Critical Reviews in Toxicology

http://informahealthcare.com/txc
ISSN: 1040-8444 (print), 1547-6898 (electronic)

Crit Rev Toxicol, 2015; 45(3): 185–208
 DOI: 10.3109/10408444.2014.1003423

informa healthcare

REVIEW ARTICLE

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

Helmut Greim[1], David Saltmiras[2,6], Volker Mostert[4,5], and Christian Strupp[3,6]

[1]*Technical University Munich, Arcisstr. 21, 80333 Munich, Germany,* [2]*Monsanto Company, 800 North Lindbergh Blvd., 63167 St. Louis, MO, USA,* [3]*ADAMA MAH BV Amsterdam NL Schaffhausen Branch, Spitalstrasse 5, 8200 Schaffhausen, Switzerland,* [4]*Knoell Consult GmbH, Dynamostr. 19, 68165 Mannheim, Germany,* [5]*Extera, Nelly-Sachs-Str. 37, 40764 Langenfeld, Germany, and* [6]*Glyphosate Task Force, http://www.glyphosatetaskforce.org/*

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

History

Received 6 November 2014
Revised 19 December 2014
Accepted 28 December 2014
Published online 24 February 2015

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Address for correspondence: David Saltmiras, Monsanto Company, 800 North Lindbergh Blvd., 63167 St. Louis, MO, USA. Tel: +1 (314) 684-8856. E-mail: david.a.saltmiras@monsanto.com

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 broad-leaved 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

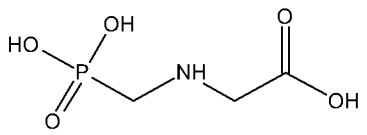

Figure 1. Structure of glyphosate acid.

sodium-, potassium-, ammonium- and isopropyl ammonium-salt 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 re-evaluation (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

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	*ca* 20%	Rat, *in vivo*
Dermal absorption	< 1%	Human, *in vitro*, 0.015 g glyphosate/L
Rat LD50 oral	> 2000 mg/kg bw	
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 ↑) NOAEL = 100 mg/kg bw/day (2-yr rat)	Critical study used for ADI setting
Reproductive toxicity	Reduced pup weight at parentally toxic doses. NOAEL = 300 mg/kg bw/day	
Developmental toxicity	Post-implantation loss, fetal BW & ossification ↓; effects confined to 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 Based on developmental toxicity in rabbits	Safety factor 100
Acceptable Operator Exposure Level (AOEL)	0.1 mg/kg bw/day Based on maternal toxicity in rabbit teratogenicity study	Safety factor 100 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 ♂ and 6 ♀
Administration route:	Oral, capsule
Doses:	0, 20, 100, 500 mg/kg bw/day
Duration:	1 year
Findings:	≥ 500 mg/kg bw/day: NOAEL (♂ + ♀) 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 ♂ and 4 ♀
Administration route:	Oral, capsule
Doses:	0, 30, 300, 1000 mg/kg bw/day
Duration:	1 year
Findings:	300 mg/kg bw/day: NOAEL (♂ + ♀) 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 reached by highest dose
Substance:	Glyphosate (95.7% pure)
Species/Strain	Dog/Beagle, groups of 4 ♂ and 4 ♀
Administration route:	Oral, capsule
Doses:	0, 30, 125, 500 mg/kg bw/day
Duration:	1 year
Findings:	≥ 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 ♂ and 4 ♀
Administration route:	Oral, diet
Concentration:	0, 1600, 8000, 50 000 ppm diet (♂ about 34.1, 182, 1203 mg/kg bw/day; ♀ about 37.1, 184, 1259 mg/kg bw/day)
Duration:	1 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 focal pneumonia (♀), minor clinical chemistry changes of Cl ↑, albumin ↓, P ↓ (♀)
Authors:	**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 ♂ and 4 ♀
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:	1 year
Findings:	15 000 ppm diet: NOAEL (♀) ≥ 30 000 ppm diet: NOAEL (♂): 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_fSD, groups of 24 ♂ and 24 ♀
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 (♂+♀) 20 000 ppm diet: parotid salivary glands (focal basophilia of the acinar cells considered non-adverse adaptive response, ♂: 13/24, ♀: 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

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/10.3109/10408444.2014.1003423).

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 ♂ and 50 ♀
Administration route:	Diet
Concentration:	0, 30, 100, 300 ppm diet (♂ about 0, 3, 10, 31 mg/kg bw/day; ♀ about 0, 3, 11, 34 mg/kg bw/day)
Duration:	26 months
Findings:	≥ 300 ppm diet: NOAEL (♂ + ♀) 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				Females			
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 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 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.

	Dose (mg/kg bw/day)			
Tumors	0	3.05	10.3	31.49
Interstitial cell tumor – B	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 control animals/total number examined (% per study)					Range
Terminal sacrifice	4/65 (6.2)	3/11 (27.3)	3/26 (11.5)	3/24 (12.5)	3/40 (7.5)	6.2–27.3%
All animals	4/116 (3.4)	5/75 (6.7)	4/113 (3.5)	6/113 (5.3)	5/118 (4.2)	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 according to GLP and OECD guideline requirements, with no deviations.			
Substance:	Glyphosate (96.5% pure)			
Species/Strain:	Rat/Sprague-Dawley, groups of 50 ♂ and 50 ♀ (10 rats per sex per dose were included for interim sacrifice after 12 months).			
Administration route:	Diet			
Concentration:	0, 2000, 8000, 20 000 ppm diet (♂ about 0, 89, 362, 940 mg/kg bw/day; ♀ about 0, 113, 457, 1183 mg/kg bw/day)			
Duration:	2 years			
Findings:	8000 ppm diet: NOAEL (♂+♀) 20 000 ppm diet: cataracts (♂), >20% reduced cumulative body weight gain through months 18–20 (♀), 13% increased liver weight (♂). Local effects: inflammation of gastric mucosa			
Select neoplasms:	Pancreatic islet cell adenoma, skin keratoacanthoma (males), thyroid C cell adenoma			
Tumor	Dose (mg/kg bw/day)			
Males	0	89	362	940
Findings for dead and moribund sacrificed animals				
Pancreas: Islet call adenoma – B	1/34 (3%)	4/28 (14%)	2/33 (6%)	4/32 (13%)
Skin: Keratoacanthoma – B	0/36	1/31 (3%)	2/33 (6%)	1/32 (3%)
Thyroid: C cell adenoma – B	0/36	2/29 (7%)	1/31 (3%)	1/33 (3%)
Thyroid: C cell carcinoma – M	0/36	1/29 (3%)	2/31 (6%)	1/33 (3%)
Findings for animals sacrificed at termination				
Pancreas: Islet call adenoma – B	0/14	4/19 (21%)	3/17 (6%)	3/17 (6%)
Skin: Keratoacanthoma – B	0/13	2/19 (11%)	2/17 (12%)	2/17 (12%)
Thyroid: C cell adenoma – B	0/14	2/19 (11%)	*7/17 (41%)	4/17 (24%)
Thyroid: C cell carcinoma – M	0/14	0/19	0/17	0/17
Females	0	113	457	1183
Findings for dead and moribund sacrificed animals				
Pancreas: Islet call adenoma – B	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 carcinoma – M	0/28	0/28	1/33 (3%)	0/32
Findings for animals sacrificed at termination				
Pancreas: Islet call adenoma – B	2/22 (9%)	1/22 (5%)	1/17 (6%)	0/18
Thyroid: C cell adenoma – B	2/22 (9%)	2/22 (9%)	5/17 (29%)	4/18 (22%)
Thyroid: C cell carcinoma – M	0/22	0/22	0/17	0/18

B benign, *M* malignant
*Statistically higher than controls ($p < 0.05$, Fisher's Exact Test with the Bonferroni Inequality).

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

Study owner:	Cheminova (1993a)
Reliability/ Justification:	1 Study performed according to GLP and OECD 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 ♂ and 35 ♀per dose were included for 1-year interim sacrifice)
Administration route:	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 ↓, salivary glands (histopathology, organ weight ↑); evidence of weak liver toxicity (alkaline phosphatase ↑, ♀: organ weight ↓)
Select neoplasms:	No neoplasms from this study were identified for 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/10.3109/10408444.2014.1003423). 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 treatment-related 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/10.3109/10408444.2014.1003423).

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 compound-related, 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 Schwebda (1996)			
Reliability/Justification:	1 Study performed according to GLP and OECD guideline requirements, with no deviations.			
Substance:	Glyphosate (96.0–96.8% pure)			
Species/Strain:	Rat/Wistar, groups of 50 ♂ and 50 ♀			
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: ≥ NOAEL (♂+♀) Only mild effects on clinical chemistry (liver enzymes), without histopathological changes.			
Select neoplasms:	Hepatocellular adenoma, hepatocellular carcinoma			
Tumor		Dose (mg/kg bw/day)		
Males	0	7.4	73.9	741
Findings for dead and moribund sacrificed animals				
Hepatocellular adenoma – B	9/30 (30%)	9/30 (30%)	6/32 (19%)	6/21 (29%)
Hepatocellular carcinoma – M	12/30 (40%)	12/30 (40%)	9/32 (28%)	5/21 (24%)
Findings for animals sacrificed at termination				
Hepatocellular adenoma – B	15/20 (75%)	13/20 (65%)	4/16 (25%)	15/20 (75%)
Hepatocellular carcinoma – 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 moribund sacrificed animals				
Hepatocellular adenoma – B	2/26 (8%)	8/23 (3%)	3/17 (18%)	5/29 (17%)
Hepatocellular carcinoma – M	4/26 (15%)	4/23 (17%)	2/17 (12%)	5/29 (17%)
Findings for animals sacrificed at termination				
Hepatocellular adenoma – B	16/24 (67%)	10/25 (40%)	16/32 (50%)	8/21 (38%)
Hepatocellular carcinoma – 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 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.

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 ♂ and 50 ♀, 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 (♂ about 0, 150, 780, 1290 mg/kg bw/day; ♀ 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:	≥25 000 ppm diet: NOAEL (♂+♀)			
	Only mild toxic effects, such as clinical chemistry of questionable relevance in aged rats, without correlating histopathological organ changes.			
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		Dose (mg/kg bw/day)		
	0	150	740.6	1290
Mortality	16/50 (32%)	17/50 (34%)	18/50 (36%)	23/50 (46%)
Females		Dose (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 guideline requirements, with no deviations.			
Substance:	Glyphosate (94.6–97.6% pure)			
Species/Strain:	Rat/Sprague-Dawley, groups of 50 ♂ and 50 ♀; satellite groups of 30 ♂ and 30 ♀for interim investigations			
Administration route:	Diet			
Concentration:	0, 3000, 10 000, 30 000 ppm diet (♂ about 0, 104, 354, 1127 mg/kg bw/day; ♀ about 0, 115, 393, 1247 mg/kg bw/day)			
Duration:	2 years			
Findings:	3000 ppm diet: NOAEL (♂+♀)			
	10 000 ppm diet: cecum weight↑, distension of cecum, loose stool, follicular hyperkeratosis and/or folliculitis/follicular abscess of the skin, body weight ↓			
Select neoplasms:	Pituitary adenoma, skin keratoacanthoma (males), mammary gland fibroadenoma (females)			
Tumor	Dose (mg/kg bw/day)			
Males	0	104	354	1127
Findings for dead and moribund sacrificed animals (Table 25–10)				
Pituitary anterior adenoma – B	22/32 (69%)	21/30 (70%)	*14/32 (44%)	18/21 (86%)
Skin keratoacanthoma – B	2/32 (6%)	1/30 (3%)	0/32	1/21 (5%)
Findings for animals sacrificed at termination (after 104 weeks, Table 25–8)				
Lung adenoma – B	0/18	2/20 (10%)	1/18 (6%)	3/29 (10%)
Pituitary anterior adenoma – B	13/18 (72%)	14/20 (70%)	13/18 (72%)	21/29 (72%)
Pituitary adenoma in intermediate part – B	0/18	1/20 (5%)	0/18	0/29 (0%)
Skin keratoacanthoma – B	1/18 (6%)	2/20 (10%)	0/18	6/29 (21%)
Tumor	Dose (mg/kg bw/day)			
Females	0	115	393	1247
Findings for dead and moribund sacrificed animals				
Pituitary anterior adenoma – B	34/35 (97%)	29/31 (94%)	28/33 (82%)	31/36 (86%)
Thyroid follicular adenoma – B	0/35	2/31 (6%)	0/32	0/36
Mammary gland fibroadenoma – B	13/35 (37%)	14/31 (45%)	12/34 (35%)	20/36 (56%)
Findings for animals sacrificed at termination				
Pituitary anterior adenoma – B	12/15 (80%)	19/19 (100%)	12/16 (75%)	13/14 (93%)
Mammary gland fibroadenoma – B	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 (2001)			
Reliability/Justification	1 Study performed according to GLP and OECD guideline requirements, with no deviations.			
Substance:	Glyphosate (97.6% pure)			
Species/Strain	Rat/Wistar Alpk: AP_fSD, groups of 52 ♂ and 52 ♀ (additional 12 animals per sex and dose for 1-year interim sacrifice)			
Administration route:	Diet			
Concentration:	0, 2000, 6000, 20 000 ppm diet (♂ about 0, 121, 361, 1214 mg/kg bw/day; ♀ about 0, 145, 437, 1498 mg/kg bw/day)			
Duration:	2 years			
Findings:	6000 ppm diet: NOAEL (♂+♀)			
	20 000 ppm diet: Kidney and liver findings. Increased survival due to reduction in CPN, prostatitis, periodontal inflammation			
Select neoplasms:	Hepatocellular adenoma (males), not a statistically significant increase for the high dose using the Fisher's exact test, but statistically significant using Peto trend analysis			
		Dose (mg/kg bw/day)		
Males	0	121	361	1214
Liver				
Hepatocyte fat vacuolation	6	7	11	11
Hepatitis	3	4	2	5
Kidney				
		Dose (mg/kg bw/day)		
Females	0	145	437	1498
Liver				
Hepatocyte fat vacuolation	7	5	6	6
Hepatitis	6	5	4	4
Tumors:		Dose (mg/kg bw/day)		
Males	0	121	361	1214
Findings for dead and moribund sacrificed animals				
*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-

Table 13. Study 8 – Two-year feeding study of glyphosate in rats (Nufarm 2009b).

