0000	-000	-0-							
SPLEEN:		(15)				(15)				Ð	
No abnormality detected Increased haemosiderin Increased extramedullary haemopoiesis	sis	0 0 15				2 × 0				00 <b>-</b>	
ADREWALS:		(15)				(15)				<del>(</del> 1)	
No abnormality detected PHAEOCHROMOCYTOMA [B] Cortical CARCINOMA [M]		<del>ار</del> بر ا				400				-00	
Unilateral cellular change (cortex)	0	-				2				0	

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			SUR	SURVIVORS			   	B	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 Omg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day		Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 1 Omg kg/day	Grp 2 10mg kg/day	l Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
ADREWALS:		(15)				(15)				Ê	
Unilateral cellular change with		0				2				0	
degeneration/vascular dilatation Subcapsular pale cell focus(i) Haemorrhagic degeneration		0 భ				~ O				00	
THYMUS:		(15)				(15)				£	
No abnormality detected Epithelial hyperplasia Cystic duct(s) Increased atrophy		∞ <i>-∿-</i>			<u>_</u>	2007				-000	
OVARIES:		(15)		_		(15)				£	
No abnormality detected		4				-7				0	
Absence of recent corpus luteum Interstitial tissue increased		÷-								00	
Follicular cyst(s) Cyst(s)		2-				~-				-0	

TABLE 52 (continued)

	i											
			SUR	SURVI VORS				DE	DECEDENTS			
FINDINGS	TREATMENT	Grp 1 Omg kg/day	Grp 2 Grp 3 Grp 4 Grp 5 10mg 100mg 300mg 1000mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	15 ¥	'P 2 GrP 3 10mg 100mg 1/day kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	
UTERUS:		(15)				(15)				(2)		
No abnormality detected		<b>8</b> 0 ×				<u>с</u> и				2 0		
Dilatation in both horns						n 0						
Focal squamous metaplasia Glandular epitheliai hyperplasia Focal endometrial hyperplasia Glandular abscess(es)		0-0-				-0-0			-	0000		
BRAIN:		(15)				(15)				(2)		
No abnormality detected Compression by pituitary Fore-brain not available for examination	minatíon	15 10				0***	_			NDD		
SPINAL CORD:		(15)				(15)				(2)		
No abnormality detected		15				15				N		Ĺ
SKELETAL MUSCLE:		(15)				(15)				(2)		DK-1 E
No abnormality detected		15				15				2		

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(continued)
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TABLE

	4-										
			SUR	SURVIVORS				D	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 2 Grp 3 10mg 100mg kg/day kg/day	Grp 3 100mg kg/day	Grp 3 Grp 4 Grp 5 100mg 300mg 1000mg kg/day kg/day kg/day	Grp 5 1000mg kg/day	Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 Omg 10mg 100mg 300mg 1000mg 0mg 10mg 100mg 300mg 1000mg kg/day kg/day kg/day kg/day kg/day kg/day kg/day kg/day kg/day	Grp 2 Grp 3 10mg 100mg kg/day kg/day	P 2 Grp 3 10mg 100mg 1/day kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 5 1000mg kg/day
PANCREAS:		(15)				(15)				6)	
No abnormality detected Acinar atrophy		÷0				2 13				- 0	
SALIVARY GLAND:		(15)	(15)	(15)	(15)	(15)				£	
MANDIBULAR: NAD MANDIBULAR: cellular alteration		15	15	15	15	8**	_				
(Grade +) Total incidence for score expanded		00	00	00	00	**^				00	
finding Parotid: Nad		15	14	13	7**	1 * * *				 	
lular alterat				ſ	+	1				c	
(Grade +)		- -		<b>v</b> 0	, 						
(Grade +++)	-		. 0	0	0	. –				0	
Total incidence for score expanded		0	0	N	* * 60	*** 71				0	
PAROTID: not examined histologically	- -	•	-	0	0	0	_			ò	
SUBLINGUAL: NAD		ñ	ň	£	1	ñ				-	
SUBLINGUAL: not examined histologically	cally	0	2	~	2	0				0	

TABLE 52 (continued)

					• {			LESIUNS (NUMERIC)	שבעזר <i>ו</i>		
			SUR	SURVI VORS				B	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 0mg kg/day	Grp 1 Grp 2 Grp 3 0mg 100mg 100mg kg/day kg/day kg/day kg/day kg/day	Grp 3 100mg kg/day	6rp 4 300mg kg/day	Grp 4 Grp 5 300mg 1000mg kg/day kg/day	Grp 5 Grp 1 Grp 2 Grp 3 Grp 4 1000mg 0mg 100mg 300mg 300mg kg/day kg/day kg/day kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
SUBMANDIBULAR LYMPH NODE:										(1)	
React i ve										-	
PITUITARY:		(15)			<u> </u>	(14)				(2)	
No abnormality detected Anterior lobe ADENOMA [B] Hyperplasia Focal mineral deposit(s) Intermediate lobe cyst(s)		<sup>2</sup> mnoo				₽ <sub>NN</sub> ++				~~~~	
SKIN/SUBCUTIS:		(15)				(15)		_		(2)	
No abnormality detected Large abscess(es)		- <del>-</del>				15	-			<del>-</del> -	
MAMMARY GLANDS:		(15)				(15)				(2)	
No abnormality detected Intraductal CARCINOMA [M] Focal hyperplasia Dilated/cystic duct(s)		9444				Noom				NOOO	

TABLE 52 (continued)

		SAUVIVAUS					DECEDENTS		
F IND INGS	TREATMENT Grp 1 Om kg/da)	 Grp 2 Grp 3 10mg 100mg kg/day kg/day	Grp 4 300mg kg/day	Grp 4 Grp 5 Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 300mg 1000mg 0mg 10mg 300mg 100mg kg/day kg/day kg/day kg/day kg/day kg/day	Grp 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg y kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
MAMMARY GLANDS:	(15)	ļ 		(15)				(2)	
Aiveolar development	-			0				0	
URINARY BLADDER:	(15)	 		(15)		_		£	
No abnormality detected	-15	 		15				<del></del>	
ADRTA:	(12)			(15)				(2)	
No abnormality detected	15	 		15				2	
MESENTERIC LYMPH NODE:	(12)			(15)				(2)	
No abnormality detected Congestion	14	 		15				N 0	
THYROIDS:	(15)	 		(15)				£	
Ko abnormality detected C-CELL ADENOMA [B]		 		10				<del>-</del> 0	
Unilateral focal c-cell hyperpiasia Diffuse c-cell hyperpiasia	- ~	 	_	0.4				00	
Dilated/cystic follicle(s)		 		~				0	_

IRI 438623

continued)
22
TABLE

				FEMALE	S : INCI	DENCE	FEMALES : INCIDENCE OF LESIONS (NUMERIC)	NN) SNO	HERIC)		
			SURV	SURVIVORS	1			B	DECEDENTS		
FINDINGS	TREATMENT	Grp 1 6mg kg/day	Grp 1 Grp 2 Grp 3 Grp 4 Ong 10mg 300mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day	Grp 1 Omg kg/day	Grp 2 10mg kg/day	srp 4 Grp 5 Grp 1 Grp 2 Grp 3 Grp 4 Grp 5 300mg 1000mg 0mg 0mg 100mg 300mg 1000mg kg/day kg/day kg/day kg/day kg/day kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
PARATHYROIDS:		(14)				(12)				(2)	
No abnormality detected		14				12				2	
TRACHEA:		(15)				(15)				£	
No abnormality detected		15				15				-	
OESOPHAGUS:		(15)				(15)				(2)	
No abnormality detected		15				15				Ŋ	
STOMACH:		(15)				(15)				Ð	
No abnormality detected Dilated/cystic gland(s)		0× 40				14				-0	
DUODENUM:		(15)	<u> </u>			(15)				(1)	
No abnormality detected		15				15				٢	
JEJUNUM:		(15)				(15)				0	
No abnormality detected		15				15				۰۰	

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test between control and each treatment group: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

ontinued)	
S	
22	
31.5	
TAB	

			SURV	SURVIVORS				DE	DECEDENTS		
F IND INGS	TREATMENT	Grp 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day		Grp 1 Omg kg/day	Grp 5 Grp 1 Grp 2 1000mg 0mg 10mg kg/day kg/day kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
ILEUM:		(15)				(15)				(1)	
No abnormality detected		15				15				-	
CAECUM:		(15)				(15)				3	
No abnormality detected		15				15				-	
COLON:		(15)				(15)				6	
No abnormality detected		15				5				-	
RECTUM:		(15)				(15)				3	
No abnormality detected		15				15				-	
SCIATIC NERVE:		(15)			_	(15)				(2)	
Wo abnormality detected		15				15				2	
STERNUM:		(15)				(15)				(2)	
No abnormality detected		15				15				7	



# RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

contd.

TABLE 48

COMBINED CHRONIC TOXICITY AND CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN WISTAR RATS

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR DEAD AND MORIBUND SACRIFICED ANIMALS

Number in (): No.of Tissues evaluated/group -

		Sex		MALE	LE			E4	FEMALE	
1		Group No.	G1	G2	G3	G4	<u>G1</u>		G3	64
H	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rate	50	50	50	50	50	50	50	50
		examined	30	30	32	21	26	24	17	29
Have-	SALIVARY GLAND	AND	(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
27	ESOPHAGUS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
з.	STOMACH Adenocarcinoma	Jma 	(30)	0 ( 0E )	(32) 1	(21) 0	(26) 0	(24) 0	(17) 0	(29)
4.	DUODENUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
ъ.	ILEUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
.9	COLON		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(28)
7.	PANCREAS Islet cell adenoma Cholangio-carcinom Undifferentiated S Histiocytic sarcom	PANCREAS Islet cell adenoma Cholangio-carcinoma-metastatic Undifferentiated Sacrcoma metastatic Histiocytic sarcoma metastatic	(28) 1 0 0	(30) 1 0 0	(32) 0 1 0	(20) 0 0 0	(26) 0 1 1 0	(23) 0 0 0 0	(16) 0 0 0 0	(28) 0 0 0 0 0
.8	LIVER Cholangiocarcinoma Hepatocellular adenoma	ccinoma Lar adenoma	(30) 0 9	(30) 2 9	(32) 2 6	(21) 2 6	(26) 1 2	(23) 0	(17) 0	(29) (29)

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### RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

qui	Number in (): No.of Tissues	.of Tissues evaluated/group	đ					Ref	Ref.App. 1	160-167
		Sex		MALE	CE				FEMALE	
		Group No.	G1	G2	G3	G4	G1	62	63	64
H	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rate	50	50	50	50	50	50	50	50
		examined	30	30	32	21	26	24	17	29
	LIVER contd.		(30)	(30)	(32)	(11)	1961	1261	1611	1007
	Hepatocellul	Hepatocellular carcinoma	12	10	σ	/+ u/	1041	1-21	() + C	( 27 )
	Intrahepatic bile duct	bile duct adenoma			n C	nc	ť C	+ C	N C	nc
	Histiocytic sarcoma		5	0	0	)	o –	0 0		0 0
	Tumour emboli	-1	0	0	I H	-	łC	0 0		0 0
	Fibrosarcoma		0	1	0	0	0	00	00	00
.6	LUNGS		(30)	(30)	(32)	(21)	(26)	1.241	1217	
	Adenoma		0	0	0		) C	(=)		104
	Histiocytic	Histiocytic sarcoma-metastatic	Г	0	1	1	) –	+ C		o c
	Cholangiocar	Cholangiocarcinoma-metastatic	0	T	0	0	0	0 0	0 0	
	Hepatocellul	Hepatocellular carcinoma- metastatic	0	1	0	1	0	0	0 0	o c
	Bronchio alv	Bronchio alveolar adenoma	0	0	0	0	0	0	. –	0 0
	Squamous cel	Squamous cell carcinoma-metastatic	1	0	0	0	0	0		o c
	Giant cell tumour	umour	0	0	0	1	0	0	0	C
	Fibroma		0	0	0	0	0	Г	C	
	Round cell s	Round cell sarcoma metastatic	0	0	0	0	0	0	) <del>[</del>	0
10.	TRACHEA .		(53)	(30)	(32)	(21)	(26)	(24)	(17)	(29)

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Defendant's Exhibit 2570\_0122



# RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

	Number in (): No.of Tissues	of Tissues evaluated/group	đn					Ref	Ref.App. 1	160-167
		Sex		MALE	LE				FEMALE	i       
		Group No.	G1	G2	G3	G4	G1	G2	63	64
H	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
		examined	30	30	32	21	26	24	17	29
i.	HEART		(30)	(30)	(32)	(21)	(26)	1241	1211	1601
	Histiocytic Round cell	Histiocytic sarcoma-metastatic Round cell carcoms of nericardium	c	00	, -	) - c	00	00	0	0
				2	D	c	Э	þ	н	0
12.	AORTA		(16)	(30)	(32)	(21)	(20)	(24)	(17)	(12)
13.	SPLEEN		(30)	(30)	(32)	(21)	(26)	(24)	(11)	1901
	Cholangioca	Cholangiocarcinoma-metastatic	0	Г	0	0	0	0	0	0
14.		MESENTERIC LYMPH NODES	(27)	(26)	(31)	(21)	(23)	(20)	(17)	(28)
15.		MEDIASTINAL LYMPH NODE	(28)	(28)	(30)	(20)	(26)	(22)	(16)	1667
	Histiocytic	Histiocytic sarcoma-metastatic	н і	0	Ч	0	Ч	0	0	0
	Hepatocellu	CHOIANGIOCAICINOMA-METASTATIC Hepatocellular carcinoma-metastatic	э с	-	00	0 0		0 0	0 0	0
	Giant cell tumour	tumour	00	+ 0	0 0	C				5 0
	Histiocyctic sarcoma	.c sarcoma	0	0	0	4 <del>- 1</del>	00	00	00	00
16.	MANDIBULAR LYMPH NODE	LYMPH NODE	(29)	(29)	(32)	(21)	(26)	(24)	(17)	(29)

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Defendant's Exhibit 2570\_0123



# **RALLIS RESEARCH CENTRE** Peenya, Bangalore - 560 058.

mbe	Number in (): No.ol	No.of Tissues evaluated/group	roup					Ref	Ref.App. 1	160-167
		Sex		MALE				- H	FEMALE	       
		Group No.	<u>61</u>	G2	G3	G4	<u>G1</u>		G3	G4
LT	TISSUE AND	Dose (ppm)	0	100		10000	0	100	1000	10000
O	OBSERVATION	No.of rats	50	50	50	50	50	50	50	50
		examined	30	30	32	21	26	24	17	29
17.	KIDNEYS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
	Cholangio care	carcinoma-metastatic	0	, L	0	0	0	0	0	0
	Histiosarcoma metastat	metastatic	0	0	ч	0	0	0	0	0
18.	URINARY BLADDER	ER	(27)	(30)	(32)	(20)	(26)	(24)	(16)	(28)
	Transitional d	cell Carcinoma	0	0	0	0	0	0	0	, L
19.	TESTES		(30)	(30)	(31)	(21)	NA	NA	NA	NA
	Leydig cell tumour	umour	0	0	2	0	NA	NA	NA	NA
	Seminoma		0	0	1	0	NA	NA	NA	NA
20.	EPIDIDYMES		(30)	( 30 )	(32)	(21)	NA	NA		NA
	Undifferentiated	ted sarcoma	0	0	1	0	NA	NA	NA	NA
21.	PROSTATE		(28)	(30)	(31)	(21)	NA	NA	NA	NA
22.	SEMINAL VESICLES	LES	(29)	(30)	(31)	(21)	NA	NA	NA	NA
23.		LANDS	(28)	(26)	(31)	(21)	NA	NA	NA	NA
24.	OVARIES		NA	NA	NA	NA	(25)	(24)	(17)	(29)

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TABLE 48 contd.

# RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

contd.

qu	Number in (): No.of Tissues	.of Tissues evaluated/group	dn				Ref.A	Ref	Ref.App. 1	p. 160-167
		Sex		MALE	LE				FEMALE	
Ê		Group No.	<u>G1</u>	G2	G3	G4	G1		G3	G4
- (	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
S	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
		examined	30	30	32	21	26	24	17	29
25.	UTERUS		NA	NA	NA	NA	(26)	1.241		1001
	Adenocarcinoma	oma	NA	NA	NA	NA	20	1	1, + 1	(27)
	Anaplastic c	carcinoma	NA	NA	NA	NA	0	, –	I C	о с
	Leiomyosarcoma	oma	NA	NA	NA	NA	0	0	00	- 1
26.	VAGINA		NA	NA	NA		(26)	(24)	(17)	(29)
27.	BRAIN Squamous cell	ll carcinoma-metastatic	(30)	(30)	(32)	(21) 1	(26) 0	(24) (0	(17)	(29)
28.	IDS ell	adenoma	(26) 0	(26) 0	(29) 1	(21) 0	(26) 0	(24) 0	(17) (17)	(27)
29.	PARATHYROIDS		(4)	(2)	(2)	(7)	(3)	(2)	(3)	(1)
30.	PITUITARY Adenocarcinoma Adenoma	oma	(29) 0 2	(27) 1 2	(30) (30) 3	(20) 0 1	 (25) 5	(22) 0 8	(16) (16) 0	(29) (29)

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Number in (): No.of Tissues	of Tissues evaluated/group	dnoıb/pa					Ref	Ref.App. 1	160-167
	Sex			MALE				FEMALE	
	Group No.	G1	G2	G3	G4	<u>G1</u>	G2	63	64
TISSUE AND	-	0	100	1000	10000	0	100	1000	10000
OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
	examined	30	30	32	21	26	24	17	29
		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(53)
Cortical cel	cell adenoma	0	0	0	0		0	, T	0
Preochromocytoma	.toma	د	m	4	4	0	0	0	2
32. EYES		(30)	(30)	(30)	(21)	(25)	(23)	(17)	(29)
33. BONE MARROW	(SMEAR)	(27)	(28)	(28)	(21)	(21)	(23)	(17)	(26)
34. SKIN 		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(28)
35. NASAL PASSAGE	ш	(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
36. TONGUE		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
37. THYMUS Thymoma		(28) 0	(29)	(31)	(20) 0	(24) 0	(24) 1	(16) 0	(28) 0
38. MUSCLE FEMORAL	AL	(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
39. SPINAL CORD		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)

RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

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ber in (): No.of Tissues evalu	Number in (): No.of Tissues evaluated/group						Ref.Ar	0.	160-167
	Sex			MALE				1	
TISSUE AND	Group No. Dose (ppm)	61	G2 100	G3 1000	G4	<u>G1</u>		63	64
OBSERVATION							TOO	1000	10000
	No.of rats	2	D n	00	Dc	0 9	50	50	50
	examined	30	30	32	21	26	24	17	29
40. SCIATIC NERVES	RVES	(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
41. PREPUTIAL GLANDS	GLANDS	(30)	(30)	(32)	(21)			NA	NA
42. MAMMARY GLAND	AND		NA	NA		(23)	(22)	(16)	1801
Adenoma		NA	NA	NA	NA	1		104	(0.4)
Adenocarcinoma	noma	NA	NA	NA	NA	2	0	0	0
43. JEJUNUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
44. CECUM		(30)	(29)	(32)	(21)	(26)	(24)	(17)	(29)
45. RECTUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
46. TUMOUR/MASS Squamous ce Histiocytic	TUMOUR/MASS Squamous cell carcinoma Histiocytic sarcoma-metastatic	( 30) ( 30)	(30)	(31) (1)	(21) 0	(26) 0	(24) 0	(17)	(29)
Cholangiocarcinom Giant cell tumour	Cholangiocarcinoma-metastatic Giant cell tumour	00	0 0 0	000	+ 0 -	- H C	000	o o c	000

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# RALLIS RESEARCH CENTRE Peenya, Bangalore - 560 058.

(29)

(11)

(24)

(26)

(21)

(32)

(0E)

(30)

LYMPH NODE (OTHERS)

52.

53. PELVIC CAVITY

1

1

(29)

(11)

(24)

(21)

(32)

(0E)

									SACALF LCED AN IMALS
Number in (): No.of Tissues	of Tissues evaluated/group	dno					Ref	Ref.App. 1	160-167
	Sex		MA	MALE			[4       	FEMALE	
	Group No.	G1	G2	G3	G4	<u>G1</u>	G2	G3	G4
TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
	examined	30	30	32	21	26	24	17	29
47. OPTIC NERVES		(27)	(27)	(25)	(20)	(22)	(21)	(16)	(27)
48. BONE (FEMUR) WITH JOIN Histiocytic sarcoma-me	BONE (FEMUR) WITH JOINT Histlocytic sarcoma-metastatic	(29)	(30)	(31)	(21) 0	(26) (26)	(24)	(17)	(28)
49. TAIL		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
50. MESENTRY		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
51. STERNUM Histiocytic	STERNUM Histiocytic sarcoma-metastatic	(29) 1	(29)	(30)	(21) 0	(26) (26)	(24) 0	(17)	(29)

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Defendant's Exhibit 2570\_0128



qu	Number In (); NO.OI IISBUES		42246/2					чет	r .444.194	9/1-891
		Sex			MALE			I.I.	FEMALE	
		Group No.	61	G2	G3	G4	G1		G3	G4
H	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
		examined	20	20	18	29	24	26	32	21
	SALIVARY GLAND	AND	(20)			(29)	(24)	(1)		1101
	Duct papilloma	oma		T	I	0	0		I	0
	ESOPHAGUS		(20)		1	(29)	(24)	   	1	(21)
э.	STOMACH		(20)	(1)		(29)	(24)			1167
	Papilloma-forestomach	orestomach	0	Ч	1	0	0	I.	Ĩ	П
	DUODENUM		(20)			(29)	(24)		1	(21)
С	ILEUM		(20)	1		(29)	(24)	(1)		(21)
6.	COLON		(20)	1		(29)	(24)	1		(21)
7.	PANCREAS		(20)			(29)	(24)	i       		1101
	Islet cell adenoma	adenoma	2	1	1		0	1	I	( <del>-</del> - )
	Lymphosarco	Lymphosarcoma metastatic	1	1	ı	0	0	I	I	10
8.	LIVER		(20)	(20)	(16)	(29)	(24)	(25)	1681	1101
	Cholangiocarcinoma	rcinoma	. –	1	0	, L	0	0		172
	Hepatocellular adenoma	lar adenoma	15	13	4	15	16	01	у Г	α

**RALLIS RESEARCH CENTRE** Peenya, Bangalore - 560 058.

COMBINED CHRONIC TOXICITY AND CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN WISTAR RATS

	SUMMAKY (	OF HISTOPATHOLOGICAL (NEOPI	(NEOPLASTIC)	FINDINGS	NGS FOR	R TERMINALLY		SACRIFICED	ANIMALS	
mber	in (): No	Number in (): No.of Tissues evaluated/group	d.					Ref	Ref.App. 1	168-175
		Sex		MALE	LE			E4       	FEMALE	
TISS	TTSSIIE AND	Group No. Dose (nnm)	61 0	G2 1001	63 1000	G4	G1	G2	63	64
OBSE	OBSERVATION		50	50	20	20 10000	50	50 100	50 50	10000
		examined	20	20	18	29	24	26	32	21
8. LI	LIVER contd		(20)	(20)	(16)	(29)	(24)	(25)	(32)	(21)
He	Hepatocellular	lar carcinoma	6	16	6	19	9	11	12	4
II	itrahepati	Intrahepatic bile duct adenoma	Ч	0	0	0	0	T	0	0
H	Histiocytic	sarcoma	0	Ч	Ч	0	0	0	i m	c
μ	Tumour emboli	li	Ч	0	1	0	0	0	0	0
5	Lymphosarcoma	ma	Г	0	0	0	0	0	0	0 0
Be	Benign mixed	d intra-	0	0	Г	0	0	0	0	c
h.	hepatic bile	e duct adenoma								
9. LI	LUNGS		(20)	(4)	(3)	(29)	1241		151	1101
Bı	conchio-al	Bronchio-alveolar adenocarcinoma	0	0	Ъ	0	0	0		1
Η¢	spatocellu	Hepatocellular carcinoma- metastatic	0	0	1	0	0	0	0	00
B1	Bronchio al'	alveolar adenoma	0	0	0	0	1	0	0	R/ Pe
ΞI	Histiocytic	sarcoma	0	0	0	0	0	0	ı.	eny.
10. TH	TRACHEA		(20)	1	1	(29)	(24)	(1)		(218
Ηİ	istiocytic	Histiocytic sarcoma-metastatic	0	I	1	0	, o	ļЧ	ï	ingal O
11. HI	HEART		(20)			(29)	(24)	(1)	(1)	ARC 121
Ξ	Histiocytic	sarcoma-metastatic	o	I	1	0	0	, L	ц	H 56

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contd. 

	SUMMARY	SUMMARY OF HISTOPATHOLOGICAL	(NEOPLASTIC)	FINDINGS	NGS FOR	R TERMINALLY	20-12	SACRIFICED	ANIMALS	5
umb	Number in (): No.of Tissues	.of Tissues evaluated/group	l/group					Ref	Ref.App.	168-175
		Sex		MA	MALE				FEMALE	
		Group No.	G1	G2	G3	G4	<u>G1</u>	G2	G3	G4
2	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
			20	20	18	29	24	26	32	21
12.	12. AORTA		(20)		1	(29)	(24)	1		(21)
13.			(20)		(3)	(29)	(24)	1	(2)	(21)
14.	MESENTERIC LYMPH NODES Histiocyctic sarcoma	LYMPH NODES C sarcoma	(20) 1	тt		(29) 0	(22) 0	111	1 1 1	(21)
15.	15. MEDIASTINAL LYMPH NODE Histiocyctic sarcoma	LYMPH NODE c sarcoma	(19) (19)	(1)	11	(29) 0	(22) 0	1	1 1 1	(21) 0
16.	. MANDIBULAR LYMPH NODE Lymphoma	LYMPH NODE	(19) 0	( 6 ) 0	(5) 0	(29) 2	(24) 0	(6)	(9) 0	(21)
17.	17. KIDNEYS Lymphosarcoma	ma	(20) 0	(3)	(2)	(29) 0	(24) 0	1 1	(1) 1	(21) 0
18.	. URINARY BLADDER	DDER	(20)			(29)	(23)		1	(20)
1 1 1							i			

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COMBINED CHRONIC TOXICITY AND CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN WISTAR RATS

TABLE 49 contd.

#### (21) Ref.App. 168-175 (21) contd. NA NA G4 10000 50 21 NA NA 1000 NA NA SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS (11) 22) 22 10 G3 1000 NA NA NA NA FEMALE 50 32 NA (10) (10) G2 50 50 26 NA NA NA NA NA 0 10 (24) (24) 0 0 0 G1 50 NA NA NA NA 24 NA 1 1 1 (29) (29) (28) (29) 10000 (29) 29 NA NA NA NA NA G4 1000 18 NA NA NA GB 50 (1) NA (1) (1) 1 1 MALE 100 NA NA NA NA NA 20 G2 (2) NA (1) 1 1 1 (18) (11) (20) (19) (19) NA NA NA NA 50 NA 0 20 61 Number in (): No.of Tissues evaluated/group No.of rats No.of rats No. Dose (ppm) examined Group Leydig cell tumour COAGULATING GLANDS Sex Adenoma papillary SEMINAL VESICLES Adenocarcinoma EPIDIDYMES Hemangioma OBSERVATION PROSTATE TISSUE AND OVARIES Adenoma UTERUS TESTES 21. 22. 23. 24. 25. 19. 20.

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nbe	r in (): No	Number in (): No.of Tissues evaluated/group	dr					Ref	Ref.App. 1	168-175
				MA	MALE				FEMALE	
Ě			Gl	G2	G3	G4	G1	G2	G3	G4
T	TISSUE AND		0	100	1000	10000	0	100	1000	10000
S	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50.
		examined	20	20	18	29	24	26	32	21
26.	BRAIN		(20)			(62)	1961			
	Pituitary a	Pituitary adenocarcinoma metastatic	0	1	Î	0	1.1	I	1	(17)
27.	THYROIDS		(19)	1		(29)	(24)			(20)
		adenoma	7	1	ī	1	2	1	1	, L
28.	PARATHYROIDS	DS	(5)		1	(29)	(9)			(3)
29.	PITUITARY		(20)	(3)	(1)	(29)	(24)	(11)	(1)	(21)
	Adenocarcinoma	noma	0	0	0	0	, T	0	0	0
	Аделота		1	7	0	4	2	5	4	1
30.	ADRENALS		(20)	(3)	(4)	(29)	(24)	(4)		1101
	Cortical C(	Cortical cell adenoma	Ч	0	Ч	0	0	ò	2	1+21
	Pheochromocytoma	cytoma	9	2	2	12	1		4	
	Malignant 1	'Malignant Pheochromocytoma	0	0	г	1	0	00	• 0	4 0
31.	EYES		(20)	(3)	(4)	(29)	(24)	(3)	(7)	(21)
32.	BONE MARROW (SMEAR)	W (SMEAR)	(19)			(29)	(21)	1		(19)
33.	SKIN		(20)		1.	(29)	(24)	(4)	(0)	1101

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	•	Sex		MA	MALE				FEMALE	
		0	Gl	G2	G3	G4	<u>G1</u>	G2	G3	G4
EH	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
0	OBSERVATION	No.of rats No.of rats	50	50	50	50	50	50	50	50
İ		examined	20	20	18	29	24	26	32	21
34.	THYMUS		(20)		1	(29)	(24)	1		110)
	Thymoma		o	ı	ſ	0	Ч	I	I	110
35.	MUSCLE FEMORAL	RAL	(20)		1	(29)	(24)		1	(21)
36.	SPINAL CORD		(20)		1	(29)	(24)	1		(21)
37.	0.000	JES	(20)		ī	(29)	(23)			(20)
38.	PREPUTIAL GLANDS	LANDS	(20)		1	(29)		NA		
39.	MAMMARY GLAND Adenoma	СГ ДХ	 NA NA	NA	NA NA		(17) (17)	(8)	(17)	(20)
	Adenocarcinoma	oma	NA	NA	NA	NA	- H	10	0	4 0
40.	JEJUNUM		(20)	I	T	(29)	(24)	1		(21)
41.	CECUM Histiocytic sarcoma	sarcoma	(20) 0	(1) 1	11	(29) 0	(24) 0	1 1		(21) (21)
42.	RECTUM		(20)			(29)	(24)			(21)

COMBINED CHRONIC TOXICITY AND CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN WISTAR RATS

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Y TYVIIIIO	SUMMARY OF HISTOPATHOLOGICAL	(NEOPLASTIC)	FINDINGS	NGS FOR	R TERMINALLY		SACRIFICED	ANIMALS	S
Number in (): No.of Tissues	of Tissues evaluated/group	/droup					Ref	Ref.App.	168-175
	Sex		MA	MALE				FEMALE	
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBSERVATION	No.of rats	50	50	50	50	50	50	50	50
	examined	20	20	18	29	24	26	32	21
43. TUMOUR/MASS		(20)	(2)	(3)	(29)	(24)	(4)		
Fibroma		0	Ч	Ē	0				
Undifferenti	Undifferentiated sarcoma	0	0	0	0	<b>н</b> н	00	00	00
44. OPTIC NERVES		(16)			(29)	(23)	(1)		(18)
45. BONE (FEMUR) WITH JOIN	TNIOL HTIW	(20)		.	(29)	(24)		1	(21)
46. MESENTERY		(20)			(29)	(24)		(1)	(21)
47. STERNUM		(20)			(29)	(24)	1	1	(21)
48. LYMPH NODE (OTHERS)		(20)	(1)		(29)	(24)		1	(21)
49. PELVIC CAVITY	X	(20)			1901				

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# Tumor Incidence

	ECT ID TES: A	D: 1231 ALL	GROI	JP: Oppm		SEX: MALE		DAYS:	ALL
ID	DAYS I	TISSUE (	OF ORIGIN		$\mathbf{T}^{\dagger}$	UMOR TYPE			PETO
4029	727 I	TESTES			в	SEMINOMA			1
4043	681 M	AMMARY	GLAND		В	FIBROADENOM	IA.		1
			Total Anima Total Prima Total Anima Total Anima Total Benig Total Malig Avg. DAYS o Animal	ary Tumors: als with Tu als with Mu gn: gnant: gnant with	ltij Meta	ple Tumors: astasis:	50 2 0 2 0 0 704		

# Tumor Incidence

	ECT ID TES: A	D: 1231 ALL	GROI	JP: Oppm		SEX: MALE		DAYS:	ALL
ID	DAYS I	TISSUE (	OF ORIGIN		$\mathbf{T}^{\dagger}$	UMOR TYPE			PETO
4029	727 I	TESTES			в	SEMINOMA			1
4043	681 M	AMMARY	GLAND		В	FIBROADENOM	IA.		1
			Total Anima Total Prima Total Anima Total Anima Total Benig Total Malig Avg. DAYS o Animal	ary Tumors: als with Tu als with Mu gn: gnant: gnant with	ltij Meta	ple Tumors: astasis:	50 2 0 2 0 0 704		

Tumor Incidence

	JECT ID: 1231 GROUP ATES: ALL	P: Oppm SEX: FEMALE DAYS: AL	L
ID	DAYS TISSUE OF ORIGIN	TUMOR TYPE	PETO
4054	728 MAMMARY GLAND	B ADENOMA	2
4055	627 MAMMARY GLAND	B ADENOMA	1
4058	728 MAMMARY GLAND	B CYSTADENOMA	1
4063	643 MAMMARY GLAND	M ADENOCARCINOMA	2
4067	472 MAMMARY GLAND	B FIBROADENOMA	2
4068	728 SKIN	B SUBCUT.TISSUE,FIBROMA,HAI	RD 1
4070	550 SKIN	B SUBCUT.TISSUE,FIBROMA,HAI	RD 2
4074	728 MAMMARY GLAND	B ADENOMA	1
4076	633 MAMMARY GLAND	B PAPILLARY ADENOMA	1
4085	489 MAMMARY GLAND	B FIBROADENOMA	2
4092	729 MAMMARY GLAND	B ADENOMA	2
4095	683 MAMMARY GLAND	B FIBROADENOMA	2
4099	402 MAMMARY GLAND	B FIBROADENOMA	2

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Tumor Incidence

PROJECT ID: 1231 FATES: ALL	GROUP: 0ppm	SEX: FEMALE	DAYS: ALL
ID DAYS TISSUE OF (	DRIGIN	TUMOR TYPE	PETO
Tot Tot Tot	cal Animals/Group: cal Primary Tumors: cal Animals with Tun cal Animals with Mu cal Benign:		

Total Malignant: Total Malignant with Metastasis:

Animals with Tumors:

Avg. DAYS on Test for

455

626

1 0

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Tumor Incidence

PROJECT ID: 1231 GROUP: 3000ppm FATES: ALL	SEX: MALE DAYS: ALL
ID DAYS TISSUE OF ORIGIN	TUMOR TYPE PETO
4107 729 TESTES	B INTERSTITIAL CELL TUMOUR 1
4108 637 MAMMARY GLAND	B FIBROADENOMA 1
4115 578 MAMMARY GLAND	B ADENOMA 2
4143 730 MAMMARY GLAND	B FIBROADENOMA 2
LUNGS +	C HEPATOCELLULAR CARCINOMA 4 LYMPHOMA MALIGNANT LYMPHOCYTIC LYMPHOMA MALIGNANT LYMPHOCYTIC LYMPHOMA MALIGNANT LYMPHOCYTIC
Total Animals/Group: Total Primary Tumors: Total Animals with Tur Total Animals with Mul Total Animals with Mul	ltiple Tumors: 0

Total Animals with Multiple Tumors:0Total Benign:4Total Malignant:1Total Malignant with Metastasis:1Avg. DAYS on Test for<br/>Animals with Tumors:590

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THUNDE THETHENE	Tumor	Incidence
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PROJECT ID: 1231 FATES: ALL	GROUP: 3	3000pm	SEX: FEMALE	DAYS: ALL
ID DAYS TISSUE O	FORIGIN	TU	MOR TYPE	PETO
4161 577 MAMMARY	GLAND	В	FIBROADENOMA	2
4165 730 MAMMARY	GLAND	В	ADENOMA	2
4170 730 MAMMARY	GLAND	В	ADENOMA	1
4178 450 MAMMARY	GLAND	В	PAPILLARY ADENOR	MA 1
4179 637 MAMMARY (	GLAND	В	ADENOMA	1
4181 730 OVARIES		В	ADENOMA	1
4183 556 MAMMARY (	GLAND	В	ADENOMA	2
4188 686 MAMMARY (	GLAND	В	ADENOMA	1

Total Animals/Group:	50
Total Primary Tumors:	8
Total Animals with Tumors:	8
Total Animals with Multiple Tumors:	0
Total Benign:	8
Total Malignant:	0
Total Malignant with Metastasis:	0
Avg. DAYS on Test for	
Animals with Tumors:	637

Tumor Incidence

	JECT ATES :	ID: 1231 ALL		GROUP :	15000ppm		SEX: MALE DAYS: AL	L
ID	DAYS	TISSUE (	OF ORIG	JIN		 T'	UMOR TYPE	PETO
4221	731	MAMMARY	GLAND	-		в	ADENOMA	1
4241	733	TESTES				в	INTERSTITIAL CELL TUMOUR	1
4242	733	SKIN				В	SUBCUT. TISSUE, LIPOMA	2
4244	733	TESTES				В	INTERSTITIAL CELL TUMOUR	1
4245	627	SKIN				В	SUBCUT. TISSUE, FIBROMA	1
			Total Total Total Total Total Total	Animals Animals Benign: Malignar Malignar	Tumors: with Tum with Mul	tij eta	ple Tumors: 0 5 0	

Avg. DAYS on Test for Animals with Tumors:

711

Tumor Incidence

	JECT ID: 123 ATES: ALL	31	GROUP:	15000ppm	SEX: F	EMALE	DAYS: AL	L
ID	DAYS TISSU	E OF ORIG	JIN	T	UMOR TYP	E		PETO
4257	582 MAMMAI	RY GLAND		В	FIBROAD	ENOMA		1
4262	590 MAMMAR	RY GLAND		В	FIBROAD	ENOMA		1
4273	733 SKIN			В	SUBCUT.	TISSUE,	FIBROMA	2
4281	372 MAMMAR	RY GLAND		В	ADENÔMA			1
4285	733 MAMMAF	RY GLAND		В	FIBROAD	ENOMA		1
4290	493 MAMMAR	RY GLAND		. <b>B</b> .	ADENOMA			1
4296	734 MAMMAR	RY GLAND		$\mathbf{B}$	FIBROAD	ENOMA		2
4300	734 MAMMAF	RY GLAND		В	FIBROAD	ENOMA		1
		Total Total Total Total Total Avg. D	Primary Animals Animals Benign: Malignar Malignar AYS on 5	/Group: Tumors: with Tumor with Multi nt: nt with Met Test for	ple Tumon astasis:	8 . 0		

Animals with Tumors: 621

459

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Tumor Incidence

PROJECT ID: 1231	GROUP:	25000ppm	SEX:	MALE	DAYS:	ALL
FATES: ALL	x					

ID DAYS TISSUE OF ORIGIN

TUMOR TYPE

PETO

Total Animals/Group: Total Primary Tumors:	50 0
Total Animals with Tumors:	0
Total Animals with Multiple Tumors:	0
Total Benign:	0
Total Malignant:	0
Total Malignant with Metastasis:	0
Avg. DAYS on Test for	
Animals with Tumors:	0

Tumor Incidence

	JECT ATES:	ID: 1231 ALL		GROUP:	25000ppr	n	SEX: FEMALE	DAYS: AL	Ĺ
ID	DAYS	TISSUE (	OF ORI	GIN		T	JMOR TYPE		PETO
4351	735	MAMMARY	GLAND			в	FIBROADENOMA		1
4352	735	MAMMARY	GLAND			в	FIBROADENOMA		2
4354	402	MAMMARY	GLAND			В	FIBROADENOMA		1
4378	468	SKIN				В	ACANTHOMA		1
4392	708	MAMMARY	GLAND			В	FIBROADENOMA		1
4393	500	MAMMARY	GLAND			в	FIBROADENOMA		1
				Animals, Primary			50 6		

Total Animals/Group:	50				
Total Primary Tumors:	6				
Total Animals with Tumors:	6				
Total Animals with Multiple Tumors:	0				
Total Benign:	6				
Total Malignant:	0				
Total Malignant with Metastasis:					
Avg. DAYS on Test for					
Animals with Tumors:	591				

461

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Summary Tumor Incidence

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PROJECT ID: 1231 DAYS: ALL	FATES: ALL SEX: MALE			
GROUP :	0ppm	3000ppm	15000ppm	25000ppm
	#	#	#	#
Total Animals/Group	50	50	50	50
Total Primary Tumors	2	5	5	0
Total Animals with Tumors	2	5	5	0
Total Animals w/ Multiple Tumor	s 0	0	0	0
Total Benign	2	4	5	0
Total Malignant	0	1	0	0
Total Malignant with Metastasis	0	1	0	0

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Summary Tumor Incidence

	FATES: ALL SEX: FEMALE Oppm	3000ppm	15000ppm	25000ppm
	#	#	#	#
Total Animals/Group	# 50	# 50	# 50	# 50
Total Primary Tumors	13	8	8	6
Total Animals with Tumors	13	8	8	6
Total Animals w/ Multiple Tumors	0	0	0	0
Total Benign	12	8	8	6
Total Malignant	1	0	0	0
Total Malignant with Metastasis	0	0	0	0

### Selected Animals

GROUP : Oppm 3000ppm 15000ppm 25000ppm SEX : MALE MALE MALE MALE MALE MALE No. of ANIMALS : 50 50 50 50 4029 4107 4221 4043 4108 4241 4115 4242 4150 4245 4150 4245 4150 4245 The above animals have at least one of the following findings. * Findings selected are : LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LVMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LVMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUECUT. TISSUE, FIEROMA	SEX :         MALE         MALE         MALE         MALE         MALE         MALE         MALE           NO. Of ANIMALS :         50         50         50         50         50           4029         4107         4221           4043         4241            4043         4108         4241           4115         4242             4150         4245           4150         4245            * Findings selected are :           4150         4245            LIVER:         HEPATOCELLULAR CARCINOMA               SPLEEN:         LYMPHOMA MALIGNANT LYMPHOCYTIC               LINGS:         LYMPH NODE:		DAYS : ALL FINDINGS : * S			
No. of ANIMALS :         50         50         50         50           4029         4107         4221            4043         4108         4241             4115         4242             4113         4244             4150         4245             4150         4245            The above animals have at least one of the following findings.             * Findings selected are :              LIVER:         HEPATOCELLULAR CARCINOMA             SPLEEN:         LYMPHOMA MALIGNANT LYMPHOCYTIC             MUNGS:         LYMPHOMA MALIGNANT LYMPHOCYTIC	No. of ANIMALS : 50 50 50 50 4029 4107 4221 4043 4108 4241 4115 4242 4150 4245 The above animals have at least one of the following findings. * Findings selected are : LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUECUT. TISSUE, FIBROMA					
4043       4108       4241           4115       4242           4150       4245           4150       4245          The above animals have at least one of the following findings.           * Findings selected are :            LIVER:            HEPATOCELLULAR CARCINOMA            SPLEEN:            LUNGS:            MES. LYMPH NODE:           LYMPHOMA MALIGNANT LYMPHOCYTIC           MES. LYMPH NODE:           LYMPHOMA MALIGNANT LYMPHOCYTIC           TESTES:       INTERSTITIAL CELL TUMOUR	404341084241411542424163424441504245The above animals have at least one of the following findings.* Findings selected are :LIVER:HEPATOCELLULAR CARCINOMASPLEEN:LYMPHOMA MALIGNANT LYMPHOCYTICLINGS:LIMPHOMA MALIGNANT LYMPHOCYTICMES. LYMPH NODE:LIMPHOMA MALIGNANT LYMPHOCYTICTESTES:INTERSTITIAL CELL TUMOURSEMINOMASKIN:SUECUT. TISSUE, FIBROMA					
4043       4108       4241           4115       4242           4150       4245           4150       4245          The above animals have at least one of the following findings.           * Findings selected are :            LIVER:            HEPATOCELLULAR CARCINOMA            SPLEEN:            LUNGS:            MES. LYMPH NODE:           LYMPHOMA MALIGNANT LYMPHOCYTIC           MES. LYMPH NODE:           LYMPHOMA MALIGNANT LYMPHOCYTIC           TESTES:       INTERSTITIAL CELL TUMOUR	404341084241411542424163424441504245The above animals have at least one of the following findings.* Findings selected are :LIVER:HEPATOCELLULAR CARCINOMASPLEEN:LYMPHOMA MALIGNANT LYMPHOCYTICLINGS:LIMPHOMA MALIGNANT LYMPHOCYTICMES. LYMPH NODE:LIMPHOMA MALIGNANT LYMPHOCYTICTESTES:INTERSTITIAL CELL TUMOURSEMINOMASKIN:SUECUT. TISSUE, FIBROMA			4321		
<pre> 4115 4242  4143 424  4150 4245 The above animals have at least one of the following findings. * Findings selected are : LIVER: HEFATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA</pre>	<pre> 4115 424 4143 424 4150 4245 The above animals have at least one of the following findings. * Findings selected are : LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUECUT. TISSUE, FIBROMA</pre>					
4143 4244   4150 4245    The above animals have at least one of the following findings. * Findings selected are :   LIVER:   HEPATOCELLULAR CARCINOMA   SPLEEN:   LYMPHOMA MALIGNANT LYMPHOCYTIC   MES. LYMPH NODE:   LYMPHOMA MALIGNANT LYMPHOCYTIC   TESTES:   INTERSTITIAL CELL TUMOUR   SKIN:	4143 4244   4150 4245    The above animals have at least one of the following findings. * Findings selected are :   * Findings selected are :   LIVER:   HEPATOCELLULAR CARCINOMA   SPLEEN:   LYMPHOMA MALIGNANT LYMPHOCYTIC   MES. LYMPH NODE:   LYMPHOMA MALIGNANT LYMPHOCYTIC   TESTES:   INTERSTITIAL CELL TUMOUR   SKIN:   SUECUT. TISSUE, FIBROMA					
4150 4245 The above animals have at least one of the following findings. * Findings selected are : LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE; LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	4150       4245          The above animals have at least one of the following findings.          * Findings selected are :          LIVER:          HEPATOCELLULAR CARCINOMA          SPLEEN:          LYMPHOMA MALIGNANT LYMPHOCYTIC          MES. LYMPH NODE:          LYMPHOMA MALIGNANT LYMPHOCYTIC					
<pre>* Findings selected are : LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:</pre>	<ul> <li>* Findings selected are :</li> <li>LIVER: HEPATOCELLULAR CARCINOMA</li> <li>SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC</li> <li>LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC</li> <li>MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC</li> <li>TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA</li> <li>SKIN: SUBCUT. TISSUE, FIBROMA</li> </ul>					
LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	he above animals have at least	one of the fol.	lowing findin	ngs.	
LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LIVER: HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	Findings selected are :		· · · ·	· ·	
HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	HEPATOCELLULAR CARCINOMA SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA					
SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA			· .	5.	
SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	SPLEEN: LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	HEPATOCELLULAR CARCINOMA				
LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LYMPHOMA MALIGNANT LYMPHOCYTIC LUNGS: LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	SPLEEN:				
LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA		2	1 <u>.</u>		
LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LYMPHOMA MALIGNANT LYMPHOCYTIC MES. LYMPH NODE: LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	LUNGS :				
LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	LYMPHOMA MALIGNANT LYMPHOCYTIC TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	LYMPHOMA MALIGNANT LYMPHOCYTIC	2			
TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	TESTES: INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	MES. LYMPH NODE:				
INTERSTITIAL CELL TUMOUR SEMINOMA SKIN:	INTERSTITIAL CELL TUMOUR SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	LYMPHOMA MALIGNANT LYMPHOCYTIC	2			
SEMINOMA SKIN:	SEMINOMA SKIN: SUBCUT. TISSUE, FIBROMA	TESTES :				
SKIN:	SKIN: SUBCUT. TISSUE, FIBROMA	INTERSTITIAL CELL TUMOUR				
	SUBCUT. TISSUE, FIBROMA	SEMINOMA				
SUBCUT. TISSUE, FIBROMA		SKIN:				
	SUBCUT. TISSUE, LIPOMA	SUBCUT. TISSUE, FIBROMA				
SUBCUT. TISSUE, LIPOMA		SUBCUT. TISSUE, LIPOMA				
MAMMARY GLAND:	MAMMARY GLAND:	MAMMARY GLAND:				
ADENOMA						
FIBROADENOMA	FIBROADENOMA	FIBROADENOMA				

		-	EXCEL II GLYPHOSA	-FEB-199 NDUSTRIE ATE TECH ABLE - 2	ES LTD. INICAL	465
			Peto Sco	ore Stat	istics	
PROJECT I TISSUE : FINDING :		LULAR C	ARCINOM		ALL ATES : ALL	
			FATA	AL TUMOF	?:::::::::::::::::::::::::::::::::::::	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	
1M: Oppm	47	0.00	0	0.24	-0.24	

2M: 3000ppm	49	3000.00	1	0.26	0.74
3M: 15000ppm	49	\$15000.00	0	0.26	-0.26
4M: 25000ppm	47	\$25000.00	0	0.24	-0.24

3000.00 1

T Value : -7713.542

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#### NON-FATAL TUMORS

Group	Number of	Dose	Observed	Expected	Observed	
	Animals	Level			- Expected	
					a far a star	
1M: Oppm	47	0.00	0	0.00	0.00	
2M: 3000ppm	49	3000.00	0	0.00	0.00	
3M: 15000ppm	49	<b>%15000.00</b>	0	0.00	0.00	
4M: 25000ppm	47	\$25000.00	0	0.00	0.00	•