Study owner:	Nufarm (2009a)			
Reliability/Justification:	1 Study performed according to GLP and OECD guideline requirements, with no deviations			
Substance:	Glyphosate (95.7% pure)			
Species/Strain:	Rat/Wistar, groups of 51 ♂ and 51 ♀			
Administration route:	Diet			
Concentration:	0, 3000, 10 000, 15 000 ppm diet, the top dose was progressively increased to reach 24 000 ppm diet by Week-40 (♂ about 0, 84, 285, 1077 mg/kg bw/day; ♀ about 0, 105, 349, 1382 mg/kg bw/day)			
Duration:	2 years			
Findings:	≥ 1077/1382 mg/kg bw/day: NOAEL (♂/♀)			
	Transient liver enzyme activity for mid-dose males and high-dose males and females; equivocal nephrocalcinosis depositions at the high-dose males and females; increased adipose infiltration of the bone marrow in high-dose males			
Select neoplasms:	Skin keratoacanthoma (males), mammary gland adenocarcinoma			
Tumor			Dose (mg/kg bw/day)	
Males	0	84	285	1077
Findings for all animals				
Skin keratoacanthoma – B	2/51 (4%)	3/51 (6%)	0/51	6/51 (12%)
			Dose (mg/kg bw/day)	
Females	0	105	349	1382
Findings for all animals				
Mammary gland adenocarcinoma – M	2/51 (4%)	3/51 (6%)	1/51 (2%)	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 drinking-water 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 drinking water study in rats with 13.85% glyphosate ammonium salt (Chruscielska et al. 2000a).

Authors:	Chruscielska et al. (2000a)
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 animal data, substance composition, purity, and stability) Highest dose did not elicit toxicity.
Substance:	Ammonium salt of glyphosate, 13.85% solution
Species/Strain:	Rat/Wistar -RIZ outbred, 85 ♂ and 85 ♀ per dose group. 10 ♂ and 10 ♀each were sacrificed after 6, 12, and 18 months of exposure.
Administration route:	Drinking water
Concentration:	0, 300, 900, and 2700 mg/L Estimated glyphosate intake: ♂: 0, 1.9, 5.7, and 17 mg/kg bw/day. ♀: 0, 2.2, 6.5, and 19 mg/kg bw/day, based on assumed water consumptions of 50/57 mL/kg bw/day (♂/♀), (Gold, et al. 1984)
Duration:	2 years
Findings:	17/19 mg glyphosate/kg bw/day: NOAEL (♂/♀) No treatment-related effects
Tumors reported for 85 rats/sex/dose:	No increase in the incidence of tumors attributable to glyphosate administration

	Estimated dose (mg/kg bw/day)							
	0		1.9/2.2		5.7/6.5		17/19	
	♂	♀	♂	♀	♂	♀	♂	♀
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	–	–	–
Spleen, leukemia	0	–	2	–	0	–	1	–
Kidneys, Fibrous histiocytoma	–	–	–	–	–	–	1	–
Pituitary gland								
Adenoma	4	10	4	6	2	8	0	3
Adenoma, malignant (assumed to be carcinoma)	0	1	0	3	1	2	1	5
Carcinoma	0	–	0	–	1	–	0	–
Thyroid								
Adenoma	1	1	1	2	0	0	3	3
Carcinoma	0	–	1	–	0	–	0	–
Uterus, cervix carcinoma	–	0	–	0	–	0	–	1
Uterus, body, histiocytoma	–	3	–	1	–	0	–	1
Mammary gland								
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								
Fibroma	0		1		1		3	
Lipoma	–	–	–	–	–	–	–	1
Cystadenoma	–	1	–	–	–	–	–	–
Lymph nodes								
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 prior to institution of GLP and OECD guideline requirements			
Substance:	Glyphosate (99.7% pure)			
Species/Strain:	Mouse/CD-1, groups of 50 ♂ and 50 ♀			
Administration route:	Diet			
Concentration:	0, 1000, 5000, 10 000 ppm diet (♂ about 0, 157, 814, 4841 mg/kg bw/day; ♀ about 0, 190, 955, 5874 mg/kg bw/day)			
Duration:	24 months			
Findings:	1000 ppm diet: NOAEL (♂ + ♀) 5000 ppm diet: body weight ↓, histological changes in liver and urinary bladder (slight to mild epithelial hyperplasia in males at mid and high doses)			
Select neoplasms:	Lymphoreticular neoplasms, bronchiolar-alveolar adenocarcinoma			
		Dose (mg/kg bw/day)		
Males	0	157	814	4841
Lymphoreticular system				
Lymphoblastic lymphosarcoma with leukemia – M	1/48 (2%)	4/49 (8%)	3/50 (6%)	2/49 (4%)
Lymphoblastic lymphosarcoma without 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 with leukemia – M	1/50 (2%)	4/48 (8%)	5/49 (10%)	1/49 (2%)
Lymphoblastic lymphosarcoma without leukemia – M	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%)
[#] Total lymphoreticular neoplasms	5/50 (10%)	6/48 (13%)	6/49 (12%)	10/49 (20%)

[#]Sum of lymphoblastic lymphosarcoma, composite lymphosarcoma, and histiocytic sarcoma.
M malignant

informahealthcare.com/doi/abs/10.3109/10408444.2014.1003423). 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 non-statistically 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. Study 11 – Two-year feeding study with glyphosate in mice (Cheminova 1993b).

Study owner:	Cheminova (1993b)			
Reliability/Justification:	1 Study performed according to GLP and OECD guideline requirements			
Substance:	Glyphosate (98.6% pure)			
Species/Strain:	Mouse/CD-1, groups of 50 ♂ and 50 ♀			
Administration route:	Diet			
Concentration:	♂+♀: 0, 100, 300, 1000 mg/kg bw/day (regular adjustment of dietary concentration)			
Duration:	24 months			
Findings:	≥1000 mg/kg bw/day: NOAEL (♂+♀) no treatment-related effects			
Select neoplasms:	Bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma, pituitary adenoma (females)			
		Dose (mg/kg bw/day)		
Males	0	10	300	1000
Bronchiolar-alveolar adenoma – B	9/50 (18%)	15/50 (30%)	11/50 (22%)	13/50 (26%)
Bronchiolar-alveolar carcinoma – 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 adenoma – B	7/50 (14%)	3/50 (6%)	3/50 (6%)	6/50 (12%)
Bronchiolar-alveolar carcinoma – 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 non-statistically 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).

Study owner:	Arysta Life Sciences (1997b)			
Reliability/Justification:	1 Study performed according to GLP and OECD guideline requirements, with no deviations.			
Substance:	Glyphosate (94.6–97.6% pure)			
Species/Strain	Mouse/CD-1, groups of 50 ♂ and 50 ♀			
Administration route:	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			
Findings:	8000/1600 ppm diet: NOAEL (♂/♀) 8000 ppm diet (♀): retarded growth 40 000 ppm diet: pale-colored skin ♂, loose stool, retarded growth, reduced food consumption and food efficiency, cecum distension and increased absolute and relative cecum weight, without histopathological findings of increased incidence of anal prolapse, consistent with histopathological erosion/ulcer of the anus			
Select neoplasms:	Lung adenoma, lung adenocarcinoma, lymphoma			
		Dose (mg/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%)
		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

Table 18. Study 13–18-Month feeding study with glyphosate in mice (Feinchemie Schwebda 2001).

Study owner:	Feinchemie Schwebda (2001)
Reliability/Justification	2 Study performed according to GLP and OECD guideline requirements, with no deviations, but possible viral infection may have confounded interpretation of results
Substance:	Glyphosate (>95% pure)
Species/Strain	Mouse/Swiss albino, groups of 50 ♂ and 50 ♀
Administration route:	Diet
Concentration:	0, 100, 1000, 10 000 ppm diet (♂ about 0, 14.5, 150, 1454 mg/kg bw/day; ♀ about 0, 15.0, 151, 1467 mg/kg bw/day)
Duration:	18 months
Findings:	1000 ppm diet: NOAEL (♂+♀) 10 000 ppm diet (♂+♀): increased mortality
Select neoplasms:	Bronchiolar/alveolar adenoma, lymphoma

	Historical controls		Dose (mg/kg bw/day) 0	14.5	150	1454
Males						
Mortality	§11/50–27/50		+22/50 (6)	20/50 (6)	22/50 (8)	27/50 (8)
Findings for dead and moribund sacrificed animals						
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 termination						
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						
Lymphoma – M	46/250	18.4% [6–30]	10/50 (20.0%)	15/50 (30.0%)	16/50 (32.0%)	*19/50 (38.0%)
	Historical controls		Dose (mg/kg bw/day) 0	15.0	151	1467
Females						
Mortality	12/50–20/50		16/50 (7)	16/50 (7)	20/50 (2)	20/50 (3)
Findings for dead and moribund sacrificed animals						
Bronchiolar/alveolar adenoma – B	–	–	0/16	0/16	1/20 (5%)	2/20 (10%)
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 – B			1/34 (3%)	0/0	1/1 (100%)	1/30 (3%)
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 – B			1/50 (2%)	0/16	2/21 (10%)	3/50 (6%)
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.
§Nine studies, performed by the same laboratory in the timeframe encompassing the study summarized here.
+(Number of animals killed in extremis).
#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 according to GLP and OECD guideline requirements, with no deviations			
Substance:	Glyphosate (94.6–97.6% pure)			
Species/Strain:	mouse/CD-1, groups of 51 ♂ and 51 ♀			
Administration route:	Diet			
Concentration:	0, 500, 1500, and 5000 ppm diet (♂ about 0, 0, 71.4, 234, 810 mg/kg bw/day; ♀ about 0, 97.9, 300, 1081 mg/kg bw/day)			
Duration:	18 months			
Findings:	≥ 5000 ppm diet: NOAEL (♂/♀) No treatment-related effects			
Select neoplasms:	Bronchiolar-alveolar adenoma, Bronchiolar-alveolar adenocarcinoma, hepatocellular adenoma (males), hepatocellular carcinoma (males), lymphoma, pituitary adenoma (females)			
		Dose (mg/kg bw/day)		
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 bw/day)		
Females	0	190	955	5873
Bronchiolar-alveolar adenoma – B	2/51 (4%)	4/51 (8%)	2/51 (4%)	2/51 (4%)
Bronchiolar-alveolar adenocarcinoma – M	5/51 (10%)	2/51 (4%)	2/51 (4%)	3/51 (6%)
Lymphoma – M	11/51 (22%)	8/51 (16)	10/51 (20%)	11/51 (22%)
Pituitary adenoma – B	0/51	1/50 (2%)	0/51	2/51 (4%)

B benign, *M* malignant

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.

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 DNA-reactive 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

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

	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)												
Select neoplasm	Controls – 0 [% range for studies]	[a]3	[d]7.4	[a]10	[c]10	[a]31	[d]73.9	[h]86	[b]89	[c]100	[f]104	[g]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

	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)												
Select neoplasm	[e]150	[h]285	[c]300	[f]354	[g]361	[b]362	[d]740.6	[e]780	[b]940	[c]1000	[h]1077	[f]1127	[g]1214	[e]1290
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

[a]Study 1 (Monsanto) (CD) SD rats, rated unreliable for carcinogenicity evaluation.
[b]Study 2 (Monsanto) (CD) SD rats, including interim sacrifice groups.
[c]Study 3 (Cheminova) SD rats.
[d]Study 4 (Feinchemic Schwebda) Wistar rats.
[e]Study 5 (Excel) SD rats, rated unreliable for carcinogenicity evaluation.
[f]Study 6 (Arysta Life Sciences) Crj:CD SD rats, including interim sacrifice groups.
[g] Study 7 (Syngenta) Alpk:AP$_f$SD Wistar rats, including interim sacrifice groups.
[h] 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).

	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)												
Select neoplasm	Controls – 0 [% range for studies]	[a]3	[d]7.4	[c]10	[a]11	[a]34	[d]73.9	[c]100	[h]105	[b]113	[f]115	[g]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	31/50	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	12/49	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 fibroadenoma	113/384 [6–58]	16/46	NF	12/28	20/48	16/44	NF	17/29	9/51	[$]24/54	30/79	4/63
Mammary gland adenocarcinoma	40/334 [2–22]	6/46	0/30	NF	5/48	8/44	0/33	NF	3/51	[~]10/54	8/79	0/63

	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)												
Select neoplasm	[e]210	[c]300	[h]349	[f]393	[g]437	[b]457	[d]740.6	[c]1000	[e]1060	[b]1183	[f]1247	[h]1382	[g]1498	[e]1740
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 fibroadenoma	1/22	19/30	7/51	27/77	6/64	[$]27/59	NF	29/50	5/22	[$]28/57	30/78	5/51	5/64	5/50
Mammary gland adenocarcinoma	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

[a]Study 1 (Monsanto) (CD) SD rats, rated unreliable for carcinogenicity evaluation.
[b]Study 2 (Monsanto) (CD) SD rats, including interim sacrifice groups.
[c]Study 3 (Cheminova) SD rats.
[d]Study 4 (Feinchemic Schwebda) Wistar rats.
[e]Study 5 (Excel) SD rats, rated unreliable for carcinogenicity evaluation.
[f]Study 6 (Arysta Life Sciences) Crj:CD SD rats, including interim sacrifice groups.
[g]Study 7 (Syngenta) Alpk:AP$_f$SD Wistar rats, including interim sacrifice groups.
[h]Study 8 (Nufarm) Wistar Han Crl:WI rats.
[$]Recorded as adenoma/adenofibroma/fibroma.
[~]Recorded as carcinoma/adenocarcinoma.
NF not found/not reported.

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

	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)							
Select neoplasm	Controls – 0 [% range for studies]	[d]14.5	[e]85	[b]100	[d]150	[a]157	[c]165	[e]267
Bronchiolar-alveolar adenoma	31/249 [10–18]	2/22	[§]7/51	15/50	0/22	9/50	[§]14/50	[§]9/51
Bronchiolar-alveolar adenocarcinoma	10/149 [2–10]	NF	[§]5/51	NF	NF	3/50	[§]1/50	[§]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
	Tumor Incidence/number of animals examined, by dose (mg/kg bw/day)							
Select neoplasm	[b]300	[a]814	[c]838	[e]946	[b]1000	[d]1454	[c]4348	[a]4841
Bronchiolar-alveolar adenoma	11/50	9/50	[§]13/50	[§]4/51	13/50	1/50	[§]11/50	9/50
Bronchiolar-alveolar adenocarcinoma	NF	2/50	[§]6/50	[§]11/51	NF	NF	[§]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

[a]Study 10 (Monsanto) CD-1 mice.
[b]Study 11 (Cheminova) CD-1 mice.
[c]Study 12 (Arysta Life Science) CD-1 mice.
[d]Study 13 (Feinchemic Schwebda) Swiss albino mice.
[e]Study 14 (Nufarm) CD-1 mice.
[§]Recorded as lung rather than bronchiolar-alveolar.
[#]Recorded as sum of malignant lymphoblastic lymphosarcoma with leukemia, lymphoblastic lymphosarcoma without leukemia and composite lymphosarcoma.
[$]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).

	Tumor incidence/number of animals examined, by dose (mg/kg bw/day)							
Select neoplasm	Controls – 0 [% range for studies]	[d]15.0	[e]85	[b]100	[d]151	[c]153	[a]190	[e]267
Bronchiolar-alveolar adenoma	28/250 [2–20]	0/16	[§]4/51	3/49	2/21	[§]5/50	9/50	[§]2/51
Bronchiolar-alveolar adenocarcinoma	2/99 [2]	NF	[§]2/51	NF	NF	[§]2/50	3/50	[§]2/51
Bronchiolar-alveolar carcinoma	9/151 [2–10]	0/16	NF	2/49	0/20	NF	NF	NF
Malignant lymphoma	54/215 [10–100]	20/50	8/51	12/15	19/50	4/50	[#]6/50	10/51
Myeloid leukemia	2/156 [0–4]	1/50	0/51	NF	2/50	0/50	NF	1/51
Pituitary adenoma	1/232 [0–2]	0/16	1/51	0/32	0/17	1/50	0/21	0/51
	Tumor incidence/number of animals examined, by dose (mg/kg bw/day)							
Select neoplasm	[b]300	[c]787	[e]946	[a]955	[b]1000	[d]1467	[c]4116	[a]5874
Bronchiolar-alveolar adenoma	3/50	[§]12/50	[§]2/51	10/49	6/50	3/50	[§]5/50	1/50
Bronchiolar-alveolar adenocarcinoma	NF	[§]3/50	[§]3/51	4/49	NF	NF	[§]1/50	4/50
Bronchiolar-alveolar carcinoma	1/50	NF	NF	NF	5/50	0/50	NF	NF
Malignant lymphoma	9/12	8/50	11/51	[#]6/50	13/14	25/50	7/50	[#]10/50
Myeloid leukemia	NF	0/50	0/51	NF	NF	1/50	1/50	NF
Pituitary adenoma	0/23	0/50	2/51	0/44	~3/50	1/48	0/50	0/37

[a]Study 10 (Monsanto) CD-1 mice.
[b]Study 11 (Cheminova) CD-1 mice.
[c]Study 12 (Arysta Life Science) CD-1 mice.
[d]Study 13 (Feinchemic Schwebda) Swiss albino mice.
[e]Study 14 (Nufarm) CD-1 mice.
[§]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 dose-response. 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 non-existent 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

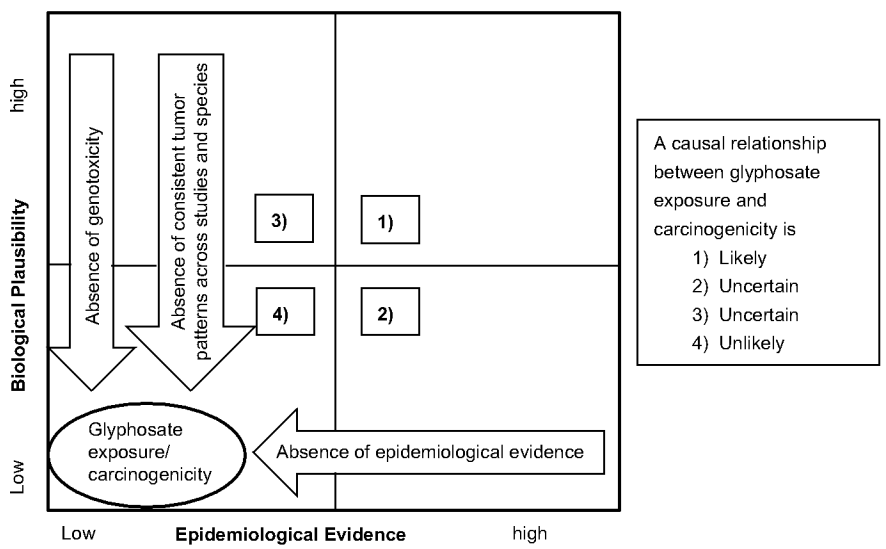

Figure 2. Likelihood of glyphosate carcinogenicity based on experimental and epidemiological data; a causal inference grid as proposed by Adami et al. (2011) to utilize both toxicological and epidemiological data.

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.

Acknowledgements

Special thanks go to Elizabeth Webb, Monsanto Toxicologist, for her detailed attention to document and data table formatting and as the reference library curator. Quality control and review of data transcription were valued services provided by Carrie Leigh Logan and Aparna Desai Nemali, Monsanto Quality Assurance Specialists.

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

NEOPLASM SUMMARY INCIDENCE TABLES

MALES

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
PITUITARY (NO. EXAMINED)	(15)	(33)	(48)	(26)	(23)	(49)	(16)	(32)	(48)	(25)	(22)	(47)
Adenoma	8	8	16	14	5	19	7	13	20	10	8	18
Carcinoma*		3	3		2	2	1	2	3	1		1
BRAIN (NO. EXAMINED)	(15)	(34)	(49)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Glioma		1	1	2	1	3				1		1
HEART (NO. EXAMINED)	(15)	(34)	(49)	(25)	(24)	(49)	(16)	(34)	(50)	(26)	(24)	(50)
Reticulum Cell Sarcoma*								1	1			
LUNG (NO. EXAMINED)	(15)	(35)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Metastatic Undifferentiated												
Sarcoma*										1		1
Reticulum Cell Sarcoma*		1	1		1	1		1	1		1	1
Malignant Lymphoma*		1	1									
Metastatic Osteogenic Sarcoma*		1	1									
Metastatic Malignant Mixed Tumor*					1	1						

*Malignant Neoplasm

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Terminal Sacrifice
Male Rats

	Group I			Group II			Group III			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
LIVER (NO. EXAMINED)	(15)	(35)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Reticulum Cell Sarcoma*		1	1		1	1		2	2		1	1
Malignant Lymphoma*		1	1					1	1			
Metastatic Undifferentiated Sarcoma*		1	1									
Neoplastic Nodule	2	1	3	2	1	3		1	1	2	1	3
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	1
Malignant Lymphoma*		1	1					1	1			
Reticulum Cell Sarcoma*		1	1								1	1
PANCREAS (NO. EXAMINED)	(15)	(35)	(50)	(26)	(23)	(49)	(16)	(34)	(50)	(26)	(24)	(50)
Islet Cell Adenoma				4	1	5		2	2	1	1	2
Islet Cell Carcinoma*										1		1
Acinar Cell Adenoma										1		1
Malignant Lymphoma*		1	1									
Reticulum Cell Sarcoma*		1	1					2	2			

*Malignant Neoplasm

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Male Rats

	Group I			Group II			Group III			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
MANDIBULAR SALIVARY GLAND												
(NO. EXAMINED)	(15)	(34)	(49)	(26)	(23)	(49)	(16)	(33)	(49)	(26)	(23)	(49)
Reticulum Cell Sarcoma*								1	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)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Angiosarcoma*		1	1									
Malignant Lymphoma*		1	1					1	1			
Reticulum Cell Sarcoma*								2	2		1	1
STOMACH (NO. EXAMINED)	(15)	(35)	(50)	(26)	(23)	(49)	(15)	(33)	(48)	(25)	(24)	(49)
Squamous Cell Carcinoma, Cardia*										1		1
JEJUNUM (NO. EXAMINED)	(14)	(35)	(49)	(25)	(21)	(46)	(14)	(34)	(48)	(25)	(24)	(49)
Reticulum Cell Sarcoma*								1	1			

*Malignant Neoplasm

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Male Rats

	Group I			Group II			Group III			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)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Tubular Adenoma	1		1		1	1						
Malignant Lymphoma*		1	1									
Reticulum Cell Sarcoma*		1	1		1	1		1	1			
Lipoma		1	1		1	1	1		1			
TESTIS (NO. EXAMINED)	(15)	(35)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Interstitial Cell Tumor				2	1	3	1		1	4	2	6
PROSTATE (NO. EXAMINED)	(15)	(35)	(50)	(25)	(22)	(47)	(16)	(33)	(49)	(25)	(24)	(49)
Reticulum Cell Sarcoma*								1	1			
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	3	1	4

*Malignant Neoplasm

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A Lifetime Feeding Study of
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Terminal Sacrifice
Male Rats

	Group I			Group II			Group III			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
PARATHYROID (NO. EXAMINED)	(11)	(16)	(27)	(15)	(15)	(30)	(5)	(23)	(28)	(13)	(14)	(27)
Adenoma					2	2						
ADRENAL (NO. EXAMINED)	(15)	(35)	(50)	(26)	(24)	(50)	(16)	(34)	(50)	(26)	(24)	(50)
Reticulum Cell Sarcoma*								1	1			
Pheochromocytoma	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		1
Sebaceous Gland Adenoma										1		1
SKELETAL MUSCLE (NO. EXAMINED)	(15)	(35)	(50)	(26)	(24)	(50)	(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)	(50)
Malignant Lymphoma*		1	1									

*Malignant Neoplasm

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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)	(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)
Osteoma										1		1
EAR (NO. EXAMINED)	(1)	(3)	(4)				(1)		(1)			
Fibroma		1	1									
Fibrosarcoma*							1		1			
Osteochondroma		1	1									
TAIL (NO. EXAMINED)	(1)		(1)	(6)	(1)	(7)	(3)	(3)	(6)	(2)	(3)	(5)
Papilloma							1		1			
Osteoma								1	1			

*Malignant Neoplasm

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
PERIOCULAR TISSUE (NO. EXAMINED)								(1)	(1)			
Squamous Cell Carcinoma*								1	1			
SUBCUTANEOUS TISSUE (NO. EXAMINED)	(4)	(6)	(10)	(9)	(3)	(12)	(6)	(4)	(10)	(3)	(4)	(7)
Fibrosarcoma*	1	1	2	1		1	1	1	2	1	2	3
Fibroma				3		3	1		1	1	1	2
Neurofibrosarcoma*										1		1
Undifferentiated Sarcoma*		1	1							1		1
Reticulum Cell Sarcoma*		1	1					1	1		1	1
Lipoma		1	1	1	1	2						
Osteogenic Sarcoma*							1		1			
Malignant Mixed Tumor*					1	1						
MEDIASTINAL TISSUE (NO. EXAMINED)		(7)	(7)		(1)	(1)		(4)	(4)		(2)	(2)
Reticulum Cell Sarcoma*											1	1
Malignant Lymphoma*		1	1									
Metastatic Osteogenic Sarcoma*		1	1									

*Malignant Neoplasm

NEOPLASM
SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
ABDOMEN (NO. EXAMINED)											(1)	(1)
Lipoma											1	1
MESENTERY (NO. EXAMINED)		(5)	(5)	(3)	(1)	(4)		(4)	(4)	(2)	(1)	(3)
Malignant Lymphoma*		1	1									
Reticulum Cell Sarcoma*		1	1					1	1			
Scirrhous Adenocarcinoma*					1	1						
ABDOMINAL CAVITY (NO. EXAMINED)								(1)	(1)			
Reticulum Cell Sarcoma*								1	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

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
MANDIBULAR LYMPH NODE (NO. EXAMINED)		(3)	(3)				(1)		(1)		(1)	(1)
Malignant Lymphoma*		1	1									
LUMBAR LYMPH NODE (NO. EXAMINED)										(1)		(1)
Metastatic Islet Cell Carcinoma*										1		1
SACRAL LYMPH NODE (NO. EXAMINED)		(1)	(1)	(2)	(1)	(3)	(2)	(1)	(3)	(1)	(2)	(3)
Reticulum Cell Sarcoma*					1	1						

*Malignant Neoplasm

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

NEOPLASM SUMMARY INCIDENCE TABLES

FEMALES

NEOPLASM
SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
PITUITARY (NO. EXAMINED)	(17)	(31)	(48)	(22)	(26)	(48)	(30)	(20)	(50)	(15)	(34)	(49)
Adenoma	13	21	34	15	14	29	20	11	31	9	17	26
Carcinoma*	2	6	8	2	5	7		5	5	4	8	12
BRAIN (NO. EXAMINED)	(18)	(32)	(50)	(23)	(26)	(49)	(30)	(20)	(50)	(15)	(35)	(50)
Invasive Pituitary Carcinoma*								1	1	1		1
Malignant Lymphoma*											1	1
Glioma											1	1
CERVICAL SPINAL CORD (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Malignant Lymphoma*											1	1
HEART (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Malignant Lymphoma*											1	1
Metastatic Fibrosarcoma*		1	1									
TRACHEA (NO. EXAMINED)	(18)	(31)	(49)	(23)	(26)	(49)	(30)	(19)	(49)	(15)	(35)	(50)
Metastatic Fibrosarcoma*		1	1									

*Malignant Neoplasm

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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)	(35)	(50)
Metastatic Fibrosarcoma*		1	1				1		1			
LUNG (NO. EXAMINED)	(18)	(31)	(49)	(23)	(27)	(50)	(30)	(19)	(49)	(15)	(35)	(50)
Reticulum Cell Sarcoma*	1	1	2		2	2		1	1		3	3
Malignant Lymphoma*					1	1					1	1
Metastatic Mammary Gland Adenocarcinoma*											1	1
Metastatic Adrenal Cortical Carcinoma*								1	1			
Metastatic Fibrosarcoma*		1	1									
LIVER (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Reticulum Cell Sarcoma*	1	1	2		2	2		1	1		2	2
Malignant Lymphoma*								1	1	1	1	2
Metastatic Fibrosarcoma*		1	1									
Hepatocellular Carcinoma*		1	1							2		2
Neoplastic Nodule	6	5	11	3	4	7	5	1	6	2	5	7

*Malignant Neoplasm

NEOPLASM
SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
MESENTERIC LYMPH NODE (NO. EXAMINED)	(18)	(24)	(42)	(23)	(16)	(39)	(29)	(19)	(48)	(14)	(33)	(47)
Malignant Lymphoma*											1	1
Reticulum Cell Sarcoma*											2	2
PANCREAS (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(34)	(49)
Islet Cell Adenoma	1	1	2		1	1	1		1			
Islet Cell Carcinoma*				1		1	1		1		1	1
MANDIBULAR SALIVARY GLAND												
(NO. EXAMINED)	(18)	(30)	(48)	(23)	(27)	(50)	(30)	(19)	(49)	(15)	(34)	(49)
Metastatic Fibrosarcoma*							1		1			
THYMUS (NO. EXAMINED)	(9)	(16)	(25)	(19)	(13)	(32)	(26)	(11)	(37)	(15)	(19)	(34)
Malignant Lymphoma*							1		1	1		1
Thymoma								1	1			

*Malignant Neoplasm

NEOPLASM
SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
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*							1		1	1	1	2
SPLEEN (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Malignant Lymphoma*								1	1	1	1	2
Reticulum Cell Sarcoma*	1	1	2		2	2		1	1		5	5
STOMACH (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Malignant Lymphoma*											1	1
Reticulum Cell Sarcoma*	1		1									
Metastatic Fibrosarcoma*		1	1									
JEJUNUM (NO. EXAMINED)	(18)	(32)	(50)	(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