T Value : 0

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#### TOTAL TUMORS \_\_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: Oppm	47	0.00	0	0.24	-0.24	0.00
2M: 3000ppm	49	3000.00	1	0.26	0.74	3.92
3M: 15000ppm	49	<b>%15000.00</b>	0	0.26	-0.26	0.00
4M: 25000ppm	47	\$25000.00	0	0.24	-0.24	0.00

T Value : %-7713.54200 Variance : %97933568.00000 Z Value : -0.77945 One Tailed Probability: 0.25000

Defendant's Exhibit 2570\_0149

	EXCEL IN GLYPHOSA	-FEB-1997 NDUSTRIES LTD. ATE TECHNICAL ABLE - Z	466				
	Peto Sco	ore Statistics					
PROJECT ID: 1231 TISSUE : SPLEEN FINDING : LYMPHOM	A MALIGNANT LYMPI	DAYS : ALL FATES : A HOCYTIC	LL				
FATAL TUMORS							
Group Number of	Dose Observed	Expected Observed					

	Animals	Level			- Expected
1M: Oppm	48	0.00	0	0.00	0.00
2M: 3000ppm	18	3000.00	0	0.00	0.00
3M: 15000ppm	21	\$15000.00	0	0.00	0.00
4M: 25000ppm	47	\$25000.00	0	0.00	0.00

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#### \_ \_ \_ \_ \_ \_ \_ \_ \_ \_ NON-FATAL TUMORS \_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected Observed	
1M: Oppm	48	0.00	0	0.00 0.00	
2M: 3000ppm	18	3000.00	0	0.00 0.00	
3M: 15000ppm	21	\$15000.00	0	0.00 0.00	
4M: 25000ppm	47	\$25000.00	0	0.00 0.00	

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T Value : 0

#### TOTAL TUMORS \_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: Oppm	48	0.00	0	0.00	0.00	1.00
2M: 3000ppm	18	3000.00	0	0.00	0.00	1.00
3M: 15000ppm	21	\$15000.00	0	0.00	0.00	1.00
4M: 25000ppm	47	<b>%25000.00</b>	0	0.00	0.00	1.00
		T Value :	0.00000			
		Variance :	0.00000			
		Z Value :	0.00000			

One Tailed Probability: 0.50000

Defendant's Exhibit 2570\_0150

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		467				
		F	eto Sco	ore Stat	istics	
PROJECT II TISSUE : 1 FINDING :	LUNGS	MALIGNAN	T LYMPI		ALL TES : ALL	
			FAT	AL TUMOR	S	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	·
	48 49	0.00 3000.00	0 0	0.00	0.00	
	49	\$15000.00	0	0.00	0.00	
4M: 25000ppm	47	<b>%25000.00</b>	0	0.00	0.00	
	T Va	alue : O				
			NON-F7	ATAL TUM	DRS	

Group	Number of	Dose	Observed	Expected	Observed
	Animals	Level			- Expected
1M: Oppm	48	0.00	0	0.00	0.00
2M: 3000ppm	49	3000.00	0	0.00	0.00
3M: 15000ppm	48	<b>%15000.00</b>	0	0.00	0.00
4M: 25000ppm	47	\$25000.00	0	0.00	0.00

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# TOTAL TUMORS

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Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: Oppm	48	0.00	0	0.00	0.00	1.00
2M: 3000ppm	49	3000.00	0	0.00	0.00	1.00
3M: 15000ppm	48	<b>%15</b> 000.00	0	0.00	0.00	1.00
4M: 25000ppm	47	<b>%25000.00</b>	0	0.00	0.00	1.00
		T Value :	0.00000			
		Variance :	0.00000			
		Z Value :	0.00000			
	One Tailed H	Probability:	0.50000			

	E : MES. LYMPH NODE FATES : ALL NG : LYMPHOMA MALIGNANT LYMPHOCYTIC FATAL TUMORS				468
	Peto Sco	ore Stati	stics		
PROJECT ID: 1231 TISSUE : MES. LYMPH NG FINDING : LYMPHOMA MA	-	FAT			
	FATA	L TUMORS			
Group Number of	Dose Observed	Expected	Observed		

	Animals	Level			- Expected
1M: Oppm	48	0.00	0	0.00	0.00
2M: 3000ppm	18	3000.00	0	0.00	0.00
3M: 15000ppm	21	\$15000.00	0	0.00	0.00
4M: 25000ppm	47	\$25000.00	0	0.00	0.00

# NON-FATAL TUMORS

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Group	Number of Animals	Dose Level	Observed	Expected Observed
1M: Oppm	48	0.00	0	0.00
2M: 3000ppm	18	3000.00	0	0.00 0.00
3M: 15000ppm	21	<b>%15000.00</b>	0	0.00 0.00
4M: 25000ppm	47	\$25000.00	0	0.00 0.00

T Value : 0

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#### TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: Oppm	48	0.00	0	0.00	0.00	1.00
2M: 3000ppm	18	3000.00	0	0.00	0.00	1.00
3M: 15000ppm	21	%15000.00	0	0.00	0.00	1.00
4M: 25000ppm	47	<b>%2</b> 5000.00	0	0.00	0.00	1.00
		T Value :	0.00000			
		Variance :	0.00000			
		Z Value :	0.00000			

One Tailed Probability: 0.50000

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15-FEB-1997 EXCEL INDUSTRIES LTD. GLYPHOSATE TECHNICAL TABLE - Z							469
		 E	Peto Sco	ore Stat	istics		
PROJECT II TISSUE : 7 FINDING :	TESTES	TIAL CELI	J TUMOUI		ALL TES : ALI		
			FAT	AL TUMOR	.S	<b></b>	
Group	Number of	Dose	Observed	Expected	Observed		
· · · · <b>E</b>	Animals	Level		·· <b>·</b>	- Expected		
1M: Oppm	48	0.00	0	0.00	0.00		
2M: 3000ppm	49	3000.00	0	0.00	0.00		
3M: 15000ppm	49	\$15000.00	0	0.00	0.00		
4M: 25000ppm	47	<b>%2</b> 5000.00	0	0.00	0.00		
	τV	alue : O					
			NON-FA	ATAL TUM	ORS		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	48	0.00	0	0.00	0.00		
2M: 3000ppm	49	3000.00	ĩ	0.36	0.64	. :	
3M: 15000ppm	49	\$15000.00	- 2	0.89	1.11	×	
4M: 25000ppm	47	\$25000.00	0	1.75	-1.75	10. -	
	T Va	alue : -25225.0	03				
			 ТОТ2	AL TUMOR	 S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1M: Oppm	48	0.00	0	0.00	0.00	1.00	
2M: 3000ppm	49	3000.00	1	0.36	0.64	2.79	
3M: 15000ppm	49	\$15000.00	2	0.89	1.11	2.25	
4M: 25000ppm	47	\$25000.00	0	1.75	-1.75	0.00	
		r Value : %-2	25225.02730				
	,	Variance : %11'	7651824.0000	00			
	:	Z Value : ·	-2.32559				
		bability:	0.01500				

		( 	EXCEL II SLYPHOS TZ	-FEB-199 NDUSTRIE ATE TECH ABLE - Z	S LTD. INICAL	470
		E	eto Sco	ore Stat		
PROJECT II TISSUE : T FINDING :	FESTES			DAYS : FA		
			FAT	AL TUMOR	S	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	· · ·
1M: Oppm	48	0.00	0	0.00	0.00	
2M: 3000ppm	49	3000.00	0	0.00	0.00	
3M: 15000ppm	49	<b>%</b> 15000.00	0	0.00	0.00	
4M: 25000ppm	47	<b>%2</b> 5000.00	0	0.00	0.00	
	T Va	lue : O				
			NON-F7	ATAL TUM		
Group	Number of	Dose	Observed	Expected		

Group	Number of	Dose	Observed	Expected	Observed	
	Animals	Level			- Expected	
1M: Oppm	48	0.00	1	0.27	0.73	
2M: 3000ppm	49	3000.00	0	0.26	-0.26	
3M: 15000ppm	49	\$15000.00	0	0.25	-0.25	
4M: 25000ppm	47	\$25000.00	0	0.21	-0.21	1841 - 18
	ту	alue : -9952.30	81	•••••		

T Value : -9952.381

#### TOTAL TUMORS )\_\_\_\_\_

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Group	Number of	Dose	Observed	Expected	Observed	ML	Value
	Animals	Level			- Expected		
1M: Oppm	48	0.00	1	0.27	0.73		3.71
2M: 3000ppm	49	3000.00	0	0.26	-0.26		0.00
3M: 15000ppm	49	<b>%15000.00</b>	0	0.25	-0.25		0.00
4M: 25000ppm	47	<b>%2</b> 5000.00	0	0.21	-0.21		0.00

T Value : %-9952.38090 Variance : %94378688.00000 Z Value : -1.02445 One Tailed Probability: 0.20000

			XCEL IN	-FEB-199 NDUSTRIE ATE TECH ABLE - Z	S LTD. NICAL	-	471
		F	eto Sco	ore Stat	istics		
PROJECT I TISSUE : FINDING :		TISSUE, F	IBROMA	DAYS : FA	ALL TES : ALL		
			FATZ	AL TUMOR	S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	48	0.00	0	0.00	0.00		
2M: 3000ppm	18	3000.00	0	0.00	0.00		
3M: 15000ppm	21	\$15000.00	0	0.00	0.00		
4M: 25000ppm	47	\$25000.00	0	0.00	0.00		
	T Va	alue : O					
			NON-FA	ATAL TUM	ORS		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	48	0.00	0	0.42	-0.42		

111. 022	10	0.00	0	v	
2M: 3000ppm	18	3000.00	0	0.07 -0.07	v E
3M: 15000ppm	21	\$15000.00	1	0.14 0.86	
4M: 25000ppm	47	\$25000.00	0	0.38 -0.38	•

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# TOTAL TUMORS

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Group	Number of	Dose	Observed	Expected	Observed	ML Value
	Animals	Level			- Expected	
1M: Oppm	48	0.00	0	0.42	-0.42	0.00
2M: 3000ppm	18	3000.00	0	0.07	-0.07	0.00
3M: 15000ppm	21	\$15000.00	1	0.14	0.86	7.38
4M: 25000ppm	47	\$25000.00	0	0.38	-0.38	0.00

T Value : 3375.00000 Variance : %130359392.00000 Z Value : 0.29560 One Tailed Probability: 0.40000

	472						
		E	Peto Sco	ore Stat	istics		
PROJECT I TISSUE : FINDING :		TISSUE, I	IPOMA	DAYS : FA	ALL TES : AL	L	
			FAT	AL TUMOR	.S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	48	0.00	0	0.00	0.00		
2M: 3000ppm	18	3000.00	0	0.00	0.00		
3M: 15000ppm	21	\$15000.00		0.00	0.00		
4M: 25000ppm	47	\$25000.00	0	0.00	0.00		
	т V	alue : O					
			NON-FA	ATAL TUM	ORS	<b></b>	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	48	0.00	0	0.00	0.00		
2M: 3000ppm	18	3000.00	0	0.00	0.00	23	
3M: 15000ppm	21	<b>%15000.00</b>	1	0.10	0.90		
4M: 25000ppm	47	\$25000.00	0	0.90	-0.90		
	TV	alue : -9000			andro andro Antonio antonio Antonio antonio Marca		
			TOTA	AL TUMOR	 S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1M: Oppm	48	0.00	0	0.00	0.00	1.00	
2M: 3000ppm	18	3000.00	0	0.00	0.00	1.00	
3M: 15000ppm	21	\$15000.00	1	0.10	0.90	10.00	
4M: 25000ppm	47	\$25000.00	0	0.90	-0.90	0.00	
		۲ Value : ۴-۶ Variance : ۴899					
	One Tailed Pro		3.00001				
		onahilitu.	0.00200				

15-FEB-1997 EXCEL INDUSTRIES LTD. GLYPHOSATE TECHNICAL TABLE - Z									473
		I	Peto Sco	ore Stat	istics				
TISSUE :	ID: 1231 : MAMMARY G : ADENOMA	LAND		DAYS : FA	ALL TES : AL				
			FAT	AL TUMOR	.S			·	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected				
1M: Opp	m 1	0.00	0	0.00	0.00				
2M: 3000ppr	m 3	3000.00	0	0.00	0.00				
3M: 15000ppr	m 1	\$15000.00	0	0.00	0.00				
4M: 25000ppi	m O	\$25000.00	0	0.00	0.00				
	τv	alue : O							
			NON-F2	ATAL TUM	ORS			· <b></b>	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected				
1M: Oppr	n 1	0.00	0	0.20	-0.20				
2M: 3000ppn		3000.00	1	0.60	0.40	х. <u>(</u>			
3M: 15000ppn		\$15000.00	1	1.20	-0.20				
4M: 25000ppn		\$25000.00	0	0.00	0.00				
	T V	alue : -1800.0	01						

#### TOTAL TUMORS

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Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: Oppm	1	0.00	0	0.20	-0.20	0.00
2M: 3000ppm	3	3000.00	1	0.60	0.40	1.67
3M: 15000ppm	1	\$15000.00	1	1.20	-0.20	0.83
4M: 25000ppm	0	<b>%25000.00</b>	0	0.00	0.00	1.00

T Value : %-1800.00085 Variance : %27360000.00000 Z Value : -0.34412 One Tailed Probability: 0.40000

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			EXCEL II GLYPHOS	-FEB-199 NDUSTRIE ATE TECH ABLE - Z	S LTD. NICAL		47
		 I	Peto Sco	ore Stat	istics		
PROJECT I TISSUE : 1 FINDING :	MAMMARY G			DAYS : FA	ALL TES : ALI	 C	
			FAT	AL TUMOR	S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1M: Oppm	1	0.00	0	0.00	0.00		
2M: 3000ppm	3	3000.00	0	0.00	0.00		
3M: 15000ppm	1	\$15000.00	0	0.00	0.00		
4M: 25000ppm	0	<b>%25000.00</b>	0	0.00	0.00		
	T V.	alue : O					
			NON-FA	ATAL TUM	ORS		
Group	Number of Animals	Dose	Observed	Expected	Observed - Expected		
	Animais	Level		1993 1997 - 1997 1997 - 1997	- Expected		
1M: Oppm	ı	0.00	1	0.58	0.42		
2M: 3000ppm	3	3000.00	2	1.33	0.67	4	
3M: 15000ppm	1	<b>%15000.00</b>	0	1.08	-1.08		
4M: 25000ppm	0	\$25000.00	0	0.00	0.00	under geheten. Na	
	T Va	alue : -14250		·			
- <b></b>			тот <i>и</i>	L TUMOR	 S		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1M: Oppm	1	0.00	1	0.58	0.42	1.71	
2M: 3000ppm	3	3000.00	2	1.33	0.67	1.50	
3M: 15000ppm	1	<b>%15000.00</b>	0	1.08	-1.08	0.00	
4M: 25000ppm	0	<b>%25000.00</b>	0	0.00	0.00	1.00	
		T Value : %-:					
	1	Variance : %11	1187504.0000	0			
	-	Z Value :	-1.35141				

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15-FEB	B-1997	
EXCEL INDUS	STRIES LTD.	
GLYPHOSATE	TECHNICAL	

TABLE - Z

	Fisher's Exact Statistics
PROJECT ID: 1231	DAYS : ALL
TISSUE : LIVER	FATES : ALL

\_ \_ \_ \_ \_ \_ \_ \_ \_ \_ \_

# FINDING : HEPATOCELLULAR CARCINOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
1M*	0	47	47								
2M	1	48	49	0.51042	1.00000	0.51042	1.02083	1.00000	?	0.969280	0.000439
ЗМ	0	49	49	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No	Chi Square
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No	Chi Square



1	5 - FEE	3-1997	
EXCEL	INDUS	STRIES	LTD.
GLYPHO	SATE	TECHNI	ICAL

TABLE - Z

Fisher's E	xact Statistics	

DAYS : ALL

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PROJECT ID: 1231 TISSUE : SPLEEN

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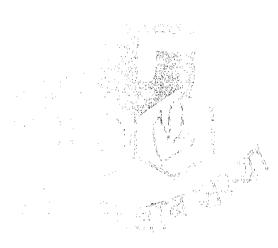
FATES : ALL

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FINDING : LYMPHOMA MALIGNANT LYMPHOCYTIC

	POS.	NEG.		ONE-TAILED	CONTROL > PROPORTION	CONTROL < PROPORTION	TWO-TAILED	PROBABILITY = OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME	CHI	SQUARE	YATES CORRE
1M*	0	48	48								
2M	1	17	18	0.27273	1.00000	0.27273	0.54545	0.27273	? 2.7	07692	0.264423
ЗМ	0	21	21	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Valu	les - No C	hi Square
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Valu	les - No C	hi Square



Defendant's Exhibit 2570\_0160

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_	LO-FER	3-1997	
EXCEL	INDUS	STRIES	LTD.
GLYPHO	SATE	TECHNI	[ CAL

TABLE - Z

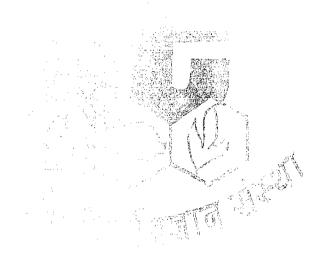
	Fisher's	Exact	Statistics
PROJECT ID:	1231	DAYS :	ALL

TISSUE : LUNGS

FATES : ALL

#### FINDING : LYMPHOMA MALIGNANT LYMPHOCYTIC

GRP	POS. RESP	NEG. RESP	TOTAL	ONE-TAILED PROBABILITY	CONTROL > PROPORTION TREATED	CONTROL < PROPORTION TREATED	TWO-TAILED PROBABILITY	PROBABILITY = OR MORE EXTREME	c	HI SQUARE	YATES CORRE
1M*	0	48	48								
2M	1	48	49	0.50515	1.00000	0.50515	1.01031	1.00000	?	0.989796	0.000107
3M	0	48	48	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No Ch	i Square
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No Ch	ni Square



	er's Exact Statistics	
PROJECT ID: 1231 TISSUE : MES. LYMPH NODE	DAYS : ALL FATES : ALL	
FINDING : LYMPHOMA MALIGNANT LY	YMPHOCYTIC	

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME	(	CHI SQUARE	YATES CORRE
											·
1M*	0	48	48								
2M	1	17	18	0.27273	1.00000	0.27273	0.54545	0.27273 ?	?	2.707692	0.264423
ЗМ	0	21	21	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No Ch	ni Square
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No Ch	ni Square

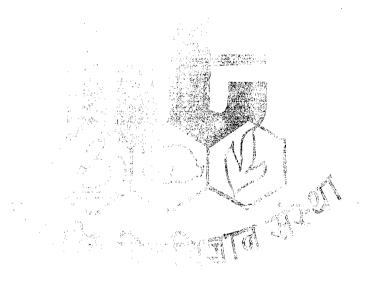


TABLE - Z

	Fisher's Exact Statistics
PROJECT ID: 1231	DAYS : ALL
TISSUE : TESTES	FATES : ALL

FINDING : INTERSTITIAL CELL TUMOUR

GRP	POS. RESP	NEG. RESP	TOTAL	ONE-TAILED PROBABILITY	CONTROL > PROPORTION TREATED	CONTROL < PROPORTION TREATED	TWO-TAILED PROBABILITY	PROBABILITY = OR MORE EXTREME		CHI SQUARE	YATES CORRE
1 <b>M</b> *	0	48	48								
2M	1	48	49	0.50515	1.00000	0.50515	1.01031	1.00000	?	0.989796	0.000107
ЗМ	2	47	49	0.25258	1.00000	0.25258	0.50515	0.49485	?	2.000430	0.489743
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	z	ero Values - No 🤇	Chi Square

#### FINDING : SEMINOMA

,

	POS.	NEG.		ONE-TAILED	CONTROL >	CONTROL < PROPORTION TWO-TAILED	PROBABILITY = OR MORE		
	P05.	MEG.		ONE-IAILED	PROPORTION	PROPORTION	= OK MORE		
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED PROBABILITY	EXTREME	CHI SQU	JARE YATES CORRE
1 <b>M*</b> .	1	47	48						
2M	0	49	49	0.49485	0.49485	1.00000 0.98969	. 0.49485	? 1.0314	67 0.000107
ЗМ	0	49	49	0.49485	0.49485	1.00000 0.98969	0.49485	? 1.0314	67 0.000107
4M	0	47	47	0.50526	0.50526	1.00000 1.01053	1,.00000	? 0.9895	0.000112
				•					
						and the second	El State		

TABLE - Z

	Fisher's Exact Statistics
PROJECT ID: 1231	DAYS : ALL
TISSUE : SKIN	FATES : ALL

FINDING : SUBCUT. TISSUE, FIBROMA

					CONTROL >	CONTROL <		PROBABILITY	
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE	
GRE	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME	CHI SQUARE YATES CORRE
11	* 0	48	48						
2M	0	18	18	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Values - No Chi Square
31	1	20	21	0.30435	1.00000	0.30435	0.60870	0.30435	? 2.319328 0.183462
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Values - No Chi Square

# FINDING : SUBCUT. TISSUE, LIPOMA

I.

						도 가지 비슷			
				CONTROL >	CONTROL <		PROBABILITY		
POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE		
RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME	CHI SQUARE	YATES CORRE
				نىرى بۇرىيا بىلەر تەربىيا بەر بەر بەر مېرىيى		rentes <b>ent</b> estados Contratos <b>de la</b> terados			
0	48	48							
0	18	18	1.00000	1.00000	1.00000	2,00000	1.00000	Zero Values - No	Chi Square
1	20	21	0.30435	1.00000	0.30435	0760870	0.30435	? 2.319328	0.183462
0	47	47	1.00000	1.00000	1,00000	2,00000	ığ. 00000	Zero Values - No	Chi Square
					i ili i i t tito come		5		
					and the second second second second second second second second second second second second second second second		and the second second		
				1. 14.5			and and and a		
					r 355 - 145				
				n - 12- 		STATE:			
				· · ·		() (() 			
	RESP 	RESP RESP 0 48 0 18 1 20	RESP         RESP         TOTAL           0         48         48           0         18         18           1         20         21	RESP         RESP         TOTAL         PROBABILITY           0         48         48           0         18         18         1.00000           1         20         21         0.30435	POS.         NEG.         ONE-TAILED         PROPORTION           RESP         RESP         TOTAL         PROBABILITY         TREATED           0         48         48             0         18         18         1.00000         1.00000           1         20         21         0.30435         1.00000           0         47         47         1.00000         1.00000	POS.         NEG.         ONE-TAILED         PROPORTION         PROPORTION           RESP         RESP         TOTAL         PROBABILITY         TREATED         TREATED           0         48         48         .         .         .           0         18         18         1.00000         1.00000         1.00000           1         20         21         0.30435         1.00000         1.00000           0         47         47         1.00000         1.00000         1.00000	POS.         NEG.         ONE-TAILED         PROPORTION         PROPORTION         TWO-TAILED           RESP         RESP         TOTAL         PROBABILITY         TREATED         TREATED         PROBABILITY           0         48         48         1.00000         1.00000         1.00000         2.00000           1         20         21         0.30435         1.00000         0.30435         07608 0           0         47         47         1.00000         1.00000         1.00000         2.00000	POS.         NEG.         ONE-TAILED         PROPORTION         PROPORTION         TWO-TAILED         = OR MORE           RESP         TOTAL         PROBABILITY         TREATED         TREATED         PROBABILITY         EXTREME           0         48         48	POS.NEG.ONE-TAILEDPROPORTIONPROPORTIONTWO-TAILED= OR MORERESPTOTALPROBABILITYTREATEDTREATEDPROBABILITYEXTREMECHI SQUARE048481.000001.000001.000002.000001.00000Zero Values - No120210.304351.000000.3043507608700.304352.319328047471.000001.000001.000002.000001.00000

#### TABLE - Z \_\_\_\_\_

### Fisher's Exact Statistics

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PROJECT ID: 1231 TISSUE : MAMMARY GLAND FATES : ALL \_\_\_\_\_

DAYS : ALL

FINDING : ADENOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
1M*	0	1	1							•	
2M	1	2	3	0.75000	1.00000	0.75000	1.50000	1.00000	?	0.444444	0.444444
ЗМ	1	0	1	0.50000	1.00000	0.50000	1.00000	1.00000	?	2.000000	0.000000
4M	0	0	0	1.00000	1.00000	1.00000	2.00000	1.00000	Ze	ro Values - No	Chi Square

#### FINDING : FIBROADENOMA

					CONTROL >	CONTROL		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTIC	N TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABLLITY	EXTREME	CHI	I SQUARE	YATES CORRE
1M*	1	0	1								
2M	2	1	3	0,75000	0.75000	1.00000	1,50000	1.00000	? 0.	.44444	0.444444
зм	0	1	1	0,50000	0.50000	1,00000	1,000d0	1.00000	? 2.	. 000000	0.000000
4M	0	0	0	1.00000	1.00000	1,00000	3 00000 2	1.00000	Zero Va	alues - No Ch	i Square
						an an an an an an an an an an an an an a	and the second sec	and a set 1			
							f into				

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Selected Animals

GRUUP :       Oppm       3000ppm       15000ppm       25000ppm         SEX :       PEMALE       FEMALE       FEMALE       FEMALE         No. of ANIMALS :       50       50       50       50         4054       4151       4257       4351         4055       4165       4262       4352         4058       4170       4273       4354         4067       4179       4281       4378         4067       4181       4290       4393         4076       4183       4296          4095            4095            4095            4095            4095            4095            4095            4095            4095            MOS       SKIN       ACMINA       ACMINA </th <th></th> <th colspan="11">DAYS : ALL FINDINGS : * Selected</th>		DAYS : ALL FINDINGS : * Selected										
SEX :     FEMALE     FEMALE     FEMALE     FEMALE     FEMALE       NO. Of ANIMALS :     50     50     50       4054     4161     4257     4351       4055     4165     4262     4352       4058     4170     4273     4354       4067     4179     4285     4392       4076     4183     4290     4393       4076     4183     4290     4393       4076     4183     4290     4393       4076     4183     4290     4393       4076     4183     4290     4393       4076     4183     4290        4092       4092       The above animals have at least one of the following findings.     *       * Findings selected are :     OVARIES:       ADENOMA     SUBCUT. TISSUE, FIBROMA       MAMMARY GLAND:     ADENOMA       ADENOMA     ADENOMA       ADENOMA     ADENOMA       PIENLARY ADENOMA       PIENDADENOMA       PIENDADENOMA       PIENDADENOMA												
No. of ANIMALS:         50         50         50           4054         4161         4257         4351           4055         4165         4262         4352           4058         4170         4273         4354           4063         4178         4281         4378           4067         4179         4285         4392           4067         4179         4285         4393           4076         4183         4296            4085         4188         4300            4092           4093            4093           4093            4093           4093            4093           4093            4094           4095            4095           4095            4095           4095            MOMAR         SUBCUT. TISSUE, FIBROMA         SUBCUT. TISUE, FIBROMA         <												
4054 4161 4257 4351 4055 4165 4262 4352 4058 4170 4273 4354 4063 4178 4281 4378 4067 4179 4285 4392 4074 4183 4296 4085 4188 4300 4085 4188 4300 4099 4099 4099 4099 4099 4095 4095 4095 4095												
4055 4165 4262 4352 4058 4170 4273 4354 4063 4178 4281 4378 4067 4179 4285 4392 4074 4181 4290 4393 4076 4183 4296 4085 4188 4300 4099 4099 4099 4099 5099 4099 509 4099 509 4099 4099 4099 4099 4099 4099 4099 4099	NO. OF ANIMALS :	50	50	50								
4058 4170 4273 4354 4063 4178 4281 4378 4067 4179 4285 4392 4074 4181 4290 4393 4076 4183 4296 4085 4188 4300 4095 4095 4099 4099 4099 4099 5. The above animals have at least one of the following findings. * Findings selected are : OVARIES: ADENOMA SUBCUT. TISSUE, FIEROMA SUBCUT. TISSUE, FIEROMA MAMMARY GLAND: ADENOMA DENOMA PAPILLARY ADENOMA FIEROADENOMA FIEROADENOMA		4054	4161	4257	4351							
4063 4178 4281 4378 4067 4179 4285 4392 4074 4181 4290 4393 4076 4183 4296 4085 4188 4300 4092 4095 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099		4055	4165	4262	4352							
4067       4179       4285       4392         4074       4181       4290       4393         4076       4183       4296          4085       4188       4300          4092         4095          4095         4095          4095         4095          4099            4099            4099            4099            4099            4099            4099            4099            VARIES:       ADENOMA           ADENOMA       SUECUT. TISSUE, FIBROMA		4058	4170	4273	4354							
4074 4181 4290 4393 4076 4183 4296 4085 4188 4300 4092 4095 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099 4099		4063	4178	4281	4378							
4076 4183 4296 4085 4188 4300 4092 4095 4099 The above animals have at least one of the following findings. * Findings selected are : OVARIES: ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA		4067	4179	4285	4392							
4085       4188       4300          4092           4095           4095           4095           4099           4099           4099           4099           4099           4099           4099           4099           4099           4099           4099           4099           4080           OVARIES:           ACANTHOMA       SUBCUT. TISSUE, FIBROMA          ADENOCARCINOMA           ADENOMA       PAPILLARY ADENOMA          FIBROADENOMA		4074	4181	4290	4393							
4092 4095 4099 4099 The above animals have at least one of the following findings. * Findings selected are : OVARIES: ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA		4076	4183	4296								
4095 4099 The above animals have at least one of the following findings. * Findings selected are : OVARIES : ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAFILLARY ADENOMA FIBROADENOMA		4085	4188	4300								
4099 The above animals have at least one of the following findings. * Findings selected are : OVARIES: ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA		4092										
The above animals have at least one of the following findings. * Findings selected are : OVARIES: ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA		4095										
<pre>* Findings selected are :     OVARIES:     ADENOMA     SKIN:     ACANTHOMA     SUBCUT. TISSUE, FIBROMA MAMMARY GLAND:     ADENOCARCINOMA     ADENOMA     PAPILLARY ADENOMA     FIBROADENOMA</pre>		4099										
OVARIES: ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA			e of the fol:	lowing finding	<b>is.</b>							
ADENOMA SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	* Findings selected ar	e :		· 								
SKIN: ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	OVARIES:		,									
ACANTHOMA SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	ADENOMA											
SUBCUT. TISSUE, FIBROMA MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	SKIN:											
MAMMARY GLAND: ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	ACANTHOMA											
ADENOCARCINOMA ADENOMA PAPILLARY ADENOMA FIBROADENOMA	SUBCUT. TISSUE, FIBR	OMA										
ADENOMA PAPILLARY ADENOMA FIBROADENOMA	MAMMARY GLAND:											
PAPILLARY ADENOMA FIBROADENOMA	ADENOCARCINOMA											
FIBROADENOMA												
FIBROADENOMA				,								
CYSTADENOMA												
	CYSTADENOMA											

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	15-FEB-1997 EXCEL INDUSTRIES LTD. GLYPHOSATE TECHNICAL TABLE - Z Peto Score Statistics									
		 I	Peto Sco	ore Stat	tistics					
PROJECT I TISSUE : FINDING :	OVARIES			DAYS F	: ALL ATES : ALI	 С				
			FAT	AL TUMO	RS					
<b>a</b>										
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected					
1F: Oppm	49	0.00	0	0.00	0.00					
2F: 3000ppm	49	3000.00	0	0.00	0.00					
3F: 15000ppm	48	\$15000.00	0	0.00	0.00					
4F: 25000ppm	50	\$25000.00	0	0.00	0.00					
	τVa	alue : 0								
				ATAL TUN	 /\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\					
Group	Number of	Dose	Observed	Expected	Observed					
	Animals	Level			- Expected					
1F: Oppm	49	0.00	0	0.00	0.00					
2F: 3000ppm	49	3000.00	1	0.35	0.65					
3F: 15000ppm	48	<b>%15000.00</b>	0	0.35	-0.35					
4F: 25000ppm	50	\$25000.00	0	0.29	-0.29					
	T Va	alue : -10705.	88							
					at a					
			TOT	AL TUMOR						
Group	Number of Animals	Do <b>se</b> Level	Observed	Expected	Observed - Expected	ML Value				
1F: Oppm	49	0.00	0	0.00	0.00	1.00				
2F: 3000ppm	49	3000.00	1	0.35	0.65	2.83				
3F: 15000ppm	48	\$15000.00	0	0.35	-0.35	0.00				
4F: 25000ppm	50	\$25000.00	0	0.29	-0.29	0.00				
	V			) .						

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			484				
		I	Peto Sco	ore Stat	tistics		
PROJECT I TISSUE : FINDING :				DAYS FA	: ALL ATES : ALI		
			FAT	AL TUMOR	RS 		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
lF: Oppm 2F: 3000ppm	48 22	0.00 3000.00	0 0	0.00	0.00		
3F: 15000ppm	22	<b>%1</b> 5000.00	0	0.00	0.00		
4F: 25000ppm	50	<b>%</b> 25000.00	0	0.00	0.00		
	T Va	alue : O					
			NON-FA	ATAL TUN	NORS		
Group	Number of Animal <b>s</b>	Dose Level	Observed	Expected	Observed - Expected		
1F: Oppm	48	0.00	D	0.35	~0.35		
2F: 3000ppm	22	3000.00	0	0.15	-0.15		
3F: 15000ppm	22	\$15000.00	0	0.15	-0.15		
4F: 25000ppm	50	\$25000.00	1	0.35	0.65		
	τ νε	alue : 13448.:	82				
			TOT	AL TUMOF	RS 		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1F: Oppm	48	0.00	0	0.35	-0.35	0.00	
2F: 3000ppm	22	3000.00	0	0.15	-0.15	0.00	
3F: 15000ppm	22	\$15000.00	0	0.15	-0.15	0.00	
4F: 25000ppm	50	<b>%25000.00</b>	1	0.35	0.65	2.82	
	п	'Value : %13	2449 01020				
		Variance : %12:		00			
		Value :	1.21247				
	One Tailed Pro		0.15000				
		-					

			EXCEL II SLYPHOS	-FEB-199 NDUSTRIE ATE TECH ABLE - Z	S LTD. NICAL		485
		I	Peto Sc	ore Stat	istics		
PROJECT I TISSUE : FINDING :	SKIN	TISSUE, F	IBROMA		ALL TES : ALI		
			FAT	AL TUMOR		· <b>- -</b>	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1F: Oppm 2F: 3000ppm 3F: 15000ppm 4F: 25000ppm	48 22 22 50	0.00 3000.00 %15000.00 %25000.00	0 0 0 0	0.00 0.00 0.00 0.00	0.00 0.00 0.00 0.00		
	т V	alue : 0					
			NON-FA	ATAL TUM			
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
	48 22 22 50	0.00 3000.00 %15000.00 %25000.00			0.00 0.00 0.86 -0.86		
	тV	alue : -8620.6	9				
			TOTZ	AL TUMOR	 S 		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1F: 0ppm 2F: 3000ppm 3F: 15000ppm	48 22 22	0.00 3000.00 %15000.00	0 0 1	0.00 0.00 0.14 0.86	0.00 0.00 0.86 -0.86	1.00 1.00 7.25 0.00	
4F: 25000ppm		<pre>%25000.00 F Value : %-% Variance : %11% Z Value :</pre>			-0.00	0.00	
	One Tailed Pr	obability:	0.00700				

	15-FEB-1997 EXCEL INDUSTRIES LTD. GLYPHOSATE TECHNICAL TABLE - Z Peto Score Statistics										
		I	Peto Sc	ore Stat	cistics						
PROJECT I TISSUE : I FINDING :	MAMMARY G			DAYS : FI	: ALL ATES : ALI						
			FAT	AL TUMOF	RS						
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected						
1F: Oppm 2F: 3000ppm 3F: 15000ppm 4F: 25000ppm	48 22 22 50	0.00 3000.00 %15000.00 %25000.00	0 0 0 0	0.00 0.00 0.00 0.00	0.00 0.00 0.00 0.00						
·	т V	alue : 0									
			NON-FA	ATAL TUN	IORS						
					· • • • • • • • • • • • • • • • • • • •						
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected						
1F: Oppm	48	0.00	1	0.41	0.59						
2F: 3000ppm 3F: 15000ppm	22 22	3000.00 %15000.00	0	0.07 0.09	-0.07 -0.09						
4F: 25000ppm	50	\$25000.00	0	0.43	-0.43						
	T V	alue : -12320.	99		and a second sec						
			TOT	AL TUMOR							
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value					
lF: Oppm	48	0.00	1	0.41	0.59	2.45					
2F: 3000ppm	22	3000.00	0	0.07	-0.07	0.00					
3F: 15000ppm	22	\$15000.00	0	0.09	-0.09	0.00					
4F: 25000ppm	50	<b>%25000.00</b>	0	0.43	-0.43	0.00					

T Value : %-12320.98830 Variance : %138366080.00000 Z Value : -1.04744 One Tailed Probability: 0.15000

15-FEB-1997

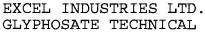


TABLE - Z

\_\_\_\_\_

DAYS : ALL

Peto Score Statistics \_\_\_\_\_

PROJECT ID: 1231 TISSUE : MAMMARY GLAND FINDING : ADENOMA

FATES : ALL

#### FATAL TUMORS \_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: Oppm	48	0.00	0	0.00	0.00
2F: 3000ppm	22	3000.00	0	0.00	0.00
3F: 15000ppm	22	\$15000.00	0	0.00	0.00
4F: 25000ppm	50	\$25000.00	0	0.00	0.00

T Value : 0

#### NON-FATAL TUMORS

Group	Number of	Dose	Observed	Expected	Observed		
	Animals	Level			- Expected		
			,				
1F: Oppm	48	0.00	4	3.39	0.61		
2F: 3000ppm	22	3000.00	5	1.04	3.96		
3F: 15000ppm	22	<b>%15000.00</b>	2	1.16	0.84	No	
4F: 25000ppm	50	\$25000.00	0	5.41	-5.41	a set a set a set a set a set a set a set a set a set a set a set a set a set a set a set a set a set a set a s	
	ту	alue · -110799	1				

T Value : -110799.1

#### TOTAL TUMORS \_\_\_\_\_

\_\_\_\_\_

Number of Dose Observed Expected Observed ML Value Group Animals Level - Expected 3.39 4 0.61 1.18 1F: Oppm 0.00 48 5 3.96 1.04 4.80 2F: 3000ppm 22 3000.00 1.72 3F: 15000ppm 22 %15000.00 2 1.16 0.84 **%25000.00**0 -5.41 0.00 4F: 25000ppm 50 5.41

> T Value : %-110799.14100 Variance : % 1264.42061E+06 Z Value : -3.11595 One Tailed Probability: 0.00100

			EXCEL II SLYPHOS, T,	-FEB-199 NDUSTRIJ ATE TECI ABLE - 2  ore Stat	ES LTD. HNICAL Z		488
PROJECT I TISSUE : 1 FINDING :	MAMMARY G			DAYS Fi	: ALL ATES : ALI		
			FAT	AL TUMOR	RS		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1F: Oppm	48	0.00	0	0.00	0.00		
2F: 3000ppm	22	3000.00	0	0.00	0.00		
3F: 15000ppm	22	<b>%15000.00</b>	0	0.00	0.00		
4F: 25000ppm	50	<b>%25000.00</b>	0	0.00	0.00		
	т V 	alue : 0	NON-F2	ATAL TUN	IORS		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected		
1F: Oppm	48	0.00	1	0.74	0.26		
2F: 3000ppm	22	3000.00	1	0.24	0.76		
3F: 15000ppm	22	%15000.00	0	0.23	-0.23	• *.	
4F: 25000ppm	50	\$25000.00	0	0.79	-0.79		
	τ ν.	alue : -20849.	08				
			TOT	AL TUMOF	RS		
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value	
1F: Oppm	48	0.00	1	0.74	0.26	1.34	
2F: 3000ppm	22	3000.00	1	0.24	0.76	4.19	
3F: 15000ppm	22	<b>%15000.00</b>	0	0.23	-0.23	0.00	

-0.79

0.00

0.79

T Value : %-20849.08200 Variance : %261083808.00000 Z Value : -1.29032 One Tailed Probability: 0.10000

4F: 25000ppm

50

**%25000.00** 0

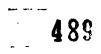


TABLE - Z \_\_\_\_

Peto Score Statistics

DAYS : ALL

\_\_\_\_\_ PROJECT ID: 1231 TISSUE : MAMMARY GLAND FINDING : FIBROADENOMA

\_ \_ \_ \_ \_ \_ \_ \_ \_ \_

FATES : ALL

#### FATAL TUMORS

-	 	-	 -	-	-	-	-	 -	-	-	_

Group	Number of Animals	Dose Level	Observed	Expected	Observed – Expected
1F: Oppm	48	0.00	0	0.00	0.00
2F: 3000ppm	22	3000.00	0	0.00	0.00
3F: 15000ppm	22	\$15000.00	0	0.00	0.00
4F: 25000ppm	50	\$25000.00	0	0.00	0.00

T Value : 0

#### NON-FATAL TUMORS

\_\_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	
1F: Oppm	48	0.00	4	3.73	0.27	
2F: 3000ppm	22	3000.00	1	1.16	-0.16	
3F: 15000ppm	22	\$15000.00	5	1.53	3.47	
4F: 25000ppm	50	\$25000.00	5	8.58	-3.58	1 A.
	т V	alue : -37904.0	5		and and an an an an an an an an an an an an an	

T Value : -37904.6

#### TOTAL TUMORS

\_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed – Expected	ML Value
1F: Oppm	48	0.00	4	3.73	0.27	1.07
2F: 3000ppm	22	3000.00	1	1.16	-0.16	0.86
3F: 15000ppm	22	<b>%15000.00</b>	5	1.53	3.47	3.26
4F: 25000ppm	50	\$25000.00	5	8.58	-3.58	0.58

T Value : %-37904.60200 Variance : % 1317.85408E+06 Z Value : -1.04414 One Tailed Probability: 0.15000

		97 ES LTD. INICAL 2	490			
		E	eto Sco	ore Stat	istics	
PROJECT II TISSUE : N FINDING :	AAMMARY G			DAYS : FF	ALL ATES : ALL	
			FAT	AL TUMOF	λs	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	
1F: 0ppm 2F: 3000ppm 3F: 15000ppm 4F: 25000ppm	48 22 22 50	0.00 3000.00 %15000.00 %25000.00	0 0 0	0.00 0.00 0.00 0.00	0.00 0.00 0.00 0.00	
41. 25000ppm		alue : 0	0	0.00	0.00	
			NON - F4	ATAL TUM	IORS	
Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	

	Animals	Level			- Expected	
1F: Oppm	48	0.00	1	0.49	0.51	
2F: 3000ppm	22	3000.00	0	0.05	-0.05	
3F: 15000ppm	22	\$15000.00	0	0.06	-0.06	
4F: 25000ppm	50	\$25000.00	0	0.40	-0.40	
	т V	alue : -11015.8	7			

T Value : -11015.87

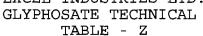
#### \_\_\_\_\_\_ TOTAL TUMORS

\_\_\_\_\_

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: Oppm	48	0.00	1	0.49	0.51	2.03
2F: 3000ppm	22	3000.00	0	0.05	-0.05	0.00
3F: 15000ppm	22	\$15000.00	0	0.06	-0.06	0.00
4F: 25000ppm	50	\$25000.00	0	0.40	-0.40	0.00

T Value : %-11015.87300 Variance : %141380704.00000 Z Value : ~0.92645 One Tailed Probability: 0.20000

#### 15-FEB-1997 EXCEL INDUSTRIES LTD.



 		· - <b></b>
Fisher's Exact	Statistics	

#### 

PROJECT ID: 1231

DAYS : ALL

#### TISSUE : OVARIES

FATES : ALL

FINDING : ADENOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
1F*	0	49	49								
2F	1	48	49	0.50000	1.00000	0.50000	1.00000	1.00000	?	1.010309	0.00000
ЗF	0	48	48	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No	Chi Square
4F	0	50	50	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No	Chi Square



Defendant's Exhibit 2570\_0175

491

TABLE - Z

#### Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL TISSUE : SKIN FATES : ALL

FINDING : ACANTHOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
1F*	0	48	48								
2F	0	22	22	1.00000	1.00000	1.00000	2.00000	1.00000	Zero	Values - No Ch	ii Square
ЗF	0	22	22	1.00000	1.00000	1,00000	2.00000	1.00000	Zero	Values - No Ch	ni Square
4F	1	49	50	0.51020	1.00000	0.51020	1.02041	1.00000 7	?	0.969897	0.000421

#### FINDING : SUBCUT. TISSUE, FIBROMA

GRP	POS. RESP	NEG. RESP	TOTAL	ONE-TAILED PROBABILITY	CONTROL > PROPORTION TREATED	CONTROL < PROPORTION TREATED	TWO-TAILED PROBABILITY	PROBABILITY = OR MORE EXTREME	CHI SQUARE YATES CORRE
1F*	0	48	48						
2F	0	22	22	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Values - No Chi Square
ЗF	1	21	22	0.31429	1.00000	0.31429	0.62857	0.31429	? 2.213439 0.162357
4F	0	50	50	1.00000	1.00000	1.00000	2.00000	1.00000	Zero Values - No Chi Square

	15-FEB-1997 EXCEL INDUSTRIES LTD. GLYPHOSATE TECHNICAL TABLE - Z	493
	Fisher's Exact Statistics	
PROJECT ID: 1231 TISSUE : MAMMARY GLAND	DAYS : ALL FATES : ALL	
FINDING : ADENOCARCINOMA		

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
15*	1	47	48								
2F	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
ЗF	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
4F	0	50	50	0.48980	0.48980	1.00000	0.97959	0.48980	?	1.052405	0.000421

#### FINDING : ADENOMA

GRP	POS. RESP	NEG. RESP	TOTAL	ONE-TAILED PROBABILITY	CONTROL > PROPORTION TREATED	CONTROL < PROPORTION TREATED	TWO-TAILED PROBABILITY	PROBABILITY = OR MORE EXTREME		CHI SQUARE	YATES CORRE
1F*	4	44	48								
2F	5	17	22	0.07879	0.97695	0.10184	0.20367	0.12762	?	2.789645	1.652850
ЗF	2	20	22	0.34281	0.72371	0.61910	1.23820	1.00000	?	0.011048	0.125843
4F	0	50	50	0.05387	0.05387	1.00000	0.10773	0.05387	?	4.343972*	2.476172

#### FINDING : PAPILLARY ADENOMA

GRP	POS. RESP	NEG. RESP	TOTAL	ONE-TAILED PROBABILITY	CONTROL > PROPORTION TREATED	CONTROL < PROPORTION TREATED	TWO-TAILED PROBABILITY	PROBABILITY = OR MORE EXTREME		CHI SQUARE	YATES CORRE
	1	47	48	<b></b>							
2F	1	21	22	0.43727	0.90435	0.53292	1.06584	0.97019	?	0.329490	0.039480
3F	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
4F	0	50	50	0.48980	0.48980	1.00000	0.97959	0.48980	?	1.052405	0.000421

#### FINDING : FIBROADENOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
1F*	4	44	48								
2F	1	21	22	0.35369	0.49517	0.85852	0.99034	1.35369	?	0.326340	0.005099
ЗF	5	17	22	0.07879	0.97695	0.10184	0.20367	0.12762	?	2.789645	1.652850
4F	5	45	50	0.26198	0.73578	0.52620	1.05240	1.52461	?	0.081565	0.004129

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TABLE - Z \_\_\_\_\_

#### Fisher's Exact Statistics

\_\_\_\_\_ PROJECT ID: 1231 DAYS : ALL

TISSUE : MAMMARY GLAND \_\_\_\_\_

FATES : ALL

FINDING : CYSTADENOMA

					CONTROL >	CONTROL <		PROBABILITY			
	POS.	NEG.		ONE-TAILED	PROPORTION	PROPORTION	TWO-TAILED	= OR MORE			
GRP	RESP	RESP	TOTAL	PROBABILITY	TREATED	TREATED	PROBABILITY	EXTREME		CHI SQUARE	YATES CORRE
		<b>-</b> -									
1F*	1	47	48								
2F	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
ЗF	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
4F	0	50	50	0.48980	0.48980	1.00000	0.97959	0.48980	?	1.052405	0.000421

#### Table 25 - 1

5 - 1 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Satellite group) Interim kill after 26 weeks of treatment

Site & Lesion	Dose			(ppm)	0	3000	10000	30000	
bree a lesion	No.	of	animals	examined	10	10	10		10
Cardiovascular System	n								
Heart:				( N= )	(10)	(10	) (10	) (	10 )
Aorta:				(N=)		(10)	) (10	$\langle \rangle$	10
Hematopoietic & Lympl	natic	Svs	tem	(11)	( 10 )	( 10	) (10	, (	10)
Bone marrow (fei	nur) :			(N=)	(10)	( 10	) (10	) (	10)
Bone marrow (sti	ernum)	:		(N=)	( 10 )	( 10	) (10	$\langle \rangle$	10
Bone marrow (ver				(N=)	(10)	( 10	) (10	{ }	10
Thymus:		·		(N=)	( 10 )	( 10	1 10	$\langle \rangle$	10)
Lymph nodes (cer	rvical	):		( N= )	1 10 5	10	\$ 10	$\{ \}$	10 {
Lymph nodes (me:	senter	ic)	:	( N= )	(10)	( 10	) (10	í ì	10 )
Spleen:				( N= )	105	2 10	\$ 110	{ }	10 5
Respiratory System				( )	( )	( 10	/ 10	, (	10 )
Trachea:				(N=)	(10)	( 10	) (10	) (	10)
Lung:				( N= ) ( N= )	( 10 )	(10 (10	) (10) (10)	$\langle \rangle$	10
Digestive System				(,	( 10 )	( 10	/ 10	, (	10 )
Submaxillary g	land:			(N=)	(10)	( 10	) (10	) (	10)
Sublingular gl				( N= )	( 10 )	10	\$ { 10	$\{ \}$	10 \$
Esophagus:				(N=)	(10)	( 10	) (10	12	10
Stomach (non-gl	andula	r p	ortion):	( N= )	( 10 )	10	\$ { 10	{ }	10
Stomach (glandu	lar po	rti	on) :	(N=)	( 10 )	( 10	\$ { 10	{ }	10
Small intesting				(N=)	( 10 )	( 10	1 10	$\langle \rangle$	10
Large intesting	a :			(N=)	( 10 )	( 10	) (10	$\langle \rangle$	10)
Liver:				( N- )	10	10		{ }	10
Pancreas:				(N=)	(10)	(10	(10	$\langle \rangle$	10)
Urinary System				( )	( 10 )	( 10	) (10	) (	10)
Kidney:				(N=)	(10)	( 10	) ( 10	1 (	10)
Urinary bladder	• :			(N-)	$\left(\begin{array}{c}10\\10\end{array}\right)$	( 10 ( 10	1 10	$\{ \}$	10 1
Genital System					/	( 10	, ( 10	, (	10,
Testis:				(N=)	(10)	(10	) (10	) (	10)
Epididymis:				( N= )	105	( 10	10	$\{ \}$	10 5
Seminal vesicle	e :			(N=)	(10)	( 10	) ( 10	$\{ \}$	10)
Coagulating gla				(N-)	(10)	( 10	) (10	$\langle \rangle$	10)
Prostate:				(N=)	101	10	1 10	{ }	10 5
Endocrine System						(	( 10	/ (	10 )
Pituitary:				(N=)	(10)	( 10	) (10	) (	10)
Thyroid:				( N= )	( 10 )	( 10	) (10	$\{ \}$	10 )
Parathyroid:				(N=)	(10)	( 10	(10	$\{ \}$	10 )
Adrenal:				( N= )	105	10	\$ 10	$\{ \}$	10 5
Nervous System					/	·	, ,	/ (	10 )
Cerebrum:				(N=)	(10)	(10	) ( 10	) (	10)
Cerebellum:				( N= )	( 10 )	( 10	1 10	$\{ \}$	10 )
Brain stem:				(N=)	(10)	( 10	(10	í ì	10)
Spinal cord (cer	vical	):		( N= )	( 10 )	( 10	10	$\langle \rangle$	10 1
Spinal cord (the	racic	):		( N= )	2 9 5	10		5 2	10)
Spinal cord(lum	ibar) :			( N= )	( 10 )	( 10		{ }	10 5
Sciatic nerve:				(N=)	(10)	( 10		11	10)
Musculo-Skeletal Syst	em					( 10 )	(10	, (	10)
Bone (sternum) :				(N=)	(10)	( 10	) (10	) (	10)
Bone (femur) :				(N=)		( 10	(10		10)
Bone (vertebra) :				(N=)		( 10			10)

( N= ): Number of animals examined microscopically at the site.