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
COLON (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(19)	(49)	(14)	(34)	(48)
Reticulum Cell Sarcoma*											1	1
KIDNEY (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(35)	(50)
Malignant Lymphoma*											1	1
Reticulum Cell Sarcoma*					1	1					2	2
Transitional Cell Carcinoma*							1		1			
URINARY BLADDER (NO. EXAMINED)	(18)	(32)	(50)	(23)	(25)	(48)	(28)	(20)	(48)	(14)	(30)	(44)
Transitional Cell Carcinoma*											1	1
OVARY (NO. EXAMINED)	(18)	(31)	(49)	(23)	(27)	(50)	(30)	(18)	(48)	(13)	(32)	(45)
Granulosa Cell Tumor	3	5	8	4	4	8	5	1	6	2	4	6
Theca-Granulosa Cell Tumor											1	1

*Malignant Neoplasm

NEOPLASM

SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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
UTERUS (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(29)	(20)	(49)	(15)	(34)	(49)
Squamous Cell Carcinoma*											1	1
Endometrial Sarcoma*											1	1
Adenoma							2		2		1	1
Polyp	4	1	5	1	1	2	3	2	5	2	1	3
Reticulum Cell Sarcoma*	1		1		1	1						
THYROID (NO. EXAMINED)	(18)	(29)	(47)	(23)	(26)	(49)	(30)	(20)	(50)	(14)	(33)	(47)
C-Cell Adenoma	2	3	5	2	1	3	4	2	6	1	2	3
C-Cell Carcinoma*	1		1				1	1	2	2	4	6
Follicular Adenoma		3	3	1	1	2	1		1			
Metastatic Fibrosarcoma*							1		1			
PARATHYROID (NO. EXAMINED)	(12)	(11)	(23)	(12)	(13)	(25)	(13)	(12)	(25)	(5)	(18)	(23)
Adenoma											1	1

*Malignant Neoplasm

NEOPLASM
SUMMARY INCIDENCE TABLE

Bio/dynamics Project Number M-6, 77-2062
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Glyphosate (ROUNDUP® Technical)
Terminal Sacrifice
Female Rats

	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
ADRENAL (NO. EXAMINED)	(18)	(32)	(50)	(23)	(27)	(50)	(30)	(20)	(50)	(15)	(34)	(49)
Reticulum Cell Sarcoma*		1	1		1	1		1	1		3	3
Pheochromocytoma	1		1	1	1	2	2		2	1	1	2
Cortical Adenoma	3	2	5	4	6	10	6		6		4	4
Cortical Carcinoma*		1	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[a]	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[a]	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[a]*	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		1									
EYE (NO. EXAMINED)	(18)	(31)	(49)	(21)	(27)	(48)	(30)	(20)	(50)	(15)	(32)	(47)
Periocular Fibrosarcoma*							1		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
[a]Number of Lesions/Number of Animals with Lesion

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I-70 CONTAINS TRADE SECRET OR
CONFIDENTIAL INFORMATION OF MONSANTO
COMPANY

NEOPLASM
SUMMARY INCIDENCE TABLE

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

	Group I			Group II			Group III			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	1		3	3
EAR (NO. EXAMINED)		(2)	(2)								(1)	(1)
Chondroma		1	1									
Osteochondroma		1	1								1	1
SUBCUTANEOUS TISSUE (NO. EXAMINED)	(2)	(2)	(4)	(3)	(3)	(6)	(1)		(1)	(1)	(1)	(2)
Lipoma										1	1	2
Fibrosarcoma*					1	1						
Reticulum Cell Sarcoma*					2	2						
Fibroma				1		1						
MEDIASTINAL TISSUE (NO. EXAMINED)		(2)	(2)		(1)	(1)	(1)	(1)	(2)		(2)	(2)
Fibrosarcoma*		1	1									
Reticulum Cell Sarcoma*					1	1						

*Malignant Neoplasm

NEOPLASM

SUMMARY INCIDENCE TABLE

Bio/dynamics Project Number M-6, 77-2062
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Glyphosate (ROUNDUP® Technical)
Terminal Sacrifice
Female Rats

	Group I			Group II			Group III			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)	(5)	(4)	(1)	(5)	(1)	(1)	(2)	(1)	(6)	(7)
Reticulum Cell Sarcoma*											2	2
Metastatic Adrenal Cortical												
Carcinoma*		1	1									
SKULL (NO. EXAMINED)											(1)	(1)
Fibroma											1	1
URETER (NO. EXAMINED)							(1)		(1)		(1)	(1)
Transitional Cell Carcinoma*							1		1		1	1
MANDIBULAR LYMPH NODE (NO. EXAMINED)	(2)		(2)	(1)	(2)	(3)	(6)		(6)	(3)	(3)	(6)
Malignant Lymphoma*											1	1

*Malignant Neoplasm

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

STUDY NO: 87122 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 1
PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:10-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED ----- MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	14	19	17	17
ADRENAL(S)					
-@B - CORTICAL ADENOMA		@	@	@	1
-@B - PHEOCHROMOCYTOMA		@	@	4	3
-@M - PHEOCHROMOCYTOMA		@	@	1	@
BRAIN					
BONE		--	..		(15)
SP.CORD,CERVICAL					
-@M - GLIOMA		@	1	@	@
CECUM					
DUODENUM					
EYE(S)					
-@M - NEUROFIBROSARCOMA (SCHWANNOMA)		@	@	@	1
KIDNEY(S)					
-@B - LIPOMA		1	@	@	@
-@M - LIPOSARCOMA		@	@	1	@
-@B - TUBULAR ADENOMA		@	1	@	@
LIVER					
-@B - HEPATOCELLULAR ADENOMA		1	1	3	4
-@M - HEPATOCELLULAR CARCINOMA		1	1	@	@
LUNG					
MAMMARY GLAND		(13)	(13)	(14)	(14)
-@B - ADENOMA/ADENOFIBROMA/FIBROMA		@	1	@	@
-@M - CARCINOMA/ADENOCARCINOMA		1	@	@	@
LY.NODE,MESENT.			(18)		
-@B - HEMANGIOMA		@	@	@	1
MESENTERY/OM'TUM		(3)	(1)	(2)	(2)
NOSE/TURBINATES					(16)

STUDY NO: 87122 ***** MONSANTO ENVIRONMENTAL HEALTH LAB ***** PAGE: 2
PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:16-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED - MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	14	19	17	17
NOSE/TURBINATES					(15)
-@B - PAPILLARY ADENOMA		0	0	0	1
PANCREAS					
-@B - ISLET CELL ADENOMA		0	4	3	3
-@M - ISLET CELL CARCINOMA		1	0	0	0
PAWS/FEET		(6)	(9)	(5)	(8)
PITUITARY					
-@B - ADENOMA, PARS DISTALIS		13	15	14	10
PROSTATE					
PARATHYROID(S)					(16)
SKIN		(13)			
-@B - KERATOACANTHOMA		0	2	2	4
-@M - SQUAMOUS CELL CARCINOMA		0	0	0	1
-@B - BASAL CELL TUMOR		0	0	0	1
-@B - SQUAMOUS PAPILLOMA		1	1	0	0
-@B - SEBACEOUS GLAND ADENOMA		0	1	0	1
SPLEEN					
SP.CORD,THORACIC					
TESTIS(ES)					
-@B - INTERSTITIAL CELL TUMOR		1	0	1	2
THYROID(S)		0	2	7 *	4
-@B - C CELL ADENOMA		2	0	1	1
-@B- FOLLICULAR ADENOMA/CYSTADENOMA		0	0	0	1
-@M - FOLLICULAR CELL CARCINOMA					
THYMUS		(8)	(15)	(10)	(14)
-@M - LYMPHOMA / LYMPHOSARCOMA		0	0	0	1
URINARY BLADDER					

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

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:10-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED ----- MALES ---			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	14	19	17	17
SUBCUTIS		(0)	(1)	(3)	(2)
-0B - FIBROMA			0	1	1
-0M - FIBROSARCOMA			0	0	1
-0B - LIPOMA			1	2	0
ORAL CAVITY		(0)	(0)	(0)	(1)

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:10-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED ----- FEMALES			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	22	22	17	18
ADRENAL(S)					
-@B - CORTICAL ADENOMA		1	1	1	1
-@B - PHEOCHROMOCYTOMA		1	1	1	2
-@M - PHEOCHROMOCYTOMA		0	0	0	1
-@M - CORTICAL CARCINOMA		0	0	0	1
BRAIN					
BONE					
SP.CORD,CERVICAL					
CECUM					
DUODENUM					
EYE(S)					
KIDNEY(S)		0	1	1	0
-@B - LIPOMA					
LIVER		0	1	3	0
-@B - HEPATOCELLULAR ADENOMA		1	0	1	1
-@M - HEPATOCELLULAR CARCINOMA		1	0	0	0
-@B - CHOLANGIOMA					
LY.NODE,UNDESIG.		(1)	(0)	(0)	(0)
LUNG		1	0	0	0
-@B - BRONCHOALVEOLAR ADENOMA					
MAMMARY GLAND		11	15	13	14
-@B - ADENOMA/ADENOFIBROMA/FIBROMA		0	0	4	5
-@M - CARCINOMA/ADENOCARCINOMA					
LY.NODE,MESENT.		(0)	(1)	(0)	(0)
MESENTERY/OM'TUM			1		
-@B - LIPOMA					

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:10-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED — FEMALES			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	22	22	17	18
NOSE/TURBINATES					
OVARY(IES)					(17)
-#B - GRANULOSA CELL TUMOR		0	1	0	0
PANCREAS					
-#B - ISLET CELL ADENOMA		2	1	1	0
PAWS/FEET		(2)	(2)	(2)	(2)
PITUITARY					
-#B - ADENOMA, PARS DISTALIS		19	19	15	11
PARATHYROID(S)					
-#B - ADENOMA		0	1	1	0
SKIN					
-#M - SQUAMOUS CELL CARCINOMA		0	0	0	1
-#B - CLITORAL GLAND ADENOMA		1	0	0	0
SPLEEN					
SP.CORD,THORACIC					
THYROID(S)					
-#B - C CELL ADENOMA		2	2	5	4
-#B- FOLLICULAR ADENOMA/CYSTADENOMA		1	0	0	0
-#M - FOLLICULAR CELL CARCINOMA		0	0	0	1
THYMUS		(14)	(19)	(9)	(11)
-#M - LYMPHOMA / LYMPHOSARCOMA		2	3	0	0
URINARY BLADDER			(21)	(16)	(17)
-#B - POLYP/PAPILLOMA		0	0	1	0
UTERUS					(17)
-#B - POLYP		1	2	0	1
-#B - ADENOMA, ENDOMETRIAL		0	2	0	0
-#B - LEIOMYOMA		1	0	0	0

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: SCHEDULED SACRIFICES PERIODS: : 7-AUG-1989:10-AUG-1989

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED ----- FEMALES			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	22	22	17	18
UTERUS				(17)	
VAGINA		(0)	(0)	(0)	(3)
-00 - FIBROMA					1
SUBCUTIS		(1)	(0)	(2)	(3)
-0M - FIBROUS HISTIOCYTOMA		1		0	0
-00 - FIBROMA		0		0	2
-00 - LIPOMA		0		2	1

NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROUP.

* = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.05] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.
** = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.01] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.

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

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: UNSCHEDULED DEATHS

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED - MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	36	31	33	33
ADRENAL(S)			(29)		
-#B - CORTICAL ADENOMA		0	0	1	1
-#B - PHEOCHROMOCYTOMA		5	1	2	5
-#M - PHEOCHROMOCYTOMA		0	1	2	0
-#M - GANGLIONEUROMA/PHEOCHROMOCYTOMA		0	0	1	0
BRAIN					
-#M - ASTROCYTOMA		0	1	1	1
BONE			(30)		
-#M - OSTEOSARCOMA		0	0	0	1
SP.CORD,CERVICAL				(32)	(32)
-#M - ASTROCYTOMA		0	0	1	0
-#M - GLIOMA		0	1	0	0
CECUM		(31)	(27)	(29)	(26)
PERITONEAL CAV.		(0)	(0)	(0)	(1)
-#M - MALIGNANT FIBROUS HISTIOCYTOMA					1
DUODENUM		(34)	(26)	(32)	(32)
-#M - ADENOCARCINOMA		1	0	0	0
EYE(S)					
KIDNEY(S)		1	0	0	0
-#B - LIPOMA		0	1	0	0
-#M - LIPOSARCOMA		0	1	0	0
-#M - MESENCHYMAL TUMOR		0	1	0	0
-#B - TUBULAR ADENOMA					
LIVER		2	1	0	4
-#B - HEPATOCELLULAR ADENOMA		2	1	1	2
-#M - HEPATOCELLULAR CARCINOMA		0	1	0	1
-#M - HISTIOCYTIC SARCOMA		0	1	0	0
-#M - NEOPLASM, UNDETERMINED ORIGIN					
LUNG					

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PATHOLOGY SECTION
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***

SELECTION CRITERIA: UNSCHEDULED DEATHS

TISSUES WITH FINDINGS	NUMBER OF ANIMALS AFFECTED — MALES			
ANIMAL SEX :	MN	M1	M2	M3
DOSAGE GROUP:				
NO. IN GROUP:	36	31	33	33
MAMMARY GLAND	(24)	(14)	(24)	(20)
-#B - ADENOMA/ADENOFIBROMA/FIBROMA	0	0	0	1
-#M - ADENOACANTHOMA	0	0	0	1
LY.NODE,MESENT.	(33)		(32)	(29)
MESENTERY/OM'TUM	(6)	(2)	(5)	(4)
-#M - MESOTHELIOMA	0	1	0	1
NERVE, UNDESIG.	(0)	(0)	(0)	(1)
-#B - NEUROFIBROMA (SCHWANNOMA)				1
NOSE/TURBINATES		(30)		
PANCREAS	(34)	(28)		(32)
-#B - ISLET CELL ADENOMA	1	4	2	4
PAWS/FEET	(6)	(6)	(7)	(3)
-#M - SARCOMA, UNDETERMINED CELL TYPE	0	0	1	0
PITUITARY		(29)	(31)	(32)
-#B - ADENOMA, PARS DISTALIS	19	15	19	19
-#B - ADENOMA, PARS INTERMEDIA	0	0	0	1
PROSTATE	1	0	0	0
-#M - ADENOCARCINOMA				
PARATHYROID(S)		(29)	(32)	
-#B - ADENOMA	1	1	0	2
SKIN				(32)
-#B - KERATOACANTHOMA	0	1	2	1
-#M - SQUAMOUS CELL CARCINOMA	2	0	0	0
-#M - CARCINOMA/ADENOCARCINOMA, ZYMBAL'S GLAND	1	0	0	0
-#M - FIBROUS HISTIOCYTOMA	0	0	1	0
-#B - ADENOMA, ZYMBAL'S GLAND	0	0	2	0
-#B - SQUAMOUS PAPILLOMA	0	0	1	0
-#B - FIBROMA	1	0	0	0
SPLEEN		(30)		

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P A T H O L O G Y S E C T I O N
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: UNSCHEDULED DEATHS

T I S S U E S W I T H F I N D I N G S	ANIMAL SEX : DOSAGE GROUP: NO. IN GROUP:	NUMBER OF ANIMALS AFFECTED — MALES			
		MN	M1	M2	M3
		36	31	33	33
SPLEEN			(30)		
TAIL		(1)	(0)	(0)	(0)
-#B- INTRACUTANEOUS CORNIFYING EPITHELIOMA		1			
SP.CORD,THORACIC					
-#M - ASTROCYTOMA		0	0	1	0
TESTIS(ES)					
-#B - INTERSTITIAL CELL TUMOR		1	0	2	0
THYROID(S)			(29)	(31)	
-#B - C CELL ADENOMA		0	2	1	1
-#M - C CELL CARCINOMA		0	2	0	1
-#B- FOLLICULAR ADENOMA/CYSTADENOMA		0	1	2	1
THYMUS		(22)	(14)	(17)	(20)
-#M - LYMPHOMA / LYMPHOSARCOMA		1	0	0	0
URINARY BLADDER		(35)			
SUBCUTIS		(6)	(1)	(1)	(3)
-#M - FIBROUS HISTIOCYTOMA		2	0	0	0
-#B - FIBROMA		2	0	0	2
-#M - FIBROSARCOMA		1	0	0	0
-#B - LIPOMA		1	0	0	0
-#M - SQUAMOUS CELL CARCINOMA		0	0	0	1
G I TRACT		(1)	(0)	(0)	(0)
-#M - MUCINOUS ADENOCARCINOMA		1			
TOOTH		(1)	(1)	(0)	(0)
-#M - ODONTOGENIC TUMOR		1	0		
-#B - ODONTOGENIC TUMOR		0	1		
MULTIPLE TISSUES		(1)	(1)	(0)	(0)
-#M - FIBROUS HISTIOCYTOMA		1	0		
-#M - LYMPHOMA/LYMPHOSARCOMA		0	1		

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PRINTED: 13-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: UNSCHEDULED DEATHS

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED			
		FEMALES			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	28	28	33	32
ADRENAL(S)					
-#B - CORTICAL ADENOMA		0	1	1	0
-#B - PHEOCHROMOCYTOMA		0	0	1	0
BRAIN					
-#B - GRANULAR CELL TUMOR		0	1	0	0
BONE					
SP.CORD,CERVICAL					(31)
CECUM		(23)	(24)	(32)	(27)
-#M - NEUROFIBROSARCOMA		0	0	1	0
PERITONEAL CAV.		(0)	(0)	(1)	(0)
-#M - NEURO-ENDOCRINE TUMOR, GASTRIN SECRETING				1	
DUODENUM			(27)	(32)	(29)
EYE(S)					(31)
KIDNEY(S)					
-#M - TUBULAR CARCINOMA		0	1	0	0
-#B - HEMANGIOMA		1	0	0	0
LIVER					
-#B - HEPATOCELLULAR ADENOMA		0	1	2	1
-#M - HEPATOCELLULAR CARCINOMA		0	0	0	1
-#M - HISTIOCYTIC SARCOMA		0	0	1	0
-#M - HEMANGIOSARCOMA		0	0	1	0
LUNG					
MAMMARY GLAND		(27)	(24)	(32)	(30)
-#B - ADENOMA/ADENOFIBROMA/FIBROMA		14	9	11	14
-#M - CARCINOMA/ADENOCARCINOMA		6	4	9	4
-#M - CARCINOSARCOMA		1	0	0	1
LY.NODE,MESENT.			(27)	(32)	

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***

SELECTION CRITERIA: UNSCHEDULED DEATHS

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED -------- ---- FEMALES ---------			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	28	28	33	32
MESENTERY/OM'TUM		(0)	(2)	(2)	(0)
NOSE/TURBINATES					
OVARY(IES)		0	1	1	0
-#B - GRANULOSA CELL TUMOR		1	0	0	0
-#B - THECA CELL TUMOR					
PANCREAS					(31)
-#B - ISLET CELL ADENOMA		3	0	3	0
PAWS/FEET		(0)	(1)	(0)	(1)
PITUITARY					(31)
-#B - ADENOMA, PARS DISTALIS		22	24	28	20
-#M - CARCINOMA, PARS DISTALIS		0	0	0	1
PARATHYROID(S)			(27)		
-#B - ADENOMA		2	0	1	0
SKIN		(27)	(24)		(30)
-#B - ADENOMA, ZYMBAL'S GLAND		0	0	1	0
-#B - BASAL CELL TUMOR		1	0	0	0
SPLEEN		0	0	0	1
-#M - LYMPHOMA / LYMPHOSARCOMA		0	0	0	1
-#B - HEMANGIOMA		1	0	0	0
-#M - HEMANGIOSARCOMA					
SP.CORD,THORACIC					
THYROID(S)		0	0	1	2
-#B - C CELL ADENOMA		0	0	1	0
-#M - C CELL CARCINOMA		0	0	0	1
-#B- FOLLICULAR ADENOMA/CYSTADENOMA					
THYMUS		(19)	(23)	(24)	(23)
-#M - LYMPHOMA / LYMPHOSARCOMA		3	0	1	1
URINARY BLADDER			(27)		

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***

SELECTION CRITERIA: UNSCHEDULED DEATHS

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED -------- ---- FEMALES ---------			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	28	28	33	32
UTERUS					
-#B - POLYP		0	0	2	1
-#B-VASCULAR HAMARTOMA		0	0	1	0
-#M - STROMAL SARCOMA		0	0	1	0
-#B - FIBROMA		1	0	0	0
VAGINA		(1)	(0)	(2)	(0)
SUBCUTIS		(3)	(0)	(2)	(3)
-#M - FIBROUS HISTIOCYTOMA		0		0	2
-#B - FIBROMA		1		1	0
-#M - FIBROSARCOMA		2		0	0
ORAL CAVITY		(0)	(1)	(1)	(1)
-#B - SQUAMOUS PAPILLOMA, PALATE			1	0	0
-#B - CHONDROMA, ALVEOLUS			0	0	1
-#M - GRANULAR CELL TUMOR			0	1	0
TOOTH		(0)	(1)	(0)	(0)

NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROUP.

* = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.05] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.
** = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.01] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.

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

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PATHOLOGY SECTION
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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED — MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	60	60	60	60
ADRENAL(S)			(58)		
-#B - CORTICAL ADENOMA		0	0	1	2
-#B - PHEOCHROMOCYTOMA		5	7	6	8
-#M - PHEOCHROMOCYTOMA		0	1	3	0
-#M - GANGLIONEUROMA/PHEOCHROMOCYTOMA		0	0	1	0
BRAIN					
-#M - ASTROCYTOMA		0	1	1	1
BONE			(59)		(58)
-#M - OSTEOSARCOMA		0	0	0	1
SP.CORD,CERVICAL				(59)	(59)
-#M - ASTROCYTOMA		0	0	1	0
-#M - GLIOMA		0	2	0	0
CECUM		(55)	(56)	(56)	(53)
PERITONEAL CAV.		(0)	(0)	(0)	(1)
-#M - MALIGNANT FIBROUS HISTIOCYTOMA					1
DUODENUM		(58)	(55)	(59)	(59)
-#M - ADENOCARCINOMA		1	0	0	0
EYE(S)					
-#M - NEUROFIBROSARCOMA (SCHWANNOMA)		0	0	0	1
KIDNEY(S)					
-#B - LIPOMA		2	0	0	0
-#M - LIPOSARCOMA		0	1	1	0
-#M - MESENCHYMAL TUMOR		0	1	0	0
-#B - TUBULAR ADENOMA		0	2	0	0
LIVER					
-#B - HEPATOCELLULAR ADENOMA		3	2	3	8
-#M - HEPATOCELLULAR CARCINOMA		3	2	1	2
-#M - HISTIOCYTIC SARCOMA		0	1	0	1
-#M - NEOPLASM, UNDETERMINED ORIGIN		0	1	0	0
LUNG					

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***

SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED - MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	60	60	60	60
MAMMARY GLAND		(43)	(31)	(41)	(37)
-#B - ADENOMA/ADENOFIBROMA/FIBROMA		0	1	1	1
-#M - CARCINOMA/ADENOCARCINOMA		1	0	0	0
-#M - ADENOACANTHOMA		0	0	0	1
LY.NODE,MESENT.		(57)	(59)	(58)	(56)
-#B - HEMANGIOMA		0	0	0	1
MESENTERY/OM'TUM		(9)	(3)	(7)	(6)
-#M - MESOTHELIOMA		0	1	0	1
NERVE, UNDESIG.		(0)	(0)	(0)	(1)
-#B - NEUROFIBROMA (SCHWANNOMA)					1
NOSE/TURBINATES			(59)		(58)
-#B - PAPILLARY ADENOMA		0	0	0	1
PANCREAS		(58)	(57)		(59)
-#B - ISLET CELL ADENOMA		1	8	* 5	7
-#M - ISLET CELL CARCINOMA		1	0	0	0
PAWS/FEET		(12)	(15)	(12)	(11)
-#M - SARCOMA, UNDETERMINED CELL TYPE		0	0	1	0
PITUITARY			(58)	(58)	(59)
-#B - ADENOMA, PARS DISTALIS		34	32	34	31
-#B - ADENOMA, PARS INTERMEDIA		0	0	0	1
PROSTATE		1	0	0	0
-#M - ADENOCARCINOMA					
PARATHYROID(S)			(58)	(58)	(57)
-#B - ADENOMA		1	1	0	2
SKIN		(59)			(59)
-#B - KERATOACANTHOMA		1	3	4	5
-#M - SQUAMOUS CELL CARCINOMA		2	0	0	1
-#M - CARCINOMA/ADENOCARCINOMA, ZYMBAL'S GLAND		1	0	0	0
-#M - FIBROUS HISTIOCYTOMA		0	0	1	0

STUDY NO: 87122 ***** MONSANTO ENVIRONMENTAL HEALTH LAB *****
PATHOLOGY SECTION

STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE
PRINTED: 12-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED - MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	60	60	60	60
SKIN		(59)			(59)
-#B - ADENOMA, ZYMBAL'S GLAND		0	0	2	0
-#B - BASAL CELL TUMOR		0	0	0	1
-#B - SQUAMOUS PAPILLOMA		1	1	1	0
-#B - SEBACEOUS GLAND ADENOMA		0	1	0	1
-#B - FIBROMA		1	0	0	0
SPLEEN			(59)		
TAIL		(1)	(0)	(0)	(0)
-#B- INTRACUTANEOUS CORNIFYING EPITHELIOMA		1			
SP.CORD,THORACIC					
-#M - ASTROCYTOMA		0	0	1	0
TESTIS(ES)					
-#B - INTERSTITIAL CELL TUMOR		2	0	3	2
THYROID(S)			(58)	(58)	
-#B - C CELL ADENOMA		2	4	8	7
-#M - C CELL CARCINOMA		0	2	0	1
-#B- FOLLICULAR ADENOMA/CYSTADENOMA		2	1	3	2
-#M - FOLLICULAR CELL CARCINOMA		0	0	0	1
THYMUS		(38)	(38)	(36)	(43)
-#M - LYMPHOMA / LYMPHOSARCOMA		1	0	0	1
URINARY BLADDER		(59)			
SUBCUTIS		(6)	(3)	(4)	(5)
-#M - FIBROUS HISTIOCYTOMA		2	0	0	0
-#B - FIBROMA		2	0	1	3
-#M - FIBROSARCOMA		1	0	0	1
-#B - LIPOMA		1	1	2	0
-#M - SQUAMOUS CELL CARCINOMA		0	0	0	1
G I TRACT		(1)	(0)	(0)	(0)
-#M - MUCINOUS ADENOCARCINOMA		1			
ORAL CAVITY		(0)	(0)	(0)	(1)

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX :	NUMBER OF ANIMALS AFFECTED - MALES			
	DOSAGE GROUP:	MN	M1	M2	M3
	NO. IN GROUP:	60	60	60	60
ORAL CAVITY		(0)	(0)	(0)	(1)
TOOTH		(1)	(1)	(0)	(0)
-#M - ODONTOGENIC TUMOR		1	0		
-#B - ODONTOGENIC TUMOR		0	1		
MULTIPLE TISSUES		(1)	(1)	(0)	(0)
-#M - FIBROUS HISTIOCYTOMA		1	0		
-#M - LYMPHOMA/LYMPHOSARCOMA		0	1		

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX : DOSAGE GROUP: NO. IN GROUP:	NUMBER OF ANIMALS AFFECTED — FEMALES FN 60	F1 60	F2 60	F3 60
ADRENAL(S)					
-#B - CORTICAL ADENOMA		1	3	2	1
-#B - PHEOCHROMOCYTOMA		1	1	2	2
-#M - PHEOCHROMOCYTOMA		0	0	0	1
-#M - CORTICAL CARCINOMA		0	0	0	3
BRAIN					
-#B - GRANULAR CELL TUMOR		0	1	0	0
BONE					
SP.CORD,CERVICAL					(59)
CECUM		(55)	(56)	(59)	(55)
-#M - NEUROFIBROSARCOMA		0	0	1	0
PERITONEAL CAV.		(0)	(0)	(1)	(0)
-#M - NEURO-ENDOCRINE TUMOR, GASTRIN SECRETING				1	
DUODENUM			(59)	(59)	(57)
EYE(S)					(59)
KIDNEY(S)					
-#B - LIPOMA		0	1	1	0
-#M - TUBULAR CARCINOMA		0	1	0	0
-#B - HEMANGIOMA		1	0	0	0
LIVER					
-#B - HEPATOCELLULAR ADENOMA		6	2	6	1
-#M - HEPATOCELLULAR CARCINOMA		1	0	1	2
-#M - HISTIOCYTIC SARCOMA		0	0	1	0
-#M - HEMANGIOSARCOMA		0	0	1	0
-#B - CHOLANGIOMA		1	0	0	0
LY.NODE,UNDESIG.		(1)	(0)	(0)	(0)
LUNG					
-#B - BRONCHOALVEOLAR ADENOMA		1	0	0	0

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P A T H O L O G Y S E C T I O N
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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