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Table 25 - 2	Histopathology - Incidence of microscopic neoplastic lesions
	in male rats (Satellite group)
	Interim kill after 26 weeks of treatment

Site & Lesion		Dose	(ppm)	0	3000	10000	30000
DICC C	. 162101	No. of anima	ls examined	10	10	10	10
Sense	lo-Skeletal Sy Bone (vertebra Tibio-femoral Skeletal musc Organs Eye: Harderian gla umentary Syste Skin:	) 《cont.》: joint: le (m.triceps su nd:	( N= ) ( ( N= ) (	(10) (10)	(10) (10)	( 10 ) ( 10 )	$ \begin{pmatrix} 10 \\ 10 \end{pmatrix} \\ (10 )$
No.	of benign neo	plasms	( 1 ) (	0	0	0	0
No.	of malignant	neoplasms		0	0	0	0
No.	of benign & m	alignant neoplas	ms	0	0	0	0
No.	of animals wi	th benign neopla	usm (s)	0	0	0	0
No.	of animals wi	th malignant nec	oplasm (s)	0	0	0	0
No.	of animals wi	th neoplasm(s)		0	0	0	 0

(N-): Number of animals examined microscopically at the site.

Table	25 - 3	Histopathology - Incidence of microscopic neoplastic lesions
		in male rats (Satellite group)
		Interim kill after 52 weeks of treatment

Site & Lesion	Dos	е		(ppm)		0	30	000	1	0000	)	30	000	
Site & Lesion	No.	of	animals	examined		10		10		10	)		10	-
Cardiovascular Syste	m													-
Heart:				( N= ) ( N= )	(	10)	(	10	)	( 10	))	(	10	)
Aorta				( N= )	(	10)	(	10	)	(10)	))	(	10 10	j
Hematopoietic & Lymp	hatic	Sys	tem											Î
Bone marrow (fe	mur):			(N=)	(	10)	(	10	)	( 10		(	10	)
Bone marrow (st				(N=)	ļ	10)	(	10		(10		(	10	)
Bone marrow (ve Thymus:	rtebra	):		(N=)	ļ	10)	5	10			))	(	10	
Lymph nodes (ce	nuinal	۱.		$\left(\begin{array}{c} N=\\ N\end{array}\right)$	5	10 }	5	10		( 10		5	10	2
Lymph nodes (ne	Contan	:.)		$\left(\begin{array}{c} N=\\ N-\end{array}\right)$	1	10)	5	10		( 10		Ş	10	)
Spleen:	Scheel	10)		(N=) (N=)	>	10) 10)	>	10	{	( 10		5	10	2
Respiratory System				( 14- )	l	10)	l	10	)	(1(	, ,	l	10	)
Trachea:				(N - )	1	10.)	1	10	1	1 11	1	1	10	1
Lung:				( N= ) ( N= )	1	10	$\left( \right)$	10 10	{	(10)	!!	5	10	1
Digestive System				( N- )	l	10)	(	10	)	( 10	))	(	10	)
Submaxillary g	land:			(N=)	1	10)	1	10	1	( 10	1	1	10	1
Sublingular gl				(N=)	2	10)	1	10 10	{	(10)		>	10	1
Esophagus:				$(N^{-})$	2	10)	1	10		(10)		1	10 10	1
Stomach (non-gl	andula	r p	ortion):	{ N= }	2	10 }	}	10	{	$\{ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 $		}	10	ł
Stomach (glandu	lar po	rti	on) :	( N= )	2	10 )	2	10	1	( 10		2	10	Ś
Small intestin				(N=)	ì	10 )	ì	10	{		55	2	10	ł
Large intestin				(N=)	ì	10 )	ì	10	{		ŝŝ	2	10	1
Liver:				(N = )	2	10 5	}	10	{	10		}	10	ł
Pancreas:				(N=)	2	10 )	2	10	5	11		2	10	1
Urinary System						/	•		1	( 1)	' '	(	10	1
Kidney:				(N=)	(	10)	(	10	)	( 10	))	(	10	١
Urinary bladde	r:			$\left\{ \begin{array}{c} N=\\ N= \end{array} \right\}$	(	10 )	2	10 10	5		5 S	1	10	5
Genital System														'
Testis				( N= )	(	10)	(	10	)	( 10	))	(	10	)
Epididymis:				(N=)	(	10)	(	10	)	( 10	))	(	10	Ś
Seminal vesicl				(N=)	(	10)	(	10	)	( 10	))	(	10	)
Coagulating gl	and:			( N= )	(	10)	(	10	)	( 10		(	10	)
Prostate: Endocrine System				( N= )	(	10)	(	10	)	(10	))	(	10	)
Pituitary:					,	10.1	,							
(B) Anteri	on ada			( N= )	(		(	10	)	(10		(	10	)
Thyroid:	or, ade	nom	a	$(M_{-})$	1	10)	1	1	1	1 10		,	0	
(B) Follic	ular a	den	Oma	( N= )	(		l	10	)	( 10		(	10	)
(B) C-cell	adena	ma	oma			0		1		(			0	
Parathyroid:	aucito	10		(N=)	1		1	0	1	1 10		1	0	1
Adrenal:				N =	2	10) 10)	>	10 10		(10)	1		10	
Nervous System				( 1- )	1	10)	(	10	)	( 10	))	(	10	)
Cerebrum:				(N=)	1	10)	(	10	1	( 10	1	(	10	1
Cerebellum:				$\left\{ N=\right\}$	2	10 1	>	10	{	$\begin{cases} 10 \\ 10 \end{cases}$		>	10 10	{
Brain stem:				(N=)	2	10)	>	10	{	10		>	10	{
Spinal cord (ce	rvical	):		( N= )		10)	2	10	1	(10)		2	10	1
Spinal cord (the				( N= )		10 )	2	10	1	(10)		}	10	1
Spinal cord (lu				( N= )		10 5	2	10	{	10		>	9	{
Sciatic nerve:						10)	2	10	1	( 10		>	10	!

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm.

### Table 25 - 4

4 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Satellite group) Interim kill after 52 weeks of treatment

Site & Lesion	Dose		(ppm)	0	3000	10000	30000
bree a deston	No. of	animals	examined	10	10	10	10
Musculo-Skeletal Syste	m						
Bone (sternum) :			(N=)	(10)	(10)	( 10	(10)
Bone (femur) :			(N=)	101	(10)	( 10	
Bone (vertebra) :			(N=)	( 10 )	101	( 10	
Tibio-femoral jo	int:		(N=)	(10)	$\left\{\begin{array}{c}10\\10\end{array}\right\}$	10	$\{ \}_{10}^{10} \{$
Skeletal muscle	(m. tric	eps sura	e): (N=)	(10)	( 10 )	( 10	1 1 10 1
Sense Organs				/	/	( 10	, (10)
Eye:			(N=)	(10)	(10)	( 10	) (10)
Harderian gland:			(N=)	(10)	$\left(\begin{array}{c} 10\\ 10\end{array}\right)$	( 10	{ { 10 {
Integumentary System					. ,		, ,,
Skin:			(N=)	(10)	(10)	(10	) (10)
(B) Papillom	8.			1	0	0	0
(B) Fibroma				0	1	0	Õ
No. of benign neopla	SmS			1	3	3	0
No. of malignant neo	plasms			0	0	0	0
No. of benign & mali	gnant n	eoplasms		1	3	3	0
No. of animals with	benign	neoplasm	(s)	1	3	3	0
No. of animals with	naligna	nt neopla	asm (s)	0	0	0	0
No. of animals with	neoplas	:m (s)		1	3		0

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm.

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### Table 25 - 5

Histopathology - Incidence of microscopic neoplastic lesions in male rats (Satellite group) Interim kill after 78 weeks of treatment

Site & Lesion	Dos	е		(ppm)	0	30	00	10000	300	00
Site & Lesion	No.	of	animals	examined	6		5	10		8
Cardiovascular System						-				
Heart:				(N=)(	6)	(	5)	( 10	) (	8
Aorta:				(N=)( (N=)(	6)	ì	5 )	10	57	8
Hematopoietic & Lympha	tic	Svs	tem		- /		- /	( 10	, ·	• ,
Bone marrow (femu	r) :	- , -	· · · ·	(N-)(	6)	(	5)	( 10	) (	8)
Bone marrow (ster		:		(N-) (	6)	ì	5 )	( 10	57	8)
Bone marrow (vert	ebra	):		(N=) (	6)	1	5 )	( 10	57	8
Thymus:				(N=)(	6)	ì	5))))))))) 5555555	( 10	śì	8
Lymph nodes (cerv	ical	):		(N = )(	6)	1	5)	1 10	\$ ?	8
Lymph nodes (mese	nter	ic)	:	(N=)(	6)	ì	5)	(10	íì	8
Spleen:				(N=)(	6)	ì	5)	( 10	57	8
Respiratory System				. , ,		`	- ,		<i>,</i> ,	- ,
Trachea:				(N=)(	6)	(	5)	(10	) (	8
Lung:				(N=)(	6) 6)	ì	5) 5)	( 10	í ì	8
(B) Adenoma					2	•	0 í	0	, ,	0
Digestive System					-		•	U		•
Submaxillary gla	nd:			(N=)(	6)	(	5)	(10	) (	8
Sublingular glar	id:			(N=)(	6 j	ì	5 )	( 10	$\{ \}$	8
Esophagus:				(N=)	6)	2	5	( 10	$\langle \rangle$	8
Stomach (non-glar	dula	r p	ortion):	(N = )	6)	2	5 1	( 10	$\langle \rangle$	8
Stomach (glandula	r po	rti	on) :	(N-) (	6 j	ì	5)	( 10		0
Small intestine:				$\{N=\}$	6) 6)	2	5 1	10	{ }	8 8 8 8
Large intestine:				(N= ) (	6)	2	555555555555555555555555555555555555555	( 10	{ }	8
Liver:				( N= ) (	6)	2	5 1	( 10	$\langle \rangle$	8
(B) Hepatoce	llul	ar	adenoma	(	1	(	- /	1	, (	
Pancreas:				(N=)(	6)	1	0 5)	( 10	) (	1 8
Urinary System				()(	- /	•	.,	( 10	, ,	0,
Urinary bladder:				(N≈)(	6)	1	5)	(10	1 (	8
Genital System				(	- /	(	.,	( 10	, (	0
Testis:				(N=)(	6)	(	5)	( 10	) (	8
Epididymis:				N = 1	6 5	2	5) 5) 5) 5)	10	{ }	8
Seminal vesicle				(N = )	6)	ì	5)	( 10	Śł	8
Coagulating glar	nd :			(N=)(	6 )	1	5 1	( 10	$\langle \rangle$	8
Prostate:				(N = )	6 5	2	5 5	1 10	{ }	8
Endocrine System				. , ,	- /		- /	(	, ,	
Pituitary:				(N=)(	6)	(	5)	(10	) (	8
(B) Anterior	ade	nom	a		3		4	4	, (	3
Thyroid:				(N=)(		(	5)		) (	8
(B) C-cell a	dend	ma			2	•	ĩ	2	, (	1
Parathyroid:				(N=)(	6)	(		( 10	1 (	
Adrenal:				( N= ) (	6 5	1	5)	10	$\{ \}$	8
(B) Cortical	ade	nom	a		0		0	1	<i>,</i> ,	0
(B) Pheochro	mocy	tom	a		0		1	Ô		õ
Nervous System							-	•		~
Cerebrum:				(N=)(	6)	(	5)	( 10	) (	8
Cerebellum:				(N=)(	6)	1	5 1	( 10	11	8
Brain stem:				$\langle N = \rangle \langle$	6)	2	5	( 10	{ }	8
Spinal cord (cerv	ical	):		(N= ) (	6 5	2	5) 5) 5)	10	{ }	8
Spinal cord (thor	acio	):		(N=)(	6)	ì	5)	( 10	i i	888888
Spinal cord (lumb				(N=)(	6)	>	5)	( 10	( )	

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm.

Table 25 - 6 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Satellite group) Interim kill after 78 weeks of treatment

Site & Lesion	Dose	(ppm)	0	3000	10000	300	00
bree & Leston	No. of animals	examined	6	5	10	1	8
Nervous System «co Spinal cord( Sciatic nerv	lumbar) 《cont.》:	( N= ) ( ( N= ) (	6)	( 5	) (10	} {	8)
Musculo-Skeletal S Bone (sternum Bone (femur) : Bone (vertebr Tibio-femora Skeletal musc	): ):	$\left(\begin{array}{c} N=\\ N=\\ \end{array}\right)\left(\begin{array}{c}\\ N=\\ \end{array}\right)\left(\begin{array}{c}\\ N=\\ N=\\ \end{array}\right)$			) (10 ) (10 ) (10 ) (10 ) (10 ) (10		8) 8) 8) 8) 8)
Sense Organs Eye: Harderian gl: Integumentary Systi	and:	{ N= } { N= } {	6 ) 6 )	( 5 ( 5	<pre>} { 10 } { 10 10</pre>	} {	8) 8)
Skin: (B) Kera (B) Fibro	toacanthoma oma	( N= ) (	6) 1 0	(5 0 0	) (10 0 1	) (	8) 0 0
No. of benign nee	oplasms		9	6	9		5
No. of malignant	neoplasms		0	0	0		0
No. of benign & r	alignant neoplasms		9	6	9		5
No. of animals w	th benign neoplasm	(s)	6	4	7		4
No. of animals w	th malignant neopla	asm (s)	0	0	0		0
No. of animals w	th neoplasm(s)		6	4	7		4

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm.

# Table 25 - 7

# 7 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group) Terminal kill after 104 weeks of treatment

Site & Lesion	Dose	(ppm)	0	3000	10000	30000
bree & heston	No. of animals	examined	18	20	18	29
Cardiovascular System		******				
Heart:		(N=)	(18)	( 20	) (18	) (29)
(B) Schwann	Oma	( )	0	0		
Aorta:		(N=)	-	( 20	0	1
Hematopoietic & Lymph	atic System	( 11- )	( 10 )	( 20	) (18	) (29)
General:	acie bystem	( ) )	1 10 1	1 00	1 1 10	
	lear cell leukemi	( N= )		(20)		) (29)
Bone marrow (fem	iear cell leukem	1	0	1	0	0
Bone marrow (ste	iur) ·	( N= )	(18)	(20	) (18	) (29)
Bone marrow (Ste	rnum)	(N-)	(18)	(20	) (18	) (29)
Bone marrow (ver	tebra):	( N= )	(18)	(20)	) (18	) (29)
Thymus:		( N= )	(18)	(20)	) (18	) (29)
Lymph nodes (cer	vical) :	(N=)	(18)	(20	) (18	) (29)
Lymph nodes (mes	enteric):	(N=)	(18)	( 20	) (18	) (29)
Spleen:		(N=)	(18)	( 20	(18	) (29)
Respiratory System			. ,		, ( 10	, ( 10 )
Trachea:		(N=)	(18)	( 20	) (18	) (29)
Lung:		(N=)	(18)	( 20	(18	(29)
(B) Adenoma		( )	0	2		, , ,
	s cell carcinoma		õ	0	1	3
Digestive System			0	0	1	0
Submaxillary gl	and		1 10 1	1 00		
Sublingular gla	anu.	$\left\{ \begin{array}{c} N=\\ N\end{array} \right\}$	18	( 20	(18	) (29)
	.nu ·	( N= )	(18)	(20	) (18	) (29)
Esophagus:	1.1	(N=)	(18)	(20)		) (29)
Stomach (non-gla	ndular portion) :	( N= )	(18)	(20)	) (18	) (29)
Stomach (glandul	ar portion):	( N= )	(18)	(20)	) (18	) (29)
(M) Leiomyo	sarcoma		0	0	1	0
Small intestine		(N=)	(18)	( 20	) (18	) (29)
(B) Leiomyc	ma.		0	0	0	1
(M) Adenoca	rcinoma		0	0	1	ō
Large intestine	:	(N=)	(18)	( 20	) (18	1 ( 20 )
Liver:		(N=)	181	20	18	(29)
(M) Hepatoc	ellular carcinoma	()	0	0	0	) (20)
Pancreas:		( N= )	(18)	( 20		) (29)
(B) Acinar	cell adenoma	( )	0	( 20		
(B) Islet c	ell adenoma		3	1	0	1
(M) Islet c	ell carcinoma		0	0	1	0
Urinary System			0	0	1	0
Kidney:		( N- )	( 10 )	1 00		
(B) Adenoma		( N= )			50 B	) (29)
(B) Lipoma			0	0	0	1
Urinary bladder		/	0	0	0	1
Conital Sustan	•	(N=)	(18)	(20)	) (18	) (29)
Genital System						
Testis:		(N=)	(18)	( 20 )	) (18	) (29)
	itial cell tumor		1	1	0	2
Epididymis:		(N=)	(18)	( 20	( 18	) (29)
Seminal vesicle		( N= )	(18)	( 20	118	29
Coagulating gla	nd :	(N=)	( 18 )	( 20	(18	(23)
(B) Adenoma		( )	0	0	0	
Prostate:		(N=)	(18)	( 20 )		(20)
		( 1- )	( 10 )	( 20	) (18	) (29)

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm.

# Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group) Terminal kill after 104 weeks of treatment Table 25 - 8

Site &	Lesion	Dos	e		(ppm)		0	30	00	10	000	30	000
		No.	of	animals	examined		18		20		18		29
Endocr	ine System						-						
	Pituitary:				(N=)	(	18)	1	20	) (	18	) (	29)
	(B) Anteri	or ade	nom	a			13	,	14	, (	13	, (	21
	(B) Adenom	a in i	nte	rmediate	part	2	0		1		0		0
	< Mass	not i	n s	ection >			0		Ô		ŏ		1
	Thyroid:				( N= )	(	18)	(	20	) (	18	) (	29)
	(B) Follic	ular a	den	оща	( )		2	1	1	, (	0	, (	0
	(B) C-cell	adeno	ma				2		5		Ő		1
	(M) C-cell	carci	nom	a			0		0		1		ō
	Parathyroid:				( N= )	(	18)	(	20	) (	18	1 1	( 29 )
	Adrenal:				( N= )	2	18 1	2	20		18		29
	(B) Pheoch	romocy	tom	a	()		8	1	4	, (	3	, ,	4*
Nervou	is System								T		0		44
	Cerebrum:				(N=)	1	19)	1	20	1 (	10	1	00 1
	(B) Glioma				(n)	(	0	C	0	) (	18	1	(29)
	Cerebellum:				(N=)	1	10 1	1	20	1 (		1	1
	(B) Granul	ar cel	1 +	umor	( 11- )	(	10 )	(	20	) (	18	) (	(29)
	Brain stem:	ui cui		umor	(N=)	1	10 1	1		1 (	1	1	0
	Spinal cord (ce	rvieal	1:		$(N^{-})$		18) 18)	}	20	$\langle \rangle$	18		(29)
	Spinal cord (th	oracie	{ .		$(N^{-})$	3		}	20	$\langle \rangle$	18		(29)
	Spinal cord (lu	mhar) :	, .		$\left( \begin{array}{c} N \\ N \end{array} \right)$		18)	}	20	{ }	18		(29)
	Sciatic nerve:	moary.			$(N^{-})$		18)	}	20	$\{ \}$	18	2 9	(29)
Museul	o-Skeletal Sys	tom			( 14- )	(	18)	l	20	) (	18	) (	(29)
mabea	Bone (sternum) :	CCIII			( 11- )	1	10 1	1	00	、 ,	10		
	Bone (femur) :				(N=)		18)	5	20	$\{$	18	) (	29)
	Bone (vertebra)				( N= )		18)	5	20	2 (	18		(29)
	Tibio-femoral	inint:			(N=)		18)	(	20	) (	18	) (	(29)
	Skeletal musch	joint.			(N=)		18)	ļ	20	) (	18	) (	(29)
Sanco	Organs	e (m. c	ric	eps sura	e)∶ ( N= )	(	18)	(	20	) (	18	) (	(29)
Dellac	Eye:				( ) )	,		,	~ ~		-		
					( N= )	(	18)	(	20	) (	18	) (	(29)
	(B) Schwan Harderian glan	noma			( ) (	,	1	,	0		0		0
	Auricle:	d.			(N≕)	5	18) 3)	ļ	20	) (	18	) (	(29)
	Contraction and the second sec				(N=)	(		(	0	) (	0	) (	(2)
	(B) Papill	oma	1				1		-		-		0
Intor	(M) Malign umentary System	ant sc	hwa	nnoma			0				-		1
Incegu	Skin:				(								
	and the second s	2000			( N= )	(	18)	(	20	) (	18	) (	(29)
	(B) Papill						1		3		2		0
	(B) Kerato	acanth	oma				1		2		0		6
	(B) Tricho	epithe	110	ma			0		1		0		0
	(B) Sebace	ous gl	and	adenoma			0		1		0		0
	(B) Basal	cell a	den	oma			0		0		0		1
	(B) Fibrom						1		0		3		2
	(B) Lipoma						2		1		2		1
	(M) Basal	cell c	arc	i noma			0		0		ō		1
	(M) Fibros	arcoma					0		1		1		Ō
	(M) Malign	ant sc	hwa	nnoшa			0		Ō		ō		1
	Mammary gland:				( N- )	(	1)	(	3	) (		) (	(1)
	(B) Fibroa	denoma			. ,	•	ī	`	2	, (	0	/ 1	0
	(M) Adenoc	arcino	ma				Ô		õ		1		1

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm. \*: Significantly different from the control at 5 % level of probability.

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# Table 25 - 9 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group) Terminal kill after 104 weeks of treatment

Site & Lesi	Dose	(ppm)	0	3000	10000	30000
0100 W 11031	No. of anima	ls examined	18	20	18	29
No. of be	of malignant neoplasms		37	40	26	48
			0	2	7	5
	nign & malignant neoplasm		37	42	33	53
	No. of animals with benign neoplasm(s)		18	19	15	27
	No. of animals with malignant neoplasm (s)		0	2	7	5
No. of an	imals with neoplasm(s)		18	19	18	27

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Table 25 - 10

0 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group) Killed in extremis or found dead

No. of animals examined         32         30         32         21           General Organs         (M) Systemic malignant fibrous histiocytoma         0         1         0           (M) Systemic malignant fibrous histiocytoma         2         0         0         0           (B) Schwannoma         0         1         0         0           (M) System         (N-)(32)         (30)         (32)         (21)           (B) Schwannoma         0         1         1         0           (M) Myelogenic leukemia         0         2         10         0           (M) Mulignant lymphoma         0         2         10         0         0           (M) Mulignant lymphoma         0         2         10         0         0         2         12           Bone marrow (sternum):         N+-1         32         30         32         21         12           Lymph nodes (mesnetric):         N+1         32         30         32         22         12           Spleen:         (M) Histiocytic sarcoma         0         1         0         0           Masal cavity:         (N-)         32         30         32         21         30         32	Site & Lesion	Dose		(ppm)	0	3000	10000	30000	
(M)         Systemic malignant fibrous histicoytoma         0         1         0           Cardiovascular System         2         0         0         0           Cardiovascular System         (N-)(32)(30)(32)(21)         0         1         0           Heart:         (N-)(32)(30)(32)(21)         0         1         0         0           Aorta:         (N-)(32)(30)(32)(21)         0         0         1         0           Hematopoietic & Lymphatic System         (N-)(32)(30)(32)(21)         0         0         0           Morta:         (N-)(32)(30)(32)(21)         0         0         0         1         0           Mone marrow (femur):         (N-)(32)(30)(32)(21)         10         0         121         0           Bone marrow (vertebra):         (N-)(32)(30)(32)(21)         10         0         121         121           Thymus:         (N-)(32)(30)(32)(21)         121         123         130)(32)(21)         121           Lymph nodes (cervical):         (N-)(32)(30)(32)(22)(21)         10         0         10         0           Respiratory System         (N-)(32)(30)(32)(22)(21)         10         0         10         0           Moneocarcinoma         0	 site a newion	No. o	f animals	examined	32	30	32	21	_
(M)         Systemic malignant fibrous histicoytoma         2         0         0           Cardiovascular System         (N-)(32)(30)(32)(21)           (B)         Schwannoma         0         1         0           Aorta:         (N-)(32)(30)(32)(21)           Hematopoietic & Lymphatic System         (N-)(32)(30)(32)(21)           General:         (N-)(32)(30)(32)(21)           Mond Malignant lymphoma         0         2           Done marrow (femur):         (N-)(32)(30)(32)(21)           Bone marrow (sternum):         (N-)(32)(30)(32)(21)           Bone marrow (sternum):         (N-)(32)(30)(32)(21)           Lymph nodes (cervical):         (N-)(32)(30)(32)(21)           Lymph nodes (cervical):         (N-)(32)(30)(32)(21)           Spleen:         (N-)(32)(30)(32)(21)           M         Misticocytic sarcoma         0         1         0           Respiratory System         (N-)(32)(30)(32)(21)         (S)(32)(21)           Monoma         0         1         0         0           Modenocarcinoma         0         1         0         0           Bone marrow (sternum):         (N-)(32)(30)(32)(21)         (S)(32)(21)           Monoma         0         1         0         0 </td <td>General Organs</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	General Organs								
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	(M) Systemic (M) Systemic	histic	ocytic sam	Coma	0	0	1	0	
Cardiovascular System       Heart:       (N-)(32)(30)(32)(21)         Henatopoietic & Lymphatic System       0       1       1       0         General:       (N-)(32)(30)(32)(21)         (M) Malignant Lymphoma       0       2       1       0         Bone marrow (femur):       (N-)(32)(30)(32)(21)       0       0       0         Bone marrow (femur):       (N-)(32)(30)(32)(21)       0       0       0         Bone marrow (sternum):       (N-)(32)(30)(32)(21)       1       0       0         Lymph nodes (cervical):       (N-)(32)(30)(32)(21)       1       1       0       0         Lymph nodes (mesenteric):       (N-)(32)(30)(32)(21)       1       1       0       0       1       0       0         Misticocytic sarcoma       0       1       0       0       1       0       0         Modenocarcinoma       0       1       0       0       1       0       0         Modenocarcinoma       0       1       0       0       1       0       1         Modenocarcinoma       0       1       0       0       1       0       1         Modenocarcinoma       0       1       0	histioev	toma	IGHC TIDES	Jus	2	0	0	0	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Cardiovascular System				4	v	U	U	
(B)         Schwannoma         0         1         1         0           Acrta:         (N-)         (32)         (30)         (32)         (21)           General:         (M)         Myelogenic leukemia         0         0         0         0         0         0           (M)         Malignant lymphoma         0         2         1         0				( N= )	(32)	( 30	) (32	) (21)	
Hematopoietic & Lymphatic System       (N-)(32)(30)(32)(21)         General:       (N-)(32)(30)(32)(21)         (M) Malignant lymphoma       0         Bone marrow (femur):       (N-)(32)(30)(31)(21)         Bone marrow (sternum):       (N-)(32)(30)(32)(21)         Bone marrow (vertebra):       (N-)(32)(30)(32)(21)         Thymus:       (N-)(32)(20)(32)(21)         Lymph nodes (cervical):       (N-)(32)(20)(32)(21)         Lymph nodes (mesenteric):       (N-)(32)(30)(32)(21)         Spleen:       (N-)(32)(30)(32)(21)         MO Histiocytic sarcoma       0       1       0         Masal cavity:       (N-)(32)(30)(32)(21)       (N-)(32)(30)(32)(21)         MAsal cavity:       (N-)(32)(30)(32)(21)       (N-)(32)(30)(32)(21)         Modenoma       0       1       0         Modenocarcinoma       0       1       0         Modenocarcinoma       0       1       0         Boneach (non-glandular portion):       (N-)(32)(30)(32)(21)       (So)(32)(21)         Stomach (non-glandular portion):       (N-)(32)(30)(32)(21)       (So)(32)(21)         Modenoma       0       0       0       0         Modenocarcinoma       0       0       0       0		na			~	1	1	0	
General:         (N-)(32)(30)(32)(21)           (M) Malignant lymphoma         0         2         1         0         0           Mome marrow (femur):         (N-)(32)(30)(31)(21)         0         0         0         21         0           Bone marrow (femur):         (N-)(32)(30)(31)(21)         0         0         21         0           Bone marrow (vertebra):         (N-)(32)(30)(32)(21)         0         0         22         1           Lymph nodes (cervical):         (N-)(32)(20)(30)(32)(21)         0         0         1         0           Spleen:         (N-)(32)(30)(32)(21)         0         0         1         0         0           Mome Mais (cervical):         (N-)(32)(30)(32)(21)         0         0         1         0         0           Respiratory System         (N-)(32)(30)(32)(21)         0         0         1         0         0           Masal cavity:         (N-)(32)(30)(32)(21)         0         0         1         0         0           Masal cavity:         (N-)(32)(30)(32)(21)         0         0         0         0         0         0           Masal cavity:         (N-)(32)(30)(32)(21)         0         0         0         0 </td <td></td> <td>tin Su</td> <td>tom</td> <td>( N= )</td> <td>(32)</td> <td>( 30</td> <td>) (32</td> <td>) (21)</td> <td></td>		tin Su	tom	( N= )	(32)	( 30	) (32	) (21)	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	General:	cic by:	сещ	(N = )	( 22 )	( 20	1 / 20	) ( 01 )	
(M) Malignant lymphoma       0       2       1       0         Bone marrow (femur):       (N-) (32) (30) (31) (21)         Bone marrow (vertebra):       (N-) (32) (30) (32) (21)         Bone marrow (vertebra):       (N-) (32) (30) (32) (21)         Lymph nodes (cervical):       (N-) (32) (30) (32) (21)         Lymph nodes (mesenteric):       (N-) (32) (30) (32) (21)         Spleen:       (N-) (32) (30) (32) (21)         (M) Histicocytic sarcoma       0       1       0         Respiratory System       (N-) (0) (2) (0) (3)       (32) (21)         (M) Adenocarcinoma       0       1       0         (B) Adenoma       0       1       0       0         (B) Adenoma       0       1       0       0         (B) Adenoma       0       1       0       0         (B) Adenoma       0       0       0       1         (B) Adenoma       0       0       0       1         Submaxillary gland:       (N-) (32) (30) (32) (21)       29)       30) (32) (21)         Stomach (non-glandular portion):       (N-) (32) (30) (32) (21)       21)         M) Malignant schwannoma       0       1       0         (M) Malignant schwannoma       0 <td></td> <td>ic leul</td> <td>cemia.</td> <td>( 11 )</td> <td></td> <td></td> <td></td> <td></td> <td></td>		ic leul	cemia.	( 11 )					
Bone marrow (femur):       (N-) (32) (30) (31) (21)         Bone marrow (sternum):       (N-) (32) (30) (32) (21)         Bone marrow (vertebra):       (N-) (32) (29) (32) (21)         Lymph nodes (cervical):       (N-) (32) (29) (30) (32) (21)         Lymph nodes (mesenteric):       (N-) (32) (30) (32) (21)         Spleen:       (N-) (32) (30) (32) (21)         M() Histicoytic sarcoma       0         Nasal cavity:       (N-) (32) (30) (32) (21)         Lung:       (N-) (32) (30) (32) (21)         Lung:       (N-) (32) (30) (32) (21)         Bone marrow (sternum):       (N-) (32) (30) (32) (21)         Masal cavity:       (N-) (32) (30) (32) (21)         Lung:       (N-) (32) (30) (32) (21)         Bone marrow (matrix)       (N-) (32) (30) (32) (21)         (B) Adenoma       0       0         M() Adenocarcinoma       0       0         Sublingular gland:       (N-) (32) (30) (32) (21)         Stomach (non-glandular portion):       (N-) (32) (30) (32) (21)         Stomach (glandular portion):       (N-) (32) (30) (32) (21)         M() Malignant schwannoma       0       1       0         (M) Malignant schwannoma       0       1       0         (B) Acinar cell adenoma       0       1	(M) Malignan	t lympł	oma		100			-	
Bone marrow (sternum): Bone marrow (vertebra): $(N_{-})$ (32) (30) (32) (21) $(N_{-})$ (32) (29) (30) (21) $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ $(12)$ 	Bone marrow (femu	r) :		( N= )		( 30			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$					(32)		) (32		
Lymph nodes (cervical): Lymph nodes (mesenteric): Spleen: (M) Histiocytic sarcoma Masal cavity: Trachea: Lung: (B) Adenoma Submaxillary gland: Sublingular gland: Stomach (non-glandular portion): Stomach (glandular portion): M) Alignant schwannoma Liver: (B) Adenoma (M) Alignant schwannoma Liver: (B) Adenoma (C) (C) (C) (C) (C) (C) (C) (C) (C) (C)		ebra):							
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		i a a 1) :		1				//	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Lymph nodes (mese	nteric)	:	1 1					
	Spleen:				32		32		
Respiratory System       Nasal cavity: $(N-)$ (0) (2) (0) (3)         Trachea: $N-$ ) (32) (30) (32) (21)         Lung: $(N-)$ (32) (30) (32) (21)         (B) Adenoma       0       1       0         (M) Adenocarcinoma       0       0       1       0         Digestive System       0       1       0       0       1         Submaxillary gland: $(N-)$ (32) (29) (30) (21)       0       1       0         Submaxillary gland: $(N-)$ (32) (29) (30) (21)       0       1       0         Submaxillary gland: $(N-)$ (32) (30) (32) (21)       0       1       0         Submach (non-glandular portion): $(N-)$ (32) (30) (32) (21)       1       0       1       0         Stomach (glandular portion): $(N-)$ (32) (30) (32) (21)       1       0       0       1       0         MM Haignant schwannoma       0       1       0       0       1       0       0         (M) Malignant schwannoma       0       1       0       0       1       0       0         (B) Acinar cell adenoma       0       0       1       0       1       1       0       1       1         (		tic sar	coma	,					
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$								v	
Lung: $(N - )(32)(30)(32)(21)$ (B) Adenoma01(M) Adenocarcinoma00Digestive System00Submaxillary gland: $(N - )(32)(29)(30)(21)$ Subligular gland: $(N - )(32)(29)(30)(21)$ Esophagus: $(N - )(32)(30)(32)(21)$ Stomach (non-glandular portion): $(N - )(32)(30)(32)(21)$ Stomach (glandular portion): $(N - )(32)(30)(32)(21)$ Stomach (glandular portion): $(N - )(32)(30)(32)(21)$ Small intestine: $(N - )(32)(30)(32)(21)$ M Malignant schwannoma $(N - )(32)(30)(32)(21)$ (B) Hepatocellular adenoma $0$ $1$ (M) Hepatocellular carcinoma $0$ $1$ (B) Adenoma $0$ $1$ (B) Adenoma $0$ $1$ (B) Adenoma $0$ $1$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Adenoma $0$ $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$ (B) Interstitial cell tumor $0$				( N= )	(0)		) ( 0	) (3)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$					(32)		) (32	) (21)	
(M) Adenocarcinoma       0       0       0       0         Digestive System       Submaxillary gland:       (N=) (32) (29) (30) (21)         Sublingular gland:       (N=) (32) (29) (30) (32) (21)         Stomach (non-glandular portion):       (N=) (32) (30) (32) (21)         Stomach (non-glandular portion):       (N=) (32) (30) (32) (21)         Stomach (glandular portion):       (N=) (32) (30) (32) (21)         Stomach (glandular portion):       (N=) (32) (30) (32) (21)         M Malignant schwannoma       0       1       0         Large intestine:       (N=) (32) (30) (32) (21)         (M) Malignant schwannoma       0       1       0         (B) Hepatocellular adenoma       0       1       0       0         (B) Acinar cell adenoma       0       1       0       1         (B) Adenoma       0       0       1       0       1         (B) Adenoma       0       0       1       1       0       1         (B) Adenoma       0       0       0       32) (21)       30       32) (21)         (B) Adenoma       0       0       0       32) (21)       30       32) (21)         (B) Adenoma       0       0       0       32)				(N=)					
Digestive System       N=       0       0       1         Submaxillary gland:       N=       (32)       (29)       (30)       (21)         Sublingular gland:       N=       (32)       (29)       (30)       (21)         Esophagus:       N=       (32)       (29)       (30)       (21)         Stomach (non-glandular portion):       N=       (32)       (30)       (32)       (21)         Stomach (glandular portion):       N=       (32)       (30)       (32)       (21)         Stomach (glandular portion):       N=       (32)       (30)       (32)       (21)         Small intestine:       N=       (32)       (30)       (32)       (21)         (M) Malignant schwannoma       0       1       0       0         Liver:       (N=)       (32)       (30)       (32)       (21)         (B) Hepatocellular adenoma       0       1       0       0       1       0         (B) Acinar cell adenoma       0       1       2       0       1       0       1         (B) Adenoma       0       0       0       0       3       3       3       3       3       3       3	1 6	cinoma							
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Digestive System				v	0	U	1	
Sublingular gland: Esophagus: $(N=)(32)(29)(30)(21)(N=)(32)(21)$ Stomach (non-glandular portion): Stomach (glandular portion): $(N=)(32)(30)(32)(21)(N=)(32)(30)(32)(21)$ Stomach (glandular portion): M Malignant schwannoma (M) Malignant schwannoma Large intestine: $(N=)(32)(30)(32)(21)(N=)(32)(21)(N=)(32)(30)(32)(21)$ (M) Malignant schwannoma Large intestine: $(N=)(32)(30)(32)(21)(N=)(32)(30)(32)(21)(N=)(32)(30)(32)(21))$ (B) Hepatocellular adenoma (M) Hepatocellular carcinoma $0$ $1$ (B) Acinar cell adenoma (B) Islet cell adenoma $0$ $1$ (B) Adenoma (B) Islet cell adenoma $0$ $1$ (B) Adenoma (B) Islet cell adenoma $0$ $1$ (C) Finary bladder: (C) (B) Adenoma $(N=)(32)(30)(32)(21)(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21))(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21))(30)(32)(21)(30)(32)(21))(30)(32)(21)$	Submaxillary gla	nd:		(N=)		( 29	) (30	) (21)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Sublingular glan	d :				( 29	) (30	(21)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$							) (32	) (21)	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Stomach (glandula)	aular p	ortion):						
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Small intestine:	porti	ion).						
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(M) Malignan	t schwa	nnoma	( ) 					
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Large intestine:			( N= )	(32)		) (32	) (21)	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$				( N= )	(32)	( 30	) (32	) (21)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	(B) Hepatoce	llular	adenoma				1	-	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Pancreas:	ITUTAr	carcinoma		•		2		
(B) Islet cell adenoma       1       0       1         Urinary System       1       0       0       1         Kidney:       (N=)(32)(30)(32)(21)       0       0       3         Urinary bladder:       (N=)(32)(30)(32)(21)       0       3         Genital System       (N=)(32)(30)(32)(21)       0       3         Genital System       (N=)(31)(30)(32)(21)       2       0       0         (B) Interstitial cell tumor       2       1       0       0         (B) Interstitial cell tumor       2       1       0       0         Semicle series       (N-)(31)(30)(32)(21)       2       1       0		ell ade	noma	( 4- )					
Urinary System       (N=) (32) (30) (32) (21)         (B) Adenoma       0 0 3         Urinary bladder:       (N-) (32) (30) (32) (21)         Genital System       (N-) (32) (30) (32) (21)         Testis:       (N-) (31) (30) (32) (21)         (B) Interstitial cell tumor       2 1 0 0         Epididymis:       (N-) (31) (30) (32) (21)	(B) Islet ce	ll ader	oma		100		-		
(B) Adenoma $(N - )(31)(30)(32)(21)$ Urinary bladder: $(N - )(31)(30)(32)(21)$ Genital System $(N - )(31)(30)(32)(21)$ Testis: $(N - )(31)(30)(32)(21)$ (B) Interstitial cell tumor $2$ Epididymis: $(N - )(31)(30)(32)(21)$							U	•	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Kidney:			( N= )	(32)	( 30 )	) (32	) (21)	
Genital System       (N-)(31)(30)(32)(21)         (B) Interstitial cell tumor       2       0       0         Epididymis:       (N-)(31)(30)(32)(21)       2       1       0       0         Semiclassical cell tumor       (N-)(31)(30)(32)(21)       0       0       0	(B) Adenoma			( 11 )		-		3	
Testis: $(N = ) (31) (30) (32) (21)$ (B) Interstitial cell tumor $2$ $1$ $0$ Epididymis: $(N - ) (31) (30) (32) (21)$ Semistricity $(N - ) (31) (30) (32) (21)$				(N=)	(32)	(30)	) (32	) (21)	
(B) Interstitial cell tumor Epididymis: (N-)(31)(30)(32)(21) (N-)(31)(30)(32)(21)				( N= )	(31)	( 20 )	( 20	) ( 01 )	
Epididymis: (N-)(31)(30)(32)(21)	(B) Intersti	tial ce	ll tumor	( 11- )	2		0		
	Epididymis:		and his operations.	(N-)	(31)		) ( 32		
	 Seminal vesicle:			( N= )	(32)	( 30 )			

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm

Table 25 - 11

Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group) Killed in extremis or found dead

Site & Lesion	Dose	(ррм) О	3000	10000 30000
	No. of animals ex	amined 32	30	32 21
Genital System 《cont.》 Seminal vesicle Coagulating glan Prostate: Penis:	(cont. ) :	(N=)(32) (N=)(32) (N=)(32) (N=)(32) (N=)(1)	(30) (30) (30) (0)	$\begin{pmatrix} 32 \\ 32 \end{pmatrix} \begin{pmatrix} 21 \\ 21 \end{pmatrix} \\ \begin{pmatrix} 32 \\ 32 \end{pmatrix} \begin{pmatrix} 21 \\ 21 \end{pmatrix} \\ \begin{pmatrix} 0 \\ 2 \end{pmatrix} \end{pmatrix}$
Endocrine System Pituitary: (B) Anterior Thyroid: (B) Follicul (B) C-cell a (M) Follicul	ar adenoma	(N-)(32) (N-)(32) 1 2 1	(30) (21) (29) 0 4 0	(32)(21) 14* 18 (31)(21) 1 0 2 4
(M) C-cell c: Parathyroid: Adrenal: (B) Cortical (B) Pheochron	arcinoma adenoma	(N=)(32) (N=)(32) 1 6 0	0 (28) (30) 2 4 0	$\begin{array}{ccc} 0 & 0 \\ 0 & 1 \\ (31) & (21) \\ (32) & (21) \\ 0 & 0 \\ 2 & 6 \\ 1 & 0 \end{array}$
Cerebrum: (B) Glioma	acic): ar):	(N=)(32) 1 (N=)(32) (N=)(32) (N=)(32) (N=)(32) (N=)(32) (N=)(32) (N=)(31)	( 30 ) 0 ( 30 ) ( 30 ) ( 30 ) ( 30 ) ( 30 ) ( 30 )	$\left(\begin{array}{c}32\\1\\0\\0\\0\\32\\1\\2\\2\\1\\32\\1\\32\\1\\32\\1\\32\\$
Bone (sternum) : Bone (femur) : (B) Osteochon Bone (vertebra) : Bone (others) : (M) Osteosard Tibio-femoral jo Skeletal muscle Sense Organs Eye:	ndroma coma	(N=)(32)	$ \left(\begin{array}{c} 30\\ 30\\ 0\\ (30)\\ (30)\\ (30)\\ (30)\\ (30)\\ (29)\\ (29) \end{array}\right) $	$ \begin{pmatrix} 32 \\ 31 \end{pmatrix} \begin{pmatrix} 21 \\ 21 \end{pmatrix} \\ \begin{pmatrix} 0 \\ 32 \\ 8 \end{pmatrix} \begin{pmatrix} 21 \\ 3 \end{pmatrix} \\ \begin{pmatrix} 32 \\ 3 \end{pmatrix} \\ \begin{pmatrix} 21 \\ 3 \end{pmatrix} \\ \begin{pmatrix} 31 \\ 32 \end{pmatrix} \begin{pmatrix} 21 \\ 21 \end{pmatrix} \\ \begin{pmatrix} 21 \\ 21 \end{pmatrix} \\ \begin{pmatrix} 30 \end{pmatrix} \begin{pmatrix} 21 \end{pmatrix} $
Harderian gland: Ear: (M) Zymbal's	gland carcinoma	(N=)(32) (N=)(0)	(29) (1) 0	$\begin{pmatrix} 30 \\ 1 \end{pmatrix} \begin{pmatrix} 21 \\ 0 \end{pmatrix}$
Integumentary System Skin: (B) Papilloma (B) Keratoaca (B) Basal cel (B) Fibroma (B) Lipoma		- (N-)(32) 0 2 0 3 2 0		$\begin{array}{cccc} 1 & - \\ (32) & (21) \\ 1 & 0 \\ 0 & 1 \\ 0 & 2 \\ 0 & 3 \\ 0 & 0 \\ 1 & 1 \end{array}$

(N=): Number of animals examined microscopically at the site.
 Malignancy: (B). benign neoplasm: (M). malignant neoplasm.
 \*: Significantly different from the control at 5 % level of probability.

Table 25 - 12	Histopathology - Incidence of microscopic neoplastic lesions	
	in male rats (Main group)	
	Killed in extremis or found dead	

. .

Site & Lesi	Dos	e		(ррп	)	0	3	000	10	000	30	000	
Ditto a hebr		of	animal	s examin	ed	32		30		32		21	
Integumenta	y System «cont	. »											-
Skin	(cont. 》:			( N	= )	( 32 )	(	30	1 (	32)	1	21	1
	1) Liposarcoma					1		0		ō,	1	0	'
2	1) Hemangiosarc					0		0		1		0	
	1) Malignant he	man	gioperio	cytoma		0		0		Õ		1	
1	1) Osteosarcoma					0		1		0		1	
	1) Histiocytic	sar	coma			0		0		1		ō	
	y gland:			( N	= )	( 2)	(	2)	) (	1)	(	1	)
1	3) Adenoma					1		0		0	`	0	1
	3) Fibroadenoma					1		1		1		0	
Body Caviti	4) Adenocarcino	ma				0		0		0		1	
Inora	cic cavity:			( N	= )	(0)	) (	0 )	) (	1)	(	0	)
AL Jon	4) Malignant me	sot	helioma					-		1		-	1
	nal cavity:	,		( )	= )	(1)	(	4)	) (	3)	(	1	)
	1) Malignant sc					0		0		1		0	Î
	1) Malignant me	sot	helioma			0		1		0		0	
No. of ber	nign neoplasms					45		42		26		39	
No. of ma	ignant neoplas	ms				8		7		12	•••••	6	••••
No. of ber	ign & malignan	t n	eoplasm	5		53		49		38	••••••	45	
No. of an	mals with beni	gn 1	neoplası	n (s)		26		28		18		20	
No. of an	mals with mali	gnai	nt neop	l asm (s)		8		7	•••••	12		4	
No. of an	mals with neop	las	m (s)			30		28	•••••	24		20	

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm.