T I S S U E S W I T H F I N D I N G S	ANIMAL SEX :	----- N U M B E R O F A N I M A L S A F F E C T E D -------- ---- F E M A L E S ---------			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	60	60	60	60
MAMMARY GLAND		(58)	(54)	(59)	(57)
-#B - ADENOMA/ADENOFIBROMA/FIBROMA		25	24	27	28
-#M - CARCINOMA/ADENOCARCINOMA		13	10	14	9
-#M - CARCINOSARCOMA		1	0	0	1
LY.NODE,MESENT.			(59)	(59)	
MESENTERY/OM'TUM		(0)	(3)	(2)	(0)
-#B - LIPOMA			1	0	
NOSE/TURBINATES					
-#M - SQUAMOUS CELL CARCINOMA, NASOLACRIMAL DUCT		0	1	0	0
OVARY(IES)					(59)
-#B - GRANULOSA CELL TUMOR		0	2	1	0
-#B - THECA CELL TUMOR		1	0	0	0
PANCREAS					(59)
-#B - ISLET CELL ADENOMA		5	1	4	0
PAWS/FEET		(2)	(3)	(2)	(3)
PITUITARY					(59)
-#B - ADENOMA, PARS DISTALIS		45	48	46	34
-#M - CARCINOMA, PARS DISTALIS		1	0	0	1
PARATHYROID(S)		(59)	(57)	(59)	
-#B - ADENOMA		2	1	2	0
SKIN		(59)	(56)	(59)	(58)
-#M - SQUAMOUS CELL CARCINOMA		0	0	0	1
-#B - ADENOMA, ZYMBAL'S GLAND		0	0	1	0
-#B - BASAL CELL TUMOR		1	0	0	0
-#B - CLITORAL GLAND ADENOMA		1	0	0	0
SPLEEN		0	0	0	1
-#M - LYMPHOMA / LYMPHOSARCOMA		0	0	0	1
-#B - HEMANGIOMA		0	0	0	0
-#M - HEMANGIOSARCOMA		1	0	0	0

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*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***
SELECTION CRITERIA: ALL DEATHS REPORTED

TISSUES WITH FINDINGS	ANIMAL SEX :	----- NUMBER OF ANIMALS AFFECTED ----- FEMALES			
	DOSAGE GROUP:	FN	F1	F2	F3
	NO. IN GROUP:	60	60	60	60
SP.CORD,THORACIC				(59)	
THYROID(S)					
-#B - C CELL ADENOMA		2	2	6	6
-#M - C CELL CARCINOMA		0	0	1	0
-#B- FOLLICULAR ADENOMA/CYSTADENOMA		1	0	0	1
-#M - FOLLICULAR CELL CARCINOMA		0	0	0	1
THYMUS		(43)	(51)	(39)	(44)
-#M - LYMPHOMA / LYMPHOSARCOMA		5	3	2	1
URINARY BLADDER			(58)	(59)	(59)
-#B - POLYP/PAPILLOMA		0	0	1	0
UTERUS					(59)
-#B - POLYP		1	2	2	2
-#B-VASCULAR HAMARTOMA		0	0	1	0
-#M - STROMAL SARCOMA		0	0	1	0
-#B - ADENOMA, ENDOMETRIAL		0	2	0	0
-#B - LEIOMYOMA		1	0	0	0
-#B - FIBROMA		1	0	0	0
VAGINA		(1)	(0)	(2)	(3)
-#B - FIBROMA		0		0	1
SUBCUTIS		(4)	(1)	(4)	(6)
-#M - FIBROUS HISTIOCYTOMA		1	1	0	2
-#B - FIBROMA		1	0	1	2
-#M - FIBROSARCOMA		2	0	0	0
-#B - LIPOMA		0	0	2	1
ORAL CAVITY		(0)	(1)	(1)	(1)
-#B - SQUAMOUS PAPILLOMA, PALATE			1	0	0
-#B - CHONDROMA, ALVEOLUS			0	0	1
-#M - GRANULAR CELL TUMOR			0	1	0
TOOTH		(0)	(1)	(0)	(0)

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P A T H O L O G Y S E C T I O N
STUDY TYPE: CH SPECIES: RAT SUBSTANCE: GLYPHOSATE PRINTED: 12-JUL-90

*** SUMMARY INCIDENCE OF HISTOPATHOLOGIC NEOPLASMS ***

SELECTION CRITERIA: ALL DEATHS REPORTED

NOTE: A NUMBER IN PARENTHESES OPPOSITE A TISSUE NAME INDICATES THE TOTAL NUMBER EXAMINED WHEN LESS THAN THE NUMBER OF ANIMALS IN THE GROUP.

* = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.05] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.
** = SIGNIFICANTLY DIFFERENT [P LESS THAN OR EQUAL TO 0.01] FROM CONTROL USING FISHER'S EXACT TEST WITH THE BONFERRONI INEQUALITY.

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

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
ABDOMEN:			(1)				(1)			(2)	(2)
Vasculitis			0				0			0	1
Focal chronic inflammation			0				1			0	0
Fat necrosis			1				0			2	1
ACCESSORY SEX GLAND(S):								(1)		(1)	(1)
CLITORAL GLAND: cystic duct(s)								1		0	1
CLITORAL GLAND: abscess(es)								0		1	0
ADRENALS:		(49)	(25)	(17)	(21)	(49)	(48)	(26)	(29)	(30)	(49)
No abnormality detected		15	16	13	10	15	6	5	5	6	6
Unilateral focal cortical hyperplasia		0	0	0	2	0	0	2	1	1	1
Focal cortical hyperplasia		1	1	0	0	3	1	0	0	0	0
Unilateral CORTICAL CARCINOMA [M]		0	0	0	0	1	0	0	0	1	0
Metastasising CORTICAL CARCINOMA [M]		0	0	0	0	0	0	0	0	1	0
Unilateral CORTICAL ADENOMA [B]		2	0	0	0	0	0	0	0	0	0
Unilateral focal medullary hyperplasia		5	0	0	1	7	3	1	1	0	1
Bilateral focal medullary hyperplasia		1	0	0	1	3	1	0	1	0	0
Focal medullary hyperplasia		0	0	0	0	0	1	0	0	0	0
Unilateral PHAEOCHROMOCYTOMA [M]		1	0	0	0	1	0	0	0	0	0
Unilateral PHAEOCHROMOCYTOMA [B]		7	1	1	1	8	5	0	0	1	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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
ADRENALS:		(49)	(25)	(17)	(21)	(49)	(48)	(26)	(29)	(30)	(49)
Bilateral PHAEOCHROMOCYTOMA [B]		1	0	0	0	1	1	0	0	0	0
Infiltration by histiocytic cells		0	0	0	0	1	0	0	0	0	0
Haemorrhagic degeneration		6	1	1	2	1	35	18	21	18	32
Only one examined		1	1	0	1	0	0	1	0	0	0
Accessory cortical nodule		1	0	0	0	0	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	2	0	1	0	0	0	0
Medulla not examined		0	0	0	0	0	0	0	1	0	1
Only one medulla examined		0	0	0	0	0	3	0	1	1	1
Subcapsular hyperplasia		1	0	0	0	0	0	0	0	0	0
Diffuse cortical hyperplasia		0	0	0	0	1	0	0	0	0	0
Cortical small-cell focus(i)		1	0	0	0	0	0	0	0	0	0
Zona glomerulosa not examined histologically		0	0	0	0	0	1	0	0	0	0
Focal cortical cell vacuolation		8	3	1	1	2	2	1	0	0	1
Diffuse cortical cell vacuolation		0	0	0	0	1	0	0	1	0	0
Necrosis		1	0	0	1	0	2	0	2	0	0
Focal cortical cell hypertrophy		18	3	4	3	15	18	5	8	13	23
Grade(++++) focal cortical cell hypertrophy		0	0	0	0	0	0	1	0	0	1
Increased haemopoiesis		0	0	0	0	0	2	0	0	0	1
Haemopoiesis		0	0	0	0	1	0	0	2	4	0
Unilateral atrophy		0	0	0	0	0	1	0	0	1	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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
ADRENALS:		(49)	(25)	(17)	(21)	(49)	(48)	(26)	(29)	(30)	(49)
Angiectasis		0	0	0	1	0	0	0	0	0	0
Autolysed, diagnosis difficult		5	7	3	3	1	2	1	2	2	3
Extra section(s) examined		0	0	0	0	1	0	0	0	0	0
AORTA:		(50)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected		50	25	18	20	50	50	28	29	30	50
Medial mineralisation		0	0	1	1	0	0	0	0	0	0
Autolysed, diagnosis difficult		0	0	1	0	0	0	0	0	0	0
BRAIN:		(50)	(25)	(19)	(21)	(50)	(49)	(28)	(29)	(30)	(50)
No abnormality detected		38	18	15	16	42	34	14	20	16	33
GRANULAR CELL TUMOUR [M]		0	0	0	0	1	0	0	0	0	0
Meningeal infiltration by histiocytic cells		0	0	0	0	1	0	0	0	0	0
Compression by pituitary		10	5	3	4	5	9	12	9	12	11
Infiltration by lymphoma cells		0	0	0	1	0	0	0	0	0	0
Focal chronic meningitis		0	0	1	0	0	0	0	0	0	0
Focal gliosis		0	0	0	0	0	0	0	0	0	2
GLIOMA [M]		2	1	0	0	1	0	1	0	0	0
Autolysed, diagnosis difficult		1	0	1	0	0	0	0	0	0	2

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)	(28)	(29)	(30)	(50)
Infiltration by pituitary tumour		1	1	0	1	0	6	4	1	2	6
Forebrain not available for histological examination		0	0	0	0	5	3	0	0	0	0
Cerebellum not examined histologically		0	0	0	0	0	1	0	0	0	1
CAECUM:		(42)	(8)	(6)	(12)	(43)	(43)	(23)	(23)	(26)	(42)
No abnormality detected		42	8	6	12	43	41	23	23	26	42
Infiltration by histiocytic cells		0	0	0	0	0	1	0	0	0	0
Infiltration by lymphoma cells		0	0	0	0	0	1	0	0	0	0
Autolysed, diagnosis difficult		0	0	0	1	0	1	0	1	1	1
CERVIX:							(1)				
No abnormality detected							1				
COLON:		(43)	(11)	(7)	(13)	(44)	(46)	(25)	(26)	(27)	(44)
No abnormality detected		43	11	6	13	42	46	25	26	27	44
Infiltration by histiocytic cells		0	0	0	0	1	0	0	0	0	0
Perivasculitis		0	0	0	0	1	0	0	0	0	0
Hypertrophy in muscle layer		0	0	1	0	0	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(11)	(7)	(13)	(44)	(46)	(25)	(26)	(27)	(44)
Dilatation		0	0	1	0	1	0	0	0	0	0
Autolysed, diagnosis difficult		1	1	1	1	1	2	0	2	0	2
DUODENUM:		(47)	(12)	(10)	(14)	(46)	(47)	(26)	(27)	(29)	(46)
No abnormality detected		46	12	10	14	45	46	26	27	29	45
CARCINOMA [M]		0	0	0	0	0	0	0	0	0	1
Infiltration by histiocytic cells		0	0	0	0	0	1	0	0	0	0
Serosal perivasculitis		1	0	0	0	0	0	0	0	0	0
Autolysed, diagnosis difficult		4	2	3	2	2	3	0	1	0	3
EYES:		(3)			(1)	(2)		(1)	(1)		
No abnormality detected		1			0	2		0	0		
Panophthalmitis		1			0	0		1	0		
Keratitis		1			0	0		0	0		
Haemorrhage		0			1	0		0	1		
Autolysed, diagnosis difficult		1			0	0		0	0		
HEART:		(50)	(24)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(49)
No abnormality detected		12	7	5	6	13	32	20	21	21	31

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)
Infiltration by histiocytic cells		0	0	0	0	0	1	1	0	0	1
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	0	0	0	1	0	0	0
Cardiomyopathy(mineralised)		1	1	0	1	0	0	0	0	0	0
Cardiomyopathy											
	(Grade +/-)	3	5	1	1	6	5	5	5	4	4
	(Grade +)	18	8	7	10	21	8	2	2	4	12
	(Grade ++)	15	3	5	3	7	0	0	0	0	0
	(Grade +++)	1	0	0	0	0	0	0	0	0	0
Total incidence for score expanded finding		37	16	13	14	34	13	7	7	8	16
Metastasis from primary in adrenal		0	0	0	0	0	0	0	0	1	0
Atrial thrombus		0	1	1	0	0	0	0	0	0	0
Myocarditis		0	0	1	0	3	3	1	2	1	1
Vascular mineralisation		0	0	1	0	0	0	0	0	0	0
Focus(i) of mast-cell infiltration		0	0	0	0	0	1	0	0	0	0
Endocarditis		0	0	0	0	1	1	0	0	0	0
Autolysed, diagnosis difficult		0	0	0	0	0	1	0	0	0	0
ILEUM:		(42)	(8)	(7)	(12)	(43)	(45)	(23)	(25)	(25)	(42)
No abnormality detected		42	8	7	12	43	44	23	25	25	42

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
ILEUM:		(42)	(8)	(7)	(12)	(43)	(45)	(23)	(25)	(25)	(42)
Infiltration by lymphoma cells		0	0	0	0	0	1	0	0	0	0
Autolysed, diagnosis difficult		0	0	1	0	0	0	0	1	1	1
JEJUNUM:		(43)	(9)	(8)	(15)	(45)	(45)	(24)	(26)	(28)	(44)
No abnormality detected		42	9	8	15	45	45	24	26	28	44
Mucosa damaged		1	0	0	0	0	0	0	0	0	0
Autolysed, diagnosis difficult		0	0	1	3	1	1	0	1	1	1
KIDNEYS:		(50)	(50)	(50)	(50)	(50)	(50)	(49)	(50)	(49)	(50)
No abnormality detected		7	12	10	6	8	9	12	17	10	13
Mesenchymal TUMOUR [M]		0	0	0	0	0	1	0	0	0	0
Unilateral TUBULAR ADENOMA [B]		1	0	0	0	0	0	0	0	0	0
Metastasising urothelial CARCINOMA [M]		0	0	0	1	0	0	0	0	0	0
Infiltration by histiocytic cells		0	0	0	0	2	1	1	0	1	1
Abnormal shape		0	0	0	1	0	0	0	0	0	0
Urothelial hyperplasia											
	(Grade +/-)	1	1	0	0	0	2	3	3	0	1
	(Grade +)	1	1	2	2	3	14	11	9	9	0***
	(Grade ++)	1	0	0	0	0	2	3	1	0	0
Total incidence for score expanded finding		3	2	2	2	3	18	17	13	9	1***

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)	(50)	(49)	(50)
Nephropathy											
	(Grade +/-)	5	8	5	9	15*	14	7	5*	6	13
	(Grade +)	20	17	16	20	10*	9	12	10	19*	7
	(Grade ++)	9	8	12	7	9	2	2	0	1	6
	(Grade +++)	6	4	0*	1	0*	0	0	0	0	1
Total incidence for score expanded finding		40	37	33	37	34	25	21	15	26	27
Infiltration by lymphoma cells		0	0	0	2	0	0	0	0	0	0
Basophilic tubules		1	0	1	1	4	1	1	0	0	0
Tubular dilatation		2	1	1	3	0	2	4	10*	3	4
Pelvic dilatation		1	0	1	3	1	0	0	1	1	1
Papillary necrosis		1	0	0	1	1	0	0	0	0	0
Cortical tubular hyaline inclusions		0	1	0	0	2	1	1	0	0	1
Mineral deposit(s)		0	0	2	0	0	0	0	0	0	0
Cortical brown pigment deposit(s)		0	0	0	1	1	1	0	3	2	0
Lymphocytic infiltration		1	0	0	0	1	1	1	0	0	0
Cortical tubular vacuolation		0	0	0	0	0	1	0	1	0	0
Pyelonephritis		0	0	1	1	0	0	0	0	0	0
Pyelitis		0	0	0	2	2	0	2	1	1	0
Perivasculitis		0	0	0	0	0	0	0	0	0	1
Glomerular nephropathy		0	0	1	0	0	0	0	0	0	0
Tubular necrosis		0	0	0	0	0	2	1	0	1	1

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)	(50)	(49)	(50)
Inflammatory cell infiltrate		0	0	1	0	0	0	0	0	0	1
Focal inflammation		0	0	1	0	0	1	1	0	0	0
Cyst(s)		2	0	1	2	1	1	1	0	2	0
Autolysed, diagnosis difficult		7	14	9	4	7	7	3	5	4	6
Tumour infiltration		0	0	0	0	0	0	1	0	0	0
LACRIMAL GLANDS:		(1)				(1)					
No abnormality detected		1				0					
Focal cellular atypia		0				1					
LIVER:		(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
No abnormality detected		2	2	6	6	1	8	2	5	5	7
Haemangioma present		0	0	1	0	0	0	0	1	0	0
Focal hepatocellular hyperplasia		0	0	1	0	0	0	0	0	1	0
HEPATOCELLULAR CARCINOMA MULTIPLE [M]		0	1	0	0	0	0	0	0	0	0
HEPATOCELLULAR CARCINOMA [M]		0	0	1	0	0	0	0	0	0	0
HEPATOCELLULAR ADENOMA MULTIPLE [B]		0	0	0	1	0	0	1	3	0	0
HEPATOCELLULAR ADENOMA [B]		2	1	1	1	2	0	0	0	1	2
Infiltration by histiocytic cells		0	0	0	1	1	1	1	0	2	2

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
LIVER:		(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Foamy hepatocytes (bifurcation of median lobe)		0	1	0	0	0	0	0	0	0	0
Foamy hepatocytes		8	1*	5	7	4	5	9	6	11	6
Portal tract sclerosis											
	(Grade +/-)	5	1	1	2	1	1	1	3	5	5
	(Grade +)	8	22**	11	19*	13	2	3	2	3	3
	(Grade ++)	5	2	4	2	2	1	0	0	0	0
Total incidence for score expanded finding		18	25	16	23	16	4	4	5	8	8
Spongiosis hepatis		17	18	22	17	11	0	1	1	1	0
Clear cell focus(i)											
	(Grade +/-)	1	0	1	1	1	0	1	0	0	0
	(Grade +)	8	4	7	5	7	4	3	0	5	3
	(Grade ++)	1	3	1	4	5	2	0	0	0	0
	(Grade +++)	0	0	0	0	1	0	0	0	0	0
Total incidence for score expanded finding		10	7	9	10	14	6	4	0*	5	3
Pale cell focus(i)											
	(Grade +/-)	1	0	0	2	0	0	1	1	1	0
	(Grade +)	9	8	9	3	8	5	5	6	7	3
	(Grade ++)	2	6	6	1	2	1	2	0	0	1
	(Grade +++)	0	0	0	0	2	0	0	0	0	1

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
LIVER:		(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Total incidence for score expanded finding		12	14	15	6	12	6	8	7	8	5
Basophilic focus(i)											
	(Grade +/-)	1	2	1	0	0	1	0	0	3	1
	(Grade +)	9	2	5	2	5	11	6	10	15	11
	(Grade ++)	0	0	2	0	3	7	8	14	5	2
	(Grade +++)	0	0	0	0	0	3	1	2	1	0
Total incidence for score expanded finding		10	4	8	2*	8	22	15	26	24	14
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	1	0	1	1	0	0	2
Dilated sinusoids		1	1	0	0	0	0	0	0	0	0
Bile duct hyperplasia											
	(Grade +/-)	4	1	0	1	1	0	3	1	0	3
	(Grade +)	15	13	15	19	11	4	8	8	5	3
	(Grade ++)	8	9	5	2	3	2	2	0	2	5
Total incidence for score expanded finding		27	23	20	22	15*	6	13	9	7	11
Extramedullary haemopoiesis		1	0	0	0	1	4	2	0	1	5
Lymphocytic infiltration		1	0	0	0	1	0	0	0	0	0
Haemocyst(s)		0	0	0	0	0	0	1	0	0	0
Vacuolation		18	13	11	12	15	13	16	18	16	13

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
LIVER:		(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Necrosis		0	2	2	1	0	3	4	0	4	5
Inflammatory cell infiltrate		2	3	2	3	5	2	6	3	2	2
Chronic periportal inflammation		0	0	0	0	1	0	0	0	0	0
Focal inflammation		1	0	4	5	4	1	0	0	1	2
Periportal hypertrophy		0	0	0	0	0	1	1	0	0	0
Centrilobular hypertrophy		0	0	1	0	0	0	1	0	0	0
Subcapsular fibrosis		3	0	0	0	0	0	0	0	0	0
Diffuse degeneration		0	1	1	0	0	0	0	0	0	0
Bile duct cyst(s)		0	0	1	1	0	2	0	2	2	2
Cyst(s)		0	0	0	0	0	1	0	0	0	0
Congestion		5	0	0	0	3	1	0	0	0	0
Angiectasis		16	8	13	12	13	15	22	10	12	13
Autolysed, diagnosis difficult		5	6	9	3	3	7	3	2	4	5
Increased mitotic rate		0	0	1	0	1	0	1	0	0	0
Extra section(s) examined		0	0	0	0	0	0	0	0	1	2
Tumour infiltration		0	0	0	0	0	0	1	0	0	0
LUNGS:		(50)	(49)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
No abnormality detected		20	29	20	27	25	25	36*	34	35	24
Metastasising SQUAMOUS-CELL CARCINOMA MULTIPLE [M]		0	0	0	1	0	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
LUNGS:		(50)	(49)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Metastasising ALVEOLAR/BRONCHIOLAR CARCINOMA MULTIPLE [M]		0	0	0	0	0	0	0	1	0	0
ALVEOLAR/BRONCHIOLAR ADENOMA [B]		2	0	1	2	0	0	0	0	0	0
SARCOMA [M]		0	0	0	0	0	1	0	0	0	0
Infiltration by histiocytic cells		0	0	0	1	2	0	1	0	2	2
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	1	0	0	1	0	0	1
Interstitial pneumonitis		2	4	4	2	3	3	1	2	1	3
Increased alveolar macrophages		9	7	5	1*	6	3	2	2	1	3
Food present		1	0	0	0	0	0	0	0	0	0
Focal alveolitis		13	9	16	13	8	16	9	12	9	12
Metastasis from primary in uterus		0	0	0	0	0	0	1	0	0	0
Metastasis from primary in thyroid		0	0	0	1	0	0	0	0	0	0
Metastasis from primary in kidney		0	0	0	1	0	0	0	0	0	0
Metastasis from primary in adrenal		0	0	0	0	0	0	0	0	1	0
Alveolar pigmented macrophages		0	1	1	0	0	0	0	0	0	0
Perivascular lymphocytic infiltration		2	1	0	0	0	0	0	0	0	0
Grade(++++) granuloma(ta)		0	0	0	0	0	0	0	0	0	1
Granuloma(ta)		0	3	0	2	1	0	0	0	0	0
Focal chronic pleurisy		0	0	1	0	0	0	0	0	0	0
Oedema		1	0	3	0	1	0	0	0	0	0
Inflammatory cell infiltrate		0	0	1	1	0	2	0	0	1	2

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
LUNGS:		(50)	(49)	(49)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Haemorrhage(s)		0	0	1	0	0	0	1	0	0	0
Alveolar epithelialisation		0	1	0	0	0	1	0	0	0	1
Congestion		4	3	3	1	5	0	0	0	0	1
Bronchopneumonia		1	0	0	0	0	0	0	0	0	0
Autolysed, diagnosis difficult		3	8	3	4	1	4	2	4	2	4
Tumour metastasis (primary site unknown)		0	0	1	0	0	0	1	0	0	0
Only two lobes available for histological examination		0	0	0	0	0	0	0	0	0	1
Only one lobe examined		0	0	0	0	0	0	1	0	0	0
LYMPH NODE(S):		(10)	(6)	(5)	(5)	(15)	(23)	(9)	(15)	(21)	(28)
Infiltration by histiocytic cells		0	1	0	0	0	0	1	1	0	0
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	1	0	1	1	0	0	1
Lymph nodes local to mass or with necropsy findings with no abnormality detected		5	3	3	3	9	15	3	10	16	16
Lymph nodes local to mass or with necropsy findings but were not available for histological examination		1	1	0	1	2	1	1	2	2	3
Tumour metastasis		0	0	0	1	0	0	0	0	1	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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(6)	(5)	(5)	(15)	(23)	(9)	(15)	(21)	(28)
Pigmented macrophages		0	0	0	0	0	2	0	0	0	2
Reactive		3	1	2	0	3	9	3	4	4	11
Cyst(s)		1	0	0	0	1	1	0	0	0	1
Congestion		0	1	0	0	1	0	1	1	2	1
Autolysed, diagnosis difficult		0	0	0	0	1	0	0	0	0	0
LYMPHORETICULAR/HAEMOPOIETIC TISSUE:		(1)	(2)		(3)	(5)	(4)	(2)	(1)	(2)	(5)
HISTIOCYTIC SARCOMA [M]		1	1		1	3	3	1	1	2	3
LYMPHOMA in thymus only [M]		0	1		0	1	0	0	0	0	0
LYMPHOMA [M]		0	0		2	1	1	1	0	0	2
MAMMARY GLANDS:		(45)	(25)	(17)	(21)	(47)	(50)	(28)	(29)	(30)	(50)
No abnormality detected		16	11	7	11	22	3	2	5	1	2
FIBROADENOMA MULTIPLE [B]		0	0	0	0	0	10	6	5	8	12
FIBROADENOMA [B]		0	0	0	0	1	19	6	12	11	17
CARCINOMA MULTIPLE [M]		0	0	0	0	0	1	0	0	0	2
Metastasising CARCINOMA [M]		0	0	0	0	0	0	0	0	1	0
CARCINOMA [M]		0	1	0	0	0	6	1	1	2	4
ADENOMA [B]		0	0	0	0	0	2	1	3	4	3
Focal alveolar hyperplasia		0	0	0	0	0	0	2	1	4	1

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(17)	(21)	(47)	(50)	(28)	(29)	(30)	(50)
Infiltration by histiocytic cells		0	0	0	0	0	0	1	0	0	1
Mammary development		28	14	10	10	24	40	24	16	28	38
Focus(i) of pigmented macrophages		0	0	0	0	0	0	0	1	0	0
Focal lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0
Chronic inflammation		0	0	0	0	0	1	0	2	0	0
Inflammation		0	0	0	0	0	2	0	0	0	0
Abscess(es)		0	0	0	0	0	0	0	0	0	1
Autolysed, diagnosis difficult		0	1	0	0	0	1	0	0	1	1
MESENTERIC LYMPH NODE:		(50)	(24)	(19)	(21)	(50)	(48)	(28)	(29)	(30)	(49)
No abnormality detected		47	23	19	19	44	46	28	26	30	45
Haemangioma present		1	1	0	0	0	0	0	0	0	0
Infiltration by histiocytic cells		1	0	0	0	2	0	0	1	0	0
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	0	0	1	0	0	0	1
Lymphoid depletion		0	0	0	1	0	0	0	0	0	0
Pigmented macrophages		0	0	0	0	0	1	0	1	0	2
Reactive		0	0	0	0	1	0	0	1	0	1
Cyst(s)		1	0	0	0	0	0	0	0	0	0
Congestion		0	0	0	1	2	1	0	1	0	0
Autolysed, diagnosis difficult		1	0	0	0	1	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
MESENTERY:					(1)						(1)
MESOTHELIOMA [B]					0						1
Abscess(es)					1						0
OESOPHAGUS:		(49)	(24)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected		49	24	19	20	50	50	28	29	30	49
Infiltration by histiocytic cells		0	0	0	0	0	0	0	0	0	1
Infiltration by thyroid tumour		0	0	0	1	0	0	0	0	0	0
OPTIC NERVE:		(1)		(1)	(1)						
No abnormality detected		1		1	1						
Autolysed, diagnosis difficult		0		1	0						
OVARIES:							(50)	(28)	(29)	(29)	(50)
No abnormality detected							19	13	9	9	20
Unilateral GRANULOSA/THECAL CELL TUMOUR [B]							0	0	1	0	0
Infiltration by histiocytic cells							1	0	0	1	0
Only one examined							1	0	0	0	0
Cystic follicle(s)							10	4	7	4	10

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
OVARIES:							(50)	(28)	(29)	(29)	(50)
Stromal hyperplasia							1	2	1	2	4
Bursal cyst(s)							2	0	1	2	1
Atrophy							21	12	12	15	19
Autolysed, diagnosis difficult							4	1	1	0	3
Tumour infiltration							0	1	0	0	0
PANCREAS:		(50)	(24)	(17)	(21)	(49)	(49)	(27)	(29)	(29)	(49)
No abnormality detected		21	13	13	16	37**	41	21	24	26	42
Islet hyperplasia		2	0	0	0	1	0	0	0	0	0
EXOCRINE CARCINOMA [M]		0	0	0	0	0	1	0	0	0	0
EXOCRINE ADENOMA [B]		3	0	1	0	0	0	0	0	0	0
ISLET ADENOMA [B]		7	1	2	2	1	1	2	2	2	1
Infiltration by histiocytic cells		0	0	0	0	1	1	0	1	0	0
Dilated duct(s)		1	0	0	0	0	0	1	0	0	0
Acinar atrophy		9	7	1	3	6	4	3	1	1	4
Pigment deposit(s)		0	0	0	0	0	0	0	1	0	0
Lymphocytic infiltration		0	0	0	0	1	0	0	0	0	0
Granuloma(ta)		1	0	0	0	0	0	0	0	0	0
Thrombus (canalised)		0	0	0	0	1	0	0	0	0	0
Perivasculitis		1	0	0	0	1	1	0	0	0	2
Interstitial oedema		0	1	0	0	0	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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:		(50)	(24)	(17)	(21)	(49)	(49)	(27)	(29)	(29)	(49)
Perivascular inflammatory cell infiltrate		0	1	0	0	0	0	0	0	0	0
Acinar hypertrophy		3	1	0	0	1	0	0	0	0	0
Ductal hyperplasia		4	1	0	0	1	0	0	0	0	0
Autolysed, diagnosis difficult		3	9	5	5	3	1	1	2	0	4
Extra section(s) examined		0	0	0	0	0	0	0	1	0	0
Infiltration by uterus tumour		0	0	0	0	0	0	1	0	0	0
PARATHYROIDS:		(44)	(20)	(17)	(19)	(46)	(46)	(26)	(23)	(24)	(41)
No abnormality detected		42	20	17	18	46	45	26	23	23	38
Unilateral focal hyperplasia		1	0	0	0	0	0	0	0	0	0
Unilateral ADENOMA [B]		1	0	0	0	0	1	0	0	0	1
Only one examined		14	5	6	1	15	9	4	6	5	15
Fibrosis		0	0	0	0	0	0	0	0	0	2
Haemorrhagic cyst(s)		0	0	0	1	0	0	0	0	0	0
Cyst(s)		0	0	0	0	0	0	0	0	1	0
Autolysed, diagnosis difficult		0	0	0	0	0	0	0	0	0	1
PITUITARY:		(50)	(24)	(19)	(21)	(50)	(49)	(28)	(29)	(30)	(49)
No abnormality detected		15	10	8	9	24	7	3	9	2	6
Only anterior lobe examined		5	5	1	0	6	0	0	1	0	3