# Table 25 - 13

Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main and satellite groups) All animals examined

Site & Lesion	Dos	е	(ppm)	0	30	000	10000	30000	
	No.	of animals	examined	76		75	80	78	
General Organi	S								
(M) (M)	Systemic his	tiocytic sam	coma	0		0	1	0	
(m)	Systemic mal histiocytoma	ignant fibro	ous	0					
Cardiovascula	System			2		0	0	0	
Heart:	Jocan		( N- )	( 70	) (	75	1 / 00	1 ( 70	
(B)	Schwannoma		( 11- )	( 10	) (	10	) (80		)
Aorta:			( N= )	( 76	) (	75	) (80	) (78	١
Hematopoietic	& Lymphatic	System			<i>,</i> ,	,	( 00	/ (10	,
General			( N= )	(76	) (	75	( 80	) (78	)
(M) (M)	Myelogenic 1	eukemia		1		0	0	0	1
(M)	Malignant ly Mononuclear	mphoma		0		2	1	0	
Bone man	row (femur) :	cell leukem		0	× /	1	0	0	2
Bone man	row (sternum)	:	(N=) (N=)	(76)	$\{ \}$	75	(79	) (78	)
Bone man	row (vertebra)	):	(N = )	(76	$\langle \rangle$	75 ) 75 )	(80	) (78	2
Thymus:			(N=)	( 76		74	(80)	) (78)	ł
Lymph no	des (cervical)	:	(N=)	( 76		74	(78	) (78 ) (78	ł
Lymph no	des (mesenter	i e) :	( N= )	( 76		75 )	( 80	) (78	{
Spleen:			( N= )	( 76		75 )			{
(M)	Histiocytic :	sarcoma		0	/ <b>\</b>	1	0	0	,
Respiratory Sy Nasal ca	stem							v	
Trachea:	wity:		( N= )	( 0	) (	2)	( 0	) ( 3	)
Lung:			( N= )	( 76	) (	75)	(80	) (78	)
	Adenoma		(N=)	(76	) (	75)	(80)		)
	Squamous cell	carcinoma		2		3 0	1	3	
· (M)	Adenocarcinor	a		Ő		0	1	0	
Digestive Syst	em			v		v	0	1	
Submaxil	lary gland:		(N=)	(76)	) (	74)	(78)	(78	١
Sublingu	lar gland:		(N=)	( 76		74 )	( 78		1
Esophagu	s:		(N=)	(76)		75)	( 80		í
Stomach	non-glandular glandular por	portion):	(N=)	(76)		75)	( 80 )	(78	Ś
(M)	Leiomyosarcon	· tionj :	(N=)	(76)	) (	75)	(80)	(78	)
Small in	testine:	14	( N- )	0		0	1	0	
	Leiomyoma		( N= )			75)			)
	Adenocarcinon	a		0		0	0	1	
(M)	Malignant sch	wannoma		õ		1	1	0	
Large in	testine:		(N=)	( 76 )	11	75)	(80)	(78	1
Liver:			(N=)	( 76 )	1	75 1	80	(78	1
(B)	Hepatocellula	r adenoma		1		0	2	1	,
(M) Domonos	Hepatocellula	r carcinoma		0		1	$\overline{2}$	1	
Pancreas			( N= )	(76)	( 1	75)	(80)	(78	)
(D) (R)	Acinar cell a Islet cell ad	aenoma		0		1	1	2	
(M)	Islet cell ad	rainora		4		1	1	1	
Urinary System	Loree Cell Ca	reinoma		0		0	1	0	
Kidney:			( N= )	( 70 )	1 .		1	1	
	Adenoma			1 76 1	11	75)	(80)	(78)	1

(N=): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

T-11-	05 14	TT:
Table	25 - 14	Histopathology - Incidence of microscopic neoplastic lesions
		in male rats (Main and satellite groups)
		All animals examined

Site & Lesion	Dos	е		(ррш)	0	3	000	10	0000	30	0000	
	No.	of	animals	examined	76		75		80		78	
Urinary System	(cont.)				-							
Kidney 《				(N=)	( 76	) (	75	)	( 80	1	( 78	1
(B)	Lipoma				0		0	/	0	,	1	,
Urinary	bladder:			(N=)	( 76	) (	75	)	( 80	1	( 78	1
Genital System								'	( 00	/		/
Testis	•			(N-)	(75	) (	75	)	( 80	)	78	1
(B)	Interstitial	cel	tumor		3	· ·	2		0	/	2	'
Epididym				(N=)	(75	) (	75	) (	( 80	) (	78	)
Seminal	vesicle			(N=)	(76		75	) (	80	5 1	78	
	ing gland:			(N=)	(76	) (	75	) (	80	) i	78	
	Adenoma				0		0		0		1	'
Prostate	•			(N=) (	(76	) (	75	) (	80	) (	78	)
Penis:				(N=) (	( 1	) (	0	) (	0	) (		í
Endocrine Syst												
Pituitar	y:			(N=)	(76	) (	75	) (	80	) (	78	)
(B)	Anterior ade	noma			38		40		33		42	
(B)	Adenoma in i	ntern	iediate	part	0		1		0		0	
m • •	< Mass not i	n sec	etion >		0		0		0		1	
Thyroid:				(N=)(	( 76	) (	74	) (	79	) (	78	1
(B)	Follicular a	denou	1a		3		2	· ·	1	<i>,</i> ,	0	'
(B)	C-cell adeno	ma			6		10		5		6	
(M)	Follicular a	denoc	arcinon	na	1		0		Ő		ŏ	
	C-cell carci	noma			2		0		1		1	
Parathyr	oid			( N= ) (	76	) (	73	) (	79	) (	78	)
Adrenal:	· · · · ·			( N= ) (	76	) (	75	) (	80		78	
(B)	Cortical ade	noma			1		2	8	1		0	'
(B)	Pheochromocy	toma			14		9		5*		10	
Nervous System	Cortical ade	nocar	cinoma		0		0		1		0	
Cerebrum												
				( N= ) (	76	) (	75	) (	80	) (	78	)
	Glioma				1		0		1		1	
Cerebell	Malignant re	ticul	OSIS	/	_1		0		0		0	
	Granular cel	1		( N= ) (	76	) (	75	) (	80	) (	78	)
Brain st		i cun	or	( xr x )	0		0		1		0	
	ord (cervical)			(N=)(	76	) (	75	) (	80	) (	78	
Spinal of	ord (thoracic)			(N=)(	76	) (	75	) (	80	) (	78	)
Spinal of	ord (lumbar) :			(N=)(	75	) (	75	) (	80	) (	78	)
Sciatic	oru (rumbar) ·			(N=)(	76	) (	75	) (	79	) (	77	)
Musculo-Skelet	al Sustam			(N≃)(	75	) (	75	) (	79	) (	77	)
Bone (ster				( xr x (	-	· ·						
Bone (fem				$\left( \begin{array}{c} N = \end{array} \right) \left( \begin{array}{c} \end{array} \right)$	76	) (	75	) (	80	) (	78	)
	Osteochondro			(N=)(	76	) (	75	) (	79	) (	78	)
Bone (ver		1d		1 11 1 1	0	、 <i>.</i>	0		1		0	
Bone (othe	are):			(N = )(	76	<b>(</b>	75	) (	80	) (	78	)
M	)steosarcoma			(N=)(	6	) (	4	) (	10	) (	9	)
Tihio-fer	noral joint:			( ) )	0	· ·	0		1		0	
Skeletal	muscle (m. tr	1000		(N = )	76	) (	75	) (	79	) (	78	)
Shorotal	mascie (m. ti	rcep	a surae	): (N=)(	76	) (	75	) (	80	) (	78	)

(N-): Number of animals examined microscopically at the site.
 Malignancy: (B). benign neoplasm: (M). malignant neoplasm.
 \*: Significantly different from the control at 5 % level of probability.

# Table 25 - 15 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main and satellite groups) All animals examined

Site & Lesion	Dos	e		(p)	pm)			0		30	00		100	000		300	000	
	No.	of	Eanimals	exam	ine	d		76			75			80			78	
Sense Organs																		
Eye:				(	N=	)	(	76	)	(	74	)	(	78	1	1	78	1
(B) Schwa								1		`	0	'		0	'	1	0	'
Harderian gla	nd:			(	N=	)	(	76	)	(	74	)	(		1	(	78	1
Ear:				(	N=	)	(	0	j	Ì	1	í	ì	78 1	í	2	0	1
(M) Zymba	l's gla	nd	carcinoma				`	-	1		Ō	'	1	1	'	(	-	'
Auricle				(	N=	)	(	3	)	(	1	)	1	Ô	1	(	2	)
(B) Papil	loma							1		•	0	'	•	_	'	1	õ	
(M) Malig	nant sc	hwa	annoma					0			0			-			1	
Integumentary System	n																-	
Skin:				(	N=	)	(	76	)	(	75	)	(	80	)	(	78	)
(B) Papil	loma							2		100	5			3	<i>`</i>		0	'
(B) Kerate	Dacanth	oma	1					4			3			0			7	
(B) Trich	pepithe	lic	oma					0			1			0			0	
(B) Debac	eous gl	and	d adenoma					0			1			0			0	
	cella	der	ioma					0			0			0			3	
(B) Fibro								4			4			4			35	
(B) Lipom	B							4			2			2			1	
(M) Squam	ous cel	1 0	arcinoma					0			0			1			1	
	cell c		einoma					0			0			0			1	
(M) Fibro	sarcoma							0			1			1			0	
(M) Lipos								1			0			0			0	
(M) Heman	giosarc	oma	1					0			0			1			0	
(M) Malig	nant he	mar	ngiopericy	toma				0			0			0			1	
(M) Osteo:	sarcoma							0			1			0			1	
(M) Malig	nant sc	hwa	innoma					0			0			0			1	
(M) Histic	beytie	sar	Coma					0			0			1			0	
Mammary gland				(	N=	)	(	4	)	(	5	)	(	2	)	(	2	)
(B) Adenor								1			0			0			0	í
(B) Fibros								2			3			1			0	
(M) Adenoo Body Cavities	arcino	ma						0			0			1			2	
Thoracic cavit				1			,											
(M) Malig		a . +	hal:	(	N=	)	(	0	)	(	0	)	(	1	)	(	0	)
Abdominal cav	tanc me	500	nerioma	1	NT.	1	1	-			-			1			-	
(M) Malig	ant co	hun		(	N=	)	(	-	)	(	5	)	(	4	)	(	2	)
(M) Malig	ant mo	ent	holiomo					0			0			1			0	
		500	nerroma				_	0			1			0			0	
No. of benign neop	lasms							92			91			64			92	
No. of malignant m	neoplas	ms						8			9		•••••	19			11	
No. of benign & ma							1	100			00		•••••	83		1	03	
No. of animals wit	h beni	gn	neoplasm (s	;)	<del>a pina</del>			51			54			43			51	
No. of animals wit								8			9			19			9	
								-						TO			9	

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm; (M). malignant neoplasm.

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### Table 26 - 1

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 26 weeks of treatment

Site & Lesion	Dos	e		(ррш)	0	3000	10000	3000	0
	No.	of	animals	examined	10	10	10	1	0
Cardiovascular System	1						-		
Heart:				(N=)	( 10 )	( 10	1 1 10	1 1 1	• •
Aorta:				(N=) (N=)		(10)	) (10 ) (10		))
Hematopoietic & Lymph	otio	C	am	( 4- )	( 10 )	( 10	) (10	) (10	) j
Bone marrow (fem	ur):	by St	сещ	( ) )	1 10 1	1 10			
Bone marrow (ste	iur).			( N= )	(10)	(10	) (10	) (10	
Bone marrow (ver	tohno	· .		(N=)	(10)	( 10	) (10	) (10	
Thymus:	cept.a	,.		(N=)	(10)	(10	) (10		))
Lymph nodes (cer	wine l'	۱.		( N= )	(10)	( 10	) (10	) (10	))
Lymph nodes (mes	vical,	; .)		(N=)	(10)	(10	) (10)	) (10	
Spleen:	enter	10)		(N=)	(10)	(10	) (10	) (10	
Respiratory System				(N=)	(10)	(10	) (10)	) (10	))
Trachea:				( )		-			
				(N=) (N=)	(10)	( 10 ( 10	(10)	) (10	))
Lung: Digogative Sugton				(N=)	(10)	(10	) (10)	) (10	) )
Digestive System									
Submaxillary gl	and			(N-) (	(10)	(10)	) (10)	) (10	))
Sublingular gla	nd:			(N−) (	(10)	( 10 )	(10)	) (10	
Esophagus:				(N=)(	(10)	( 10	) (10	) (10	
Stomach (non-gla	ndula	r pc	ortion):	(N⇒)(	(10)	( 10	( 10	(10)	
Stomach (glandul	ar poi	rtic	on) :	(N=) (	10)	( 10	( 10		5 í
Small intestine				(N=)(	10 )	( 10 '	( 10 )		
Large intestine	:			(N=)(	10 )	( 10	(10	(10)	
Liver:				(N) (	10 )	( 10	( 10	10	
Pancreas:				(N=)(	10 )	( 10	( 10	(10)	
Urinary System					/	( 10	( 10 )	( 10	, ,
Kidney:			10 C	(N=) (	10)	( 10 '	( 10 )	( 10	11
Urinary bladder	:			(N=) (	10) 10)	(10)	2 10		1
Genital System				(,)	10 )	( 10 )	(10)	(10	, ,
Ovary:				(N = )	10 1	( 10 )	( 10 )	1 10	• •
Uterus:				(N=)( (N=)(	10 1	$\left\{\begin{array}{c} 10\\10\end{array}\right\}$	(10)		! {
(B) Polyp/e	ndomet	tria	1 stroma	1 nolvn	1 1	0	0	(10	; )
Vagina:				(N=) (	10)	(10)		( 10	
Endocrine System				()(	10 )	(10)	(10)	(10	' )
Pituitary:				(N=)(	10 )	(10)	( 10 )	1 10	
(B) Anterio	r ader	noma		( 11 ) (	10,	(10)			
Thyroid:				(N=) (	10)	1	0	( 10	
Parathyroid:				$\langle N = \rangle$	10 5	$\left\{\begin{array}{c} 10\\ 10\end{array}\right\}$	$\left(\begin{array}{c} 10\\ 10\end{array}\right)$	{ 10	
Adrenal:				(N=) (	10)	(10)		(10	
Nervous System				( 11- ) (	10)	(10)	(10)	(10	)
Cerebrum:				(N=) (	10.)	( 10 )	( 10 )	1 10	
Cerebellum:				(N=) (	10)	(10) (10)	(10)	( 10	
Brain stem:							(10)	(10	
Spinal cord (cer	vical	:			10	(10)	(10)	( 10	
Spinal cord (tho	racio			(N≕)(	10)	(10)	(10)	(10	
Spinal cord (lum)	har):			(N=)(	10)	(10)	(10)	(10	
Sciatic nerve:	uar).			(N=)(	10)	(10)	(10)	(10	
Musculo-Skeletal Syst	0.04			( N- ) (	10)	(10)	(10)	(10	)
Bone (sternum) :	ещ			(					
				(N=)(	10)	(10)	(10)	( 10	)
Bone (femur) :				(N~)(	10)	(10)	(10)	( 10	
Bone (vertebra) :			*2	(N=)(	10)	(10)	(10)	( 10	

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm.

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### Table 26 - 2

# 2 Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 26 weeks of treatment

Site	е. Т.	neion	Dose	(ppm)	0	3000	10000	30000
JICC .	* 110	.31011	No. of anim	als examined	10	10	10	10
Muscu	10-5	Skeletal Sy	stem «cont.»					
	Bor	ne (vertebra)	(cont. ) :	(N=)	(10)	( 10 )	( 10	) (10)
	Tit	io-femoral	joint:	(N-)	10 5	10	1 10	$\begin{pmatrix} 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 $
	Ske	eletal musc	le (m triceps s	urae): (N=)	10 1	( 10	1 10	1 10 1
Sense						,		, ( 10 )
	Eye			(N=)	(10)	(10)	( 10	) (10)
Inton	mar	derian gla	nd:	(N=)	(10)	(10)	(10	$\left\{\begin{array}{c}10\\10\end{array}\right\}$
Integ	Ski	itary System	<b>n</b>	( )				
		mary gland		(N-)	(10)	( 10	(10	$\left(\begin{array}{c}10\\10\end{array}\right)$
	mau	mary grand		(N=)	(10)	(10)	(9)	) (10)
No.	of	benign neop	plasms		2	0	0	0
No.	of	malignant m	neoplasms		0	0	0	0
No.	of	benign & m	alignant neopla	SMS	2	0	0	0
No.	of	animals wi	th benign neopl	asm (s)	2	0	0	0
No,	of	animals wi	th malignant ne	oplasm (s)	0	0	0	0
No.	of	animals wit	th neoplasm (s)		2	0	0	

( N= ): Number of animals examined microscopically at the site.

## Table 26 - 3

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 52 weeks of treatment

Site & Lesion	Dos	e		(ppm)	0	3000	10000	300	000
	No.	of	animals	examined	10	10	10		10
Cardiovascular System									
Heart:				(N=)	( 10 )	( 10	) ( 10	1 1	10 1
Aorta:				( N= ) ( N= )	10 1	10	) (10 ) (10	$\langle \rangle$	10)
Hematopoietic & Lymph	atic	Svs	tem	(11)	( 10 )	( 10	) (10	) (	10 )
Bone marrow (fem	ur) :	-3-	· · ·	(N=)	(10)	( 10	1 / 10	1 1	10.1
Bone marrow (ste	rnum)	:		(N=)	10	(10)	$\{ (10) \\ (10) $	$\{ \}$	10)
Bone marrow (ver	tebra	):		(N- )	10 1	10	<pre>{ 10 } ( 10 10</pre>	$\{ \}$	10)
Thymus:				(N-)	( 10 )	( 10	) (10	$\langle \rangle$	10)
Lymph nodes (cer	vical	):		( N= )	10 5	( 10	\$ { 10	$\{ \}$	10)
Lymph nodes (mes	enter	ic)	:	(N-)	10 1	( 10	) (10	$\langle \rangle$	10)
Spleen:				( N= )	10 1	10	\$ 2 10	$\{ \}$	10 )
Respiratory System				( )	,	( 10	) (10	) (	10)
Trachea:				· ( N- )	(10)	( 10	) ( 10	) (	10 )
Lung				(N=) (N=)	105	( 10 ( 10	) (10 ) (10	$\{ \}$	10 {
Digestive System				. ,	,	( 10	, ( 10	) (	10)
Submaxillary gl	and:			(N-)	(10)	( 10	) (10	) (	10)
Sublingular gla	nd:			(N=)	( 10 )	( 10	5 ( 10	$\{ \}$	10 5
Esophagus				(N=)	(10)	( 10	) (10	$\{ \}$	10)
Stomach (non-gla	ndula	r p	ortion):	(N-)	(10)	( 10	) (10	$\{ \}$	10 5
Stomach (glandul	ar po	rti	on) :	(N-)	(10)	( 10		í ì	10 )
Small intestine	: 1			(N=)	(10)	( 10	5 ( 10	5 2	10 1
Large intestine	:			(N=)	(10)	( 10	) (10	52	10 )
Liver:				(N-) (	(10)	( 10	) (10	$\{ \}$	10 1
Pancreas				(N-) (	(10)	(10	) (10		10 )
Urinary System						•	/ (	, ,	10 )
Kidney:				( N= ) ( ( N= ) (	(10)	(10	) (10	) (	10)
Urinary bladder	:			(N=)(	10)	(10)	) { 10 } ( 10	57	10 1
Genital System									/
Ovary: Uterus:				(N=)( (N=)(	10) 10)	(10 (10	) (10	) (	10)
			1	(N=)(	10)	(10	) { 10	) (	10)
(B) Polyp/e Vagina:	naome	tri	al stroma		0	, 1	1		1
(B) Polyp				( N= ) (			) (10	) (	10)
Endocrine System					0	0	1		0
Pituitary:				( 11 - ) /	10.1	1			
(B) Anterio	a da	0.000		( )(	10)	(10	) (10	) (	10)
Thyroid:	auci	тоща	1	(N - )	10.)	1	3		1
Parathyroid:				(N=)( (N=)(	10)	( 10		4 2	10)
Adrenal:				$\left\{ \begin{array}{c} N = \\ N = \end{array} \right\}$	10)	(10	(10	1 1	10)
Nervous System				( 11- ) (	10)	(10	) (10	) (	10)
Cerebrum:				(N=) (	10 \	( 10	( 10	× /	10.1
Cerebellum:				(N=)( (N=)(	10) 10)	( 10	(10		10)
Brain stem:				(N-)	10 }	(10)	(10		10)
Spinal cord (cerv	vical)	:		(N=)(	10)	(10)	) (10		10)
Spinal cord (thor	acic)	:		(N=)(	10	(10)	) (10 ) (10		10)
Spinal cord (lumb	ar):			(N-)(	10 )	( 10 )	(10		10)
Sciatic nerve:				(N-) (	10)	( 10	(10		10)
Musculo-Skeletal Syste	m			()(	10)	(10)	(10	) (	10)
Bone (sternum) :				( N- ) ( ( N- ) (	10)	{ 10 } { 10 }	( 10 ( 10	) (	10) 10)
Bone (femur) :					1	1 10	(10	1	10 ]

( N= ): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm

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### Table 26 - 4

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 52 weeks of treatment

Site & Lesion	Dose	(ppm)	0	3000	10000	30000
	No. of animal	s examined	10	10	10	10
Musculo-Skeletal Sy	stem 《cont.》					
Bone (femur) 《	cont. 》: chondroma		0	0	(10)	1
Tibio-femoral Skeletal musc		ae): (N=)	(10)	(10)		$\left\{\begin{array}{c}10\\10\\10\end{array}\right\}$
Sense Organs Eye: Harderian gla	nd:					$\left\{\begin{array}{c} 10\\ 10\\ 10\end{array}\right\}$
Integumentary System Skin:						
Mammary gland (B) Fibros	adenoma	( N= ) (	(10) 1	(10) 0	(10) 1	(10) (10) 0
No. of benign neop	olasms		2	2	6	3
No. of malignant :	neoplasms		0	0	0	0
No. of benign & ma	alignant neoplasm	S	2	2	6	3
No. of animals wi	th benign neoplas	m (s)	2	2	4	2
No. of animals with	th malignant neop	lasm (s)	0	0	0	0
No. of animals with	th neoplasm(s)		2	2	4	2

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm.

## Table 26 - 5

5 Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 78 weeks of treatment

Site & Lesion	Dose		(ppm)	0	30	000	100	000	300	000
Site a lesion	No. of	animals	examined	8		9		8		8
Cardiovascular Syste	n							-		
Heart:			(N=) (	9)	1	0)	1	0 1	1	•
Aorta:			(N≕)( (N=)(	8)	>	9) 9)	}	8)	5	8) 8)
Hematopoietic & Lymp	hatic Syst	em	(11)(	0)	(	a )	(	8)	(	8)
Bone marrow (fe	mur):	- u	(N=)(	8)	(	0)	1	01	1	~ 1
Bone marrow (st	ernum) :		(N = )	8)	>	9) 9)	}	8)	5	8)
Bone marrow (ve	rtebra):		$\left( N = \right)$	8)	>	9	>	8)	}	8) 8)
Thymus:			(N=)(	8)	>	9)	}	8)	ł	8)
Lymph nodes (ce	rvical):		$n = \frac{1}{2}$	8)	}	9	>	8)	>	8
Lymph nodes (me.	senteric):		(N= { }	8)	}	9)	}	8)	>	8)
Spleen:			$\langle N = \langle \rangle$	8)	>	91	>	8	}	8
Respiratory System			( ) (	0)	(	5)	(	0)	(	0)
Trachea:			(N=)(	8)	1	0)	1	01	1	0 1
Lung:			2 N- { }	8)	>	9) 9)	}	8)	>	8
Digestive System			()(	• ,	(	0)	(	0)	(	0)
Submaxillary g	land:		(N=)(	8)	1	9)	1	01	1	0)
Sublingular gli	and:		$\langle N= \rangle$	8)	>	9)	>	8) 8)	>	8)
Esophagus:			(N= ) }	8)	>	9)	>	8)	5	8 l
Stomach (non-gla	andular po	rtion):	$\left\{ N = \right\}$	8)	>	3	>	8	>	8)
Stomach (glandu	ar portio	n) :	(N=)	8)	2	9)	1		5	8)
Small intesting	3:	,	(N=)(	8)	>	9)	}	8)	5	8)
Large intesting			(N = )(	8)	>	9)	ļ	8)	Ş	8)
Liver:			$\left\{ N = \right\}$	ŝ)	>	9	>	8)	5	8)
Pancreas:			(N=)(	8)	>	9)	}	8) 8)	Ş	8)
Urinary System			(	0)	(	а)	l	8)	l	8)
Kidney:			(N=)(	9)	1	0)	1	٥ ١	1	01
Urinary bladder	• :		N= { }	8)	>	9) 9)	>	8)	>	8 {
Genital System			( 1 ) (	0)	(	a )	(	0)	(	8)
Ovary:			(N=) (	8)	1	0)	1	01	1	0.1
Uterus:			(N=)( (N=)(	8) 8)	2	9) 9)	>	8)	>	8) 8)
(M) Adenoca	rcinoma		( ) (	0	(	1	(	°,	C	0)
Vagina:			(N=)(	8)	(	9)	(	8)	1	8)
(B) Polyp			( ) (	0	1	0,	(	0)	C	0)
Endocrine System				•		~		v		1
Pituitary:			(N=)(	8)	(	9)	(	8)	1	8)
(B) Anterio	r adenoma		( / (	6	1	5	(	4	(	2)
Thyroid:			(N=)(	8)	(	9)	(	8)	(	8)
(B) C-cell	adenoma			õ,	(	°,	(	1	C	0)
Parathyroid:			(N = ) (	81	1		(	-	1	4
Adrenal:			(N= { }	8)	1	9) 9)	>	8)	>	8)
Vervous System			( ) (	0,	(	5)	(	0)	(	0)
Cerebrum:			(N=)(	8)	(	( )	1	01	1	٥ ١
Cerebellum:			(N= { }	8)	2	9 ) 9 )	>	8)	}	8)
Brain stem:			(N=) (	81	2	9)	1	8)	1	8)
Spinal cord(cer	vical) :		$\left\{ N = \right\}$	8) 8)	2	9 \$	}	8	>	8
Spinal cord (tho	racie) :		(N=)	8)	2	9)	2	8)	>	8)
Spinal cord (lum	bar) :		(N-)	8)	2	9)	2	8)	>	8)
Sciatic nerve:			(N-)(	81	>	9 1	>	8)	5	8)

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm.

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### Table 26 - 6

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Satellite group) Interim kill after 78 weeks of treatment

Site & Lesion	Dose	(ppm)	0	3000	10000	30000
bite a Lesion	No. of anima	als examined	8	9	8	8
Musculo-Skeletal	System					
Bone (sternu Bone (femur) Bone (verteb Tibio-femor	m) : : ra) :	( N= ) ( ( N= ) ( ( N= ) ( ( N= ) ( ( N= ) ( urae) : ( N= ) (	8) 8) 8) 8) 8)	(9) (9) (9) (9)	) ( 8 ) ( 8 ) ( 8 ) ( 8	$ \begin{pmatrix} 8 \\ 8 \\ 8 \end{pmatrix} \\ \begin{pmatrix} 8 \\ 8 \\ 8 \end{pmatrix} \\ \begin{pmatrix} 8 \\ 8 \\ 8 \end{pmatrix} \\ \begin{pmatrix} 8 \\ 8 \end{pmatrix} $
Eye:		(N=)(	9)	1 0	) ( 0	) / 0)
Harderian g Auricle: (B) Pap		( N≕ ) ( ( N= ) (	8)	(9) (9) (0)	$\left( \begin{array}{c} 8\\ 8\\ \end{array} \right)$	
Integumentary Sys	tem		_	-	1	-
Skin: (B) Lip Manmary gla	Oma nd:	(N=)(	0	(9)	) ( 8	) (8)
	noma	( N- ) (	8) 0	(9)	) ( 8	) (8)
	roadenoma		1.	3	2	Ő
(M) Ade	nocarcinoma		1	1	0	0
No. of benign n	eoplasms		7	10	9	10
No. of malignan	t neoplasms		1	2	0	0
No. of benign &	malignant neoplas	SmS	8	12	9	10
No. of animals	with benign neopla	asm (s)	7	5	4	8
No. of animals	with malignant neo	oplasm (s)	1	2	0	0
No. of animals	with neoplasm(s)		7	6	4	

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm.

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### Table 26 - 7

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main group) Terminal kill after 104 weeks of treatment

Site & Lesion	Dose	(ppm)	0	3000	10000	30000
	No. of animals	examined	15	19	16	14
Cardiovascular Syste	n					1997 B
Heart:		(N=)	(15)	( 10 )	( 10	1 1 1 1
Aorta:		(N-) (N-)	15	(19)	(16)	
Hematopoietic & Lymp	hatic System	(11)	(10)	(19)	(10	) (14)
Bone marrow (fe	mur):	(N=)	(15)	( 10 )	1 10	1 1 1 1
Bone marrow (st	ernum) :	(N=)	(15)	(19)	(16	(14)
Bone marrow (ve	rtebra):	( N= (	15	(19)	( 16 ( 16	$\left( \begin{array}{c} 14 \\ 14 \end{array} \right)$
Thymus:		( N= {	15	2 19	16	(14)
Lymph nodes (cer	rvical):	(N-)	(15)	( 19 )	16	
Lymph nodes (me	senteric):	(N=)	(15)	( 19 )	( 16	
Spleen:		( N= )	15	19	16	(14)
Respiratory System		()	(10)	(10)	( 10 )	(14)
Trachea:		(N=)	(15)	(19)	( 16	(14)
Lung		(N=) (N=)	( 15 )	(19)	(16)	
Digestive System		()	( 10 )	( 10 )	( 10 )	(14)
Submaxillary g	land:	(N=)	(15)	( 19 )	( 16 )	( 14 )
Sublingular gli	and:	( N= )	15	19	$\begin{cases} 16 \\ 16 \end{cases}$	(14)
Esophagus:		(N=)	(15)	(19)	( 16	(14)
Stomach (non-gla	andular portion):	(N=)	( 15 )	( 19 )	( 16 )	(14)
Stomach (glandu	ar portion):	(N=)	(15)	(19)	( 16 )	(14)
Small intestine	9:	( N= )	15	119	16	) /
(B) Leiomyo	oma	( )	0	0	(10)	(14)
Large intestine		(N=)	(15)	(19)	( 16 )	(14)
(M) Maligna	int histiocytoma	( , .	1	0	( 10 )	(14)
Liver:		(N-)	(15)	(19)		(14)
(B) Hepator	ellular adenoma		1	1	( 10 )	(14)
Pancreas:		(N-)	(15)	(19)		(14)
(B) Islet o	ell adenoma		1	1	0	0
Jrinary System				-	•	v
Kidney:		(N-)(	(15)	(19)	(16)	(14)
(B) Lipoma			0	1	0	0
Urinary bladder	•:	(N-) (	(15)	(19)	(16)	
Genital System					/	、 /
Ovary:		(N=)(	(15)	(19)	(16)	(14)
	sa cell tumor		1	0	0	0
(B) Luteoma			0	0	1	0
Uterus:		(N=)(	15)	(19)	(16)	(14)
(B) Polyp/e	ndometrial stroma	l polyp	3	3	1	2
(B) Granula	r cell tumor		1	0	0	ō
(M) Adenoca	rcinoma		1	0	0	0
Vagina:		(N=)(	15)	(19)	(16)	(14)
Indocrine System						
Pituitary:		(N-) (	15)	(19)	(16)	(14)
(B) Anterio	r adenoma		12	19	12	13
(M) Anterio Thyroid:	r adenocarcinoma	( ·	1	0	0	0
	1	(N=)(	15)	(18)	(16)	
(D) rollicu (B) C_coll	lar adenoma		0	0	1	0
(B) C-cell Parathuroid	adenoma	(	1	4	2	1
Parathyroid: Adrenal:		( N- ) ( ( N- ) (	15)	(19) (19)	(16)	(14)
nul chai.		(N=)(	15)	(19)	(16)	(14)

(N=): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm.

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### Table 26 - 8

# B Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main group) Terminal kill after 104 weeks of treatment

Site & Lesion	se	(ppm)	0	3000	10000	30000
No	o. of animal	s examined	15	19	16	14
Endocrine System «cont.»						
Adrenal (cont. ) :		(N=)	(15)	(19)	(16)	(14)
(B) Cortical ad	enoma	( /	0	0	(10)	(14)
(B) Pheochromoc	vtoma		1	ŏ	2	1
Nervous System			1	U	2	1
Cerebrum:		( N= )	(15)	(19)	( 10 )	( 14 )
(M) Malignant r	eticulosis	(	0	(13)		(14)
Cerebellum:		(N=)	(15)		( 10 )	0
Brain stem:		( N= )	15	$\left\{\begin{array}{c}19\\19\end{array}\right\}$	$\{ 16 \}$	$\{14\}$
Spinal cord (cervica	1):	(N-)	(15)	(19)		(14)
Spinal cord (thoraci	el :	( N= )		(19)	$\{16\}$	(14)
Spinal cord (lumbar)	:	(N=)	1 1		(16)	(14)
Sciatic nerve:		$\left( N^{-} \right)$	(15)	(19)	(16)	(14)
Musculo-Skeletal System		( - )	(15)	(19)	(16)	(14)
Bone (sternum) :		( ) )	( 15 )	1	1	
Bone (femur) :		$\left( \begin{array}{c} N \\ N \end{array} \right)$	15	(19)	(16)	(14)
Bone (vertebra) :		(N-)	(15)	(19)	(16)	(14)
(B) Chordoma		( N= )	(15)	(19)	(16)	(14)
Bone (others) :		/ x	1	0	0	0
bone (others) :		(N-)	(4)	(1)	(0)	(1)
(B) Osteochondr	oma		2	0		1
Tibio-femoral joint	:	(N=)	(15)	(19)	(16)	(14)
Skeletal muscle (m.	triceps sur	ae): (̀N=)́∣	(15)	(19) (19)	(16)	( 14 )
Sense Organs						( )
Eye:		(N=)	(15)	(19)	(16)	(14)
Harderian gland:		(N-)	(15)	(19)	(16)	(14)
Ear:		(N=)	( O )	(1)	ini	11
Integumentary System				· - /	( .)	( - )
Skin		( №= ) (	(15)	(19)	(16)	(14)
(B) Papilloma			0	Ì O Í	1	0
(B) Fibroma			2	2	ô	ĭ
(B) Lipoma			2	õ	ĭ	ō
Mammary gland:		(N=) (				1
(B) Ādenoma		( ) (	0	1	0	(14)
(B) Fibroadenom			10	13	12	10
(M) Adenocarcin	oma		2	2	5	10
Body Cavities			-	4	J	1
Abdominal cavity:		(N=) (	(1)	(0)	(1)	( 0)
(B) Lipoma		()	ô	( 0)	(1)	(0)
(M) Malignant s	chwannoma		1	-	0	-
No. of benign neoplasms						
			38	45	36	29
No. of malignant neopla:	SmS		6	3	5	1
No. of benign & malignam	nt neoplasms	1	44	48	41	30
No. of animals with ben	ign neoplasm	ı (s)	15	19	15	14
No. of animals with mal	gnant neopl	asm (s)	4	3	5	
No. of animals with neop						
no. or animato with neor	JIASM (S)		15	19	15	14

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M). malignant neoplasm.

### Table 26 - 9

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main group) Killed in extremis or found dead

Site & Lesion	Dose	(ppm)	0	3000	10000	30000
	No. of animals	examined	35	31	34	36
General Organs						
(M) Systemic	histiocytic same	rcoma	1	0	0	0
Cardiovascular System	•		•	U	v	0
Heart:		(N=)	(35)	( 31	) (34	) (36
(B) Schwanne	)ma	(,	0	0	) ( 34	) (30
Aorta:		(N = )	(35)	( 31		
Hematopoietic & Lympha	tic System		( )	( 01	/ ( 04	) ( 30
General:		(N=)	(35)	( 31	) (34	) (36
(M) Malignar	it lymphoma	,	1	1	1	2
Bone marrow (femu	ır) :	(N=)	(35)	( 31	) (34	) (36
Bone marrow (ster	num) :	( N= )	(35)	( 31	34	36
Bone marrow (vert	ebra):	( N= )	(35)	( 31	34	) (36
Thymus:		(N=)	(35)	( 31 )	34	
Lymph nodes (cerv	ical):	(N=)	(35)	( 31	32	
Lymph nodes (mese	nteric):	(N= )	(35)	( 31 )	34	
Spleen:		(N-)	(35)	( 30	(34	) (36
Respiratory System		( )	( 00 )	( 00 )	(04	) ( 30
Nasal cavity:		(N=)	(2)	( 0 )	) ( 3	) ( 1
(M) Squamous	cell carcinoma	( )	`ī′		0	, , ,
Trachea:		(N = )	( 35 )	( 31 )	1 24	1 ( 20
Lung:		( N= )	235	$\binom{31}{31}$	24	
Digestive System		( )	( 00 )	( 31 )	( 34	) ( 30 )
Submaxillary gla	nd:	(N=)	(35)	(31)	( 32	1 20
Sublingular glan	d :	(N=)	(35)	(31)	32	) (36 ) (36
Esophagus:		(N-)	(35)	(31)	(34)	36
Stomach (non-glan	dular portion):	(N=)	(35)	(30)		(36)
Stomach (glandula	r portion):	(N-)	(35)	( 30 )		) (36
Small intestine:		(N= )	(35)	(31)	34	
Large intestine:		( N- )	35	$\binom{31}{31}$		
Liver:		(N=)	(35)	(31)		
Pancreas:		(N=)	(35)	(31)	(34)	
(B) Islet ce	ll adenoma	()	2	1	(34)	
(M) Islet ce	ll carcinoma		ō	1	Ô	1
Urinary System				•	v	U
Kidney:		(N=)	( 35 )	(31)	(34)	( 36 )
(M) Transiti	onal cell carcin	Oma	1	( 31 )	(34)	
Urinary bladder:		(N=)	( 35 )	(31)		0
(B) Papillom	a	( )	( 00 )	( 31 )	( 34 )	
Genital System			v	1	U	0
Ovary:		(N=)	( 35 )	( 21 )	( 24 )	( 90 )
Uterus:		( N= )	(35)	(31)	(34)	(36)
(B) Polyp/en	dometrial stroma	1 nolvn	( 00 )			
(M) Malignan	t schwannoma	. borab	Ō	4	0	2
Mass n	ot in section >		1		0	1
Vagina:	in socion >	(N=)	( 25 )	(21)	(24)	0
(B) Polyp		( 11- )	1	(31)		(36)
(M) Leiomyos	arcoma		0	0	0	0
Clitoral gland:		( N= )	( 1)	( 0)	( 0)	1
(1) 5	cell carcinoma	( 1- )	(1)	(0)	(0)	(0)

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm

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### Table 26 - 10

# Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main group) Killed in extremis or found dead

Site & Lesion -	ose		(p)	pm)			0		30	000		100	000		300	00	
	o. of an	imals	exam	ine	d		35			31			34			36	1
Endocrine System													-		-	the:	-
Pituitary:			(	N=	1	1	35	1	1	31	1	1	90	1	1	0.0	1
(B) Anterior a	denoma		(	R	,	(	34	,	1	29	,	(	33	)	L	36	)
Thyroid:	u on onde		(	N=	1	1	35	1	1	31	1	1	28 32	1	,	31	
(B) Follicular	adenoma	e.	(	M-	,	(	0	,	(	2	)	(	32	)	(	-	)
(B) C-cell ade	noma	8.					3			3			5			0	
Parathyroid:			(	N=	1	(		1	1	31	١	1	32	1	1	36	1
Adrenal:			2	N=	1	2	35		2	31	1	}	34		Y	30 36	
(B) Cortical a	denoma		1		'	1	0	,	(	1		(	0	,	(	30 0	,
(B) Ganglioneu	roma						õ			1			0			0	
(B) Pheochromo	cytoma						1			Ô			ő			0	
Nervous System	-						•			•			v			0	
Cerebrum:			(	N=	)	1	35	1	1	31	1	1	33	1	1	36	1
(B) Meningioma					'	,	0	'	1	1	'	(	0	,	1	0	,
(M) Malignant	reticulo	sis					1			Ô			0			0	
Cerebellum:			(	N=	)	(	35	1	1	31	1	1	33	1	1	36	١
(B) Granular c	ell tumo	r	`		'	1	0	/	1	0	1	(	1	,	1	0	1
Brain stem:			(	N=	)	(	35	1	1	31	1	1	33	1	1	36	١
Spinal cord (cervic	al):		2	N=		2	35	5	2	31		2	34		>	36	
Spinal cord (thorac	ic):		2	N=		2	35	{	2	31		}	34		>	36	
Spinal cord (lumbar			2	N=	1	2	35	5	2	31	{	2	34	{	>	36	ł
Sciatic nerve:			2	N=		2	35	{	2	31	<	>	34	<	>	36	{
Musculo-Skeletal System			(		1	(	00	,	(	01	,	ſ	04	,	(	30	,
Bone (sternum) :			(	N-	)	(	35	1	1	31	١	(	34	1	1	36	1
Bone (femur) :			2	N-		2	35	{	2	31	{	1	34	<	>	30 36	{
Bone (vertebra) :			2	N-		2	35		2	31		1	34		>	36	
Bone (others) :			1	N=		2	2	5	2	2	1	2	2	{	>	4	{
(B) Osteochond					'	1	0	,	1	õ	'	(	0	,	١,	2	,
Tibio-femoral join	t:		(	N=	)	(	35	)	(	31	1	1	34	1	1	36	١
Skeletal muscle (m	triceps	Surae	e): (	N-	í	ì	35	í	ì	31	í	ì	34	í		36	5
Sense Organs					'			'	`		1	1	01	,	1	00	,
Eye			(	N=	)	(	35	)	(	31	)	(	32	1	1	36	١
Harderian gland:			(	N=	)	(	35	)	Ì	31	Ś	ì	33	5	2	36	í
Ear			(	N=	)	ĺ	3	)	Ì	1	í	ì	1	í	2	2	í
Auricle:			(	N=	)	(	1	)	(	1	S	1	1	1	1	2	ś
(B) Fibroma						-	1			0	1		0	'		0	'
Integumentary System																•	
Skin:			(	N=*	)	(	35	)	(	31	)	(	34	)	(	36	)
(B) Papilloma						•	0	•	•	1	'		0	'	•	0	'
(B) Keratoacan	thoma						0			0			0			1	
(B) Fibroma							2			1			2			3	
(B) Lipoma							2			Ō			2			õ	
< Mass not	in sect	ion >					0			Ō			3			ŏ	
Mammary gland:			(	N=	)	(	35	)	(	31	)	(	34	)	(	36	1
(B) Adenoma			19				1			0	1		0	/	1	0	,
(B) Fibroadeno							13			14			12			20	
(M) Adenocarci	loma						8			5			6			7	

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm.

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Site & Lesion	Dose	(ррш) О	3000	10000	30000
	No. of animals ex	amined 35	31	34	36
No. of benign	neoplasms	61	59	51	62
No. of malign	ant neoplasms	14	7	7	11
No. of benign	& malignant neoplasms	75	66	58	73
No. of animal	s with benign neoplasm(s)	34	29	31	35
No. of animal	s with malignant neoplasm	(s) 12	7	7	
	s with neoplasm(s)	34	31	31	

Table 26 - 11 Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main group) Killed in extremis or found dead

# Table 26 - 12

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main and satellite groups) All animals examined

Site & Lesion	Dos	e		(ppm)	0	3	000	10	000	30	000	
	No.	of	animals	examined	78		79		78		78	
General Organs	3											
(M)	Systemic his	tiod	ytic sam	coma	1		0		0		0	
Cardiovascular	- System						-		•		v	
Heart:				(N-)	(78	) (	79	) (	78	) (	78	١
	Schwannoma				0		0	<i>,</i> ,	0	<i>,</i> ,	1	'
Aorta				(N-)	(78	) (	79	) (	78	) (	78	١
Hematopoietic	& Lymphatic	Syst	em					· ·		· ·	10	'
General				(N-)	(78	) (	79	) (	78	) (	78	1
(M)	Malignant ly	npho	ma		1		1	<i>,</i> ,	1	· ·	2	'
Bone mar	row (femur) :			(N-)	(78	) (	79	) (	78	) (	78	)
Bone mar	row (sternum)	:		(N=)	(78	57	79	\$ 1	78	57	78	{
Bone mar	row (vertebra)	:		(N-)	(78	57	79	ί	78	57	78	1
Thymus:				(N=)	(78	57	79	\$ 1	78	í ì	78	
Lymph no	des (cervical)	:		(N=)	( 78	íì	79	í i	76	Ś	78	
Lymph no	des (mesenter	i c) :		(N-)	( 78	57	79	57	78	{ }	78	{
Spleen:				(N=)	( 78	í í	78	í i	78	Ś	78	1
<b>Respiratory</b> Sy	stem			. ,		, ,		/ \		, ,	10	,
Nasal ca				(N=)	( 2	) (	0	) (	3	) (	1	1
(M)	Squamous cel	l ca	rcinoma	( ··· /	1	/ (	-	/ (	Ő	, (	ō	,
Trachea				(N=)	1 78	) (	79	) (	79	) (	70	١
Lung:				( N= )	78	$\langle \rangle$	70	< >	70	{ }	70	{
Digestive Syst	em			( )	( 10	, (	10	) (	10	, (	10	,
Submaxil	lary gland:			(N-)	(78	) (	79	) (	70		70	1
Sublingu	lar gland:			(N=)	( 78	$\langle \rangle$	79	$\langle \rangle$	76 76	{ }	78	{
Esophagu	IS:			( N= )	( 78	{ }	79	{ }		{ }	78	
	non-glandula	- n0	rtion):	(N = )	(78	{ }		{ }	78	! }	78	
Stomach	glandular poi	tio	n) :	( N= )	(78	$\langle \rangle$	78	$\langle \cdot \rangle$	78	! !	78	
Small in	testine:			(N = )	Contraction of the	{ }	78	$\langle \rangle$	78	! !	78	
	Leiomyoma			( 11- )	(78	) (	79	)	78	) (	78	)
	testine:			(N=)	0	1	0	۱ <i>(</i>	1	. ,	0	
	Malignant his	etio	outoma	( n- )	( 10	) (	79	) (	78	) (	78	)
Liver:	mari Suance nin	3010	cycoma	( ) .	1 70	1	0	· ·	0	,	0	
	Hepatocellula	ar a	danama	( N= )	( 18	) (	79	) (	78	) (	78	)
Pancreas	:	*I U	ucnoma	( N- )	1 70	× (	70	× /	0		0	
	Islet cell ad	leno	ma	( 11- )		) (	79		78	1	78	)
òmó	Islet cell ca	irei	noma		3 0		2 1		1		1	
Urinary System			TORIC		0		1		0		0	
Kidney:				(N-)	1 70	1	70	· ·	-			
	Lipoma			( N= )		) (	79	) (	78	(	78	)
òxó	Transitional	001	lannin	0.000	0		1		0		0	
Urinary	hladder:		i carein		1 70		0	. ,	0		0	
	Papilloma			( N= )	( 18	) (	79	) (	78)	(	78	)
Genital System	r aprilloma				0		1		0		0	
Ovary:				( ) )	/ == -							
	Granulosa cel	1.4		(N=)	(78)	) (	79	) (	78)	(	78	)
B	Granulosa cel Luteoma	1 0	umor		1		0		0		0	
Uterus:	LUCCOME			1	0		0	- In	1		0	
(D)	Dolum lande		1	(N=)	(78)	) (	79)	) (	78)	(	78	)
	Polyp/endomet	ria	l stroma	l polyp	5		8		2		5	~
(B)	Granular cell	tu	nor		1		0		0		0	
(M)	Adenocarcinom	A			1		1		0		0	

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm; (M). malignant neoplasm.

# Table 26 - 13

Histopathology — Incidence of microscopic neoplastic lesions in female rats (Main and satellite groups) All animals examined

Site & Lesion	Dose	(ррш)		0	3	000	1	10	000		30	000	
	No. of animals	examined		78		79	1		78			78	
Genital System «cont.»													-
Uterus 《cont.》:		( N= )	(	78	) (	79	1	(	78	1	1	78	
(M) Malignan	t schwannoma	( )	1	0	1	0	•	(	0	,	(	1	
< Mass no	ot in section >			1		õ			0			0	
Vagina:		( N= )	1	78	1	79		(	78	1	1		
(B) Polyp		()	1	1		0		(	1	,	(		
(M) Leiomyosa	arcoma			ô		õ			Ô			1	
Clitoral gland:		(N=)	(	1)	1		)	(		)	1		1
(M) Squamous	cell carcinoma			1	(	-	'	(	-	,	(	0	,
Endocrine System												v	
Pituitary:		(N=)	(	78)	(	79	)	(	77	1	(	78	1
(B) Anterior	adenoma		•	54	,	54		(	47	,	(	52	
(M) Anterior	adenocarcinoma			1		0			0			0	
Thyroid:		(N~)	(	78)	(	78	)	(	76	1	1	78	
(B) Follicula	ir adenoma		•	0		2	'		1	'	1	0	,
(B) C-cell ad	enoma			4		7			8			4	
Parathyroid:		(N=)	(	76)	(	79	)	(	76	1	1	78	١
Adrenal:		( N= ) ( N= )	1	76) 78)	1	79 79	1	2	78	{	2	78	- 2
(B) Cortical	adenoma		•	0	,	1	'	,	1	'	1	0	1
(B) Ganglione	uroma			0		1			Ô			ŏ	
(B) Pheochron	ocytoma			2		Ō			2			1	
Nervous System												-	
Cerebrum:		( N= )	(	78)	(	79	)	(	77	1	1	78	1
(B) Meningion	18.			0		1	'		0	'	1	0	'
(M) Malignant	reticulosis			1		1			Ō			õ	
Cerebellum:		(N=)	(	78)	(	79	)	(	77	)	(	78	)
(B) Granular Brain stem:	cell tumor			0		0			1	·		0	'
Spinal cond (court		(N=)	( 1	78)	(	79	)	(	77	)	(	78	)
Spinal cord (cervi	cal):	(N=)	( 1	78 )	(	79	)	(	78	5	2	78	
Spinal cord (thora	cic) :	(N=)		78 )	(	79	)	(	78	)	(	78	ĵ
Spinal cord (lumba Sciatic nerve:	r):	( N= )	(	78)	(	79	)	(	78	)	Ì	78	í
Musculo-Skeletal System		( N= ) (	( 1	78 Ś	(	79	)	(	78	)	(	78	Ĵ
Bone (sternum) :		( x											*
Bone (femur) :		(N=)( (N=)(	(	78)	(	79	)	(	78	)	(	78	)
(B) Osteochon	dnows	(N=)(	( 1	(8)	(	79	)	(	78	)	(	78	)
Bone (vertebra) :	uroma.	( ) · · · ·		0		0			0		121	1	
(B) Chordoma		( N= ) (	1	(8)	(	79	)	(	78	)	(	78	)
Bone (others) :		( ) ) (	,	1	,	0		,	0			0	
(B) Osteochon	drome	(N=)(		6)	(		)	(	2	)	(	5	)
Tibio-femoral join	ut Ulla	( 11 ) (		2	,	0			0			3	
Skeletal musele (	nt. n trigona ourse)	(N=)(	1	(8)	ļ	79	)	(	78	)		78	
Skeletal muscle ( Sense Organs	a criceps surae,	· (N=)(	1	(8)	(	79	)	(	78	)	(	78	)
Eye:		( ) ) (		10.1	,								
Harderian gland:		$\binom{N}{N}$	7	8)	5	79	Į	5	76	)		78	)
Ear:		$\left( \begin{array}{c} N= \end{array} \right) \left( \begin{array}{c} \\ \end{array} \right)$	1	8)	Ş	79	)	( 1	77		( 1	78	)
Auricle:		( N= ) (		3)	Ş	2	)	(	1	)	(	3	)
(B) Papilloma		(N=)(		3)	(	÷ .	)	(	2		(	3	)
(B) Fibroma				0		0			1			0	
1-7 1 1 51 Outd				1		0			0			0	

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm.

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### Table 26 - 14

Histopathology - Incidence of microscopic neoplastic lesions in female rats (Main and satellite groups) All animals examined

Site & Lesion	Dose		(ppm)	0	3000	10000	30000
	No. of a	nimals (	examined	78	79	78	78
Integumentary S	System						
Skin:			(N-)	(78)	(79)	(78	) (78)
	apilloma			0	1	1	0
(D) N (B) F	eratoacanthoma ibroma			0	0	0	1
	ipoma			4	3	2	4
	Mass not in sec	tion >		4	1	3	0
Mammary g	land:		(N=)	(78)	(79)	(77	(70)
(B) A	denoma		( 11 )	1	(13)	(77	) (78)
(B) F	ibroadenoma			25	30	27	30
(M) A Body Cavities	denocarcinoma			11	8	11	8
Abdominal	aguitu:		( ) .				
	ipoma		( N= )	(1)	(2)	(1)	) ( 0 )
(M) M	alignant schwann	oma.		0	0	1	-
No. of benign	neoplasms			110	116	102	104
No. of malign	ant neoplasms			21	12	12	12
No. of benign	& malignant neo	plasms	1	131	128	114	116
No. of animal	s with benign ne	oplasm (s	;)	60	55	54	59
No. of animal	s with malignant	neoplas	m (s)	17	12	12	12
No. of animal	s with neoplasm (	a)		60	58	54	60

(N=): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

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									•
REMOVAL REASON: INTERCURRENT		WALES				FEMALI	FEMALES		
ANTMALS ON STUDY ANTMALS COMPLETED	0 ppm 37	2000 ppm 36	6000 ppm 35	20000 ppm 64 26	0 ppm 64 20	2000 24 24	6000 ppm 64 13	20000 DDm 64 23	
ABDOMINAL CAVITY EXAMINED	••	40	00	••	4-	мo	00	00	
ADRENAL GLAND EXAMINED	W VOO40 0	H 07000	41000 0 M	6 19000 19	0 0000 0 7	40400 0		m0000 0	
BRAIN EXAMINED(MAIIGNAT) Astrocytoma(MAIIGNAT) Benign meningioma(BENIGN) Benign ependynoma(BENIGN) Pineal gland tumour(BENIGN)	۵000 W	80400 8	ы С С С С С С С С С С С С С С С С С С С	90400 N	00000 N	N 40000	61001	84000 84000	
CERVIX EXAMINED		1111		11113	61100 1	04000 04000	1001	21120	
DUODENUM EXAMINED	36 1 0	35 94 9	8 410	0 72 72	17 0 0	ter C	13 0 0	0 10 0	
EAR/ZYMBALS GLAND EXAMINED	۰	0	H	0	0	0	0	0	

GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN RATS

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

AND ONCOGENICITY STUDY IN RATS
SATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN R
GLYPHOSATE ACID:

# TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

MARCELLYCHMAT - NOS ERG - TANDAR		o a tem		-			c	-
	0	2000	6000	20000	0	FEMALES	S	20000
ANIMALS ON STUDY	ppm 64	DDM 64	ppm 64	DDM 64	ррш б.4	DDM 64	DDm Ad	mqq A
ANIMALS COMPLETED	37	36	35	26	50	24	13	23
EAR/ZYMBALS GLAND Squamous cell carcinoma(MALIGNANT)	(CONTINUED) 0	0 0	H	•	0	0	0	•
HARDERIAN GIAND EXAMINED	9 10 10	র ম ম	35 0 0	000 7	000	5 71 7	E O O	23 0
HEART EXAMINED	37	36	35	26	20	24	EI	23
(MALIGNANT)	н	0	0	0	0	•	•	0
KIDNEY EXAMINED	37 0	36 36	35	26 1	20	24 0	13	53 0
LACRIMAL GLAND BYAMINED	8 9 4 4	97 P M	90 0 0	000 19	6 <b>1</b> 0	23 1 0	61 00	27 0
LIMB EXXMINED	0,000	0140 1	maco	4040	N00H	4000	0000	4000
LIVER EXAMINED. Hepatocellular adenoma. (BENIGN) Liposarcoma (MALIGNANT)	37 0 0	0 N Q M	35 102	0 M O N	000	400	100	23 0
LUNG EXAMINED	37	36	35	26	20	24	13	23

GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN RATS

# TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

REMOVAL BEAGON - TUTER TITS BEAT		MALFS		-		TENSI	0		
		ā –	6000	20000	0	2000 6000	6000	20000	
ANIMALS ON STUDY ANIMALS COMPLETED	ppm 64 37	ppm 64 36	ppm 64 35	ppm 64 26	ppm 64 20	ppm 64 24	ppm 64 13	ppm 64 23	
LUNG Adenocarcinoma (MALIGNANT)		H		o	0	0	0	0	
LYNRFH NODE-NESERTERIC EXAMINED. MISSING	50 51 4	410140 M	ы с м с м с м с м с м с	0010 0	0000	0108	۴000	000 7	
LYMPHORETICULAR SYSTEM EXAMINED	υH	40	40	40	9 1	90	мO	40	
Large granular Lymphocyte leukemia (MALIGNANT) Myeloid leukaemia(MALIGNANT)	m 0	40	01	40	ώQ	цо	мo	40	
(MALITGNANT)	H	0	o	0	0	٦	0	0	
MAMMARY GLAND EXAMINED. MISEING. MISEING. Adenoma. (BENIGN). Yeibroadenoma. (BENIGN).					00400 N	8 8 100 8 100 8	m0044	80044 80044	
NASAL CAVITY EXAMINED	37 0	36	35 1	26 0	0 0	24 0	13	23 0	
(BENIGN)	00	<b>0</b> 1	40	00	••	00	40	••	
ORAL CAVITY EXAMINED. MISSING	φo	mo	40	81	но	ыo	40	00	

						5			2
REMOVAL REASON: INTERCURRENT		MALES 2000	6000		0	FEMALES 2000 6	ES	20000	
ANIMALS ON STUDY ANIMALS COMPLETED	ppm 64 37	ррш 64 36		ppm 64 26	ppm 64 20	54 24	ppm 64 13	23 23	
ORAL CAVITY Squamous cell carcinoma (MALIGNANT) Fibrosarcoma (MALIGNANT)	(CONTINUED) 0 0	D) D)	-10	04	40	40	• •	00	
PANCREAS EXAMINED	50000 M	80444 8	nomoo m	60000 N	64000 H	0000 N	m0000	m0000 N	
PARATHTROID GLAND EXAMINED	025 35	ñ u t	0 m 5 m	0 0 Q Q	61 0	18 6 0	500 1	210	
PHARYNX EXAMINED MISSING MISSING Squamous cell carcinoma(MALIGNNNT)	нн 36	900	800 800	0 0 0 Q 7	000	<b>400</b> 7	60 1	00 53	
FITULTARY GLAND EXAMINED MISSING	37 110	8 17 18	35 110	0 e 0 e 7	20 1700	53 16 16	1 1 1 1 1 1 1	23 100 0	
SALIVARY GLAND EXAMINED	9 0 9 Q	34 400	500 8	00 50 50	র ন ন	0 7 7 7 7	500 13	00 53	
SKIN EXAMINED	37 0	36 0	35	72 72	0 0 7	2 <b>4</b>	13 0	23 0	

GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN RATS

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

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TWO YEAR DIETARY TOXIC
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GLYPHOSATE ACI

# TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

REMOVAL REASON: INTERCURRENT		MALES	0009			FEMALES	Si		
ANIMALS ON STUDY ANIMALS COMPLETED	bpm 37		-	2000 26 26	ppm 64 20	2000 24 24	6000 64 13	20000 54 23	
SKIN Squamous papilloum. (BENIGN) Squamous carcinomm. (MALIGNANT) Benign basal cell tumour. (BENIGN) Basal cell carcinoma. (MALIGNANT) Pilomatrixonm (BENIGN) Keratoacanthoma (BENIGN) Sebaceous adanoma (BENIGN) Trichofolliculonma (BENIGN) Histiocytic sarcoma (MALIGNANT)	(CONTINUED) 0 1 0 5 5 0 0 0 0 0 0 0	000000110 2		00400000	******	04000000		******	
STOKACH EXALINED MISSING Squamous papilloma. (BENIGN)	6 700	00 36	38 0 0	0 0 0 E	000	0 13 7	50 T	0 73 73	
SUBCUTANEOUS TISSUE EXAMINED	@0+00	NH000	50010	64400	40004	44000	00000	-10000	
TAIL EXAMINED MISSING Fibrosarcoma. (MALIGNANT)	110	000 7	2 400	1 000	moo	000	MÓO	544	
TESTIS EXAMINED	9 H H 9	ы В Ц Ц	र्थनन ल	008 70		111			

								CONIGNI	10)
REMOVAL REASON: INTERCURRENT		0 2000	6000	20000		FEMALI	- FEMALES 2000 6000	20000	
ANLIMALS ON STUDY ANLIMALS COMPLETED	00m 64 37	-	-		ppm 64 20	ррш 64 24	e	23	
TESTIS Malignant mesothelioma(MALIGNANT)	(CONTINUED) 0	D) T	0	o	ı	1	·	ı	
THYMUS EXAMINED MISSING MISSING Fenior thymoma.(EENICA). Malignat thymoma.(MALIGNAT). Not otherwise specified sarcoma (MALIGNANT).	4100-10 0 M	8840 0 8	0 000 0	0 01 33 5	0 HH 0	0 0000 7	0 101 0 1	1 0015 7	
THYROID GLAND EXAMINED	७ननन ल	м 100	0002 M	0000 7	6400	6440 5	n000	23 23	
UTERUS EXAMINED					04004 0	24 24 24 26 26 26 26 26 26 26 26 26 26 26 26 26	ਅਜ਼ਹਮਜ ਜ	201210	

GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN RATS

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

<b>STUDY IN RATS</b>
AND ONCOGENICITY STUD
Y TOXICITY
TWO YEAR DIETAR
GLYPHOSATE ACID:

# TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

REMOVAL REASON: INTERIM		Salew			DATENA	TEMAT.		_
	•	2000	6000		٥	2000	6000	20000
ANIMALS ON STUDY ANIMALS COMPLETED	ppm 64 11	DDm 64 11	ppm 64 11	ppm 64 12	ррт 64 12	ppm 64 12	ppm 64 12	ррш 64 11
FITUITARY GLAND EXAMINED MISSING MISSING Adenome pars distalis. (BENIGN)	108	104	100	<b>1</b> 11	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	17 70 4	तन च न	104 104
THYROID GLAND BXAMINE	100	100	0 1 1 0	10 10 10	1 1 1 1	600 1700	400 100	100
UTERUS EXAMINED Stromal cell polyp(BENIGN)	11	1.1	<b>1</b> 1	1 )	514	12	12	1°

-

REMOVAL REASON: TERMINAL		MALES		·     · · · · · ·		FEMALES	Si		
ANTMALS ON STUDY	0 10 10 10 10 10 10 10 10 10 10 10 10 10	2000 DDm 64	6000 ppm 64	20000 20000	udd Py	o	6000 ppm 64	2000Ó ppm	
ANIMALS COMPLETED	16			36	32	58		30	
ADRENAL GLAND									
EXAMINED	16	5	<b>1</b> 8	<b>5</b> 6	32	<b>78</b>	38	õ	
Benign phaeochromocytoma. (BENIGN)	4	0	৯ বা	2 4	<b>&gt;</b> न	<b>5</b> 64	10	00	
Cortical adenoma (BENIGN)	•	-	0	•	0	0	•	0	
(MALIGNANT)	0	0	•	1	•	0	0	Ö	
BRAIN									
EXAMINED	16	17	18	26	32	28	39	30	
Benign meningioma. (MALLGNAMY)	••	••	• •	• •		• •	40	01	
Y TUGUT									
EXAMINED	1	,	1	ı	32	28	39	30	
Stromal cell polyp. (BENIGN) Stromal cell sarcoma (MALICNDNT)			1 1	1 1	00	•	<del>, 1</del> ,	•	
	t	I	I	I	•	>	4	5	
DUODENUM EXAMINED	16	17	18	26	32	28	39	30	
Adenocarcinoma (MALIGNANT)	•	•	0	•	0	-1	•	0	
EPIDIDYMIS	;	1							
EXAMINED	9 C	17	80	26	, ,		3 1	1	
Malignant mesothelioma (MALIGNANT)	••	• -•	.0	10	. ,				
NULTI									
EXAMINED	16	17	8	56	ē,	27	6 C	ŝ	
Leiomyosarcoma (MALIGNANT)	••	0	••	••	10	4 ल	••		
K IDNEY EXAMINED	4	4	-	36		0 C	00		
	> 1	i.	0	2	36	07	57	00	

GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICITY STUDY IN RATS

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

					}				
REMOVAL REASON: TERMINAL	0	MALES	5000	<u> </u>	0	FEMALE 2000	S	20000	
ANIMALS ON STUDY ANIMALS COMPLETED	ррш 64 16	54 DDm 17	ני גע נפ	_	DDm 64 32	ppm ppm 64 64 28 39	ррт 64 39	DDm 64 30	
KIDNEY Liposarcoma (MALIGNANT)	(CONTINUED) 0 0	•••	00	01	00	00	40	00	
LIVER EXAMINED	16 1	17 0	8 1 8	26	32	8 5 8	99 79	30 30	
LYMPH NODE-MESENTERIC EXAMINED	0 16 1	17 2 1	810 18	26 04 0	32 37 37	<b>0</b> 28 7	6 9 <b>0</b> 8 8	30 1 30	
LYNPH NODE-PANCREATIC EXAMINED	ਜਜ	00	10	40	00	40	40	00	
LYMPHORFTICULAR SYSTEM EXAMINED	40 4 0	no n o		NO N O	100 <b>4</b> H	r0 r 0	11 0 0	ৰাত ৰ ত	
MANMARY GLAND EXAMINED						000000 000000	00000 N	007004 M	
NASAL CAVITY EXAMINED	16	17	18	26	32	28	39	30	

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TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

IABLE 2/ - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPI				0200		OPLA		5 NIN	145) 0
REMOVAL REASON: TERMINAL		MALE 2000	6000		1		6000	20000	
ANIMALS ON STUDY ANIMALS COMPLETED	ррт 64 16	ppm 64 17	e		ppm 64 32	ppm 64 28	ppm 64 39	ppm 64 30	
NASAL CAVITY	(CONTINUED)	â							
Fepilitoma/s nasolachrymai duct (BENIGN)	00	00	••	00	• •	01	00	40	
ORAL CAVITY EXAMINED	000	440	MH0	000	m00	010	404	400	
PANCREAS EXAMINED	901 C	5 4 4 C	18 44 0 4	20 H B 20 5	00 gg	• 008 7	607 (	000	
PITULTARY GLAND EXAMINED MISSING MISSING Adenoma pars distalis (BENICN)	0000 H	0 10 10	0 80 4 M	1108 c	5°13 2°13	1 804c	0 0 0 <del>1</del> 0	5809 C	
SALIYARY GLAND EXAMINED	16 16	17 0	18 18 0	1 1 1	9 <u>7</u> 0	0 38 0	) 6°	9 0 0	
SKIN EXAMINED	9000 H	400M	8040 1	H 0 0 6	4005 M	8000 7	5,000 M	8444 8	

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

IABLE 2/ - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SF				0200		OPLA:	מור כיד	SPNINGS	<u>ה</u>
REMOVAL REASON: TERMINAL	0	3	6000		0	FEMALES		20000	
ANIMALS ON STUDY ANIMALS COMPLETED	ppm 64 16	ppm 64 17	ррт 64 18	ppm 64 26	ррт 64 32	ppm 64 28	ррт 64 39	00m 64 30	
SKIN Keratoacanthoma(BENIGN) Sebaceous adenoma(BENIGN)	(CONTINUED) 1 0	00 6	01	40	00	00	00	00	
SPLEEN EXAMINED	90 0 1	17 0 4	18 0 0	26 0	37 0 0 37	0 0 58	6.T 0 6	00 0 M	
SUBCUTANEOUS TISSUE EXAMINED	MN100	***	N0004	N0004	44000	m0000	PH004	vo-100	
TESTIS EXANINED	16 4 0	н Г н н	840 840	0 7 Q 7 Q					
THYMUS EXAMINED. MISSING. Benign thymoma. (BENIGN)	900 7	0 1 1 0	18 10 1	52 77 7	8 111 8	28 0 1	8710 8710	90 90 1	
THYROID GLAND EXAMINED Follicular cell adenoma.(BENIGN) Parafollicular cell adenoma.(BENIGN). Parafollicular cell carcinoma (MALIGNANT)	90H 0	1 201 1	80 N T O	0 0 M U	8 8 1 8 0 8 1 8 0	8 H O O 7	ର <b>ମ ତ</b> ମ	000 H	
UTERUS EXAMINED	1	I	ı	I	32	28	5£	30	

TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

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# TABLE 27 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (SPLIT BY REMOVAL REASON)

REMOVAL REASON: TERMINAL		2	6000			Z000	S	20000
ANIMALS ON STUDY ANIMALS COMPLETED	ppm 64 16	ppm 64 17	ррт 64 18	ррт 64 26	ppm 64 32	ppm 64 28	ppm 64 39	ppm 64 30
UTERUS Stromal cell polyp. (BENIGN) Adenocarcinoma. (MALIGNANT) Haemangioma. (BENIGN)	(CONTINUED)	· · · · ·	1111		10400	MNOO	500MH	4000
VOLUNTARY MUSCLE EXANINED. MISSING. Haemangioma. (BENIGN)	0 0 0 1 0	17 000	5	000 0	800 37	800 7	8 H O	000

## TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

	MALES MALES	MALE	2		1	FEMALES	SH	
ANTMALS ON STUDY ANTMALS COMPLETED	0 ppm 64	2000 DDM 64 64	6000 DDm 64	20000 ppm 64 64	0 64 64	2000 DDm 64	6000 DDm 64 64	20000 2000 64 64
ABDOMINAL CAVITY EXAMINED Lipoma (BENIGN)	00	40	mo	••	ъч	ъо	••	00
ADRENAL GLAND EXAMINED MISSING Benign genetone. (BENIGN) Benign phaeochromocytoma. (BENIGN) Cortical adeona. (BENIGN) Maligmant phaeochromocytoma (MALIGNANT).	40000 0 40000 0	40044 H	ю 070F0 Ю	40044 4	6 40040 0	401100 0	<u> ө</u> нооо о	40000 0
ERAIN EXAMINED	0 40000	90400 40400	400H0	90H04	9 9 9 9 0 0 0 9 9	40000 8	40004 9	41100 V
CERVIX EXAMINED. MISING. Stromal Gell Polyp. (BENIGN). Stromal Gell Barcoma. (MALIGNANT). Stromal Gell Barcoma. (MALIGNANT)						040000	Юннонн	00100 0 0
DUODENUM EXAMINED	0 H 3	0 <b>4</b> 0	0 7 5 0	040	61 0 3	13 61	00 <b>4</b>	9 9 0

ANIMALS ON STUDY ANIMALS ON STUDY DUODENUM Laiouroma (BENICAN)	64 ppm 64 (CONTINUED)	MALES - 2000 6 64 06 64 6 64 6 0 0	S 64 DDm 64		64 64 64	FEMALES	ies 64 ppm 64	 20000 64 64
EAR/ZYMBALS GLAND EXANINED	000	040	нон			- 000		
EPIDIDYMIS EXAMINED	00Hg	6444	6 6 6 7 0 0	4040 8				1111
HARDERLAN GLAND EXAMINED MISSING Anaplastic Barcoma. (MALIGNAN)	010	0 0 0	9 9 9	400 400	9 9 9 0 0	5 1 1 2 2	400	900 6
HEART EXAMINED. Malignant endocardial schwannoma Malignant endocardial schwannoma	64 1	64 0	6 0 <b>4</b>	64 0	64 0	64 0	64 0	64 0
ILEUM SXAMINBD MISSING. Leiomyosarcoma. (MALIGNANT)	57 7 0	57 0	9 1 6 0	0 N N 9	5 6 6	1.59	0 13 0	61 0
KIDNEY EXAMINED	64 0	64 0	64 0	17 6	64 0	64 0	64 0	64 0

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TABLE 28 - INTEF	IGROU	COM	PARIS	ON OF	MICRO	scopl	C NEO	INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)
ANTMALS ON STUDY ANTMALS COMPLETED	0 0 64 64	2000 2000 Dpm 64	6000 54 DDm 64	 20000 54 64		FEMALES 2000 6000 5Pm 5Pm 64 64	1255 6000 64 64	 20000 5 DPm 64
KIDNEY Liposarcoma (MALIGNANT)	(CONTINUED) 0 0	00	00		00		-0	~~
LACRIMAL GLAND EXAMINED	63 11 19 63	0 7 17 6	400 8	63 0 1 3	0 13 0	<u>ю</u> но	400	0 10
LIMB EXAMINED MISSING Squamous Squamous Benign histiocytoma. (BENIGN)	т Т	4110 1	0000	4040 4	N00H	nooo	~~~~	6000
LIVER EXAMINED Hepatocellular adanoma. (BENIGN) Liposarcoma. (MALIGNANT)	64 0 0 64	970 9	64 1 1	9 9 9 9 9 9	90 64	900 60	<b>4</b> 400	64 0 0
LUNG EXAMINED	64 0	64 1	64 0	64 0	6 <b>4</b> 0	64 0	64 0	64 0
LYMPH NODE-MESENTERIC EXAMINED	401-4 8	1 8 2 5 6	4040 4040	4000 4000	4044 4044	0 6 19 15 6	9 9 9 0 9 0 9 0 9	0,000 T
LYMPH NODE-PANCREATIC EXAMINEDEXAMINED	Ħ	0	г	÷	0	щ	H	0

## TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

ANIMALS ON STUDY ANIMALS COMPLETED	64	2000 2000 64 64	6000 5000 64	20000 DDm 64	0 54 64	2000 54 54	2000 6000 DDm DDm 64 64	20000 20000 64 54
LYMPH NODE-PANCREATIC Haemangioma(BENIGN)	(CONTINUED) 1	0 (0	•	0	0	0	0	
LYMPHORETICULAR SYSTEM EXAMINED	91	40	40	no	1 1	13 0	14 1	80
Warge granutar lymphocyce leukemia (MALIGNANT)	40	40	04	щO	<b>۵</b> 0	12 0	13	80
(MALIGNANT)	ч	o	• 0	•	ч	H	•	•
MAMMARY GLAND EXAMINED					6 6 6	<u>ю</u> но 19	900 9	40 () 9
Adenoma (BENIGN)			<b>1 1</b> 1	111		N O 4	0 H 0	0410
NASAL CAVITY EXAMINED. Fibrosarcoma (Malignant)	<b>\$</b> 9 40	64 0	1 1 1	64 0	64 0	64 0	64 0	64 0
FEDILIONA'S DESCLACHTYMAL duct (BENIGN)	000	004	400	000	000	040	400	400
ORAL CAVITY EXAMINED	800	400	104	**	404	604	nco	400

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<b>STUDY IN RATS</b>
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<b>TWO YEAR DIET</b>
GL YPHOSATE ACID:

## TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

		MALES				FEMAL	- FEMALES	
AUTMALS ON STUDY	0 DDm 64	2000 DDM 64	6000 DDm 64	20000 ppm 64	0 ppm 64	2000 DDm 64	6000 DDm 64	20000 20000 64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
ORAL CAVITY Fibrosarcoma (MALIGNANT)	(CONFINUED) 0 0	00 6	00	40	00	00	04	00
PANCREAS EXAMINED	64	64	64	64	63	ទ	64	64
MISSING	••	0,	• 1	01	-	-	0	0
Exocrime adenocarcinoma (Malignanr)	*0	N 14	~ 0	- 0	00	00	00	00
Islet cell adenoma(BENIGN) Islet cell adenocarcinoma	-	61	0	H	0	•	г	•
(MALIGNANT)) (MALIGNANT)	•	•	•	•	0	H	0	0
PARATHYROID GLAND EXAMINED	57 7	60 4	9 2 2	6 S 5	50 10 11	52	57	58
Adenoma. (BENIGN)	. 0	r <del>ci</del>		.0	<b>,</b> 0	10	0	
PHARYNX EXAMINED	6944 8944	900 900	900 8	64 0 0	900 800	400 9	9 400	66 0 0 44
PITULTARY GLAND SXMMIRED	64 13 0 0	19 19 19 19	3 10 10 10	18193 18193	63 47 0	66 13 06 13	6 1 9 0 4 1 0	8 4 4000
SALIVARY GLAND EXAMINED. MISSING	62 2	5 5 6	64 0	64 0	1	5 62	64 0	64 0

8.8       8.4		0	MALES 2000 DDM		20000	udd	2000 2000 DDm	1	 20000 DDm
CCONTINUED) 0 0 0 64 64 64 64 64 64 64 64 64 64	ANIMALS ON STUDY ANIMALS COMPLETED	64 64	64 64	64 64	64 64	64 64	64 64	64 64	64 64
400000000000 400 400 10 400000000000 4000 10 4000 00 4000000000 4000 10 4000 00 0000000 4000 0 4000 00 4000 0 4000 4000 800 800	LIVARY GLAND anoma (BENIGN)	(CONTINUE 0 0	。 6	00	04	-10	00	00	00
онолноон 400 о 400 Ци ооошонно 4000 и 400 ли ончонноо 400 о 400 би опонооо 400 о 400 юн	LN MJUNED. SSIIG. Babilloma. (BENIGN)	4000	400°	4040 8	9 10	4000 8	400, 700,	9000 9	400 9
4000 0 400 112 4000 1 4000 12 4000 0 4000 02 4000 0 4000 81 4000 0 4000 81	<pre>iign basal cell tumour. (BENICA) iign basal cell tumour. (BENICA) can cell carcinoma. (MALIGNANT) comtrixoma. (BENICA) etoeceus denoma. (BENICA) etoeceus denoma. (BENICA) concfolltouloma. (BENICA) chofolltouloma. (MALIGNANT) triocytic sarcoma. (MALICANANT)</pre>	24004004	200m0440	o4404400	0404H000	00040000			44040000
64 64 64 64 64 64 64 64 64 64 64 64 64 6	MINED. MINED. MINED. Mangiosarcoma. (MALIGNANT). . otharvise specified sarcoma. (WALIGNANT)	400 O	1000 FI	400 0 9	400 0	900 0 900 0	0 о⊢ 9	9 707 0	400 0
11 2 6 10 2 0 0	MACH Mirred Sirlo amous papilloma. (BENIGN)	64 0 0 4	64 0 0	400 400	907 007	00 <b>#</b>	640	904 9	400 9
	CUTANEOUS TISSUE MINED	11	50	10	∞ +	80 41	74	<del>م 1</del>	۰ <b>0</b>

TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

## TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

		2000	ЦĞ		0	2000	- FEMALES	20000
ANIMALS ON STUDY ANIMALS COMPLETED	64 64	64 64	ррш 64 64	ppm 64 64	ррш 64 64	DDm 64 64	ррт 64 64	ppm 64 64
SUBCUTANEOUS TISSUE	(CONTINUED)	6						
Fibrosarcoma (MALIGNANT)	-1 •	0	20	Ч	0	0	•	0
Haemangiosarcoma. (MALIGNANT)	40	<b>-</b> -		•	00	••	00	<b>н</b> (
	•	10	<b>н</b>	×	2	>0	5 M	00
TAIL EXAMINED	Ę		ų	:		:	;	
MISSING	5-11	201	50	40	8 <u>0</u>	90	40	8 m
······································	Ð	0	0	•	•	0	¢	ч
TRUTIS								
MISSING	63	63	63	64	ı	1	,	ı
Benign Leydig cell tumour. (BENIGN)	ιŋ	-1 (7)	- 10	00	11	1 1	T	
Benign mesothelioma (BENIGN)	•	न	0	.0	ı	,	1	
WALLYMAN' MEBOUNGLIOMA (MALIGNANT)	D	п	•	•	ı	ı	,	,
SUMAHT	ł							
MISSING.	0 0 1 0	0, 12 10	57	60	63	62 62	62	63
Benign thymoma. (BENIGN)	) <del>н</del>	२ न	- 0	* 01	- 03	N <del>1</del> 4		-1
Malignant thymoma (MALIGNANT) Not otherwise specified serroms	•	0	0	0		0	• <del>•</del>	10
(MALIGNANT)	0	0	0	•	0	0	0	н
THYROID GLAND								
EXAMINED	63	63	63	64	63	63	64	64
Follicular cell adenoma (TENTON)	-1 -		-1 (	•		-	0	•
Parafollicular cell adenoma (BENIGN).	101	) r-1	4 6	no	-1 -5	0 0	нc	0 ~
Paratollicular cell carcinoma						,	,	2
(INALLGNANT)	0	ч	•	0	•	•	0	г
UTERUS EXAMINED	ı	ı	ı	,	64	64	64	64

AND ONCOGENICITY STUDY IN RATS
GLYPHOSATE ACID: TWO YEAR DIETARY TOXICITY AND ONCOGENICIT

## TABLE 28 - INTERGROUP COMPARISON OF MICROSCOPIC NEOPLASTIC FINDINGS (TOTAL)

ALES2	ррш ррш ррш ррш 64 64 64 64 64 64 64		5 7 2	10 9 5		) -	1 C		64 63 64 0 1 0 0 0 0
0	1900 64 64		7	9	0		-	0	90 90 00
20000	64 64		ı	1	ı	1	ı	,	400 800
6000	64 64		,		•	,	ı		113
0 2000 6000 20000 20000 20000	64 64	ED)	•	1	,		ı	ı	64 0 64
	64 64	(CONTINUED)	•	ı	,	,	ı	ı	6 0 0 4
	ANIMALS ON STUDY ANIMALS COMPLETED	UTERUS	SCTOMAL CELL POLYD. (BENICN)	AGENOCETCLIOMA (MALIGNANT)	retouvome (BENIGN)	Squamous cell carcinoma (MaLIGNANT)	Haemanglosarcoma. (MALIGNANT)	Haemangloma (BENIGN)	VOLUNTARY MUSCLE EXAMINED

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ζ Text Table 1 Incidence and % Incidence of Neoplastic Lesions by Tissue for Terminal Kill and Interim D SPL PROJECT NUMBER: 2060-0012

Text Table 1 Incidence and % Incidence of Neoplastic Lesions by Tissue for Terminal Kill and Interim Death Animals Combined (continued)

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Text Table 1 Incidence and % Incidence of Neoplastic Lesions by Tissue for Terminal Kill and Interim Death Animals Combined (continued)

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Glyphosate

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Defendant's Exhibit 2570 0232

### **Evaluation of chronic activity and possible far** – reaching effects Part 1. Studies on chronic toxicity<sup>\*)</sup>

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Abstract: The combined test of chronic toxicity and carcinogenicity of glyphosate was performed on Wistar-RIZ rats. The herbicide was administered in water at concentrations: 0, 300, 900, 2700 mg/L. The examination of the peripheral blood parameters and the smears of bone marrow did not reveal harmful effect of the herbicide on haematopoietic system of rats. The biochemical parameters determined in blood and urine only in some cases showed significant deviations in comparison with the control group, but in any examined indices dose-effect-time occurred what could manifest the toxic influence of glyphosate. In pathomorphological studies on the organs no correlation was stated between the number of observed tumours and the concentrations of the herbicide. It indicates lack of pathogenic influence of glyphosate on neoplastic pathogenesis.

Key words: chronic toxicity, carcinogenicity, rats

The study was performed with financial support of KBN and Zakłady Chemiczne Organika "Azot" at Jaworzno.

### INTRODUCTION

Glyphosate (N-phosphonomethyl glycine) of the formula

HOOC-C H3-NH-C H2P (OH)2

is the non – selective, broad spectrum postemergence herbicide of systemic activity. It is applied to control weeds in the form of isopropylamine salt [1]. Acute toxicity of glyphosate to laboratory animals at different routes of exposure is relatively low and amounts as follows:

 $LD_{so}$  per os for rats > 5600 mg/kg b.w.

 $LD_{so}$  inhalation > 12.2 mg/l air

LD<sub>so</sub> per os for mouse 1100 mg/kg b.w.

LD<sub>so</sub> dermal for rabbit > 5000 mg/kg b.w.

In chronic studies on rats and dogs ineffective concentration of the herbicide in diet amounted to 300 mg /kg [2].

Some quantity of impurities are being formed during industrial production of biologically active ingredients. Their presence can considerably fluctuate depending on applied technology [3,4]. Such impurities can affect toxicological properties of the final product. Therefore biologically active ingredients produced after technologies elaborated in this country are under evaluation of health hazard risk of chronic exposure and far-reaching effects understood as mutagenic and cancerogenic responses and neurotoxic effects disturbing reproduction processes and inducing innate malformation of descendants.

The technology of glyphosate production was elaborated at the Institute of Industrial Organic Chemistry (patent No 150424) [5], and will be implemented at one domestic chemical works manufacturing pesticides. The range of undertaken studies to determine hazards of exposures to glyphosate comprised studies on chronic toxicity, carcinogenesis, genotoxicity, embriotoxicity and teratogenicity.

The objective of the research is evaluation of far-reaching effects of chronic exposure and cancerogenic risk assessment of given glyphosate herbicide.

### MATERIALS AND METHODS

Ammonium salt of glyphosate 13.85% solution was used in the studies. The combined test of chronic toxicity and carcinogenicity (OECD No 453 [6]) has been carried out in rats 5-6 weeks old Wistar –RIZ outbred herd from the rearing at the Pharmaceutic Institute in Warsaw. After one week the laboratory animals were randomly divided into four groups. Each group composed of 170

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Defendant's Exhibit 2570 0233

animals (85 male and 85 female). Rats were kept in metal cages (males) and plastic cages (females). The compartment was well ventilated, temperature amounted to 22 °C and lighting was automatically regulated at 12 h cycle. Joiner shavings sterilized by UV radiation were used as bedding material. Rats were fed with standard granulated fodder Murigram from the mill at Motycz.

The examined formulation was administered to rats in aqueous solutions: control,

group 1 - 300 mg/L (ppm),

group 2 - 900 mg/L (ppm),

group 3 - 2700 mg/L (ppm).

During the whole 2 year period of experimentation animals were under inspection of the veterinary surgeon and animals general appearance and behavior were being observed. Increase of body weight, consumption of fodder and water, and mortality of rats were registered.

After 6, 12 18 and 24 months of poisoning the following investigations were carried out:

⇒ hematological examination of peripheral blood:

- hemoglobin, erythrocytes, leucocytes- determined by hematological analyser (Baker Instruments 150);
- hematocrit determined in Union centrifuge for separating blood cells;
- hemogram blood smear stained by Pappenheim method and evaluated in light microscope;
- thrombocyte- were counted microscopically in Bürker chamber after Danci in Rees in Ecker solution;
- reticulocytes were counted in preparations stained with brilliant cresyl blue;
- ⇒ examination of haematopoietic system (after 24 months):
  - myelogram- was stained by May-Grünwald and Giemzy method and evaluated in light microscope Axiolab.

Blood for examination was taken from retrobulbar venous plexus in slight ether narcosis.

Bone marrow was uptaken from femoral bone:

⇒ serum biochemistry analysis for: total protein, urea, glucose, free cholesterol, electrolytes: calcium, sodium, potassium, inorganic phosphor, alkaline phosphatase activity, alanine/asparagine aminotranspherase activity (ALAT/ AspAT), gama glutamyl transpeptidase GGT).

Biochemical and enzymatic parameters were determined in clinical analysers (Synchrom 4) after 6 and 12 months and in 700 type after 18 and 24 month of experimentation (Beckman firm with usage of the firm reagents).

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⇒ biochemical examination of urine: total protein, glucose, urobilinogen, bilirubin, ketones, nitrites and blood.

Analyses were performed using dry tests "Multistix" of Ames firm. To obtain urine, rats were kept 18 hours in glass cages of "Simex" type.

⇒ pathomorphological examinations were performed in all animals died during whole period of experimentation and in killed animals after 12 and 24 months (10 males and 10 females from each level of dosage), and in all animals, which survived 2 years period of intoxication. Postmortem macroscopic examination of the organs of rats were conducted after 6 and 18 months of experimentations.

During autopsy of rats after 12 and 24 month of poisoning the following organs were weighed: brain, heart, lungs, liver, spleen, kidneys, adrenals, testis/ovaries. Above mentioned organs and thyroid, bladder, stomach, small and large intestines, rectum and oesophagus were subjected microscopic examination. Slides were prepared by paraffin technique after fixation in 10% solution of formalin. Hematoxylin and eosin stain.

Non-parametric Kruskal-Wallis statistical method was used.

### RESULTS

No differences in appearance and behavior between poisoned with glyphosate animals at 300, 900 and 2700 ppm dosage and control animals were being observed during 24 months of experimentation.

Non-significant difference in mean rat body mass in successive monthly observations and at the end of experiment between intoxicated and control animals were noted.

During the experiment period 208 rats died (108 males and 100 females), 240 animals were narcotized after 6, 12 and 18 months (in accordance with experiment schedule) and 232 rats survived up to the end of the experiment (112 males and 120 females).

Lack of significance between general number of died animals from experimental and control groups at all levels of dosage was shown by the analysis of mortality distribution in 24 months period of rats intoxication by glyphosate. This distribution expressed by percentage index for increasing herbicide concentration in water amounted to:

• 42 (K), 42. 54 and 44% (males),

• 38 (K), 45. 53 and 60% (females).

The index was calculated from 55 rats in the group e.i. number of animals which were planned to remain in the experiment for 24 months. This assumption

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adopted sharpens criteria of the experiment in comparison with percent of initial number of animals used for examination (85 rats), but it is more precise.

No significant differences in fodder consumption between rats from experimental and control group occurred during 24 months of intoxication.

The mean values of hematological parameters examined after 6, 12 18 and 24 months of rats intoxication by glyphosate at all levels of the dosage were approximate to control values. Dose- effect relationship did not occur and therefore single significant deviations should be recognized as accidental and not connected with toxic influence of the herbicide.

No changes in percent composition of individual kinds of white blood cells (neutrophilic and eosinophilic granulocytes, monocytes and lymphocytes) were shown in morphological evaluation of peripheral blood smears (leucograms) performed in male and female poisoned rats after 6, 12,18 and 24 months comparison with control animals.

After 24 months, in rats exposed to the highest glyphosate dose, no significant qualitative or quantitative changes in nucleated marrow cells, reticular cells, and lymphatic cells were found in the myelogram, in comparison to the controls. Normoblastic red blood cells constituted mostly polychromatophilic erythrocytes. The percent of normoblasts and basophilic was at equal level. In total, the mean value in control males was 18.55% and females 22.53%, whereas in treated rats it amounted to 20.76 in males and to 18.78 in females. In humans, 10-30% of red blood cells is considered to be within the normal range.

Granulocytes consisted mostly of neutrophilic divided elements, rod neutrophils, neutrophilic metamyelocytes and neutrophilic myelocytes, both in treated and control groups. The percent in total granulocytes in nucleated bone narrow cells was 68.61% in control males, and 62.56% in control female. In treated groups, it was 62.72% in male rats, and 65.% 43 in female rats. For humans, in normal myelogram, leucocytes (granulocytes) amount to 62-77%.

White blood cells to red blood cells ration in control female rats was 2.78:1, in treated female rats 3.90:1, whereas in control males 3.70:1, and in treated males 3.02:1

The lymphatic system consisted of mature lymph cells. The percentage of these cells in the myelogram of treated rats was comparable to the control, and was within the normal range (3-12%). The percentage value of regular plasmacytes in control treated rats was almost equal, but slightly decreased when compared to the normal value for human marrow cells (1.5-6%).

The results of peripheral blood parameters and bone marrow smear examination led to the conclusion that glyphosate does not induce pathological changes in the haematopoietic system in rats exposed to 300, 900 and 2700 ppm for 24 months.

### Defendant's Exhibit 2570 0236

Serum profile of treated rats only in a few cases revealed significant changes in biochemical parameters as compared to the control; however, no incidence of dose-response-time relationship indicating the effect of herbicide on any of the parameters was seen.

Decrease of urea and creatine levels were observed in females after 6 months. Deviations in electrolytes: increase of sodium ions was noted in females after 12 months. Increase of potassium ions, and decrease of calcium ions was determined in females, and at the highest dosage level decrease of triglycerides in females was observed. In males after 18 and 24 months of intoxication the values of examined biochemical and enzymatic parameters in experimental groups did not differ significantly in comparison with control group.

The biochemical parameters of urine such as glucose, ketones, bilirubin, and urobilinogen in intoxicated and control rats did not show deviations from the standards. Protein and blood were at the same level in poisoned and control rats.

The macroscopic changes of the organs of animals were evaluated in 20 rats (10 males and 10 females) from each level of dosage, sacrified in accordance with experimental schedule after 6, 12 18 and 24 months.

No anatomomorphological changes were determined in postmortem examination after 6 months. After 12 and 18 months those changes regarded individual animals. Interstitial and purulent lungs inflammation in old animals (after 24 months) were mainly determined, both in intoxicated and control rats.

In microscopic examinations many pathomorphological changes of circulatory disturbances of retrogressive progressing inflammatory and neoplastic character were determined.

Congestion, erythrorrhagia, hemorrhages, and swellings should be cited among circulatory disturbances. Retrogressive changes occurred mainly in the parenchymatous organs. The adipose degeneration of liver and its cells bionecrosis and gangrene were found. The adipose degeneration of adrenal cortex cells and hyaline renal cylinder casts were detected. The progressive changes were detected mainly in the form of Brawier-Kupffer cells growth in liver and hyperplasia of its biliary canaliculus. The inflammatory changes were detected mainly in lungs. The suppurative pneumonia and purulent inflammation of bronchi were stated in 168 rats (39.4%). Those inflammations occurred in 49% of the control group, and in intoxicated groups respectively: 32.4% in group 1, 55.1% in group 2, and 41.5 in group 3. It should be underlined that pathological states of the respiratory system of laboratory rats are typical and their intensification depends on animals origin and environmental conditions amounting even to 90% (frequently ending of animals death).

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Neoplastic changes were stated in 127 rats. Within this number 36 were control animals, 31 rats from group 1, 26 from group 2, and 34 rats from group 3.Localization kind, and frequency of neoplasm occurrence are shown in tables 1 and 2.

Neoplastic proliferation was observed in lungs, spleen, kidneys, pituitary glands, thyroid, thymus, adrenal glands, mammary gland, subcutaneous tissue, skin, testes, prostate, uterus, and mesenteric lymph nodes.

In the total number of these neoplasma, 25 were classified as malignant (6 in control group, 6 in group 1, 5 in group 2 and 8 in group 3) (Fig. 1). Lack of correlation between number of neoplasms and values of herbicide concentration applied was stated. It indicates lack of phatogenic influence of glyphosate on neoplastic pathogenesis.

Enumined annex	Wind of monthem		Gr	oup .	
Examined organ	Kind of neoplasm	0	1	2	3
	Lymphoma	2	2	1	3
Lungs	Adenocarcicioma	1	-	-	-
	Histocytoma malignum			1	-
Spleen	Leucemia	0	2	0	1
Kidneys	Fibrohistiocytoma	-	-	-	1
	Adenoma	4	5	2	0
Pituitary gland	Adenoma malignum	ΰ	0	1	1
	Carcinoma	0	0	1	0
Thyroid	Adenoma	1	1	0	3
Thyroid	Carcinoma	0	1	0	0
Adrenal glands (medulla)	Adenoma	1	2	1	0
Thymus	Lymphoma	•.	•	-	2
Testis	Leydigoma		3	6	1
Subcutaneous tissue	Fibroma	0	1	1	3
Lymph nodes	Lymphoma	0	0	0	1
Skin	Carcinoma	2	-	•	•
Prostate	Adenoma	1		-	
Total:		12	17	14	16

Table 1. Localization, kind and frequency of neoplasms occurrence in male rats chronically exposed to glyphosate

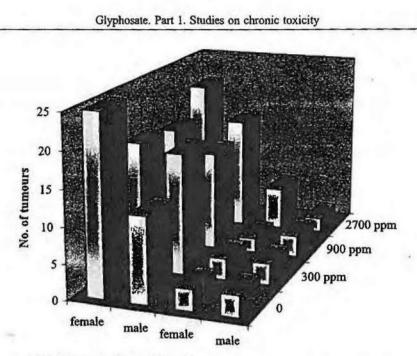
K. Chruścielska et al.

Table 2.	Localization, kind and frequency of neoplasms occurrence in female
	rats chronically exposed to glyphosate

Enamined survey	Wind of seasons		Gr	oup	
Examined organ	Kind of neoplasm	0	1	2	3
	Lymphoma	•	-	-	1
Lungs	Histiocytoma			-	1
	Histocytoma malignum	1		-	•
Ditaitany aland	Adenoma	10	6	8	3
Pituitary gland	Adenoma malignum	1	3	2	5
Thyroid	Adenoma	1	2	0	3
Adrenal glands (medulla)	Adenoma	2	2	2	2
Uterus- cervix	Carcinoma	0	0	0	1
Uterus - body	Histiocytoma	3	1	0	1
	Fibroma	0	0	1	0
Mammary gland	Fibroadenoma pericanaliculare	3	2	• 3	3
	Fibroma	1	2	-	-
Subcutaneous tissue	Lipoma	-	-	-	1
	Cystadenoma	1	-	-	)
Lumph nodes	Lymphoma	1	-	1	-
Lymph nodes	Lymphoma malignum	· 1	÷	-1-1	-
Total:		25	18	17	21

18

A Children Marries 1/2 Children



tumours malignant tumours

Fig. 1. Total number of tumours and malignant tumours during chronic exposure to glyphosat.

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K. Chruścielska, J. Brzeziński, K. Kita, D. Kalhorn, I. Kita, B. Graffstein, i P. Korzeniowski

### Glifosat

Ocena działania przewleklego i możliwych skutków odległych Cz.1. Badanie toksyczności chronicznej

### Streszczenie

Celem pracy była ocena odległych następstw przewlekłego narażenia z oszacowaniem ryzyka kancerogennego oddziaływania glifosatu.

Kombinowany test toksyczności przewlekłej i rakotwórczości wykonano na szczurach stada Wistar-RIZ. Preparat podawano w wodzie w stężeniach: 0; 300; 900 i 2700 mg/L. Badania parametrów krwi obwodowej i rozmazu szpiku kostnego nie wykazały szkodliwego wpływu związku na układ krwiotwórczy szczurów. Wskaźniki biochemiczne oznaczone w surowicy krwi i moczu tylko w nielicznych przypadkach wykażywały istotne odchylenia w porównaniu z grupą kontrolną, ale w żadnym z badanych wskaźników nie/wystąpiła wyraźna zależność dawka-efekt-czas co świadczyłoby o toksycznym oddziaływaniu glifosatu na badany parametr.

W badaniach patomorfologicznych narządów nie stwierdzono korelacji pomiędzy liczbą obserwowanych nowotworów, a wielkością stosowanych stężeń. Wskazuje to na brak wpływu glifosatu na rozwój choroby nowotworowej.

Defendant's Exhibit 2570 0241

77-2061

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### Table 17 C

### A Chronic Feeding Study of Glyphosate (ROUNDUP® Technical) in Mice Pathology Report

Summary-Incidence of Neoplastic Findings - Male Mice Total - Male Mice

> CONTAINS TRADE SECRET OR OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY

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BID/DYNAMICS, INC. Department of Pathology East Millstone, NJ 08873	*** PATH/TOX SYSTEM OUTPUT A CHRONIC FEEDING STUDY OF CLYPHOSATE (ROUNDUP TECHNICAL	ИТРИТ STUDY NICOL)	x 2 * 1 *	ICE		PRINTED: 23-MAR-83 PAGE: 2
	INCIDENCE SUMMARY WITH PERCENTAGES	PERCEN	TAGES			STUDY NUMBER: 772061
		2	H O	а П В	1 12 0 1	ANIMALS-AFFECTED
TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=A DEATH=ALL;FIND=M,B,X,I,S;SUBSET=AL	J.WEEKS=ALL SEX1 SUBSET=ALL GROUP:			<b> </b>	-4-	
ORGAN AND FINDING DESCRIPTION	NUMBER :	20	50	50	50	
** TOP DF LIST ** PITUITARY GLAND (PG)	······ NUMBER EXAMINED:	1 01 1 10 1 10	18		30 31 1	·
BRAIN (BN)	LEUKEMIC MANIFESTATIONS,	40 0 2 2 2	0 0 0 7 0 8 0 8 0 8 0 8 0 8 0 8 0 8 0 8	50 24 24	50 0 2	
CERVICAL SC (SCO)	NUMBER EXAMINED:	49	48	50	50	
THORACOLUMBAR SC (SC1)	NUMBER EXAMINED:	10	8	10	23	INF
HEART (HT)	LEUKEMIC MANIFESTATIONS	47 0 2 2	49 1 2 X	40 47 42	50 1 22	VISE COI DRMATH ANTO C
AORTA (AD)	NUMBER EXAMINED:	46	50	20	47	ON
TRACHEA (TR)	NUMBER EXAMINED	48	50	50	49	OF
ESOPHAGUS (ES)	NUMBER EXAMINED:	48	20	50	48	
LUNGS (LU)ALVEDLAR ADENOMA B- BRONCHIOLAR-ALVEDLAR ADENOMA		48 5 102	50 9 182	50 9 182	50 9 182	
M- BRONCHIOLAR-ALVEOLAR ADENOCARCINDMA	НА	4 82	д 8 <b>%</b>	0 4 X	1 22	
		0 X 0	0 0	0 0	0X 0	
		× 00	020	020	0	
S- LIPOSARCOMA		0× 0	א ס ס	0 X 0	0 0 0	01
S- COMPOSITE LYMPHOSARCOMA		0 0 X 0	0 0 X	0 0 7 0	0 0	56
** CONTINUED ON NEXT PAGE ** //  /	,				Ň	

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Defendant's Exhibit 2570\_0243

5	A/TOX SYS			1		PRINTED: 23-MAR-83 PAGE: 3
EAST MILLSIUNE, NJ 08873	UF GLYPHOSATE (ROUNDUP TECHNICAL) IN M INCIDENCE SUMMARY WITH PERCENTAGES	IECHNICAL) AITH PERCENT	IN MICE Ages	CE	8	STUDY NUMBER: 772061
		<b>X</b>	a w n	Ш	- 0 F - A N	I H A L S - A F F E C T E D
TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL	SEX: GROUP:	+		ł	-4	
ORGAN AND FINDING DESCRIPTION	NUMBER I			20	50	
** FROM PREVIOUS PAGE ** LUNGS (LU)	ITH LEUKENIC MANIFESTATIONS	48 1 2 <b>X</b>	1 1 1 1 1 1 1 1 1 1 1 1 1 1		10 11 12 1	
S- LYMPHOBLASTIC LYMPHDSARCDMA		0 0	1 2X	0X 0	02	
LIVER (LI)	······································	49 5 102	50 6 12 <b>x</b>	50 6 122	50 4 8%	
B- HEPATOCELLULAR ADENOMA		0 N	0 X 0	1 57	20	i ORM
		0 20	8 0	× 00	17 4 X	ATION
		0 %	0 87	0%	0 2 2	
S- HISTIOCYTIC SARCOMA		020	1 2 <b>X</b>	0 X 0 0	0 2	
S- LEIOMYOSARCOMA		0 X 0	0× 0×	0× 0	0 22	
		0 X 0	0 X	020	0 0	
S LIPOSARCOMA		0 20	0 0 X 0	1 22	1 2x	
S- HEMANGIDENDOTHELIOMA		070	040	0 0	0 0	
S- COMPOSITE LYMPHOSARCOMA * CONTINUED ON NEXT PAGE **		1 22	0 0	0	0×0	0157

BIO/DYNAMICS, INC. Department of Pathology		TUTPUT STUDY	*			PRINTED: 23-MAR- Page: 4
EAST MILLSTONE, NJ 08873	RY RY	UTH PERCENTAGES	IN NI TAGES	ICE		STUDY NUMBER: 772061
			N U H I	B E R	- 0 F - A N I	MALS-AFFECTED-
TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL	=ALL;WEEKS=ALL \$;SUBSET=ALL GROUP;		-23-	1		
ORGAN AND FINDING DESCRIPTION	NUHBER	1 50	1 20	20	50	
** FROM PREVIOUS PAGE ** LIVER (LI) NUMBER EX S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			х		50 7 7 7 7	
		0 0	х 0 0	0 X 0	0 X	
GALLBLADDER (GB)	NUMBER EXAMINED:	45	32	36	41	С
MESENTERIC LN (LND)	······································	48 0 0 2 2	50 1 2 <b>x</b>	46 02 02	49 0 12	THERWI
S LEIOMYDSARCOMA		0 X 0	0 20	0X 0	0×0	se co R <i>M</i> Ati
S- GRANULDCYTIC LEUKEMIA		0 2 0	0 0 0	0×	0%	он о
		0 0	а 9 9	0 0 0	0 02	NT'AL F
COMPOSITE LYMPHOSARCOMA		1	0 X 0	52	0 D X	<b>ڊ</b>
LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	ITH LEUKEMIC MANIFESTATIONS	1 2X	4 7 7	1 52	0 2	
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	ITH LEUKEMIC MANIFESTATIONS	0 0	0 20	- 2	13 4%	
		0 20	0 <sup>21</sup> 0 0	0	0 0	
М- LYHPHORLASTIC LYMPHOSARCOMA		0 X	- 22	ير د م	0 2 2	01
** CONTINUED ON NEXT PAGE **						58
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Defendant's Exhibit 2570\_0245

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BIO/DYNAMICS, INC. Department of Pathology East Millstone, NJ 08873	*** PATH/TOX SYSTEM OUTPUT A CHRONIC FEEDING STUDY DF GLYPHDSATE (ROINDUP TECHNICAL)		LW N1	L L		PRINTED: 23-MAR-83 PAGE: 5
	INCIDENCE SUMMARY W	PERCEN	rages			STUDY NUMBER: 772061
		2	ЯНЛ	ы В С	- 0 F - A N I	HALS-AFFECTED
TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL	IEEKS=ALL SEX; SET=ALL GROUP;					
DRGAN AND FINDING DESCRIPTION	NUMBER :	50	50	50	50	
** FROM PREVIOUS PAGE ** HESENTERIC LN (LNO)	NUMBER EXAMINED:	48 48 02	20 20	4 4 9 0 7 0 7 0	 49 02	
		020	0 0 0	0 0	20 0	
HEDIASTINAL LN (LN1)	NUMBER EXAMINED:	20 0 7 7	44 1 1 2 2	4 0 0 2 0 2 0	49 0 12	
		0 0	0 0 0	020	0 0	ERWIS INFOR INSAN
		0 X 0	020	02	0 0	MATIC
		0 0	א 0 0	0 0 0 0	0 2	Dr: OF
		1 22	020	122	0 0 X	
	UKEMIC MANIFESTATIONS	57	0 <b>7</b>	57 57	دی 4 ۲	
M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	UKEMIC MANIFESTATIONS	0 X 0	0 0 0	22	0 0	
И- LYMPHOBLASTIC LYMPHOSARCOMA		0 X 0	0 0 X	02	0 0	
S- LYMPHOBLASTIC LYMPHOSARCOMA		0× 0	0X 0	02	0 2	
SALIVARY GLANDS (SG)	······ NUMBER EXAMINED:	49 0 02	0 X 0 0 2 0	49 0 2	50 0 02	0159

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님	*** PATH A CHR	UTPUT STUDY	* *			PRINTED: 23-MAR-B3 PAGE: 6	
EAST MILLSTONE, NJ 08873	OF GLYPHOSATE (ROUNDUP TECHNICAL) IN MICE Incidence Summary With Percentages	PERCEN	IN M. TAGES	ICE	1	STUDY NUMBER: 772061	
		2	NUN	BER	- 0 F - A N I N	H A L S - A F F E C T E D	
TABLE INCLUDES; SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SURSET=ALL	=ALL;WEEKS=ALL SEX; S;SURSET=ALL GROUP;	1-1-		1.			
DRGAN AND FINDING DESCRIPTION	NUMBER :		20	50	50		
** FROM PREVIOUS PAGE ** SALIVARY GLANDS (SG) S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	ITH LEUKEMIC MANIFESTATIONS	44 49 1	000 100	- 46 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1	50 10 10		
THYHUS (TH)	······ KUMBER EXAMINED:	N	0	-	1		
PLEEN (SP)	····· RAMINED:	48 0 02	49 0 12	50 1 2X	49 0 0 %		<u> </u>
B HEMANGIDMA		0 0	0 7 0	0 0	0 0 z 0	11×10	
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		0%0	0X 0	0 %	020	ICN C	
S ENDOMETRIAL ADENOCARCINOMA		0 0	0 0	0 X	0× 0	NTIAL >F	0
		0 X 0	0 X	0 0 X	0X 0		R
		1 2X	020	1	0 20		
S LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	TH LEUKEMIC MANIFESTATIONS	1	8 4 4 10	5 5 7 5 7 5	0X 0		
H- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	TH LEUKEMIC MANIFESTATIONS	020	ы 4 4	0 X 0 0	1 2 X		
COMPOSITE LYMPHOSARCOMA		0 20	0 0 0	0 0	0×0		
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BID/DYNAMICS, INC. DEPARTMENT OF PATHOLOGY A CHRONIC FEEDING STUDY EAST MILLSTONE, NJ 08873 INCIDENCE SUMMARY WITH PERCENTAGES	STEM OUTPUT *** EDING STUDY TECHNICAL) IN H WITH PERCENTAGES	*** 1 IN MI 1 AGES	E	PRINTED: 23-MAR PAGE: 7 STUDY NUMBED: 7700.	23-MAR-83 7
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ORGAN AND FINDING DESCRIPTION	50	50	20	20	
** FROM PREVIOUS PAGE ** SPLEEN (SP) NUMBER EXAMINED: M- LYMPHOBLASTIC LYMPHOSARCOMA	4 80 20 20	1 6 <b>4</b>	1 20 20 1	49 02	
S- LYMPHORLASTIC LYMPHOSARCOMA	0×0	0 0	0 0 0 0	02	
STOMACH (ST)NUMBER EXAMINED: M- LEIOMYOSARCOMA	40 0 10 10	·	48 0 8 7 8	MO	1)
M- GASTRIC ADENOCARCINOMA	0 X 0	0	0 X	NSAN 8	RWISE NFORA
	1 2X	0 X 0	0 0	TO CC	E CON KATIO
DUODENUM (DU)NUMBER EXAMINED: S- COMPOSITE LYMPHOSARCOMA	х 0 0 7 7	м 0 о М Ф	4 0 0 4 0 0 X	MPANY	SECRET I
PANCREAS (PA) NUMBER EXAMINED: S- HISTIOCYTIC SARCOMA	ч 80 4 9	•	4 7 7 7 7 7	50 0 1 × ·	OR L
	0 0 X			0 2	
S- COMPOSITE LYMPHDSARCOMA	0 20	0 0 Z	020	0 0 X	
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS	0 0	0%	2X 2	0 ×0	
JEJUNUM (JE) NUMBER EXAMINED: S- COMPOSITE LYMPHOSARCOMA	46 0 20 22	4 20 20 4	7 0 0 7 7	47 0 22 0 22	0161

BIO/DYNAMICS, INC. Department of Pathology East Millstone, NJ 08873	C2	UTPUT STUDY NICAL)	*** ) IN MICE	щ	RINTED I PAGE I
	INCIDENCE SUMMARY WITH PERCENTAGES		NTAGES N U M B	ы В	- DF - A N I M A L S - A F F E C T E D
TABLE INCLUDES; SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL	ALL;WEEKS=ALL 5;SUPSET=ALL GROUP;	-1-	-23-		-4-
ORGAN AND FINDING DESCRIPTION	NUMBER :	50	20	20	
** FROM PREVIOUS PAGE ** ILEUM (IL)	······································		N		48 0 2 2
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKENIC	TH LEUKEMIC MANIFESTATIONS	1 2x	0%	×0	02
CECUM (CE)	NUMBER EXAMINED:	х 0 7	4 9 9 7 7 7 7	х 0 0	IN
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	TH LEUKEHIC MANIFESTATIONS	5 <b>7</b>		0 0 0	FORM
COLON (CO)	NUMBER EXAMINED:	46 1 2%			
S LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC	TH LEUKEMIC MANIFEŠTATIONS	070	02	0 0 0	)F
KIDNEYS (KD)	NUMBER EXAMINED:	46 0 7	46 0 2%		50 3 62
S- B/ HISTIOCYTIC SARCOMA		0 0 0	х 1	020	0 20
S B/ LEIOMYDSARCOMA		0 0	0 0	0	0 0
		0 0	0X 0	0	0
S- B/ СОМРОSITE LYMPHDSARCDMA		5%	0× 0	02	1G2 2
** CONTINUED ON NEXT PAGE **					

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DLOGY	<b>T P</b>	OUTPUT *	* *	1	PRINTED: 23-MAR-83 Page: 9
EAST MILLSTONE, NJ 08873 DF	GLYPHOSATE (ROUNDUP TECHNICAL) IN MICE INCIDENCE SUMMARY WITH PERCENTAGES		AGES		STUDY NUMBER: 772061
		z	≞ ¥⊃ Z	ы В	- D F - A N I H A C G - A F F E C T E D
TABLE INCLUDES: SEX=MJGROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBGET=ALL	SEX: GROUP:				-4
RGAN AND FINDING DESCRIPTION	NUMBER:	50	20	20	50 #
. FROM PREVIDUS PAGE ** IDNEYS (KD)	KEMIC MANIFER EXAMINED: KEMIC MANIFESTATIONS	ĸ	ж	50 4 X 4 X	50 2 4%
		0 X 0 0	0 X 0	0 20	0 2
TESTES (TE)	NUMBER EXAMINED:	4 10 14 14	48 0 4	7 7 9 0 0	
S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS	UKEMIC MANIFESTATIONS	0 20	54 57	070	OTHER IN
S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEU	UKEMIC MANIFESTATIONS	0 X 0 0	020	1 27	WISE FORM (SANT
EPIDIDYHIDES (EP)	NUMBER EXAMINED:	4 0 0 2 2 2	48 1 2x	20 02	
PROSTATE (PR)	NUMBER EXAMINED:	49	47	50	entia DF PAN
.URINARY BLADDER (UB)	NUMBER EXAMINED:	48 0 02	46 1 22	47 0 0 2 2	4.L Y
		070	0X 0	020	0 کې .
S- COMPOSITE LYMPHOSARCOMA		0 0 X	0 0 X 0	020	0×0
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKER	NIC MANIFESTATIONS	57 57	1 22	02	0 20
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08873 OF GLYPHOSATE INCIDENCE	(ROUNDUP TECHNICAL) IN MICE Summary With Percentages	CENTAC	N NTC	ا ا	STUDY	JDY NUMBER: 772061
		z	a H N	н 24	- OF - ANIMALS -	- AFFECTED
TABLE INCLUDES: SEX=M;GRQUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL	SEX: GROUP: -1-			1		
ORGAN AND FINDING DESCRIPTION	NUMBER 1 5	50 50 11 50	1	1	50	
** FROM PREVIOUS PAGE ** DVARIES (OV) NUMBER EXA B- U/ LUTEOMA	EXAMINEDI	א	א	א_	0 0 0	
M- B/ MALIGNANT TERATOMA		- 1 0 X 0	020	0 0	0	
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I- B/ ENDOMETRIAL ADENOCARCINOMA			0	0 X	0 X 0	FORM.
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BIG/DYNAMICS, INC. Department of Pathology East Millstone, NJ 08873	H/TOX SYS RONIC FEE (ROUNDUP	TPUT 3 TUDY ICAL)	*** IN MICE	ш		£8-
	INCLUENCE SUMMARY WITH PERCENTAGES		IAGES U M B	а Ш	STUDY NUMBER: 772061 - D F - A N T M A D S - A F F F F T F P	
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S COMPOSITE LYMPHOSARCOMA Continued on Next Page **		1 22	020	مح 0 ک	01( 1	ഹെംഭം
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BID/DYNAMICS, INC. DEPARTMENT UF PATHOLOGY EAST MILLSTONE, NJ 08873	*** PATH/TOX SYSTEM DUTPUT *** A CHRONIC FEEDING STUDY DF GLYPHOSATE (ROUNDUP TECHNICAL) IN M INCIDENCE SUMMARY WITH PERCENTAGES	TEM OUTPUT DING STUDY TECHNICAL)	*** IN MICE	ICE		PRINTED: 23-MAR-83 PAGE: 12 Study Number: 772861
		2	R N	B E R	- D F - A N I M A L	S-AFFEC
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BIO/DYNAMICS, INC. Department of Pathology	*** PATH/TOX 5YST A CHRONIC FEEI	TPUT *	* * *			PRINTED: 23-MAR-B3 PAGE: 14
EAST MILLSTONE, NJ 08873	DF GLYPHOSATE (ROUNDUP TECHNICAL) IN M INCIDENCE SUMMARY WITH PERCENTAGES	TECHNICAL) IN MICE VITH PERCENTAGES	IN MI AGES	CE	بيد الله الله الله الله الله الله الله الل	STUDY NUMBER: 772061
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<pre>BLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL</pre>	SEX: GROUP:		-23-			
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	ITH LEUKEMIC MANIFESTATIONS	0 X 0	0 X 0	0×0	1 502	entrat Of
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NAL CORD (SC)		0	0	0	o	
GASTROINTESTINES (GI)	NUMBER EXAMINED:	0	0	0	D	
TERS (UR)	NUMBER EXAMINED:	0	0	-	Û	0
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EAST MILLSTONE, NJ 08873 UF GLYPHUSATE INCIDENCE	CRUUNDUP IECH	PERCENTA	2	1		BER 1 77	
	1	2 2	A E D	і 92 Ш	OF - ANIMALS - AF	ш 	
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ORGAN AND FINDING DESCRIPTION	NUMBER:	20	0	1			
HEAD SECTIONS (NT)	NUMBER EXAMINED:	10 0 0 2	80 07 07	0 0 0	0 0		
JUNCTION (JU)	NUMBER EXAMINED:	0	0	0	0		
CORRELATE #1 (G1)	NUMBER EXANINED:	0	0	0	0		
CERVIX (CV)	NUMBER EXAMINED:	х 0 0	х 0 0 0	м Сос	0 X 0		INF
JUSCLE DTHER (MU)	NUMBER EXAMINED:	0 0,0 0 0,0	х 0 0	می	0 0 0		ORMATI
CORRELATE #2 (G2)	NUMBER EXAMINED:	0	0	0	8		NTIDENTI, ON OF COMPAN
		·					0169

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## Table 18 C

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A Chronic Feeding Study of Glyphosate (ROUNDUP® Technical) in Mice Pathology Report

Summary-Incidence of Neoplastic Findings - Female Mice Total - Female Mice

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TARLE INCLUDES: SEXEF;GROUP=ALL;SCREFN=ALL;UFEKS=ALL DEATHILLSTONE, NJ 00873 INC INC TARLE INCLUDES: SEXEF;GROUP=ALL;SCREFN=ALL;UFEKS=ALL DEATH=ALL;FIND=M,R,X,I,SSURSET=ALL	· · · · · · · · · · · · · · · · · · ·	37 P. M. 1				PAGE: 2
	INCIDENCE	FRCENT	IN M	ICE		STUDY NUMBER: 772061
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FINDING DESCRIPTION	NUMBER	0 S I	ا ا ا	<b>6</b>	0 1 1	
** TOP OF 1.15T ** PITU/TARY GLAND (PG)	NIMMER EXAMINED:	35	12	44	37	
BRAIN (BN) NUMHER EXA 	NUMMER EXAMINED: PHIC MANJFESTATIONS,	05 02	46 0 2 0 2	20 27 27	50 0 02	
CERVICAL SC (SCO)	NUMBER FXAMINED:	48	49	49	49	
THORACOLUMBAR SC (SC1)	NUMBER FXAMINED:	10	6	æ	12	IHTC I
HEART (HT)		20 20 20	20 20 20	4 7 0 11 11	49 0 10 X	AINS TR ERWISE NFORM NSANT
ADRTA (AD)	NUMBER EXAMINED:	47	49	49	47	CON ATIC
	NUMBER FXAMINED	47	20	20	48	FIDE
ESOPHAGUS (ES)	NUMRER FXAMINED:	4月	20	20	. 50	NTIA <b>)F</b>
LUNGS (1.U)	NUMBER EXAMINED:	49 18 202	50 9 182	44 70 70 70 70	50 1 2 x	
BRUNCHIDLAR-AI VEDLAR ADENOCARCINOMA		1 22	3 6%	4 82	4 132	
		0 0	1 2 7	0 X 0 X	0 0	
S I.EIDMYDSARCOMA		0 0 %	1 2%	0× 0	0 02	
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		1	0 0	5 6 7	1	
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KIU/DYNAMICS, INC. Department of Pathology East Mill.Stone, NJ 08873	*** PAT 0 CH 0F GLYPHUSATF 1AC FDEARF	*** PATH/IOX SYSTEM OUTPUT *** A CHRONIC FFEDING STUDY GLYPHOSATF (ROUNDUP TFCHNICAL) IN MICE JANE DEADE SUMMARY WITH PEDISENIALES	TPUT # TUDY TCAL ) EDCENT	IN MI DEFG	CE		PRINTED: 23-MA PAGE: 3 Stlidy Niimber; 772041
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LIVER (LJ)	•	NUMRER FXAMINFD:	49 1 22	50 77 77	4 1 2 2 2	49 0 02	1
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5	*** PATH/IDX SYSTEM OUTPUT A CHRONIC FFEDING STUDY DE FLYPDHORDE (DOUNDUD TECHNICAL)		1W N1	Ц		PRINTFD: 23-MAR-83 PAGE: 4
EAST MILLSTUNE, NJ VERV.3		ERCEN	IAGE S	1		STUDY NUMBER: 7720
		2	H N N N	2 2 2	+ + 	ANIMALS HAFFECTED
TARLF INCLUDES: SEX=F;CROUP=ALL;SCREEN=ALL,WEEKS=ALL DEATH=ALL;FIND=M,R,X,I,SSBURGET=ALL	MEEKS=ALT SEX: RIGET=ALL GROUP :		-FEMALF -23-	1	-4-	
URGAN AND FINDING DFSCRIPTION	NUMBER :	20	05		20 	
<pre>** FROM PREVIOUS PAGE ** LIVER (1.1)</pre>	NUMMER EXAMI C MANTEFSTATIONS	49 1 2%	50 4 82	49 44 82	6 – <sup>60</sup> X	
S- LYMPHOBLASTIC LYMPHOSARCOMA		9 0 %	3× 10	0 Z O	2 N 7 N	
GALLEI ADDER (GR)	NUMBER EXAMINED:	36	42	41	44	
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	EUKEMIC MANJFESTATIONS	0	3 9%	1 22	1 2X	
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KIC/DYNAMJCS, JNC. DEPARTMENT OF PATHOLOGY EAST MILLSTONE, NJ 08873	*** PATH/TOX SYSTEM DUTPUT *** A CHRIMIC FEFDING STUDY DF GLYPHOSATE (RUNNUP TECHNICAL) IN MICE	DUTPUT STUDY HNJCAL	* * * * *	41.CF		PRINTED: 23-MAR PAGE: 5
					R - 0 F - 6	5 - 4 F F C T E D
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		0 0	9 0 %	0		
SALIVARY GLANDS (SG)		20 0 1 2 0	05 05	50 7 7	47 0 102	020
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BIN/DYNAMICS, INC. DEPARTHENT OF PATHOLOGY EAST MILLSTONE, NJ 08873 DF GLYPHOSATE (ROUNDUP	/TOX_SYSTEM_OUTPUT_*** CNLC_FEEDING_STUDY (ROUNDUP_TECHNICAL)_IN_MICE	*** (	HICE			23-MAR 6
INCIDENCE	SUMMARY WITH PERCENTAGES	NTAGES	14	R - 0 F - A N I	STUDY NUMBER: 7 M A L S - A F F E C 1	772061 T E D
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AND FJNDJNG DESCRIPTION	к:	50	65	00		
** FROM PREVIDUS PACE ** SALIVARY GLANDS (SC)	INFD: 50	ŧ	1	•		
THYMUS (TM)	NED: 2	ŧIJ	n:	-		
SPLEEN (SP)NUMRER EXAMINED: M- HEMANGIDENDOTHELIOMA	NFD: 50 1 2%	48 0 20	4 4 7 7 7 7	49 1 2 X		
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S- FNDOMFTRIAL ADFNOCARCINOMA	1 2X	2 0 7 0	0 77 0 77	0 1) X		FIDEN
S- HEMANGJOENDDTHEILIOHA	20 0	0 7 0 7	6 8	1 2X		TIAL
S- COMPOSITE LYNPHOSARCOMA	4 4	9 9 X 9 X	0 0 0	1 22		
S- LYMPHORLASTIC LYMPHOSARCOMA WITH LEUKFHIC HANTFESTATIONS	1 7 X	4 N N	4 N 7	0 2	ι	
M- I.YMPHORI ASTIC I.YMPHOSARCOMA WITH I.EUKEMIC MANTFESTATIONS	0 70	0 X 0	4 N	0 2		
М- СОМРИЗІТЕ І ҮНРНОЗАКСОНА	1 72	1 22	1 22	5 10%		(
** (:CUT(NUFT) DN NEXT PAGE **						0205

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Defendant's Exhibit 2570\_0262

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BEO/DYNAMICS, INC. DEPARTMENT OF PATHOLOGY DEPARTMENT OF PATHOLOGY DE GLYPHOSATF (ROUNDUP TECHNICAL) IN MICE EAST MILLSTONF, NJ 08873 INCIDENCF SUMMARY WITH PERCENTAGES	UTPUT STUDY NTCAL)	*** The h	NCE		PRINTED: 23-MAR-83 PAGE: 7 Study Numrer: 772061
		NUNBE	1	R - D F - A N I M A L	S-AFFECTED
TARLE INCI UDES: SEX=F;GRUIP=ALL;SCRFEN=ALL;WEEKS=ALI DEATH=ALL;FIND=M,R,X,T,S;SUBSET=ALL GRUUP;			н. F -З-	-4-	
URGAM AND FINDING DESCRIPTION	50	20	5	50	
** FROM PREVIAUS PAGE ** SPLEEN (SP) NUMBER FXAMENED: M- LYMPHOBLASTIC LYMPHOSARCOMA	1 20 20	44 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 4 4	-=- 49 1 2%	
S- I.YMPHORLASTIC I.YMPHOSARCOMA	8 8	220	0 87 8	1 27	
STOMACH (ST)NUMRFR EXAMINED: M- I.EIOMYOSARCOMA	48 0 02	49 0 2	50 27 27	50 02	OT
M- GASTRIC ADFNOCARCINUMA	9 0%	0 17 0	1	10 2	HER WI
	0%	07 07	0 87 87	0 0 2 0	ISE CO RMATI
DUUDFNUM (DU)NUMRER EXAMINED: S- COMPOSITE LYNPHOSARCOMA	43 1 22	47 0 02	44 0 20	49 0 11 2	DE SECRE INFIDENT ION OF COMPAN
PANCREAS (PA)NUMBER FXANJNED: S- HISTIOCYTIC SARCOMA	47 0 10 22	6 0 X 0 X 0 X 0 X 0 X 0 X 0 X 0 X 0 X 0	44 0 2 0 2	58 0 0.2	IAL
	070	1 22	0 % 0	0 2 X 0	
	9 N 7	1 2 2	0 2 2 7	1 22	
	1 27	1 22	1 22	0	
JEJUNUM (JE)	5 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	4 0 20 22	4 0 2 2 2 2	84 0 20 20	0206

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5	*** PATH A CHR	atuby	* *	Ĺ		PRJNTFD: 2. PAGE: 8	23-MA 8
EAST MILLSTONE, NJ 08873	DF GLYPHNSATE (KUHNNUP TECHNICAL) IN MICH Incidence Summapy With Percentages	UTH PERCENTAGES	IN NI	÷.		STUDY NUMBER: 7	77206
		2	N U W	R F R	- OF - ANIMAL	. S - AFFECT	a U
TAHLE INCLUDES: SEX=FJCROUP=ALLJSCRFFN=ALLJWFEKS=ALL DEATH=ALLJFIND=H, B, X, I, SJSURSET=ALL	<pre>sFN=aL1.WFEKS=aL1. SFX:</pre>	-1-	-FEMALE	1	-4-		
URGAN AND FINDING DESCRIPTION	NUMBER		20	5 . 5	50 1		
** FROM PREVIOUS PAGE ** ILFUM (JL.)		ж	4 20 20 20 20	х	49 0 12		
S- I.YMPHORIASTIC I.YMPHOSARCOMA WITH I EUKEMIC MANIFESTATIONS	A WITH I EUKEMIC MANIFESTATIONS	0 X 0	א 0 0	× 0 0	0%		
CECUM (CF)	NUMBER FXAMINFD:	44 1 22	45 0 2 2	40 9 2 2 2 2	50 10 24		
	A WITH LFUKEMIC MANJFESTATIONS	8% 8	بر 10 10	х 0	0 2 7	INFC	
COLON (CO)	······································	44 1 2 X	4 0 2 2 2 2 2	84 0 20	50 02	ISE CON DRMATIC ANTO CC	S TRADE
	A WITH LEUKEMIC MANJFFSTATIONS	1	0	0× 0	20	N OT	
KIDNEYS (KD)	······································	20 20 20	50 0 2	20 20 20	50 0 0,2		
		۲ 0	200	0 0	0 %		
		0 0 X 0	1	0 0 X	072		
		8 8 7	1	0 12	ہ 2		
S- B/ COMPOSITE 1 YHPHOSARCOMA		2 7 7	1	- 22	2 47	(	
** CONTLAUFD ON NEXT PAGE **						)207	

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Defendant's Exhibit 2570\_0264

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BIN/DYNAMICS, INC. Department uf Pathuingy East Mill.Stunf, NJ 10873	*** PATH/TUX SYSTEM O A CHRONIC FFFDING OF GLYPHOSATF (ROUNDUP TECH INCLDENCE SUMMARY WITH			*** • JN MJCF vtages	Ë	ω	PRINTED: 23-MAR-83 Page: 9 Study Number: 772061
			Z	NUMBE	8	- DF - ANIMALS	AFFECTED
TARL F. INCLUDFS: SEX=F;GROUP=ALL;F DEATH=ALL;FIND=M,	SEX=F;GRONP=ALL;SCRFFN=ALL;WFEKS=ALL DEATH=ALL;FIND=M,R,X,I,S;SNBSET=ALL	SFX: GROUP:		-FEMAI F	1	- <b>t</b> -	
ORGAN AND FINDING DESCRIPTION	Z	NUMBER:	20		20	C 0	
KIDNEYS (KD)	EMIC MANIFESTA	NFD:	י א		י א	50 51 22	
S- B/ I.YMPHORLASTIC LYMPHOSARCOMA	ISARCOMA		020	0%	0 0 X	1 ? 2	
TESTFS (TE)	HUMMFR EXAMINED:	ANT NE D :	2 4 C	0 X 0 0	200 200	بر 10	
S U/ LYMPHORI.ASTIC I.YMPHOSARCOMA WITH I.FUK	ISARCOMA WITH LEUKFMIC MANIFESTATIONS	SNL	0 0 %	0 0 0	0770	0 1) Z (1)	OTH
S B/ LYMPHOBLASTIC I YMPHOSARCOMA WITH 1.FUK	ISARCOMA WITH LEUKFMIC MANIFESTATIONS	SNC	0 20	0%	0 70 0	0 U X	ier wis Infor
EPIDJDYHJDFS (FP)		AMJ NED :	200 000	0X 0	0 0 7 0	8 8	TRADE S E CONF MATION NTO CO
PRUSTATE (PR)	NUMBER EXAMINED:	AMJ NED :	0	6	0	0	NDEN
URINARY BLADDER (UB)	···· NUMBER	EXAMI NED :	47 80 202	4 50 70 70	40 0% 0%	4R 0 10,2	TIAL
			0 0	1 2X	0 H X	0 20	
			- 2 7	1 22	0%	0 × 0	
	COMA WITH I FUKEMIC MANIFESTATIONS		1 22	22	4 N	0 20	
							0208

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BID/DYNAMICS, INC. DEPARTMENT DE PATHOLNCY 	*** PATH/TOX SYSTFM NUTPUT * A CHRONTC FFEDING STUDY DF ELYPHOGATE (POLINDIP TECHNICAL)	TPUT * TUDY	*** 1N MICE	CE		PRINTED: 23-MAR-83 Page: 10
	INC.I DENCE	FRCFNT	IAGES	i		STUDY NUMBER' 7/20
		2	E E N	* * *		
TARLE INCLUDES: SEX=FICROUP=ALL;SCRFFN=ALL;WFFKS=ALL DEATH=ALL;FIND=M,R,X,I,S;SUBSFT=ALL	SFX: GROUP:		-EFMALF			
URGAN AND FINDING DESCRIPTION	NUMBER :	1021	105	0 i 10		
** FROM PRFVIOUS PACE ** Ovaries (DV)	NUMBER EXAMINED:	47 8 11 x	47 0 20	50 1 2X	47 0 11 X	
		20 0	1	0 %	0 0	
		0 0	1 22	02	0 2	
S- B/ I.F.JONYOSARCOMA	·	0 0	1 2%	0 0 0	0 0	
I B/ FNDOMF.TRIAL ADFNOCARCINDMA		1	0 0 X 0	х 00	0 0	THERV INF( MONS
S- U/ I_YMPHORI_ASTIC IYMPHOSARCOMA WITH I_EUKEMIC MANIFESTATIONS	H LEUKEMJC MANJFESTATJONS	0 22	1 22	00	0 02	VISE CO DRAGA
	H LEUKENIC MANJFESTATIONS	1	۲0 0 م	74	0 2	TION
S- B/ COMPOSITE LYNPHOSARCOMA		0 0	0	0% 0%	1 2X	ENTEAI OF
UTERUS (UT)		49 22 42	48 1 22	49 1 22	50 1 2	
		л А Ч	3 62	N 7 5	3 52	
M- ENDOMETRJAI, STROMAL CELI SARCOMA		0 0	1 22	0 70	0 20	
R- HEMANGJOMA		0	1 22	0× 0	0 1) Z	<b>)</b> ;20
** CONTINUED ON NEXT PAGE **						\$

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BID/DYNAMICS, INC. Department of Patholngy East Millstonf, NJ 08873	*** PATH/TOX SYSTEM OUTPUT * A CHRONIC FFEDING STUDY OF GLYPHOSATE (ROUNDOUP TECHNICOL) INCTDENCF SUMMARY WITH PERCENT		*** IN MJCF ITAGES	<u>لد</u> ت	STUDY	PKINTED: 23-MAR83 Page: 11 Study Numrer: 772061
	an an an an an an an an an an an an an a	Z		α 		C 1
TARLE INCLUDES: SEX=F;GRRUP=ALL;SGRFFN=ALL;WEFKS=AL DEATH=ALL;FIND=M,R,X,I,S;SUBSFT=ALI	JEFKS=ALI SFX: BSFT=ALI GROUP:		-2	ł	- 4-	
URGAN AND FINDING DESCRIPTION	NUMBER :	1 20	1 20	100	- C10 - III -	
** FROM PREVIOUS PAGE ** UTERUS (UT)	NUMPER FXAMINFD:	N	×	ĸ	50 1 1 1	
		0 0 0	0 0 %	0× 0	۲ ۲۲	
S- LYNPHOR.ASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS	EUKEMIC MANIFESTATIONS	א 50	3 57	1	0 0	
THYROID GI.AND (TH)		43 10 20	37 0 1	49 1 2%	48 0 11 X	OTI
PARATHYRUID GLS. (PT)	NUMBER EXAMINED:	1,1	18	27	15	HER V Irnf(
ADRENAL GLANDS (AD)		к 00 11	47 0 20	44 0 70 70	49 10 8 %	IS TRAD VISE CO! ORMATH ANTO C
S- U/ I.YMPHORIASTIC I.YMPHOSARCOMA WITH LEI	H LEUKEMIC MANJFESTATIONS	0	א 0 ט	24 9 X	0 2	NFIDEN ON OI
	H LEUKEMIC MANJFESTATJONS	0 X 0	ے 2	0%	0 2 2	ITIAL F
SKIN/SURG/FARS (SK)	NUMBER EXAMJNED:	40 02 02	45 1 22	49 1 22	4R 0 2	ł
M- I.IPOSARCOMA		- 2	۲8 84	020	0 2 X 0	
		1 7%	80%	0×0	0 2 0	0
СОМРОЗІТЕ І ҮНРНОЗАКСАМА		0 0 70	0× 0	א 10	9 2 7	240
** CONTINUED ON NEXT PACE **						)

5	*** PATH A CHR	SYSTEM DUTPUT FFFDING STUDY	* *	L		PRINTED: 23-MAR-B3 PAGE: 12
EAST MILLSTONE, NJ 08873	OF GLYPHOSATE (RUINDUP TECHNICAL) IN MICH INCIDENCE SUMMARY WITH PERCENTAGES	CHNICAL H PERCE	VTAGFS	1111		STUDY NUMBER: 772061
		1	W II N	H F A	R = (1 F = A N	IMALS-AFFECTED
TARLE INCLUDES: SEX=F;CROUP=ALL;SCREEN=ALL;WEEKS=ALL DEATH=ALL;FIND=M,R,X,I,S;SUBSET=ALL;	8	SFX:		FFMAN.F 23	-4-	
URGAN AND FINDING DESCRIPTION	NUMRER	R: 50		<b>0</b>   0   1	1 11 11	
** FROM PREVIOUS PAGE ** SKIN/SUBG/FARS (SK)	H LEUKFMIC MANIFESTATIONS			49 33 52	44 10 20 20	
MAMMARY (MG)	NUMBER FXAMINED.	Di 38 22 52	36 4 112	40 40 4	ЗН 1 3Х	
S- LYMPHOR ASTIC LYMPHOSARCAMA WITH LEUK	TH LEUKEMIC MANJFERTATIONS	50 07	24	1 72	0 0	c.
MUSCLE (SM)	NUMBER EXAMINED	D: 50 1 22	20 20 20 20	05 05	4 0 20 20	ONT AIN OTHERV INFO MONS
	rh leukemjc manifestations	1 22		1 22	0 0	VISE CO DRMA
NERUF (NF)	NUMBER EXAMINED:	:D: 41	10 97	49	47	ONFI TIOP
~ ကို		-D: 41 8 02	37 0 20	41 0 2 0 2	45 0 2 2	DENTIAI GOF
HARDFRIAN GLAND (HG)	····· EXAMINED:	.D1 45 2 42	48 9 0 20	49 1 22	44 0 20	
H I IPUSARCOMA		0 0	0%	0 07	0 102	
	LYMPHOSARCOMA WITH LEUKENIC MANJFFSTAFIONS	0 0 0	5 0 3	1 24	0 0	•
BONF (BO)	· · · · · · · · · · · · · · · · · · ·	FD: 47	5 F	49	41	0241
	<b>۔</b> ۲					,

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BIR/DIMARILS, JAL. Departhent de Pathol.ngy Fact milistome, nj ohrzi	AN PATH/INX SYSTEM DUIPUT A CHRAVIC FFEDING STUDY AF CLARATE (VOLUMNIA TECHATCAL)			Ļ	PRINTED: 23-MAR-83 PAGE: 13
	INCT PENCE SUMMARY V	ITHPERCENT	IN HICF TAGES	CF	STUDY NUMBER 1 772061
			N II N	E R	- U F - A N I M A L S - A F F E C T E D
TARI F. INCI UDFSI SEX=FIGROUP=AILIJSGRFFN=ALLIJWEEKS=A DEATH=ALLIFIND=M,K,X,I,SJURSET=AL	II SEX: I GROUP:	+ + 1	-FEMALE-		
URGAN AND FINDING DESCRIPTION	. NUMHER :	50	50		50
** FROM PREVIOUS PAGE ** BONF MARROW (FM)	UKENIC MANJESTALINS	44 10 10 20	4 4 4 4 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	1 N N N N N N N N N N N N N N N N N N N	=- 49 1 2%
		9 0 X	0 0 0	020	2 4X
		0 0	0 0	× 0 •	С
SEMINAL VESICLES (SV)	NUMPER EXAMINED:	C	8	8	ATM THEI III MON
TAJI. (TA)	NUMBER EXANINED:	13	10	0	RV/19 NFOR
COAGULAT. GLAND (CG)	NUMBER EXANINED:	0	8	0	SE CO VMA
ABDQMFN (AB)	NUMPER EXANJNED:	0	c	0	onf Tíoi
SMALL INTESTINES (SI)	NUMBER EXANINED:	C	c	8	iden 1 Oi
PREPUTIAL GLAND (PP)	NUMRFR FXAMJNFD:	c	8	-	ITIA F
MESFNTERY (MF)		с С 9 3	1 0 2 2	2 0 0 0 0	
		0 97 97	1 1002	07 07	020
GENERAL COMMENTS (GC)	NUMBER EXAMINED:	c	•	c	E

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MIN/DYNAMJCS, JNC. Departhent of Pathol Ogy	* *	TUX SYST	NUTPUT STUDY	* *	1		PRINTED: 23-MAR-83 PAGE: 14
EAST MILLISTONE, NJ 08873	DF GLYPHOSATE. INCJDFNCF	(RUUNUP	TECHNICAL) IN MICE 11th Percentages	NTAGES	IICE .		STUDY NUMBER: 772061
				MUN	BFR	ו 10 1	ANIMALS-AFFECTED
TARLE INCLUDES: SEX=F;GROUP=ALL;SCRFFN=ALL;WFEKS=ALL DEATH=ALL;FIND=M,B,X,I,S;SUBSFT=ALL	N=ALL;WFEKS=ALL I,S;SUBSFT=ALL	SFX: GRUUP:			al , F	-4	
URGAN AND FINDING DESCRIPTION		NUMBER :	2: 50 	. 20			
-	2	NUMRFR FXAMINFD:	1 1 1 1002	0 0 0	6 0 <sup>2</sup> 0	0 0 0	
LYMPH NODE (LN)		NUMRFR EXAMINED:		4 0 0 7	20 20 20	1 0 2 2	
			0 0	1 25%	020	0 0	
S- COMPOSITE LYMPHOSARCOMA			2 40%	1 25%	0	1 1002	INFO
M- COMPOSITE LYMPHOSARCOMA			1 202	0 70	07	20	ISE CC RMAT NTO
S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEHIC		MANJFFSTATIONS	1 202	1 252	0 70	0 0	ION C
M- LYNPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC		MANJFFSTATJONS	0%	с <sup>х</sup>	0 70	0	)F
PENIS (PE)		NUMBER EXAMINED:	0 :0	=	c	c	×
ABDUMINAL CAVITY (AC)	2	NUMBER EXAMINED:	0 :0	-	6	Ŧ	
CAVITY (CA)	<b>4</b> • • • • • • • • • • • • • • • • • • •	NUMBER FXAMINED:	0 ic	0	-	Ŧ	
SPINAL CORD (SC)	<b>4</b>	NUMBER EXAMINED:	0 ; c	=	6	c	
GASTROINTESTINES (GI)		NUMRFR EXAMINED:	8 	6	0	8	
URETERS (UR)	۲۵	NUMBER EXAMTNED:	0 ;;	0	0	6	
ADJPOSE TJSSUF (AT)	۲ 	NUMBER FXAMINED.		6 0 0	200 200	50 00	0223

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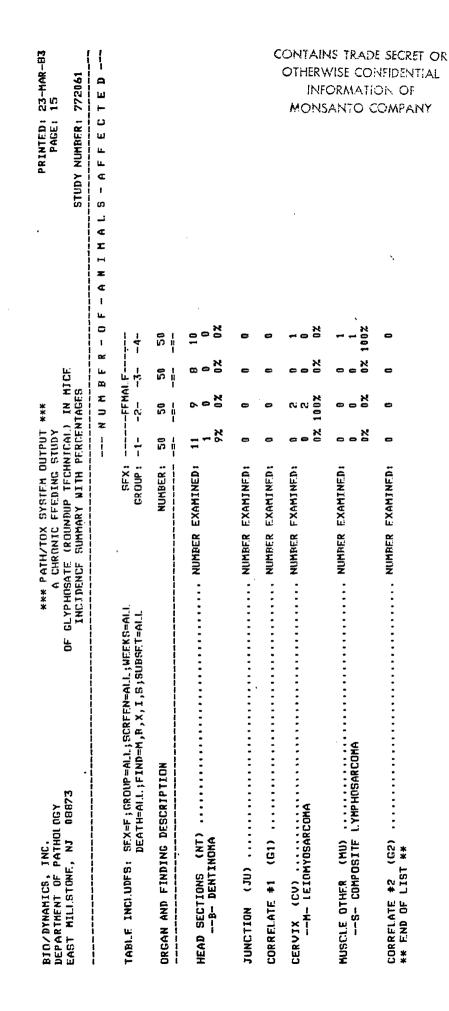


TABLE 15

Glyphosate 104 Week Dietary Carcinogenicity Study in Mice Incidence of Histological Findings : Males and Females

[				N.	INCIDENCE	ъ	I) SNCIS	LESIONS (NUMERIC)	-	
				MALES	s			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	6rp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	GENERALISED CONDITION:		(11)	(5)	(4)	6)	(9)	(1)	(3)	(2)
	Amyloidosis		\$	<b>e</b> -+	-	7	м	~	•	'n
	ABDOMEK:			6		(2)	£			£
	Haemorrhage(s) Inflammation/fat necrosis			0-			0-			0-
	ACCESSORY SEX GLAND(S):			£	Ð	6	_			
	PREPUTIAL GLAND: purulent inflammation/abscess(es)			~	-	<del></del>				
	ADRENALS:		(50)	(23)	(12)	(48)	(05)	(32)	(54)	(50)
	No abnormality detected Unilateral PHAEOCHROMOCYTOMA [M] Unilateral subcapsular CORTICAL CARCINOMA	CARCINOMA	200	5		0 52 0 52	400		400	400
	LmJ Unilateral PHAEOCHROMOCYTOMA [B] Unilateral CoRTICAL ADENOMA [3] Unilateral subcapsular CoRTICAL ADENOMA [B]	ADENOMA	o+o	00 <del>-</del>	00N	-00	00 <del>-</del>	000	~ ~ ~ ~	000
Figures in brackets Significance of diff	ts represent the number of animals from which this tissue was examined histologically. differences in a pairwise (Fisher's) test: * P<0.05, ** P<0.01, *** P<0.001	s from which s) test: * 1	h this P<0.05,	tissue 1 ** P<0	Has exa .01, **	mined h * P<0.0	istolog 01	ically.	_	_

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		=	ICIDENC	E OF LE	SNO1S	INCIDENCE OF LESIONS (NUMERIC)		
		MALES	S			FEMALES	ES	
FINDINGS	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
ADREMALS:	(50)	(23)	(21)	(48)	(50)	(32)	(24)	(50)
Subcapsular hyperplasia	19	5	4	14	40	29	18	40
(Associated) subcapsular hyperplasia		¥ 1		0.	<b>e</b> (	0	0	0
l Unilateral medullary hyperplasia Foral contical hyperplasia		c	- c	- ^	o c 	o -	o c	o c
Diffuse cortical hyperplasia	0	0	0	0	-	• •	) <b>0</b>	0
Unitateral focus(i) of subcapsular	-	0	0	•	0	0	0	0
medullary cell(s) infiltration by lymphoma cells	-	c	c	~	۲	~	•	-
Increased corticomedullary pigmented	. 0	0	0	.0	<b>וא</b> ו 		- M	- 20
foamy cells Unilateral focus(i) of cellular change		0	0		0		0	0
(cortex)					1			;
		<u>ہ</u>	o (	c	rvi •	4	~ ~	~ c
unitaterat infombus Unitateral inflammatory cell infiltrate	00		- c	-	- 0	00	>-	
Focal/diffuse cortical hypertrophy	14	-	- LA	- <b>0</b>	-	0	0	0
Focal cortical degeneration	0	-	0	~	0	0	0	0
Congestion	0	-	0	0	0	0	0	0
Amyloidosis	<b>vo</b>	÷	-	2	м	Ś		м
		_	_	_	-   ·		_	_
ackets represent the number of animals from which this tissue was examined histologically.	h this	tisette	NAC PYR	mined h	ietoloa	ically		

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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	;	2	CIDENCE	: OF LES	INCIDENCE OF LESIONS (NUMERIC)	UMERIC;	~	
		MALES	s	_		FEMALES	LES	
FINDINGS TREATMENT Gr 0 0 mg	Grp 1 G 0 1 mg/kg m /day /	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
AORTA:	(50)	(57)	(20)	(50)	(48)	(32)	(24)	(50)
No abnormality detected Lymphoma cells in surrounding tissue	49	54	0 20	48	3 45	2 M	<b>4</b>	48
BONE:					(2)		£	
Metastasising OSTEOSARCOMA [M]					0		-	
BRAIN:	(65)	(57)	(12)	(05)	(05)	(33)	(24)	(50)
No abnormality detected MENINGIOMA [B] Compression by pituitary Compression by lymphoma cells Meningeal infiltration by lymphoma cells Mineral deposit(s) Meningeal inflammatory cell infiltrate Focus(i) of bacterial inflammation Cerebral haemorrhage(s) Yentricular dilatation Cerebral cyst(s)	400+400000	0000400000	*-00k-0000	* %000-000-0	40-N4-0-0-	N00-400000	<sup>2</sup> 0000000	Mo++ 80+000

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Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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			MALES	INCIDENCE OF LESIONS (NUMERIC) LES   FEMAL		SIONS (	VUMERIC) FEMALES	LES	
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
CAECUM:		(42)	(18)	(16)	(11)	(1)	(33)	(22)	(4)
No abnormality detected Mucosal hyperplasia		38 0	18	15	6£ 0	43	0 29	22 0	42 45
Infiltration by lymphoma cells Submucosal oedema Mucosal necrosis with/without		- MO			-0-	0 + 0	040		o <del>-</del> -
inflammation Amyloidosis		0	•	0	•	0		0	•
CERVIX:						(2)			(2)
Dilatetion/cyst(s)						N			2
COAGULATING GLANDS:		£	£		£				
Dilated Inflammation		-0							
COLON:		(27)	(12)	(19)	(87)	(4)	(33)	(23)	(67)
No abnormality detected Infiltration by lymphoma cells		44	21	¢	48 0	48	32	53	49
Submucosal oedema		ŝ	0		0	0	0	0	

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			NI I	ICIDENCI	E OF LES	STOKS (	INCIDENCE OF LESIONS (NUMERIC)		
			MALES	s			FEMALES	LES	
F I ND I NGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
DIAPHRAGM:			£	£		9		£	
Chronic inflammatory cell infiltrate Contains secondary tumour	trate		0-	o-	_	-0		o-	
DUODEKUM:		(42)	(21)	(16)	(47)	(4)	(31)	(19)	(48)
No abnormality detected Infiltration by tymphoma cells Inflammation in muscle layer Amyloidosis Submucosal focus of pancreatic tissue	tissue	8-04+	<u>+0000</u>	20000	040-040	4-0M0	804-90	#F000	3-0M0
EYES:		5	6	Ð	(2)	(3)	£	(2)	(2)
No abnormality detected Unilateral keratitis		-v -	-0	-0		мo	- 0	ND	NO
GALL BLADDER:		(77)	(42)	(63)	(41)	(77)	(43)	(77)	(97)
No abnormality detected Mucosal hyperpiasia Mesothelial hyperplasia Infiltration by lymphoma cells		900F	0075	₩000	¥00+	8°0 ← v	M004	40-4	200 N

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Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001</pre>

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			NCIDENC	INCIDENCE OF LESIONS (NUMERIC)	) SNOIS	NUMERIC		
		MALES	ES			FEMALES	LES	
FINDINGS	MENT Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
GALL BLADDER:	(44)	(42)	(43)	(11)	(77)	( 73 )	(44)	(97)
Dilated Inflammation Cyst(s) Contains secondary tumour	N-00	N000	M←←+	mooo	0007	*	1000 N	N-00
HARDERIAN GLAND:	£	(2)		(2)				
Unilateral ADENOMA [8] Unilateral bacterial abscess(es)				N 0				
HEART:	(50)	(22)	(12)	(50)	(50)	(33)	(57)	(50)
We abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells Cardiomyopathy with/without necrosis Myocardial mineral deposit(s) Widespread myocardial vacualation Atrial thrombosis Perivasculitis Inflammatory changes Haemorrhage(s)	000040400	2000-000×00	Noonoonnmo		0004000+M00	0400-NN0	00	

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Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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				1	INCIDENCE		SIONS (	OF LESIONS (KUMERIC)	~	
				MALES	ES			FEMALES	LES	
FINDINGS	8	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	6rp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 тg/kg /day
HEART:			(50)	(25)	(12)	(50)	(50)	(33)	(24)	(50)
Focal 1 Valvule Amylofc Epicarc Contair	Focal fibrosis Valvular bacterial endocarditis Amyloidosis Epicardial lymphoid cell(s) Contains secondary tumour				-000-	0000+	0-0-0	000	000	00000
ILEUM:			(43)	(19)	(16)	(1)	(45)	(32)	(22)	(48)
No abno Infiltr Amyloic	No abnormality detected Infiltration by lymphoma cells Amyloidosis		6 - 36 		200		04w	¢ - 3		v - 4¢
JEJUNUM:			({}})	(19)	(18)	(45)	(48)	(30)	(20)	(48)
No abne Infiltr Amyloic	No abnormality detected Infiltration by lymphoma cells Amyloidosis		×-5	°-0-	200 8	5-m	5-15	м - 56	00%	404 40-
KIDNEYS:			(50)	(05)	(50)	(05)	(50)	(67)	(50)	(50)
No abno Unilate	abnormality detected ilateral TUBULAR CARCINOMA [M]	_	8 <del>-</del>	~~	<b>0</b> 0	40	¥0	~ 0	00	*

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					INCIDENCE	Ъ.	LESIONS (	(NUMERIC)		
				MALES	s			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	KIDNEYS:		(05)	(50)	(50)	(50)	(50)	(67)	(50)	(50)
	Unilaterat TUBULAR ADENOMA [B] Unilaterat focus(i) of tubutar Lucrostari		<del>⊷</del> <del>~</del>	-0	00	00	00	0-	00	00
		s s) s) kening	-000000	0-000000044000-440	00-01-0000-0000-000	0-4-MW4-00400MWN	00-0+0+00000000	0N&0NMM4-00-+0000-0	00000000000000000000000000000000000000	0000000-0-0-000000
Figures in brackets Significance of diff	<pre></pre>	s from which this s) test: * P<0.05,		tissue was ** P<0.01,	ias exar 01, ***	examined his	 histologically. .001	ically.		

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				5	INCIDENCE	Ь	LESIONS (1	(NUMERIC)		
				MALES	s			FEMALES	LES	
Ē	SBNICN	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
KIDNEYS:	EYS:		(50)	(50)	(50)	(50)	(50)	(67)	(20)	(50)
	terstitial/perivascular lymphoid	bid	м	Ś	4	\$	Ś	9	м	10
	Tubular hypertrophy Tubular hypertrophy Cortical tubular eosinophilic droplet(s)	oplet(s)	00	- 01	100	00	001	o-:	0 10 1	000
	cystis) Congestion Amyloidosis Contains secondary tumour		-0.00	0000	, , , , , , , , , , , , , , , , , , ,	^ m -		-004	10-0	
LIVE			(50)	(05)	(50)	(50)	(05)	(65)	(50)	(05)
2 	No abnormality detected HEPATOCELLULAR CARCINOMA(TA) [M] HEPATOCELLULAR ADENOMA(TA) [B] (Associated) HEPATOCELLULAR ADENOMA(TA)	IOMA(TA)	-88+ 7	2021	5°1°2	4 0 J 5	20	2000	<u></u> 6000	0000 
	loj Infiltration by histiocytic cell Infiltration by lymphoma cells Focal ovel-cell hyperplasia	Ø	0 N 0 0	N00.	0-0,	ты 		месо	M 80 0 0	<u> </u>
	Hepatocyte atypia Contains haemangiosarcoma Hepatocyte rarefaction		00M	-0-	-00	M		00N	000	0
Figures in brackets Significance of diff	Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: * P<0.05, ** P<0.01, *** P<0.001	s from whic s) test: *	 h this P<0.05,	tissue ** P<0	Нас еха Нас еха .01, **	mined h * P<0.0	istolog 01	ically.	_	
				?			5			

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				=	INCIDENCE	Ъ	LESIONS (	(NUMERIC)	~	
				MALES	S		   	FEMALES	LES	
HI	RD I N GS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
LIVER:			(95)	(02)	(50)	(50)	(50)	(49)	(50)	(50)
Kec	crosis with inflammation		-	-	0	2	0		+-	0
	offer cell pigmentation		0	0	0	м	-	0	0	0
Pad	le/clear cell focus(i)		г'n	~	0	0	0	0	0	0
8as	sophilic focus(i)		m	0	0	-	0	-	0	0
Fac	cus(i) of lymphoid cell(s)		4	~1	9	N	•0	Ś	9	<del>0</del>
EX1	tramedullary haemopoiesis		•	2	<b>0</b>	۲N 1	m I	\$ 	<u>م</u>	m
Hei	patocyte vacuolation		• •	5	<b>4</b> + 1	m	~	4		•
	rombus		<u> </u>	••	•	0,	0	<del>.</del> (	0	0
Per	rivasculitis								-	<u> </u>
	Focus(i) of mineralisation	4	• •				00	- -	••	0,
	ntritubutar nepatucyte entarge ootst of docemensticn/macrosis	TUAU		- n		- 1/	<b>~</b>	4 6	- 14	- 14
	ct(s) of degeneration/licerosis st(s)	_		. C				- C	- ר	C
	lated sinusoids/angiectasis	_	0	0	~~	0	0			
Vas	scular amyloidosis		m	-	0	0	2	m	-	N
	Increased cell turnover		~1	-	-	4	-	м	2	-
Vas	ascular endotheliat pavementing	λq I	0	-	0	0	0	0	0	0
ner	eutrophils									
In	nflammatory changes with/without	It	9	5	~	=	2	~	9	80
i e	ineralisation									
E E	uitinucleate hepatocytes		0	0	0	0	0	0	0	-
C01	ontains secondary tumour		0	0	-	-	rv	-	0	0
			_							
Figures in brackets r	represent the number of animal	s from which	h this		Was exa	mined h	examined histologically.	ically.		
Significance of diffe		s) test: *	P<0.05,	** P<0.01,	.01, **	*** P<0.001	01			

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					INCIDENCE	Ъ	LESIONS (NUMERIC)	NUMERIC		
				MALES	S			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	LUNGS:		(05)	(50)	(05)	(95)	(50)	(67)	(50)	(50)
		-	18	17	5	5	5	8	17	12
	ALVEOLAR/BRONCHIOLAR CARCINOMA(TA) ALVEOLAR/BRONCHIOLAR ADENOMA(TA) [	TA) [M]	- -	~5	a 🗧	۰ ت	мr	м м	- M	<u>v</u> vo
	(Associated) ALVEOLAR/BRONCHIOLAR		m	0	-	м	0	~	0	m
	Infiltration by histiocytic cells	ls	01	N +	o-	← <	ۍ ج	<del>، -</del> «	NR	0
	Alveolar epithelialisation		10	- 0	- ~	→ <del>-</del> -	2	,0	- c	20
	Focal adenomatosis	-	0	0	-	0	0	0	0	0
	<pre>[ Interstitial/perivascular lymph Interstitial pneumonitis</pre>	lymphoid cells	0 M	<u>0</u> -		ом	м-	~ ~	~o~	۵÷
	Increased alveolar macrophages		-	9	60	13	• •0	0		• 0.
	B.A.L.T. increase		~ ~	I	<b>m</b> i	~	~ ~	0	~ ~	0
	Alveolitis Deriveculitie		4 ⊂	N -	∽ -		40	<u> </u>		<u>د</u> م -
	Alveotar oedema		0	- 0	- 0	0	. 0	10	- 0	- ~
	Inflammatory changes		-	-	0	0	-	-	4	0
	_		Ö		-	-	~	-4	-	m
	<pre>Focal alveolar fibrosis</pre>		0	0	-	0	•	0	0	-
	Focal pleural eosinophilic deposit(s)	sit(s)	0	0	0	0	0	0	-	0
	Congestion		~	м	m	~	-	-	0	-
	Bronchopneumonia		-	0	2	0	•	0	0	0
	1			_		_	_		_	
Figures in brackets Significance of dif	ickets represent the number of animals from which this f differences in a pairwise (Fisher's) test: * P<0.05,	ls from which this 's) test: * P<0.05,	h this °<0.05,	tissue was ** P<0.01,	Was exa .01, **	mined h * P<0.0	examined histologically. *** P<0.001	ically.		

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		=	ICIDENC	INCIDENCE OF LESIONS (NUMERIC)	) SNOIS	KUMER 1 C		
		MALES	ŝ			FEMALES	LES	
FINDINGS	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
LUNGS:	(50)	(50)	(05)	(50)	(50)	(67)	(05)	(50)
Focal pleural fibrosis/thickening Solitary focus of vascular mural	00	00	-0	00	00	- 0	00	
Contains secondary tumour		•	-	-	0	0	2	-
LYMPH NODE(S):	(8)	(12)	6	(20)	(18)	(16)	(15)	(13)
One or more has lymphoid hyperplasia One or more infiltrated by histiocytic		00	00		00	<b>₩</b>	0 N	
out of more infiltrated by lymphoma	2	0	0	<u>м</u>	8	~	• 	4
One or more has vascular medial hymertronby	0	•	•	0	-		•	•
Une or more has extramedullary	0	0	<b>.</b>	•	<u>،</u>	0 	0	0
One or more reactive	00			00	<u>~</u> -	0 (	o -	<u> </u>
One or more has inflammatory cell			) <del>-</del>	) <del>-</del>	• •	10 	- 0	, <del></del>
one or more has plasmacytosis	-	~	•	m	0	<b>-</b>	-	0
	_		_	_	-	_	_	_

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Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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				INCIDENCE	Ч	LESIONS (NUMERIC)	NUMERIC		
			MALES	S			FEMALES	LES	
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
LYMPH NODE(S):		(8)	(12)	(6)	(20)	(18)	(16)	(15)	(13)
		0	0	0	-	0	0	0	0
macrophages One or more congested One or more has amyloidosis One or more contains secondary tumour	tumour	000	000	000	000		NTT	0 0 N	000
LYMPHORETICULAR/HAEMOPOIETIC TISSUE:	sue:	(4)	(7)	Ĵ	(8)	(14)	(15)	(12)	(14)
HISTIDCYTIC SARCOMA [M] LYMPHOMA [M]		¢ 0	N N	0-	6 2	0 14	3 12	ma	13
MAMMARY GLANDS:		(77)	(14)	(20)	(75)	(4)	(33)	(24)	(50)
No abnormality detected CARCINOMA(TA) [M] ADENOACANTHOMA MULTIPLE [B] Alveolar development Infiltration by lymphoma cells Dilated/cystic duct(s) Increased secretion present Thrombosis Inflammation		40000-00N	*0000000	00000000	×00000000	N00NT-00	8 Noonmoooo	×-00m-0-0	40+000M00
<pre>Figures in brackets represent the number of animals from which this Significance of differences in a pairwise (Fisher's) test: * P&lt;0.05,</pre>	als from which r's) test: *	h this P<0.05,	tissue was ** P<0.01,	Has exal	<pre>examined histologically.     *** P&lt;0.001</pre>	istolog 01	ically.	_	_

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			ī	INCIDENCE	QF	LESIONS (	(NUMERIC)	~	
			MALES	ES		   	FEMALES	LES	
F I ND I KGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
MAMMARY GLANDS:		(77)	(14)	(20)	(42)	(4)	(33)	(24)	(50)
Amyloidosis Site only examined		٥ĥ	12 0	4	0 H	00	00	- 0	•
MEDIASTIKUM:						-	£		
Infiltration by lymphoma cells									
MESENTERIC LYMPH NODE:		(46)	(20)	(18)	(47)	(48)	(31)	(22)	(67)
No abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells Lymphoid hyperplasia Extramedullary haemopoiesis Increased lymphocytolysis/lymphoid	s	Monoco		2000NN		N08044		20000	Mosoco
depterion Pigmented macrophages Reactive		-0	- 0	-0	NO	м <del>с</del>	~ ~	00	-0
Plasmacytosis Dedema		00	00	00	⊷ c	00	~	00	0 ~
Inflammatory changes Cyst(s)		N 0		NO	- o	0-			- N

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				INCIDENCE OF	E OF LE	) SNOIS	LESIONS (NUMERIC)		
			MALES	S			FEMALES	LES	
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
MESENTERIC LYMPH NODE:	K NODE:	(99)	(20)	(18)	(17)	(48)	(31)	(22)	(46)
Congestion Amyloidosis Contains secon	ngestion yloidosis intains secondary tumour	<u> </u>	m ← o	MOO	4 M F	400	440	0	0 tr M
MESENTERY:				(2)	£	(3)		ε	£
Infiltration E Infiltration E Perivasculitis Chronic, activ Contains secon	Infiltration by histiocytic cells Infiltration by lymphoma cells Perivasculitis Chronic, active inflammation Contains secondary tumour			000 <b></b> -	-0000	00-00			0-000
KASAL CAVITY:					£	Ð			
Mucosal inflammation Haemorrhage(s)	mmation )				04	-0			
OE SOPHAGUS:		(50)	(57)	(21)	(50)	(50)	(32)	(77)	(20)
No abnormality detected Submucosal inflammation	y detected flammation	50	05	21	0°0	ño	32	0 54	5 7 7 8 8
Figures in brackets represent th Significance of differences in m	represent the number of animals from which this tissue was examined histologically. ferences in a pairwise (fisher's) test: * P<0.05, ** P<0.01, *** P<0.001	l ch this P<0.05,	tissue ** p<0	Has exa .01, **	mined h	istolog 01	i cally.	_	_

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FINDINGS         FEMALES         MALES         FEMALES           FINDINGS         TREATMENT GEP 1 [GFP 2 GFP 3 GFP 4 GFP 1 [GFP 2 GFP 3 GFP 4 marks         TOD0 0 1000 0 1000 0 3003 10000 0 1000 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			_							
Grp 1       Grp 2       Grp 3       Grp 4       Grp 1       Grp 2       Grp 3         mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg         mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg         mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg       mg/kg         /day       /day       /day       /day       /day       /day       /day       /day         /day       /day       /day       /day       /day <t< th=""><th></th><th></th><th></th><th>MAL</th><th>ES</th><th></th><th></th><th>FEMA</th><th>LES</th><th></th></t<>				MAL	ES			FEMA	LES	
(50) (33) (34) (50) (33) (34) (31) (32) (33) (34) (31) (32) (33) (33) (32) (33) (33) (33) (33) (33) (34) (34) (35) (33) (33) (34) (34) (35) (33) (33) (33) (33) (34) (34) (35) (33) (33) (33) (33) (33) (33) (33		TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	- 0,	Grp 2 100 mg/kg /day		Grp 4 1000 mg/kg /day
	OVARIES:						(50)	(33)	(24)	(50)
а	No abnormality detecte						æ •	м (		
а	UNITATERAL GRANULUSA L UNITATERAL metastasisi TIMAND FMJ						- 0	⇒ <b>o</b>	⇒ •	
а	Unilateral tubulostron Unilateral focus(i) of	nal ADENOMA [B] f tubulostromal			_		00	00	0-	N M
а	hyperplasia (Associated) bilateral Hyperplasia	l tubulostromal					0	•		-
20 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Unilateral focus(i) of Numerolasia	f papillary					•	0	•	2
0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Bilateral Sertoliform	tubular hyperplasia erclasia					- ^	<u> </u>	00	0 M
0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Infiltration by histic	ocytic cells			-		101	0	→ ← ⊔ 	) <del>-</del> - (
4 + 4 - 4 - 4 - 4 - 4 - 4 - 4 - 4 - 4 -	Unitateral mineral dep	Juna certs Dosit(s)						00	n 0 	V 0
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Pigment deposit(s)						4.		c	o •
4 9 6 36 27 20 0 0 0							- m	- M		- M
	Absence of recent corp	ous luteum					4	0	\$	9
	Cyst(s) Unitateral angiectasis	10					80	22	20	<u>Б</u>

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		-	INCIDENCE	E OF LE	OF LESIONS (NUMERIC)	NMERIC	~	
		MALES	ES		 	FEMALES	LES	
FINDINGS	T Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
QVAR1ES:					(50)	(33)	(24)	(50)
Amyloidosis Increased luteal tissue Contains secondary tumour					~ • •	m+0	0 M F	m-0
PANCREAS:	(50)	(22)	(20)	(4)	(02)	(33)	(54)	(50)
No abnormality detected ISLET ADENOMA [B] Islet hyperplasia Infiltration by histiocytic cells Infiltration by lymphoma cells Cystic duct(s) Costised replacement by fat Acinar atrophy Focus(i) of lymphoid cell(s) Acinar-cell vacuolation Perivasculitis Interstitial oedema Interstitial endema Interstitial inflammation with/without pecrosis Focal acinar hypertrophy Interstitial fibrosis	<u>4000000000000000000000000000000000000</u>	×00000+00ND0MM 00	Moroororveoor oo	А-о+1000NN0000 00	0000×+0000×+0		~000000000000 00	00000000000000000000000000000000000000

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001</p>

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			Ξ	INCIDENCE	ő	LESIONS (	(NUMERIC)	~	
			MALES	ES		   	FEMALES	LES	
F I KD I NGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
PANCREAS:		(50)	(25)	(20)	(65)	(50)	(33)	(77)	
Decreased islet tissue Contains secondary tumour		00	- 0		00		00	00	
PARATHYROIDS:		(77)	(19)	(19)	(42)	(£7)	(28)	(12)	
No abnormality detected Infiltration by lymphoma cells Lymphocytic infiltration Unilateral mast-cell infiltration Unilateral cyst(s) Amyloidosis	Ę	%←0004	°°°°°°≁		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<u>404004</u>	N0+++N	000-000	
PITUITARY:		(47)	(54)	(20)	(44)	(4)	(32)	(23)	
<pre>Ko abnormality detected Anterior lobe ADENOMA [B] Intermediate lobe ADENOMA [B] Cellular change Infiltration by lymphoma cells Focal mineral deposit(s) Thrombus Perivasculitis</pre>			Noo-0000	\$0000000	400-00	2-0NN0	0000-N000	0000000	

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				Í	INCIDENCE OF LESIONS (NUMERIC)	E DF LES	I ONS ()	UMERIC		
				MALES	S		_	FEMALES	LES	
	FINDLAGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	Pitultary:		(47)	(77)	(02)	(77)	(67)	(32)	(23)	(50)
	Focal haemorrhage(s) Anterior lobe cyst(s) Congestion		0-0	000	00-	000	- o o	0-0	00 <del>-</del>	- o o
	PROSTATE:		(48)	(57)	(12)	(50)				
	No abnormality detected Metastasising SARCOMA [M] Contains haemangiosarcoma Hyperplasia Infiltration by histiocytic cells Infiltration by lymphoma cells Inflammation		200000 200000	×00000%	00000-X	40+0+0M				
	RECTUM:		(97)	(21)	(19)	(48)	(47)	(32)	(23)	(4)
	No abnormality detected Infiltration by lymphoma cells		4 t-	21	6	48 0	670	0 32	0	6,0
	SALIVARY GLAND:		(20)	(57)	(12)	(50)	(50)	(33)	(54)	(05)
	No abnormality detected		32	19	19	31	27	17	17	27
Figures in brackets Significance of diff	ckets represent the number of animals from which this tissue was examined histologically. f differences in a pairwise (Fisher's) test: * P<0.05, ** P<0.01, *** P<0.001	from which test: * F	1 this 2<0.05,	tissue : ** P<0	Mas exa .01, ***	mined h	istolog 01	ically.	_	

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				=	NCIDENCE	QF	LESIONS (I	(NUMERIC)	~	
				MALES	S			FEMALES	ES	
	FIKDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	SALIVARY GLAND:		(05)	(54)	(21)	(50)	(50)	(33)	(54)	(50)
	SUBMAXILLARY: infiltration by lymphoma	иррота	-	0	0	м	8	2	M	m
	mucous medial		<u> </u>	00	00		<u>ہ</u> ۔	ъo	40	-0
	SUBMAXILLARY: acinar atrophy SUBMAXILLARY: bacterial focus(i)	•		0 - 1	001	- 0 0	~ 00	001	000	00¥
	SUBMAXILLARY: YYNPHOIG TOCI SUBMAXILLARY: perivasculitis		<u> </u>	<b>n</b> 0 (		> (	> «	• • •	<u> </u>	≗ (
	SUBMAXILLART: CAPSULAT TIDFOSIS SUBMAXILLART: Amyloidosis		- 00				-0-			
	SUBLINGUAL: INTILLERION DY LYNN Ceils	on ona	>	-	5	-	-	>	-	>
	SUBLINGUAL: lymphoid foci SUBLINGUAL: acinar-cell entargement	nent		<u> </u>	00	~~	- c	o	00	00
	SUBLINGUAL: amyloidosis		0	00		• • •	0 1	0		00
	PAROTID: REFILEMENT DY LYMPHONE PAROTID: acinar-cell vacuolation	חם כפווג ח		- -	-0	- ~	• •	10		→ <del>-</del>
	PAROTID: acinar atrophy		0	0	0	0	0	-	0	0
	PAROTID: lymphoid foci PARDTID: inflemmation			o •	00	~	~ ~	C		мс
	PAROTID: amyloidosis		· •	-	0	- 73	2	ю ма 	•	N
Figures in brackets Significance of diff	ckets represent the number of animuls from wh differences in a pairwise (Fisher's) test:	l ls from which 's) test: * P.	ich this * P<0.05,	tissue was ** P<0_01,	L Has exami 		ned histologically P<0.001	f fcally.	_	_

L				=	CIDENCI	INCIDENCE OF LESIONS (NUMERIC)	I) SNOIS	NUMERIC	~	
				MALES	S			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
<u>l</u>	SCIATIC NERVE:		(4)	(77)	(12)	(4)	(50)	(33)	(23)	(50)
	No abnormality detected Inflammatory changes Lymphoma cells in surrounding tissue	ssue	\$mo	0 1 23	005	<del>4</del> 00	000	£ Е О О	5	148
	SEMINAL VESICLES:		(54)	(10)	(6)	(54)		-		
	No abnormality detected Unilateral mucosal hyperplasia Infiltration by histiocytic cells Infiltration by lymphoma cells Dilated with secretion Inflammation Hacmorrhage(s) Cellular infiltrate in secretion Contains secondary tumour	ν, Γ	0-00 <sup>5</sup> 0000	40000000	-0000	000757770				
	SKELETAL MUSCLE:		(50)	(77)	(12)	(20)	(4)	(33)	(77)	(05)
	No abnormality detected Infiltration by lymphoma cells Mineral deposit(s) Lymphocytic infiltration		\$00F	000%	0000	4 8 7 0 7	00%	ñ-0-	2740	0055
Figures in brackets Significance of diff	<pre>kets represent the number of animals from which this tissue was examined histologically. differences in a pairwise (Fisher's) test: * P&lt;0.05, ** P&lt;0.01, *** P&lt;0.001</pre>	ls from which 's) test: * P	h this P<0.05,	tissue ** P<0	Was exa .01, **	* P<0.0	istolog 01	rically.	_	_

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			Ξ	INCIDENCE	Ч	LESIONS (	(NUMERIC)	~	
			MALES	ES			FEMALES	LES	
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
SKELETAL MUSCLE:		(50)	(54)	(21)	(50)	(67)	(33)	(54)	(50)
Perivasculitis Myositis Areas of intramuscular hacmorrhage(s)	Bge(s)		000	-00			0 <del>-</del> 0		-00
SKIN/SUBCUTIS:		(50)	(54)	(21)	(50)	(50)	(23)	(24)	(50)
No abnormality detected SQUANOUS-CELL CARCINOMA [M] SARCOMA(TA) of unknown cell ori PAPILLOMA(TA) [B] LIPOMA [B]	origin [M]	00775	<del>2</del> 0000		200 Å	40440	80000	200	300
Focus(i) of epidermal hyperplasia Infiltration by histiocytic cells Infiltration by lymphoma cells Enidermal uterration with	i a I s	0004	0000	000m	04	oov+	00-0	0005	-00+
inflammation/necrosis Mast-cell accumulation					0		) <del></del>	. 0	· 。
Subcutaneous oedema Inflammation		o	- o	<u> </u>	о N 	0	<u> </u>	00	00
Focus(i) of granulation tissue Increased subcutaneous fat		<u> </u>	00	00	- 0	<u> </u>	0 **	00	<u> </u>
Subcutaneous squamous epithelial cyst(s)	il cyst(s)	•	•	0	0	-	0	0	· •

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				NI.	INCIDENCE	10	LESIONS (	(NUMERIC)		
				MALES	S			FEMALES	LES	
<u>-</u>	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	6rp 4 1000 mg/kg /day
	skin/suacutis:		(50)	(57)	(12)	(50)	(50)	(33)	(54)	(50)
	Focal subcutaneous congestion Subcutaneous sebaceous duct dilatation	atation	00	00	00	- 0	00	00	00	0-
	SPINAL CORD:		(05)	(57)	(12)	(50)	(20)	(33)	(77)	(05)
	No abnormality detected LUMBAR : GANGLIONEUROMA [B] THORACIC : meningeal hyperplasia THORACIC : white matter mineralisation Infiltration by lymphoma cells Spinal canal dilatation Axonal degeneration Cyst(s)	a isation	400-0-	200000	<u>20000000</u>		4000-000	×000-000	*	400+00NF
	SPLEEN:		(50)	(26)	(12)	(50)	(20)	(33)	(77)	(50)
	No abnormality detected SARCOMA of unknown cell origin [ Contains haemangiosarcoma Infiltration by lymphoma cells Lymbhoid hyperplasia Spienic contraction	E	NOONON	800-0M	-0000N	44M00		N0-N0-	00400	000005
Figures in brackets Significance of diff	ets represent the number of animals from which this i differences in a pairwise (risher's) test: * P<0.05,	ls from which this 's) test: * P<0.05,	this <0.05,	tissue was examined histologically ** P<0.01, *** P<0.001	tas exar 01, **'	nîned hi r P<0.00	istolog 01	ically.	_	

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TABLE 15 (continued)

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				a	INCIDENCE		OF LESIONS (NUMERIC)	NUMER 1 C		
				MALES	s			FEMALES	.ES	
	FIND INGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	SPLEEN:		(50)	(26)	(12)	(05)	(50)	(33)	(77)	(05)
	~	oiesis		← eo i	0.0	- 5	° 5	- ÷	- =	0
	Increased lymphocytolysis Increased brown pigment deposit( Perivasculitis	(s)		M 0 0	-00	N O O	0 v 0	-00	0-0	- 01
	Large focus(i) of necrosis Congestion in the red pulp			0						001
	Amyloldosis Abscess(es) Incressed callularity of red nul	<u> </u>	<u>vo-</u>	- 0 0	- 0 0	n 0 0	v – c	*00		v o c
	Cell vacuolation in the red pulp Chronic inflammatory thickening of	of the	- 0 0				)	000		
	capsule Contains secondary tumour		0	0	•	0	0	-	<b>e</b>	0
	STERNUM: No abnormality detected Bone marrow infiltration by lymphoma	рһота	45	0 50	0 19	37	37	4 19	4 7	53
	cells Fibrous osteopathy Pigment deposit(s)		00	00	00	00	mo	no	00	8 <del>-</del>
Figures in brackets Significance of diff	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	ls from whic 's) test: *	h this P<0.05,	tissue was ** P<0.01,	Has exe .01, **	<pre>examined histologically.     *** P&lt;0.001</pre>	istolog 01	lically.	_	

			н	INCIDENCE	9F	CESIONS (	(NUMERIC)	~	
			MALES	ES			FEMALES	LES	i i
FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 Mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
STERHUM:		(20)	(22)	(21)	(05)	(50)	(32)	(57)	
ocal bone ncreased	sis	0	0 10	0 21	0 4	<del>м –</del>	0		
Increased haemopolesis Decreased haemopolesis tymphoid foci in marrow						- 0 0	000		
Maldevelopment of one rib Increased lymphoid cells in marrow	10,	000	, o o -	000		) o -		000	
Increased meduilary trabecular bone	оле	<b>-</b>	0	°	0	~	<u>г</u> л	M	
STOMACH:		(50)	(57)	(12)	(67)	(50)	(33)	(77)	_
No abnormality detected SquAMOUS-CELL CARCINOMA [N] Squamous ebithelial hyperplasia		фот	°00	÷00	<u></u> М	62 O F	°	٥ 0 م	
Focal glandular mucosal hyperplasia Diffuse glandular mucosal hyperplasia	asia Olasia	- M un	) C	) <b>C</b> -1	- 00	- N F	> ← œ	» m n	
Infiltration by lymphoma cells Dilated glands in muscle laver		c	. o c	· o c	· r	- - -	) m c	1 M C	
Dilated mucosal glands				~ <del>-</del>	J	5 N	2 10	 -	_
Submucosal lymphoid cell(s) Perivasculitis		<u> </u>	00	00	00	~ ~	c	0 C	
Submucosal oedema		0	0		• •	0	, <del></del>	) O	

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				ī	I NC I DENCE	0	LESTONS (	(NUMERIC)	~	
				HALES	S			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
S	STOMACH:		(50)	(24)	(21)	(67)	(50)	(33)	(54)	(67)
	Inflammation Submucosal haemopoiesis Amyloidosis Contains secondary tumour		0000	0000	000-	-000		0-00	-00-	
	SUBMANDIBULAR LYMPH NODE:		(2)	(2)		(2)	(8)	£	£	3
	No abnormality detected Infiltration by lymphoma cells Lymphoid hyperplasia Pigment deposit(s) Reactive Plasmacytosis Cyst(s)		000-0000	00000000		0m00++00		0-00000-	0-000000	0000000
Ŧ	TESTES:		(50)	(54)	(12)	(05)				
	No abnormality detected INTERSTITIAL-CELL ADENOMA(TA) [8] Unilateral focal interstitial-cel hyperplasia	11	0 M V	400	004					

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				Ē	INCIDENCE		STORS (	OF LESIONS (NUMERIC)		
				MALES	S			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	TESTES:		(50)	(77)	(21)	(50)				
	Diffuse interstitial cell hyperplasia Unilateral rete testis hyperplasia Infiltration by histiocytic cells Unilateral infiltration by lymphoma cell Tubular atrophy/mineralisation Depressed spermatogenesis Sperm accumulation Unilateral coagulative necrosis Unilateral rete testis inflammation Interstitial congestion Amyloidosis FPIDIDYMIS: infiltration by histiocytic cells FPIDIDYMIS: infiltration by lymphoma cells FPIDIDYMIS: spermatocele(s) EPIDIDYMIS: tubular dilatation EPIDIDYMIS: vacular endothelial Cells FPIDIDYMIS: vacular endothelial	lasia ia soma cells ion tiocytic bhoma	8400 <sup>8</sup> 080440 + NNF0	N00040-0000N 0 000-	-000M0N000-0 0 -000	WEEEE4N000F E EN00	<u></u>			
Figures in brackets Significance of diff	represent erences in	ls from whic 's) test: *	 h this P<0.05,	tissue ** P<0	Has exa 01, **	mined h * P<0.0	 istolog 01	ically.		

				1	INCIDENCE	Ъ	LESIONS (A	(NUMERIC)	0	
				MALES	s			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	THORAX:				(1)	£		£		
	PLEURA: inflammation Infiltration by lymphoma cells Contains secondary tumour				00-	040		-00		
	THYMUS:		(42)	(21)	(16)	(41)	(95)	(12)	(23)	(77)
	abnormality detected filtration by lymphon mphoid hyperplasia ithelial hyperplasia creased lymphocytolys cal foamy cell accum rombus cus(i) of necrosis cus(i) of necrosis scull finfiltration ronic inflammatory ce ssall's corpuscle en ssular mural thicken ngestion rophy of hyaline ch	La te	Nm-000000000000	2000-00000-0-NO		м м м	×= ×0 + 0 + 0 0 0 0 0 0 0 - 0			KON - 0 - 0 0 NNOO
Figures in brackets Significance of diff	ickets represent the number of animals from wh of differences in a pairwise (Fisher's) test:	<pre>s from which this s) test: * P&lt;0.05,</pre>	ich this * P<0.05,	tissue was ** P<0.01,		examined histologically. *** P<0.001	istolog 01	ically.		

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		É	INCIDENCE		) SNOIS	OF LESIONS (NUMERIC)		
		MALES	s			FEMALES	LES	
FINDINGS	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
:SUMART	(42)	(12)	(16)	(41)	(97)	(31)	(23)	(77)
Contains secondary tumour Germinal centre development	00	••	- 0	00	00		00	<del>ب</del> بـ
THYROIDS:	(50)	(54)	(21)	(50)	(50)	(32)	(57)	(50)
<pre>Ko abnormality detected Unilateraf FOLLICULAR ADENOMA [B] Unilateral focus(i) of follicular-cell hynamilasia</pre>	105	200	₩-0	0058	M 0 0	005	÷	0-158
Unitateral focus(i) of c-cell hyperplasia Infiltration by lymphoma cells Dilated/cystic follicle(s)		000	001	0 ~ <sup>6</sup>	0 ~ 2	4 0 0	- 0 v	0 7 7
Focuse() of lymphoid cell(s) Perivasculitis Unilateral inflammatory cell infiltrate Amyloidosis			00	00	4-02	000N	N00+	-00-
TRACHEA:	(50)	(54)	(21)	(20)	(50)	(32)	(57)	(50)
No abnormality detected Infiltration by lymphoma cells in lamina propria	<u> </u>	*00 5	00	<u>йо</u>	02 O	32		<u> </u>

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Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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				1	INCIDENCE		OF LESIONS (NUMERIC)	NUMERIC	~	
				MALES	S			FEMALES	LES	
	FINDINGS	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	6rp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
	URETER:						6			
	Infiltration by lymphoma cells									
	URINARY BLADDER:		(67)	(23)	(19)	(50)	(67)	(32)	(23)	(67)
	No abnormality detected Infiltration by histiocytic cells Infiltration by lymphoma cells submucosal lymphoid focus(i) perivasculitis Inflammation Focal transitional-cell hypertrophy submucosal haemorrhage(s) Dilatation Large plug of seminal fluid in lumen UTERUS: No abnormality detected STROMAL TUMOUR [B] POLYP(S) [B] LEIOMYOMA(TA) [B]	ls Lumen	×0-*0*00*0	-00M0V0-0-	0000000	00-40-90-00	0-000 000 000 000 000 000 000 000 000 0	тааат <u>щ</u> олооооме	2-wwaaaaaa (, weaea	Nov-0-0-0 0 0N-NN
Figures in brackets Significance of diff	ckets represent the number of animals from which this i if differences in a pairwise (Fisher's) test: * P<0.05,	als from which 's) test: *	h this P<0.05,	<pre>tissue was examined histologically. ** p&lt;0.01, *** p&lt;0.001</pre>	was exa .01, **	mined h * P<0.0	istolog 01	ically.		

				1	INCIDENCE	5	LESIONS (N	(NUMERIC)		ļ	
		•		MALES	s			FEMALES	LES		
	SDN I GN I 4	TREATMENT	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	
	UTERUS:						(05)	(33)	(24)	(50)	
	Cystic endometrial hyperplasia Endometrial hyperplasia Contains haemangiosarcoma Infiltration by histiocytic cells Infiltration by lymphoma cells Dilated/cystic gland(s) Mesothelial hyperplasia Extramedullary haemopoiesis Adenomyosis Thrombosis Patrononisis Myometrial inflammation Mural haemorrhage(s) Fat necrosis Dilatation Angiectasis Pigmented macrophages in muscle layer VAGINA: POLYP [B]	ls Layer					M-004F-0N-ND-00N-	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	N 00MNM00-00-0-NOO	M+000000+044000000	
Figures in brackets Significance of dif	<pre>1                                      </pre>	ls from which 's) test: * P	1 this 2<0.05,	tissue   ** p<0	tas exa 01, **	mined h * P<0.0	istolog 01	ically.		_	

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				INCIDENCE OF LESIONS (NUMERIC)	E OF LE	SIONS (	NUMERIC	~	
			MALES	ES			FEMALES	LES	
FINDINGS	TREATMENT         Grp 1         Grp 2         Grp 3         Grp 4         Grp 1         Grp 2         Grp 3         Grp 4           0         1000         300         1000         0         1000         300         1000         300         1000         300         1000         300         1000         1000         300         1000         300         1000         300         1000         1000         300         1000         1000         1000         1000         100         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         1000         10	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day	Grp 1 0 mg/kg /day	Grp 2 100 mg/kg /day	Grp 3 300 mg/kg /day	Grp 4 1000 mg/kg /day
VASCULAR SYSTEM:		(2)	(9)	(3)	6	9	6	(2)	6
HAEMARGIOSARCOMA [M] Perivasculitis Vascular endothelial pavementing by neutrophils	yd gni	010	0 0	0 M O	4100	000	0 0 0	0 1 0	- 00

Figures in brackets represent the number of animals from which this tissue was examined histologically. Significance of differences in a pairwise (Fisher's) test: \* P<0.05, \*\* P<0.01, \*\*\* P<0.001

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#### Histopathology - Incidence of microscopic neoplastic lesions in male mice Terminal kill after 78 weeks of treatment Table 20 - 1

Site & Lesion	Dose	(pp	om)			0		16	300		8	000		40	000	
	No. of animals	exami	ne	d		26			34			27			29	1
Hematopoietic & Lymph	atic System			A												
General:		(	N=	)	(	26	)	(	34	)	(	27	)	(	29	
(M) Maligna	nt lymphoma			1		0	ŕ		0		`	0			2	
Respiratory System															-	
Lung:		(	N=	)	(	26	)	(	34	1	1	27	1	(	29	
(B) Adenoma			20	1	,	5	'	1	13		1	10		(	-	1
(M) Adenoca	ceinoma					0			0			4			1	
Digestive System						v			U			4			1	
Liver:		1	N=	1	1	26	1	(	34	١	1	27	١	1	90	
	ellular adenoma	(	I	'	1	8	,	1	13		(			(	29	
(B) Hemangie	ona					1						9			5	
(M) Henatoe	ellular carcinoma					0			0			0			0	
Urinary System						U			U			2			0	
Kidney:		1	M	١	1	0.0	1	1	<b>n</b> /	1	,			,		
(B) Adenoma		(	И=	)	(	26	1	(	34	)	(	27	)	(	29	
Urinary bladder		,	17		,	0		,	0			0			2	
		l	N=	)	(	26	)	(	34	)	(	27	)	(	29	1
(D) Iransit	ional cell papill	oma				0			2			0			0	
Genital System Testis:		1	1.	,	,		N	,								
		(	N=	)	(	26	)	(	34	)	(	27	)	(	29	1
(B) Interst	itial cell tumor					0			1			0			0	1
Endocrine System																
Thyroid:		(	N=	)	(	26	)	(	34	)	(	27	)	(	29	1
(B) Follicul	ar adenoma					0			1			0			0	
Vervous System																
Cerebrum:		(	N=	)	(	26	)	(	34	)	(	27	)	(	29	1
(B) Lipoma						0		•	1	'		0	'	•	0	'
Musculo-Skeletal Syste	em.														•	
Bone (others) :		(	N=	)	(	3	1	(	1	)	(	4	1	(	1	١
(B) Osteoma		•		1	•	õ	'	1	Ô	1	1	1	1	1	0	1
Sense Organs						•			•			r			v	
Harderian gland:		(	N=	1	(	26	1	(	34	1	1	27	1	(	29	١
(B) Adenoma		(		1	1	20	/	(	A	,	(	- 0	,	(	23	1
Integumentary System						4			4			V			4	
Skin:		( )	N.	١	1	26	1	1	34	١	1	27	١	1	00	1
(B) Papillon	8	( )	"	,	ſ	1	,	(	1	,	(		)	l	29	,
(M) Hemangio						0			ô			0			0	
							-								1	
						17			36			20			16	
No. of malignant neo	plasms		*****			0			0			6			4	
No. of benign & mali	gnant neoplasms					17			36			26			20	
No. of animals with	benign neoplasm(	s)				13		1	25			17			14	
No. of animals with	malignant neopla:	sm (s)				0	*****		0			6			4	
No. of animals with						13			25			20			15	

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm.

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#### Table 20 - 2

Histopathology - Incidence of microscopic neoplastic lesions in male mice Killed in extremis or found dead

Site & Lesion	Dose	(թթտ)	0	1600	8000	40000
Side a lesion	No. of animal	s examined	24	16	23	21
Hematopoietic & Lymp	hatic System					
General:		(N=)	(24)	(16)	(23)	( 21 )
(M) Malign	ant lymphoma	( )	2	2	0	4
Lymph nodes (me	esenteric):	( N= )	$(2\bar{4})$	$(1\bar{6})$		
(M) Malign	ant lymphoma	· · · /	0	1	, 10,	0
Spleen:		( N= )	(24)	(16)	(23)	(21)
(M) Histic	cytic sarcoma	( )	1	0	0	0
Respiratory System			-	U	v	v
Nasal cavity:		(N=)	(0)	(0)	(0)	(1)
(M) Adenoc	arcinoma	. ,	` _ <b>`</b>	· - /	· - /	ì
Lung:		(N-)	(24)	(16)	(23)	(21)
(B) Adenom			3	1	3	4
(M) Adenoc	arcinoma		1	1	2	3
Digestive System						
Small intestin		( N= )	(24)	(16)	(23)	(21)
(B) Papill	ary adenoma		0	1	0	0
(M) Adenoc	arcinoma		0	0	0	1
Liver:		( N= ) (	(24)		(23)	(21)
(B) Hepato	cellular adenoma		6	2	6	2
(M) Histio	cytic sarcoma		1	0	0	0
Genital System	cellular carcinom	18	0	1	1	1
Testis:		( ) ( ) (		( (0))	(	
(B) Hemang	i ama	(N=)(		(16)		
Endocrine System	TOILLA		1	0	0	0
Thyroid:		( ) ) (	011	1 10 1	(	1
	ular adenoma	( N= ) (	24)	(16)	(23)	(21)
Adrenal:	urar auenoma	( 11 ) (	04.	( 10 )	( 00 )	0
	B cell tumor	( N= ) (	24)	(16)	(23)	(21)
Musculo-Skeletal Sys	tem		0	1	U	0
Bone (others) :	Con	(N=)(	6)	(1)	(2)	( 1)
(B) Osteom	a	( 11- ) (	1	$(1)_{0}$	( 2)	$(1)_{0}$
(M) Osteos	arcoma		Ô	0	1	ő
Sense Organs			v	U	1	0
Harderian gland	d:	(N=)(	28 1	(16)	(23)	(21)
(B) Adenomi	a	( 1 ) (	1	(10)	( 40 )	( 21 )
Integumentary System			1	U	1	1
Skin:		(N = ) (	21)	(16)	(23)	(21)
(M) Hemangi	iosarcoma	( ) (	0	0	(23)	(21)
(M) Leiomyc	osarcoma		õ	õ	1	1
(M) Osteosa	reoma		ő	0	0	1

(N→): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

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Site	& T.	esion	Dose	9		(ppm)	0	1600	8000	40000
			No.	of aniu	uals ez	kamined	24	16	23	21
		benign neop	lasms				12	6	10	7
No.	of	malignant n	eoplası				5	5	5	13
		benign & ma	lignant	neopla	ISMS		17	11	15	20
		animals wit					10	5	8	6
No.	of	animals with	n malig	nant ne	oplasm	1 (s)	5	5	5	12
		animals with					12	9	10	15

#### Table 20 - 3 Histopathology - Incidence of microscopic neoplastic lesions in male mice Killed in extremis or found dead

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#### Table 20 - 4 Histopathology - Incidence of microscopic neoplastic lesions in male mice All animals examined

Site & Lesi	on	Dos	e		(	ppn	1)			0		160	0		80	000		40	000	1
		No.	of	animals	exa	mir	ec	ł		50		5	0			50			50	1
Hematopoiet Genera	ic & Lympha	tic	Syst	em																
		4 1	1.			( )	=	)	(	50	)	(5		)	(	50	)	(	50	)
Lumph	<li>A) Malignar nodes (mese</li>	it ly	upho	oma.		1 1		`	,	2			2			0			6	
Lympt	I) Malignar	t l.	IC) ·			( 1	=	)	(	50	)	(5	0	)	(	50	)	(	50	)
Spleen	iy marignar	it iyi	npno	ma		1 1		1	1	0	1		1		,	_0		,	0	
opreen (	1) Histiocy	tio		0.000		( 1	=	)		50	)	(5	0	)	(	50	)	(	50	)
Respiratory	System	uic .	bal C	oura						1			0			0			0	
Nasal	cavity:					( )	_	1	1	0	1	1	^	•	1	•	1	,		
()	1) Adenocar	cino	na			( 14	-	,	(	0	)		0	)	(	0	)	(	1	)
Lung:	,	ornor				N	-	١	( )	50	۱.	( 5	0	1	1	50	1	1	1	1
- (E	) Adenoma					( 11		/	1.	8	,	1		,	•	50	)	(	50	)
()	) Adenocar	cinon	aa							1			ŧ			13 6			11	
Digestive Sy	stem									1			L			0			4	
	intestine:					N	-	)	( 5	50	1	( 5(	1	1	(	50	١	(	50	1
(E	) Papillar	y ade	nom	a				'		0	· ·		í	1	1.	0	)	1	00	)
(M	Adenocar	cinom	ia							õ		Ċ				õ			1	
Liver:					(	N	- 1	1	( 5	50 )	) (	50			( (	50	1	1	50	1
(B	) Hepatoce Hemangio	llula	r a	denoma			'			4		15				15	)	1	1000	1
(B	) Hemangion	na							-	1		10			4	0			7	
(M	Histiocy	tie s	arec	oma						1		Č				ŏ			0	
(M	Hepatoce	llula	r ca	arcinoma						ô		1				3			1	
Urinary Syst	em									v		1				9			1	
Kidney	:				(	N=	- )	(	( 5	0)	1	50	1			50	1	1	EO	1
	Adenoma						/	1		0 '	(	0				0	)	(	50	)
Urinary	bladder:				(	N=	. )	(		õ)	(	50		1		~	1	1	4	•
(B)	Transitio	onal	cell	nanille	oma	11	1	(		0,	(	2		1	, a	0	)	(	50	)
Genital Syste	em			papiri	o mu					v		4				U			0	
Testis					(	N=	1	1	5	0)	(	50	1	(	E	0	1	(	-0	1
(B)	Interstit	ial	cell	tumor	1	п	,	1		0	(	1	)	(		0	)	(	50	)
(B)	Hemangion	a								1		0				0			0	
Endocrine Sys	stem									1		0				U			U	
Thyroid	:				(	N=	1	1	5	0)	1	50	١	(	5	0	•	( )	0	1
(B)	Follicula	r ade	enon	a	X		'	1	0	n'	1	00	,	(		•	,	( )	50	)
Adrenal	:				1	N-	1	(	5	0)	1	50	١	(		0,0			0	<b>\</b>
(B)	Benign B	cell	tum	or	(	11	1	1	0	n'	(	<sup>30</sup>	,	(	D	0)	,	( 3	50	,
Nervous Syste	m	10000 B							2	0		1				0			0	
Cerebru	m :				1	N-	1	1	50	))	(	EO	١	1	-	~ `				
(B)	Lipoma				(	11-	,	1	5	,,	(	50	)	(	5	0)			50	
Musculo-Skele	tal System								(	,		1				U			0	
Bone (ot	hers) :		3)		(	N=	١	1	(	))	1	0	1	1		• 1		,	•	
	Osteoma				(	n	)	1	1	, ,	(		)	(		6)			2)	
(M)	Osteosarc	oma							0	1		0				1			0	
Sense Organs									C	,		0				1			0	
Harderi	an gland:				(	N=	١	1	10	))	1	50	1	1	-	• •		-	~	
(B)	Adenoma				(	14	)	(	40	, ,	(	50	)	1	50	))	1	5	( 0	
Integumentary	System								e	)		4			1	L			3	
Skin:	- 1 <b>9</b> (1996)				(	N-	1	(	FC	1	1	En	١	1	F/	1		-	~ `	
	Papilloma				C	11-	1	(	10	))	(		)	(		))	(	5	( 0	
	Hemangios	arrom	a						1			1			(				0	
6.9		-1 - 0 0 10							0			0			(	)			2	

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

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Site & Lesion	Dose	(ppm)	0	1600	8000	40000
	No. of anima	ls examined	50	50	50	50
	em 《cont.》 : myosarcoma osarcoma	( N= )	(50) 0 0	(50) 0 0	(50) 1 0	(50) 1 1
No. of benign ne	oplasms		29	42	30	23
No. of malignant	neoplasms		5	5	11	17
No. of benign &	malignant neoplasm	ns	34	47	41	40
No. of animals w	ith benign neoplas	sm (s)	23	30	25	20
No. of animals w	ith malignant neop	lasm (s)	5	5	11	16
No. of animals w	ith neoplasm(s)		25	34	30	30

Table 20 - 5 Ilistopathology - Incidence of microscopic neoplastic lesions in male mice All animals examined

Malignancy: (M), malignant neoplasm.

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#### Table 21 - 1 Histopathology - Incidence of microscopic neoplastic lesions in female mice Terminal kill after 78 weeks of treatment

Site & Lesion	Dose	(ppm)	)		(	)	1	600	)	8	000	)	40	0000	)
	No. of animals	examin	ed		32	2		36	;		4(	)		35	i
Hematopoietic & Lymphat	tic System		RC.				-		-			1			
General:		( N	- )	1	( 32	1 5	(	36	1	(	4(	1	(	35	1
(M) Malignant	t lymphoma	1	1		1	i'	1		*	1	4		(	30	
Thymus:		( N·	- )	1	( 32	5)	(	35		(	40		1		
(M) Malignant	lymphoma	1.11	1		02	5	1	0		(	40	, ,	(	35	)
Spleen:	•	( N=	- )	1	( 20	1	(			(	10	1	(	0	1
(B) Hemangion	18	( 11	,	1	02	; /	ſ	0		(	40	, ,	(	35	
Respiratory System					U			0			1	2		0	
Lung:		( N=	- )	1	20	1	1	90	1	1	10		1	05	•
(B) Adenoma		( 11	)	(	04	, ,	(	36	,	(	40		(	35	
(M) Adenocarc	inoma				í			4			12			4	
Digestive System	ritolite				1			1			3			0	
Small intestine:		( N-	. )	1	00	١	1	00	1	1	10	•	,	-	
(B) Adenoma		( N=	)	(	•		l	36	•	(	40	)	(	35	)
Liver:		( )1	1	1	0		1	0		,	1			0	
	lular adenoma	( N=	)	1	32	)	(	36	)	(	40	)	(	35	)
Urinary System	rurar adenoma				1			1			1			0	
Urinary bladder:		( ))	1	,	00		,								
(B) Leiomyoma		( N-	)	(	32	)	(	36	)	(	40	)	(	35	)
Genital System					0			0			1			1	
Uterus:		( 11		,			,	-							
(B) Endometration	1	( N=	)	(		)	(	36	)	(	40	)	(	35	)
(D) Homeneteria	al stromal polyg a	þ			0			2			0			0	
(D) Letanglona	1				0			0			1			2	
(B) Leiomyoma					1			0			2			1	
(M) Histiocyti	ic sarcoma				0			1			0			0	
(M) Leiomyosar	Coma				2			1			0			0	
Endocrine System														-	
Pituitary:		( N=	)	(	32	)	(	36	)	(	40	)	(	35	1
(B) Anterior a	adenoma				0	150	•	1	'	`	0	'	1	0	,
Thyroid:		( N=	)	(	32	)	(	36	)	1	40	)	(	35	1
(B) Follicular	· adenoma				0			1	'	•	0	'	1	0	,
Adrenal:		( N≕	)	(	32	)	(	36	)	1	40	1	(	35	)
(B) Benign A c	ell tumor			•	0	'	•	1	/		2	,	1	0	,
(B) Pheochromo	eytoma				0			2			0			Ő	
Sense Organs								1			v			v	
Harderian gland:		( N=	)	(	32	1	(	36	١	1	10	1	1	35	1
(B) Adenoma		<b>,</b>	'	•	1	,	1	3	)	( .	0	,	(	3	,
Integumentary System					-			U			0			0	
Skin:		( N=	1	(	32	1	(	36	1	(	10	1	1	9F -	1
(B) Papilloma		(	,	1	1	,	(	0	)	( '	10 10	)	L	35	)
(B) Lipoma					1			0			~			0	
(M) Liposarcom	a				0						1			0	
Mammary gland:		( N=	1	1	~	)	1	0		1	0	1	1	1	0
(B) Adenoma		( 11-	11			,	( .	36)	1	( 4	10	)	(	35)	)
(M) Adenocarci	noma				0			1			0			0	
Body Cavities	noma				0			2			0			0	
Abdominal eavity:		( )	1	,	- 1		,			,			,		
(B) Hemangioma		( N=	) (		5	)	(	4)		(	3	)	(	4)	È.
(b) nemangroma					0			0			0			1	

(N-): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm. \*: Significantly different from the control at 5 % level of probability.

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Site	& I.	esion	Dose	(ppm)	0	1600	8000	40000
			No. of anima	als examined	32	36	40	35
		benign neop	lasms		12	16	22	12
No.	of	malignant r	neoplasms		7	5	9	4
			alignant neoplas		19	21	31	16
			h benign neopla		11	12	18	11
No.	of	animals wit	h malignant neo	plasm(s)	7	5		4
			h neoplasm(s)		16	16	21	12

Table 21 - 2 Histopathology - Incidence of microscopic neoplastic lesions in female mice Terminal kill after 78 weeks of treatment

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Site & Lesion	Dose	(ppm)	0	1600	8000	40000
	No. of animal:	s examined	18	14	10	15
Hematopoietic	& Lymphatic System					
General		(N=)	(18)	(14)	(10)	(15)
(M)	Myeloid leukemia	( )	0	0	0	1
	Malignant lymphoma		2	Å	3	Å
Spleen:		( N= )		(14)		( 15)
(M)	Hemangiosarcoma	( )	0	( 14 )	1 1	(10)
(M)	Histiocytic sarcoma		ŏ	ŏ	ò	1
Respiratory 5	ystem		v	v	v	1
Lung:	•	(N-) (	18)	(14)	(10)	(15)
(B)	Adenoma	( ) (	1	1	0	(10)
(M)	Adenocarcinoma		ô	î	Ő	1
	< Nodule/mass not in se	ection >	õ	Ô	1	ō
Digestive Sys	tem			•	-	v
Liver		(N-)(	18)	(14)	(10)	(15)
(B)	Hemangioma	. , ,	0	0	0	1
Genital System	11					-
Ovary:		(N=)(	18)	(14)	(10)	(15)
	Hemangioma		0	0	0	1
Uterus:	-	( N= ) (	18)	(14)	(10)	
(M)	Leiomyosarcoma		0	0	0	1
Endocrine Syst	tem					•
Thyroid		( N- ) (	18)	(14)	(10)	(15)
(B)	Follicular adenoma		0	1	0	0
Musculo-Skelet	al System					
Bone (fen		(N=)(	18)	(14)	(10)	(15)
(B)	Osteoma		0	0	0	1
Skeletal	muscle (others) :	(N-)(	0)	(3)	(3)	(1)
(M)	Rhabdomyosarcoma		- '	1	2	Ì Ô Í
Sense Organs						
	n gland:	(N-)(	18)	(14)	(10)	(15)
	Adenoma		0	0	0	2
Integumentary	System					
Skin:		(N=)(	18)	(14)	(10)	(15)
(M)	Basal cell carcinoma		0	1	0	0
(M)	Hemangiosarcoma		0	0	1	Õ
Manumary	gland:	(N=)(	18)	(14)	(10)	(15)
D. I. C. I. (M)	Adenocarcinoma		0	1	1	0
Body Cavities					-	
Thoracic	cavity:	(N=)(	2)	(4)	(4)	(7)
(M)	Osteosarcoma		0	` Ő ´	ô	1
Abdomina	l cavity:	(N-) (	3)	(5)	(6)	$(\hat{5})$
(M)	Osteosarcoma		0	0	0	1

#### Table 21 - 3 Histopathology - Incidence of microscopic neoplastic lesions in female mice Killed in extremis or found dead

(N-): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm: (M), malignant neoplasm.

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Site	& I.	esion	Dose	(ppm)	0	1600	8000	40000
			No. of anima	ls examined	18	14	10	15
No.	of	benign neop			1	2	0	6
		malignant r	neoplasms		2	8	8	10
			lignant neoplas		3		8	16
			h benign neopla	sm (s)	1	1	0	5
No.	of	animals wit	h malignant neo	plasm (s)	2	8	7	9
			h neoplasm(s)	*********	3	8		11

Table 21 - 4 Histopathology - Incidence of microscopic neoplastic lesions in female mice Killed in extremis or found dead

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Table 21 - 5

Histopathology - Incidence of microscopic neoplastic lesions in female mice All animals examined

Site & Lesion	Dose	(ppm)	1		0		1	600		8	000		40	000	
	No. of animals	examin	ed		50			50			50			50	1
Hematopoietic & Lymphat	ic System				-										
General:		( N=	- )	) (	50	)	(	50	)	(	50	1	(	50	1
(M) Myeloid In			1		0		1	Ő		(	0		(	1	
(M) Malignant	lymphoma				6			4			8			7	
Thymus:		( N=	= )	) (	49	)	(	49	)	(	50	)	(	50	1
(M) Malignant	lymphoma				0	1		0	'	· ·	1	'		0	1
Spleen:		( N=	= )	1 (	50	)	(	50	)	(	50	)	(	50	1
(B) Hemangioma (M) Hemangiosa	1				0	ŕ		0	1		1	'		0	1
(M) Hemangiosa	arcoma				0			0			1			0	
(M) Histioeyti	ic sarcoma				0			0			0			1	
Respiratory System														-	
Lung:		( N=	- )	(	50	)	(	50	)	(	50	)	(	50	)
(B) Adenoma					8			5			12	1.62		5	í
(M) Adenocarci	noma				1			2			3			1	
Digestive System	nass not in sec	tion >			0			0			1			0	
Small intestine:		( )	`	1	-	•	,	-		,	-				
(B) Adenoma		( N=	• )	(	50	)	(	50	)	(	50	)	(	50	)
Liver:		( M	1	1	0	1	,	0	1	,	1		,	0	
(B) Hepatocell	ulan adamama	( N=	)	1		)	(	50	)	(	50	)	(	50	)
(B) Hemangioma					1			1			1			0	
Urinary System					0			0			0			1	
Urinary bladder:		( N=	١	1	50	1	1	EO	١	1	FA	1	1	FA	•
(B) Leiomyoma		( n-	,	1	0	,	(	50	1	(	50	)	(	50	)
Genital System					V			0			1			1	
Ovary:		( N=	١	1	FO	1	1	-	1	1		1	,	-	•
(B) Hemangioma		( n-	1	(	00	)	1	50	)	(	50	)	(	50	)
Uterus:		( N=	١	1	50	1	1	0	1	1	0	1	1	1	`
	l stromal poly	- 1 )	1	(	0	)	1	50 2	)	(	50	)	(	50	)
(B) Hemangioma	i beromat pory	4			0			0			1			0	
(B) Leiomyoma					1			0			$\frac{1}{2}$			2	
(M) Histiocyti	e sarcoma				0			1			ő			1	
(M) Leiomvosar	coma				2			1			0			0 1	
Endocrine System					4			1			U			T	
Pituitary:		( N-	1	(	50	1	1	50	)	1	50	1	1	50	1
(B) Anterior a	denoma	1 -1	'	1	0	,	1	1	,	(	0	,	(	0	,
Thyroid:		( N=	1	(	50	)	(	50	)	1	50	1	1	50	1
(B) Follicular	adenoma	(	1	1	0	/	1	2	)	1	00	,	(	0	,
Adrenal:		( N=	)	(	50	)	(	50	١	(	50	)	٢	50	1
(B) Benign A ce	ell tumor		1	1	0	/	1	1	,	(	2	,	1	0	,
(B) Pheochromod	evtoma				0			2			õ			õ	
Musculo-Skeletal System					•			4			v			U	
Bone (femur) :		( N=	)	(	50	)	(	50	)	(	50		(	50	1
(B) Osteoma					0			0	'	1	0		1	1	1
Skeletal muscle (ot)	ners):	( N=	)	(	0	)	(	3	)	(	4		(	3)	1
(M) Rhabdomyosa	rcoma			•	-		1	1		1	2		1	0	
Sense Organs								-			4			V	
Harderian gland:		( N=	)	(	50	)	( !	50	1	(	50		(	50 )	
(B) Adenoma		100 1000		•	1		•	3			0			5	

(N=): Number of animals examined microscopically at the site. Malignancy: (B), benign neoplasm; (M), malignant neoplasm.

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Site & Lesion	Dose		(ppm)	0	1600	8000	40000
orte a heston	No.	of animals	examined	50	50	50	50
Integumentary Sys	tem						
Skin:			(N=)	(50)	(50)	(50)	(50)
	illoma			1	0	0	0
	oma			1	0	1	Õ
	al cell ca	rcinoma		0	1	0	0
	osarcoma			0	0	0	1
(M) Hem	angiosarco	ma		0	0	1	0
Manumary gla			( N= )	(50)	(50)	(50)	(50)
	noma .			0	1	0	0
Body Cavities	nocarcinom	a.		0	3	1	0
Thoracic ca			( ) )		1		
(M) Ost	eosarcoma		( N⇒ )	(4)	(6)	(5)	(10)
Abdominal e	avity:		(N=)	(8)	(9)	( 0)	( 1
	angioma		( 14- )		(9)	(9)	(9)
	eosarcoma			0	0	0	1
	coour conta			0	0	U	1
No. of benign n	eoplasms			13	18	22	18
No. of malignan	t neoplasm:	5		9	13	17	14
No. of benign &	malignant	neoplasms		22	31	39	32
No. of animals	with benig	n neoplasm	(s)	12	13	18	16
No. of animals	with malig	nant neopla	.sm (s)	9	13	16	13
No. of animals	with neonla	asm (s)		19	24	28	23

Table 21 - 6 Histopathology - Incidence of microscopic neoplastic lesions in female mice All animals examined

(N=): Number of animals examined microscopically at the site. Malignancy: (B). benign neoplasm: (M). malignant neoplasm. Feinchemie Schwebda 2001, 'Carcinogenicity Study with Glyphosate Technical in Swiss Albino Mice.', unpublished, Study No.: Toxi: 1559.CARCI-M, Rallis India Ltd., Bangalore, India.



G4 10000 20 20 (20) (20) (20) (10) (20) (20) (20) (20) (20) contd. Ref.App.: 39-42 & 43-46 0 G3 1000 20 20 (20) (20) (20) (20) (16) (19) (20) (10) (20) 0 FEMALES G2 100 16 16 (16) (16) (16) (16) (16) (15) (16) (13) (16) ы 19 (16) (16) (15) (16) (16) (16) (16) (16) (16) 16 010 0 G4 10000 (27) (27) (26) (26) (27) (27) (27) (26) 27 (26) 0 1000 22 22 (20) (22) (22) (22) (20) (22) (22) (20) (22) GB 0 MALES G2 20 20 (20) (20) (20) (20) (19) (20) (20) (20) (19) 0 Benign M: Malignant MM: Metastatic I: Infiltrative (22) (22) (22) 1 [5] (21) (21) (22) (22) (22) (22) G1 22 22 []: Percentage value
(): No. of Tissues evaluated/group 0 Dose (ppm) No. of mice No. of mice examined Endometrial stromal sarcoma Group No. Sex -infiltrative(I) SALIVARY GLAND Adenoma (B) ESOPHAGUS DUODENUM STOMACH JEJUNUM OBSERVATION Number in [ Number in ( TISSUE AND RECTUM ILEUM CECUM COLON

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TABLE 20

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

Number in []: Percentage value

		Sex		MALES	BS			FEMI	FEMALES	
		Group No.	G1	G2	G3	G4	<u>61</u>	G2	63	G4
IS	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	1000
BS.	OBSERVATION	No. of mice	22	20	22 .	27	16	16	20	20
İ		No. of mice examined	22	20	22	27	16	16	20	20
10.	PANCREAS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
	Endometrial	Endometrial stromal sarcoma	100 C				•	•		
	-infiltrative(I)	.ve(I)	0	0	0	0	0	1	0	0
								[9]		
÷	11. LIVER		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
	Hemangiosarcoma(M)	coma (M)	0	0	Г	0	0	0	0	0
					[5]					
	Endometrial	Endometrial stromal sarcoma								
	-metastatic(MM)	( MM )	0	0	0	0	0	2	ч	0
								[13]	[5]	
	Hepatocellul	Hepatocellular adenoma(B)	Ģ	-	0	-1	0	0	0	0
				[2]		[4]				
	Hepatocellul	Hepatocellular carcinoma(M) .	0	0	0	1 [4]	0	0	0	0
12.	GALL BLADDER		(22)	(18)	(20)	(24)	(13)	(14)	(16)	(17)
13.			(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
	Squamous cel	Squamous cell carcinoma-metastatic(MM)	0	л [5]	0	0	0	0	0	0

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CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

TABLE 20 contd.

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

	o. of itssues evaluated/group	•	MALES				FEMI	FEMALES	
	Group No.	G1	G2		G4	G1	G2	G3	G4
TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	1000
OBSERVATION	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20		27	16	16	20	20
13. LUNGS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sa	stromal sarcoma					•			•
-metastatic(MM)	c (MM)	0	0	0	0	0	0	Ч	0

G4 10000 20 20

0 0 0

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10

0 0

0 0

0

Bronchio-alveolar carcinoma(M)

Bronchio-alveolar adenoma(B)

TRACHEA

14.

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(20) (20)

(10)

(16)

(16)

(26)

(22)

(20)

(22)

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(20)

(16)

(16)

(27)

(22)

(20)

(22)

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1 [6]

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0

0

0

0

Endometrial stromal sarcoma

-infiltrative(I)

i

MESENTERIC LYMPH NODES

17.

SPLEEN

16.

HEART

15.

Hemangioma(B)

contd.

(20) 2 [10]

(20)

(16)

(16) 1 [6]

(25)

(22)

(20)

(22)

(20) 

(20)

(16)

(16)

(27)

(22)

(20)

(22)

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Defendant's	Exhibit 2570	0318

B: Benign M: Malignant MM: Metastatic I: Infiltrative



G4 10000 (16) (20) (20) 1. contd. 20 NA NA NA Ref.App.: 39-42 & 43-46 0 0 0 0 1000 20 20 [ 100 ] (20) (20) (20) NA 1) 1 0 0 FEMALES G2 100 16 (16) (15) (16) NA Î 60 0 1 -(16) (16) (16) NA NA NA 16 16 (1) 5 0 0 0 0 0 G4 10000 (27) (27) (27) 1 [4] (27) 27 [2] (2) 0 0 0 2 G3 1000 22 22 (22) (21) (22) (22) (2) 0 0 0 0 MALES G2 100 20 20 (20) (20) (18) (20) Î 0 0 0 B: Benign M: Malignant MM: Metastatic I: Infiltrative 1 (22) 22) (22) (22) 22 0 1 î 0 0 in []: Percentage value
in (): No. of Tissues evaluated/group 1 0 No. of mice examined Endometrial stromal sarcoma -metastatic(MM) Endometrial stromal sarcoma Endometrial stromal sarcoma
-infiltrative(I) No. of mice Dose (ppm) Group No. MEDIASTINAL LYMPH NODE MANDIBULAR LYMPH NODE Renal cell adenoma(B) Leydig cell tumour(B) Sex -infiltrative(I) URINARY BLADDER KIDNEYS OBSERVATION ------TESTES TISSUE AND Number 18. 22. 19. 20. 21.

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Defendant's Exhibit 2570\_0319

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CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

TABLE 20 contd.

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Number

1



G4 10000 contd. (20) 20) -20 NA NA i NA NA Ref.App.: 39-42 & 43-46 1 5 50 0 63 1000 20 20 (20) (20) NA NA 1 NA NA [5] [2] (1) FEMALES G2 100 16 2 [13] [13] (16) (16) NA NA NA NA (1) N (16) (16) G1 16 16 NA NA NA NA -[9] 0 -G4 10000 27 27 (27) (27) (27) (27) NA NA NA NA NA NA NA G3 1000 22 22 (22) (20) (22) (22) NA NA NA NA NA NA NA NA MALES G2 100 20 20 (20) (20) (20) (20) NA NA NA NA NA NA NA B: Benign M: Malignant MM: Metastatic I: Infiltrative (22) (22) (22) 22) NA NA NA NA NA NA NA in []: Percentage value
in (): No. of Tissues evaluated/group of mice examined Endometrial stromal sarcoma(M) . Endometrial stromal sarcoma No. of mice No. of mice Dose (ppm) Group No. Sex COAGULATING GLANDS -infiltrative(I) Leiomyosarcoma(M) SEMINAL VESICLES Hemangioma(B) 23. EPIDIDYMES PROSTATE OBSERVATION OVARIES UTERUS 29. VAGINA TISSUE AND Number 24. 25. 26. 27. 28.

TABLE 20 contd.

### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

Number

Defendant's Exhibit 2570\_0320

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

Number in []: Percentage value Number in (): No. of Tissues evaluated/group

Ref.App.: 39-42 & 43-46

	Sex		MALES	ES			FEM	FEMALES
	Group No.	Gl	G2		G4	G1	G2	G3
TISSUE AND	Dose (ppm)	0	100		10000	0	100	1000
OBSERVATION	w	22	20		27	16	16	20
	No. of mice examined	22	20		27	16	16	20
30. THYROIDS		(22)	(20)		(22) (25)	(16)	(16)	(19)
31 SUTURNER								

	Cross No	5	00				10		
TTSSUE AND	Dree (nnm)	ל פיד	100	1000	10000	C T	62	63	64 10000
OBSERVATION	No. of mice	22	20	22 22	27 27	0 16	100	1000	10000
	No. of mice examined	22	20	22	27	16	16	20	20
30. THYROIDS		(22)	(20)	(22)	(25)	(16)	(16)	(19)	(20)
31. PARATHYROIDS	DS	(19)	(19)	(22)	(23)	(15)	(16)	(13)	(19)
32. PITUITARY Adenoma(B) 		(22) 0	(20) 0	(21) 0	(27) 0	(14) 0	(16) 0	(17) 0	(18) 1 [6]
33. ADRENALS Endometria	ADRENALS Endometrial stromal sarcoma	(22)	(19)	(22)	(27)	(16)	(16)	(20)	(20)
-infiltrative(I)	tive(I)	0	o	0	o	0	1 [6]	o	0
34. EYES WITH	EYES WITH OFTIC NERVE	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
35. BONE MARROW (SMEAR	DW (SMEAR)	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(19)
36. SKIN Squamous c	SKIN Squamous cell carcinoma(M)	(22) 1 [5]	(20) 1 [5]	(22) 0	(27) 0	(16) 0	(16) 0	(20) 0	(20) 0
37. THYMUS		(20)	(18)	(17)	(19)	(13)	(14)	(17)	(11)
	Metastatic T:			· · · · · · · · · · · · · · · · · · ·			/ = = /	1	



### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

value
Percentage
••
Ξ
in
Number

		Sex		MALES	SS			FEMI	FEMALES	
		Group No.	G1	<u>G2</u>	G3	G4	G1	G2	G <u>3</u>	G4
SSI	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
BSE	Z	No. of mice	22	20	22	27	16	16	20	20
		No. of mice examined	22	20	22	27	16	16	20	20
38.	MUSCLE FEMORAL		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
39.	SPINAL CORD		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
40.	SCIATIC NERVES		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
41.	MAMMARY GLAND		NA	NA	NA	NA	(16)	(16)	(20)	(20)
42.	TUMOUR/MASS (Sacral) Hemangiosarcoma(M)	acral) a(M)	(22) 0	(20) 0	(22) 0	(27) 0	(16) 0	(16) 1 [6]	(20) 0	(20) 0
	43. BONE (FEMUR) WITH JOINT Osteoma(B)	TH JOINT	(22) 1 [5]	(20) 0	(22) 0	(27) 1 [4]	(16) 1 [6]	(16) 0	(20) 0	(20) 0
4.	44. TAIL Hemangioma(B)		(1) 1 1001	() .	(-) -)	(- -)	(1)	Î I	(-)	۱ <u>آ</u>
	Hemangiosarcoma(M)	la (M)	0	1	I	I	1 [100]	I	1	ı

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TISSUE AND Desce (prom)         Genup No. Dose (prom)         Gin Cold         Gin Cic Cic Cic Cic         Gin Cic Cic Cic Cic Cic Cic         Gin Cic Cic Cic Cic Cic Cic Cic Cic Cic Cic		Sex		MALES	ES			FEMI	FEMALES	
SUE AND         Dose (ppm)         0         100         1000         16		Group No.	G1	G2	G3	G4	G1	G2	G3	G4
RIVATION         No. of mice         22         20         22         27         16	ISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	1000
No. of mice examined         22         27         16         16           MBSENTERY Endometrial stromal sarcoma -infiltrative(I)         (2)         (2)         (1)         (1)         (3)         (5)         (           -infiltrative(I)         0         0         0         0         0         1         (20)           STERNUM WITH MARROW         (22)         (19)         (22)         (19)         (27)         (15)         (16)         (           STERNUM WITH MARROM         (22)         (3)         (5)         (4)         (3)         (5)         (4)         (5)         (16)	BSERVATION	No. of mice	22	20	22	27	16	16	20	20
MESENTEX         (1)         (			22	20	22	27	16	16	20	20
Endometrial stromal sarcoma       0       0       0       1         -infiltrative(I)       2       0       0       1         STERNUM WITH MARROW       (22)       (19)       (27)       (15)       (16)         STERNUM WITH MARROW       (22)       (19)       (22)       (7)       (15)       (16)         STERNUM WITH MARROW       (22)       (19)       (27)       (15)       (5)       (5)         Endometrial stromal sarcoma       0       0       0       0       0       0       0         Endometrial stromal sarcoma       0       0       0       0       0       0       0         Infiltrative(I)       8       0       0       0       0       0       0       0         BRAIN-CEREBRUM       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (21)       (21)       (16)       (16)       (16)	5. MESENTERY		(2)	(2)	(1)	(1)	(3)	(5)	(5)	(4)
-infiltrative(I)       0       0       0       1         STERNUM WITH MARROW       (22)       (19)       (27)       (15)       (16)         STERNUM WITH MARROW       (22)       (19)       (22)       (27)       (15)       (16)         STERNUM WITH MARROM       (3)       (5)       (4)       (3)       (5)       (5)         EXMPH NODE (OTHERS)       0       0       0       0       0       0       0         Endometrial stromal stromal stroma       0       0       0       0       0       0       0         Endometrial stromal stroma       0       0       0       0       0       0       0         Infiltrative(I)       0       0       0       0       0       0       0         BRAIN-CEREBELUM       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (21)       (21)       (21)       (16)       (16)	Endometrial	. stromal sarcoma						•	•	•
STERNUM WITH MARROW       (22)       (19)       (27)       (15)       (16)         LYMPH NODE (OTHERS)       (3)       (5)       (4)       (3)       (5)       (5)         Endometrial stromal stromal stromal stromal stromal stromal stromal stromal stromal stromal stromal stromal stromal stroma       (3)       (5)       (4)       (3)       (5)       (5)         Endometrial stromal stromal stroma       0       0       0       0       0       0       0         Infiltrative(I)       sarcoma       0	-infiltrat	ive(I)	0	0	0	0	0	1 [20]	0	0
LYMPH NODE (OTHERS)       (3)       (5)       (4)       (3)       (5)       (5)         Endometrial stromal sarcoma       0       0       0       0       0       0       0         -metastatic(MM)       0       0       0       0       0       0       0       0       0         Endometrial stromal sarcoma       0       0       0       0       0       0       0       0         Endometrial stromal sarcoma       0       0       0       0       0       0       0       0       0         BRAIN-CEREBRUM       (22)       (20)       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-CEREBELLUM       (21)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (22)       (27)       (16)       (16)         SUPERFICIAL.ING.L.NODE       (22)       (20)       (21)       (27)       (16)       (16)		H MARROW	(22)	(10)	(22)	(27)	(15)	(16)	(20)	(19)
Indometrial stromatic (MM)       0	7. LYMPH NODE		(3)	(2)	(4)	(3)	(5)	(5)	(2)	(1)
Endometrial stromal sarcoma       0	-metastati		0	0	0	o	0	0	ц Т	0
-infiltrative(I) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 BRAIN-CEREBRUM (22) (20) (22) (27) (16) (16) BRAIN-CEREBELLUM (21) (20) (22) (27) (16) (16) (16) BRAIN-MEDULLA (22) (20) (22) (27) (15) (16) (16) (16) SUPERFICIAL.ING.L.NODE (22) (20) (21) (21) (21) (16) (16)	Endometrial	stromal sarcoma							[JU]	
BRAIN-CEREBRUM       (22)       (20)       (27)       (16)       (16)         BRAIN-CEREBELLUM       (21)       (20)       (22)       (27)       (16)       (16)         BRAIN-CEREBELLUM       (22)       (20)       (22)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (22)       (27)       (15)       (16)         SUPERFICIAL.ING.L.NODE       (22)       (20)       (21)       (27)       (16)       (16)	-infiltrat	ive(I)	o	0	0	0	0	o	1 [20]	0
BRAIN-CEREBELLUM       (21)       (20)       (27)       (16)       (16)         BRAIN-MEDULLA       (22)       (20)       (22)       (27)       (15)       (16)         SUPERFICIAL.ING.L.NODE       (22)       (20)       (21)       (27)       (16)       (16)			(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
BRAIN-MEDULLA (22) (20) (22) (15) (15) (16) SUPERFICIAL.ING.L.NODE (22) (20) (21) (27) (16) (16)		ELLUM	(21)	(20)	(22)	(27)	(16)	(16)	(19)	(18)
SUPERFICIAL.ING.L.NODE (22) (20) (21) (27) (16) (16)		ЧТ.	(22)	(20)	(22)	(27)	(15)	(16)	(20)	(19)
		ING.L.NODE	(22)	(20)	(21)	(27)	(16)	(16)	(19)	(19)

TABLE 20 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

Number in []: Percentage value Number in (): No. of Tissues ev

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

# SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF DEAD AND MORIBUND SACRIFICED MICE

Number in []: Percentage value

		Sex		MALES	ES			FEM	FEMALES	
		Group No.	G1	G2	G3	G4	G1	G2	G3	G4
TIS	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBS.	OBSERVATION	No. of mice	22	20	22	27	16	16	20	20
Ì		No. of mice examined	22	20	22	27	16	16	20	20
52.	HEMOLYMPHOR	52. HEMOLYMPHORETICULAR SYSTEM	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(00)
	Histiocytic sarcoma(M)	sarcoma(M)	Ч	, L	0	ц	0	, N	1-7	
			[2]	[5]		[4]		[13]	[5]	[5]
	Malignant lymphoma(M)	ymphoma (M)	ნ	12	13	13	6	10	13	12
			[41]	[ 60 ]	[59]	[48]	[ 56 ]	[ 63 ]	[65]	r 601
	Myeloid leukemia(M)	kemia(M)	7	Ч	,	Ţ	5	, н ,	2	, L
			[6]	[5]	[5]	[4]	[13]	[9]	[10]	[2]

B: Benign M: Malignant MM: Metastatic I: Infiltrative

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

TABLE 21

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

		Sex		MALES	ES			FEM	FEMALES	
		Group No.	G1	<u>G2</u>		G4	G1	G2	G3	G4
TIS	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBS	OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
		No. of mice examined	28	30	28	23	34	34	30	30
i i	SALIVARY GLAND	đ	(28)	(1)	(1)	(23)	(34)	(1)	(-)	(30)
2.	ESOPHAGUS		(28)	(-)	(-)	(23)	(34)	Î.	(-)	(30)
э.	STOMACH		(28)	(30)	(28)	(23)	(34)	(	(-)	(30)
4.	DUODENUM		(28)	(0E)	(28)	(23)	(34)	<u>〔</u>	(-)	(30)
5.	JEJUNUM		(28)	(-)	(-)	(23)	(33)	(34)	(30)	(30)
6.	ILEUM		(27)	(-)	( - )	(23)	(34)	(34)	(30)	(30)
7.	CECUM		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
8.	COLON	,	(28)	(-)	(-)	(22)	(33)	(-)	(-)	(30)
9.	RECTUM		(27)	(-)	(-)	(22)	(33)	(34)	(30)	(30)
10.	10. PANCREAS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

Number in []: Percentage value

	Sex		MALES				FEMI	FEMALES	
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
	No. of mice examined	28	30	28	23	34	34	30	30
11. LIVER		(28)	(5)	(9)	(23)	(34)	(4)	(2)	(30)
Hepatocellular adenoma(B)	<pre>c adenoma(B)</pre>	4	4	'n	2	5	ેન	10	2
		[14]	[80]	[50]	[6]	[9]	[25]	[ 100 ]	[7]
Hepatocellular carcinoma(M	c carcinoma(M)	1 [4]	0	0	1 [4]	0	0	0	0
12. GALL BLADDER		(27)	(-)	Ĵ	(22)	(32)	(-)	(-)	(30)
13. LUNGS Bronchio-alveolar adenoma(	olar adenoma(B)	(28) 0	(2) 2 [100]	-) -	(23) 0	(34) (34) 1 [3]	(	(1) 1 [100]	(30) 1 [3]
		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
		(28)	(2)	(-)	(23)	(34)	(-)	(-)	(30)
16. SPLEEN		(28)	(30)	(27)	(23)	(34)	(33)	(27)	(30)
17. MESENTERIC LYMPH NODES Hemangioma(B)	APH NODES	(28) 1	(29) 0	(27) 0	(23) 1	(34) 0	(32) (0	(28) 0	(30) 2
Hemangiosarcoma(M)	na (M)	<b>1</b> 0	0	1 [4]	0	0	0	0	[ 0

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

-¢ -Ninthor

		Sex		MALES	SS			FEM	FEMALES	
		Group No.	G1	G2	1	G4	G1	G2	63	G4
LIS	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
DBS.	OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
		No. of mice examined	28	30	28	23	34	34	30	30
8	18. MEDIASTINAL LYMPH NODE	LYMPH NODE	(-)	(-)	(-)	(1)	(1)	(-)	(-)	Ĵ
6	19. MANDIBULAR LYMPH NODE	LYMPH NODE	(28)	(30)	(28)	(23)	(34)	(33)	(28)	(30)
20.		KIDNEYS Malignant hybernoma-infiltrative(I)	(28) 1	(9) 0	(4) 0	(23) 0	(34) 0	(2) 0	(1) 0	(30)
	Renal cell adenoma(B)	adenoma (B)	<del>,</del> 0	o	1 [25]	0	0	0	0	0
21.	URINARY	BLADDER	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
.2.	22. TESTES Leydig cell tumour(B)	. tumour(B)	(28) 1 [4]	(1) 1 [100]	(1) 0	(23) 1 [4]	NA NA NA	NA NA NA	NA NA NA NA	NA NA NA NA
	23. EPIDIDYMES Leiomyoma(B)		(28) 0	(1) 1 [100]	(-)	(23) 0	NA NA NA NA	NA NA NA NA	NA NA NA NA	NA NA NA NA
4.	24. PROSTATE		(28)	(-)	(-)	(23)	NA	NA	NA	NA

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	Sex		MALES	ES			FEM	FEMALES	
	Group No.	15	<u>G2</u>	1	64	5	62	63	54
ISS	TISSUE AND Dose (ppm)	0	100	1000	10000	0	100	1000	10000
BSE	OBSERVATION No. of mice	28	30	28	23	34	34	30	30
	No. of mice examined	28	30	28	23	34	34	30	30
25.	SEMINAL VESICLES	(28)	(18)	(10)	(23)	NA	NA	NA	NA
26.	0	(27)	(- )	-	(22)	NA	NA	NA	NA
27.	OVARIES	NA	NA	NA	NA	(34)	(13)	(13)	(29)
	Granulosa cell tumour(B)	NA	NA	NA TH	NA	0	0	0	[
		NA	AN	AN	AN	c	c	c	[۲]
	ruceolia ( p )	AN	AN	AN	AN	C	C	D	1.21
28.	UTERUS	NA	NA	NA	NA	(34)	(15)	(10)	(30)
	Leiomyoma(B)	NA	NA	NA	NA	0	0		0
		NA	NA	NA	NA			[10]	
	Endometrial stromal sarcoma(M)	NA	NA	NA	NA	Ч	0	2	г
		NA 	NA	NA	NA	[3]		[20]	[3]
29.	VAGINA	NA	NA	NA	NA	(2)	-	(-)	(2)
30.		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
31.	-	(22)	-	(-)	(22)	(30)	(-)	(-)	(29)

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

Number in []: Percentage value

TISSUE AND OBSERVATION			MALES	ES			FEM	FEMALES	
BSERVATION	Group No.	G1	G2		G4	G1	G2	63	G4
)BSERVATION	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	28	30	28	23	34	34	30	30
	No. of mice examined	28	30	28	23	34	34	30	30
		(27)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
33. ADRENALS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(29)
rnsdebaur	subcapsular cell adenoma(B)	D	ı	1	0	0	1	I	ч
Pheochrom	Pheochromocytoma(B)	0	T	1	0	o	I	ı	[2] T [2]
34. EYES WITH C	EYES WITH OPTIC NERVE	(28)	(-)	(1)	(23)	(34)	(2)	(1)	(30)
35. BONE MARROW (SMEAR)	OW (SMEAR)	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
36. SKIN Squamous ( 	SKIN Squamous cell carcinoma(M)	(28)	(8) 0	(6) (6)	(23) 0	(34) 0	(8) 1 [13 <sub>]</sub>	(4) 1 [25]	(30) 0
37. THYMUS Lymphoma(B) 	B)	(24) 0	ĵ.	() -	(19) 0	(33) 1 [3]	()  )	() 	(30)
38. MUSCLE FEMORAL	MORAL	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

		Sex		MALES	S			FEM	FEMALES	
		Group No.	G1	G2	1	G4	61	<u>G7</u>	6.9	64
SI	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
BSI	OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
		No. of mice examined	28	30	28	23	34	34	30	30
39.	SPINAL CORD		(28)	( - )	(-)	(23)	(34)	(-)	(-)	(30)
40.	SCIATIC NERVES	S	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
41.		a (M)	NA NA NA	NA NA NA	NA NA NA	AN AN AN	(34) 1 [3]	(1) (1)	Ĵ,	(30) 1 [3]
42.			(-)	(-) -)	() 	(1) 1 [100]	ĵ,	(-)	(	0
43.	BONE (FEMUR) WITH JOINT Osteoma(B)	TNIOL HTIW	(28) 0	Ĵ	î ı	(23) 0	(34) 0	(2) 2 [100]	(1) 1 [100]	(30) 3 [10]
14.	44. MESENTERY Lipoma(B) Endometrial atromal sarco	tromal sarcoma	( - -)	î '	Ĵ,	(1) 1 [100]	(2) 1 [50]	(1) 0	(1) 1 [100]	(2)
	-infiltrative(I)	e(I)	ı	I	t	0	o <sup>.</sup>	o	0	1 [50]

Defendant's Exhibit 2570\_0330

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

Number in []: Percentage value

		Sex		MALES	ES			FEM	FEMALES	
		Group No.	Gl	G2	1.	G4	G1	G2	63	64
TIS	TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBS	OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
		No. of mice examined	28	30	28	23	34	34	30	30
45.		TH MARROW	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
46.	LYMPH NODE (OTHERS)	(OTHERS)	(5)	(3)	(5)	(2)	(3)	(6)	(3)	(9)
47.	BRAIN-CEREBRUM	BRUM	(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
48.		ЗЕТГОМ	(28)	(-)	(-)	(23)	(33)	(-)	(-)	(29)
49.	BRAIN-MEDULLA	LLA	(28)	(-)	(-)	(23)	(33)	(-)	(-)	(30)
50.	ומו		(2)	(5)	(5)	(2)	(1)	(4)	(1)	(-)
51.		SUPERFICIAL.ING.L.NODE	(28)	(1)	(2)	(23)	(34)	(4)	(1)	(30)
52.		HEMOLYMPHORETICULAR SYSTEM Histiocytic sarcoma(M)	(28) 1	(30)	(28) 0	(23) 0	(34) 0	(34) 0	(30) 0	(30) 1
	Malignant lymphoma(M)	.ymphoma(M)		ю	ო	9	6	10	9	[3] 13
	Myeloid leukemia(M)	ıkemia(M)	[4] [4]	[10] 0	[11] 0	[26] 0	[26] 0	[29] 0	[20] 0	[43] 0

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### CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

## SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

Sex	Sex		MALES					FEMAL FC	
	Group No.	5	G2		G4	G1	G2	63	64
TISSUE AND	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
OBSERVATION	No. of mice	28	30	28	23	34	34	30	30
	No. of mice examined	28	30	28	23	34	34	30	30
53. BONE (OTHERS)		(-)	(-)	(-)	(-)	(-)	(-)	(1)	(1)
Osteoma (B)		ï	ı	1	I	I	1	1, 1001	1

B: Benign M: Malignant MM: Metastatic I: Infiltrative

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				MALES	LES							FEM	FEMALES			
	9 9	Oppm	200	500ppm	1500	1500ppm	5000ppm	mqq	do	Oppm	500	500ppm	1500	1500ppm	500	5000ppm
Number of Mice	LO LO	51		51	ß	51	51		20	51	LD LD	51	ß	51		51
CONDITION	=	%	=	%	=	%	<b>ء</b>	%	=	%	=	%	=	%	=	%
ADRENAL GLAND*																
Cortical adenoma b	m	9	0	0	0	0	ო	9	0	0	0	0	0	0	0	0
	٦,	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BONE																
Osteoma b	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
BONE MARROW																
Lipoma b	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	7
BRAIN *																
Meningeal sarcoma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Oligodendroglioma m	1	2	0	0	0	0	0	0	1	2	0	0	0	0	0	0
HARDERIAN GLAND**																
Adenoma b	4	8	0	0	0	0	2	4	1	2	0	0	0	0	2	4
Adenocarcinoma r	0	0	0	0	0	0	0	0	2	4	0	0	0	0	0	0
INTESTINAL TUMOUR																
Adenoma b	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
KIDNEY																
Haemangiosarcoma m	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
LIVER*																
Hepatocellular adenoma b	1	2	1	2	4	8	2	4	0	0	0	0	0	0	0	0
Hepatocellular carcinoma m	9	12	11	22	7	14	4	8	0	0	1	2	0	0	0	0
Combined	7	14	12	24	11	22	6	12	0	0	1	2	0	0	0	0
Haemangioma b	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0
Haemangiosarcoma m	2	4	-	2	H	2		2	0	0	0	0	1	2	0	0
LUNG*																
Adenoma b	6	18	7	14	9	18	4	8	2	4	4	8	2	4	2	4
Adenocarcinoma m	5	10	5	10	7	14	11	22	5	10	2	4	2	4	3	9
Combined	14	28	12	24	16	32	15	30	7	14	9	12	4	8	ъ С	10
MAMMARY GLAND																
Adenocarcinoma m	0	0	0	0	0	0	0	0	0	0	1	2	З	6	1	2
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\* Group 1 male % based on 50 animals \*\* Group 1 male % based on 49 animals

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Oppm       Number of Mice     51       Number of Mice     51       Number of Mice     51       Number of Mice     7       Network     7       Network     7       Number of Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice     7       Mice       Mice       Mice   <	500ppm 51 0 0 0 0 0		<b>1500ppm</b> 51	<b>5000ppm</b>	md	Oppm		500ppm	150	1500ppm	5000	5000ppm
Number of Mice     51       CONDITION     n       IC LYMPH NODE     n       IC LYMPH NODE     0       Histiocytic sarcoma m     0       Haemangioma b     1       Sertoli cell tumour b     Cystadenoma b       Cystadenoma b     Cystadenoma m	21	<b>E</b> <sub>0</sub>		51		ŭ			•			
CONDITION     n       IC LYMPH NODE     IC LYMPH NODE       Histiocytic sarcoma m     0       Haemangioma b     0       Sertoli cell tumour b     Cystadenoma u       Cystadenoma m     1		0				5		51		51	<b>D</b>	51
IC LYMPH NODE Histiocytic sarcoma m 0 Luteoma b Haemangioma b Sertoli cell tumour b Cystadenoma b Anaplastic sarcoma m harcoma		0	%	=	%	٥ د	u %	%	=	%	-	%
Histiocytic sarcoma m 0 Luteoma b Haemangioma b Sertoli cell tumour b Cystadenoma b Anaplastic sarcoma m		0		Ī								
Se			0	0	0 2	4	0	0	0	0	1	2
Se						_						
Se					1	2	T	2	1	2	1	2
Se					0		0	0	0	0	1	2
Anapla					0	0	0	0	0	0	1	2
Anapla					0		0	0	0	0	2	4
					0			2	0	0	0	0
						_						
Islet cell adenocarcinoma m 0 0	0	0	0	0	0 1	2	0	0	0	0	0	0
PITUITARY												
Adenoma b   0   0	0 0	0	0	0	0 0	0	1	2	0	0	2	4
SEMINAL VESICLE												
Adenoma b 2 4	0	0	0	0	0							
Leiomyosarcoma m   0   0	0 0	0	0	1	2							
SKIN/SUBCUTIS												
Fibrosarcoma m 0 0	3 6	2	4	1	2 0	0	0	0	0	0	0	0
Haemangiosarcoma m   0   0	0 0	0	0	0	0 0	0	1	2	0	0	0	0
SPLEEN												
Haemangioma b   1   2	0	0	0	0	0	0	0	0	0	0	0	0
Haemangiosarcoma m 0 0	0	0	0	0	1	2	0	0	0	0	H	2
TESTIS												
Interstitial cell tumour b 2 4	0 0	0	0	0	0	_						
THYMUS												
Histiocytic sarcoma m 0 0	0	0	0	0	0	0	0	0	1	2	0	0
UTERUS												
Endometrial stromal polyp b					2	4	2	4	З	6	4	8
Haemangioma b					0		1	2	0	0	0	0
Leiomyoma b					0	0	0	0	1	2	0	0
Squamous cell carcinoma m		_			-	2	0	0	0	0	0	0
Histiocytic sarcoma m					2	4	2	4	0	0	1	2
Leiomyosarcoma m						2	0	0	0	0	0	0

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# Table 1 Incidence and % Incidence of Neoplastic Lesions by Tissue for Terminal Kill and Interim Death Animals Combined (continued)

				MA	MALES							FEM,	FEMALES			
	do	Oppm	500	500ppm	1500	1500ppm	5000ppm	mqq	do	Oppm	500	500ppm	1500	1500ppm	500(	5000ppm
Number of Mice		51	LO	51	ß	51	51	H	цо П	51	")	51	ъ	51	0)	51
CONDITION	=	%	E	%	E	%	=	%	=	%	=	%	E	%	E	%
ABDOMINAL																
Lipoma b	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
Mesothelioma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Anaplastic sarcoma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
LYMPHOID/HAEMOPOIETIC ***																
Myeloid leukaemia m	0	0	1	2	0	0	0	0	0	0	0	0	1	2	0	0
Malignant lymphoma m	0	0	1	2	2	4	5	10	11	22	8	16	10	20	11	22
****Histiocytic sarcoma m	0	0	0	0	0	0	0	0	4	8	2	4	1	2	3	9
Combined	0	0	2	4	2	4	5	10	15	29	10	20	12	24	14	28
<b>OVERALL TUMOUR INCIDENCE</b>																
Primary benign tumours	15	29	6	12	6	18	7	14	5	10	9	12	6	12	6	18
Primary malignant tumours	14	28	20	39	17	33	20	39	23	45	15	29	17	33	18	35
Multiple benign tumours	9	12	2	4	4	8	1	2	4	8	4	8	1	2	7	14
Multiple malignant tumours	1	2	2	4	З	6	5	10	4	8	2	4	1	2	1	2

\*\*\* Histiocytic sarcomas are not generally regarded as lymphoid in origin but are usefully included here

\*\*\*\* Based on incidence from all sites and not additional to those reported for individual sites