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
PITUITARY:		(50)	(24)	(19)	(21)	(50)	(49)	(28)	(29)	(30)	(49)
CARCINOMA [M]		1	1	0	1	0	7	5	1	2	7
ADENOMA MULTIPLE [B]		0	0	0	0	0	2	0	0	0	4
ADENOMA [B]		28	12	8	7	17*	33	19	19	25	30
Focal hyperplasia		4	1	2	3	7	0	0	0	0	2
Intermediate lobe hyperplasia		1	0	0	0	0	0	0	0	0	0
Damaged		0	0	0	0	1	0	0	0	0	0
Posterior lobe not examined histologically		3	0	4	1	2	1	0	0	0	2
Cyst(s)		4	0	2	1	5	1	1	0	2	3
Autolysed, diagnosis difficult		1	1	4	2	3	2	1	2	1	1
Anatomical defect (possibly congenital)		0	0	0	0	1	0	0	0	0	0
PROSTATE:		(50)	(24)	(18)	(21)	(50)					
No abnormality detected		42	23	14	17	43					
CARCINOMA [M]		0	0	0	0	1					
ADENOMA [B]		0	0	0	0	1					
Focal lymphocytic infiltration		1	0	0	0	0					
Inflammation		6	1	4	4	5					
Interstitial fibrosis		1	0	0	0	0					
Autolysed, diagnosis difficult		0	0	2	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
RECTUM:		(43)	(12)	(8)	(13)	(44)	(46)	(26)	(28)	(27)	(43)
No abnormality detected		42	12	8	13	43	45	25	28	27	43
Infiltration by histiocytic cells		0	0	0	0	1	0	1	0	0	0
Infiltration by lymphoma cells		0	0	0	0	0	1	0	0	0	0
Lymphocytic hyperplasia		1	0	0	0	0	0	0	0	0	0
Dilatation		0	0	0	0	1	0	0	0	0	0
Autolysed, diagnosis difficult		1	2	2	1	1	3	1	4	0	1
SALIVARY GLAND:		(50)	(46)	(49)	(50)	(49)	(50)	(50)	(50)	(50)	(48)
No abnormality detected		1	1	0	0	0	1	1	1	0	0
PAROTID: NAD		35	30	25	8***	12***	35	33	31	21**	8***
SUBLINGUAL: NAD		48	45	49	50	47	49	47	49	46	45
MANDIBULAR: NAD		41	40	27**	8***	17***	38	40	37	32	21**
PAROTID: not examined histologically		0	1	3	1	0	9	7	5	7	1*
SUBLINGUAL: not examined histologically		1	0	0	0	2	0	2	0	4	2
MANDIBULAR: not examined histologically		0	0	0	0	0	0	1	0	0	0
PAROTID: FIBROMA [B]		1	0	0	0	0	0	0	0	0	0
MANDIBULAR: FIBROMA [B]		0	0	0	0	0	0	0	1	0	0
PAROTID: infiltration by histiocytic cells		0	1	0	0	0	0	0	0	0	1
MANDIBULAR: infiltration by histiocytic cells		0	0	0	0	1	0	0	0	0	1

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)

FINDINGS / TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
	MALES					FEMALES				
	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)	(46)	(49)	(50)	(49)	(50)	(50)	(50)	(50)	(48)
PAROTID: dilated/cystic duct(s)	0	1	0	0	0	0	0	0	1	0
MANDIBULAR: hyperplastic focus(i)	0	0	0	0	1	0	0	0	0	0
PAROTID: lymphocytic infiltration	1	0	0	0	1	0	0	0	0	0
MANDIBULAR: perivasculitis	0	0	0	0	1	0	0	0	0	0
MANDIBULAR: inflammation	0	0	0	0	0	1	0	0	0	1
SUBLINGUAL: acinar hypertrophy	0	0	0	0	0	0	0	0	0	1
PAROTID: ductal hyperplasia	0	0	0	0	1	1	0	0	0	1
MANDIBULAR: ductal hyperplasia	0	0	0	0	0	0	0	0	0	1
MANDIBULAR: hyperplasia	1	0	0	0	0	0	0	0	0	0
PAROTID: acinar atrophy	5	4	0	0	2	1	1	1	0	3
PAROTID: cellular alteration										
(Grade +/-)	4	4	8	3	4	1	2	2	2	5
(Grade +)	3	5	9	21***	14**	0	5	9**	9**	13***
(Grade ++)	0	0	4	17***	18***	1	1	1	9*	18***
(Grade +++)	0	0	0	0	0	0	0	0	1	2
Total incidence for score expanded finding	7	9	21**	41***	36***	2	8	12**	21***	38***
MANDIBULAR: cellular alteration										
(Grade +/-)	7	5	10	14	9	2	0	3	1	6
(Grade +)	0	0	12***	28***	22***	9	8	9	15	19*
(Grade ++)	0	0	0	0	0	0	0	0	2	1
Total incidence for score expanded finding	7	5	22***	42***	31***	11	8	12	18	26**

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(46)	(49)	(50)	(49)	(50)	(50)	(50)	(50)	(48)
Autolysed, diagnosis difficult		7	10	10	9	6	7	3	4	5	5
SCIATIC NERVE:		(50)	(25)	(19)	(21)	(50)	(49)	(28)	(29)	(30)	(49)
No abnormality detected		44	25	16	19	46	49	27	28	30	49
Infiltration by histiocytic cells		0	0	0	0	0	0	1	0	0	0
Chronic inflammatory cell infiltrate		0	0	0	0	1	0	0	0	0	0
Axonal degeneration		6	0	3	2	3	0	0	1	0	0
Autolysed, diagnosis difficult		0	0	2	0	0	0	0	0	0	0
SEMINAL VESICLES:		(2)	(2)	(2)	(2)	(2)					
No abnormality detected		1	2	2	1	2					
Serosal inflammation		1	0	0	0	0					
Haemorrhage(s)		0	0	0	1	0					
SKELETAL MUSCLE:		(50)	(25)	(19)	(21)	(50)	(50)	(27)	(29)	(30)	(50)
No abnormality detected		45	25	18	20	45	50	26	29	29	50
Infiltration by histiocytic cells		0	0	0	0	0	0	1	0	0	0
Focal lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0
Myositis		0	0	0	1	2	0	0	0	1	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)

FINDINGS / TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
	MALES					FEMALES				
	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
SKELETAL MUSCLE:	(50)	(25)	(19)	(21)	(50)	(50)	(27)	(29)	(30)	(50)
Focal inflammatory cell infiltrate	0	0	0	0	1	0	0	0	0	0
Myofibre degeneration	4	0	1	0	2	0	0	0	0	0
Autolysed, diagnosis difficult	0	0	1	0	0	0	0	0	0	0
SKIN/SUBCUTIS:	(50)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected	31	15	11	12	29	42	23	20	25	43
TRICHOEPITHELIOMA [M]	0	1	0	0	1	0	0	0	0	0
BASAL CELL TUMOUR [M]	1	0	0	0	0	0	0	1	0	0
SEBACEOUS CARCINOMA [M]	0	0	0	0	0	1	0	0	0	0
ZYMBAL'S GLAND: CARCINOMA [M]	1	0	0	0	0	1	0	1	0	0
SQUAMOUS-CELL CARCINOMA [M]	0	0	0	0	1	0	1	0	0	0
SARCOMA [M]	0	1	1	0	0	1	0	0	0	0
SCHWANNOMA [M]	0	1	0	0	0	0	0	0	0	0
PAPILLOMA [B]	0	0	0	1	0	0	0	0	0	0
FIBROSARCOMA [M]	1	1	0	2	2	0	0	0	0	0
FIBROMA MULTIPLE [B]	1	0	1	0	1	0	0	0	0	0
FIBROMA [B]	7	2	0	1	5	1	2	2	1	2
Dermal FIBROMA MULTIPLE [B]	0	1	0	0	0	0	0	0	0	0
Dermal FIBROMA [B]	2	0	2	1	2	0	0	0	0	0
LIPOMA [B]	1	0	1	0	0	0	0	0	0	2

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
SKIN/SUBCUTIS:		(50)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
INTRACUTANEOUS CORNIFYING EPITHELIOMA MULTIPLE [B]		0	0	0	0	1	0	0	0	0	0
INTRACUTANEOUS CORNIFYING EPITHELIOMA [B]		1	2	0	0	4	1	0	0	0	0
Infiltration by histiocytic cells		0	0	0	1	0	0	0	0	0	1
Subcutaneous oedema		0	1	0	0	0	0	0	0	0	0
Epithelial hyperplasia		1	0	0	0	0	0	0	1	0	0
Dermal fibrosis		0	1	0	0	0	0	0	0	0	0
Inflammation		1	0	2	1	3	0	0	1	2	0
Sebaceous cyst(s)		0	0	0	0	1	0	0	0	0	0
Dermal cyst(s)		0	1	0	0	5	1	0	1	1	0
Abscess(es)		0	0	1	0	2	0	0	1	1	0
Autolysed, diagnosis difficult		0	1	0	0	0	0	0	0	0	0
Pododermatitis		4	3	2	2	4	4	4	1	1	3
SPINAL CORD:		(50)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected		49	25	19	19	46	50	27	29	29	50
Infiltration by lymphoma cells		0	0	0	2	0	0	0	0	0	0
Haemorrhage(s)		0	0	0	1	0	0	0	0	0	0
Neuronal degeneration		1	0	0	0	4	0	1	0	1	0
Autolysed, diagnosis difficult		0	0	1	0	0	0	0	0	0	0
Cervical not examined		1	0	0	0	0	0	0	0	0	1

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
Lumbar not examined		1	1	4	0	3	0	0	2	6	4
SPLEEN:		(50)	(25)	(19)	(21)	(49)	(49)	(27)	(29)	(30)	(50)
No abnormality detected		35	16	8	9	33	12	11	5	9	18
Haemangiosarcoma present		0	0	0	0	1	0	0	0	0	0
Infiltration by histiocytic cells		0	0	0	1	1	1	0	1	1	0
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	2	0	1	1	0	0	1
Lymphoid depletion		0	0	0	0	0	1	0	0	0	1
Increased extramedullary haemopoiesis		11	7	8	9	8	26	9	13	15	21
Inflammatory cell infiltrate		0	0	0	1	0	0	0	0	0	0
Chronic serosal inflammation		1	0	0	0	0	0	0	0	0	0
Lymphoid hyperplasia		1	0	0	2	1	0	0	0	1	0
Small cyst(s)		0	0	0	0	1	0	0	0	0	0
Congestion		2	0	0	0	0	0	0	0	0	0
Increased brown pigment		1	3	3	0	4	10	7	10	6	11
Autolysed, diagnosis difficult		4	11	6	2	3	4	1	2	1	3
Infiltration by uterus tumour		0	0	0	0	0	0	1	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
STERNUM:		(50)	(25)	(19)	(21)	(50)	(50)	(28)	(29)	(30)	(50)
No abnormality detected		50	25	19	19	49	48	26	29	29	50
Infiltration by histiocytic cells		0	0	0	1	1	0	1	0	1	0
Infiltration by lymphoma cells		0	0	0	1	0	0	1	0	0	0
Bone marrow hyperplasia		0	0	0	0	0	2	0	0	0	0
Autolysed, diagnosis difficult		1	0	0	0	0	0	0	0	0	0
STOMACH:		(50)	(23)	(15)	(18)	(50)	(48)	(27)	(27)	(29)	(47)
No abnormality detected		19	17	11	13	29	33	14	20	15	23
Dilated/cystic gland(s)		23	5	3	1	17	11	10	2	14	20
Keratinised cyst(s)		0	0	0	0	0	0	0	1	0	0
Ulceration in glandular region		0	0	0	0	0	0	0	1	0	0
Ulceration in non-glandular region		3	0	1	1	1	1	2	1	0	0
Perivasculitis		0	0	0	0	2	0	0	0	0	0
Submucosal oedema in non-glandular region		2	0	0	1	0	1	1	1	0	0
Mineralisation		0	0	1	1	0	0	0	0	0	0
Inflammation		6	1	1	1	3	1	2	1	1	5
Focal hyperplasia in non-glandular region		1	0	0	0	0	0	0	0	0	0
Hyperplasia in non-glandular region		3	1	1	3	3	3	5	2	0	3
Autolysed, diagnosis difficult		8	12	8	5	6	4	1	1	2	3

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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:		(6)	(3)	(2)	(2)	(3)	(6)	(1)	(4)	(1)	(12)
No abnormality detected		0	2	1	0	1	2	0	1	0	3
Infiltration by histiocytic cells		0	0	0	0	1	0	0	1	0	0
Infiltration by lymphoma cells		0	0	0	0	0	1	0	0	0	0
Reactive		6	0	1	1	0*	3	1	2	1	7
Congestion		0	1	0	2	1	0	0	0	0	2
TESTES:		(50)	(25)	(19)	(21)	(50)					
No abnormality detected		37	21	16	18	35					
Unilateral focal interstitial cell hyperplasia		0	0	0	1	0					
Bilateral focal interstitial cell hyperplasia		0	0	0	1	2					
Unilateral INTERSTITIAL-CELL ADENOMA [B]		3	1	0	0	0					
Bilateral INTERSTITIAL-CELL ADENOMA [B]		0	0	0	0	1					
INTERSTITIAL-CELL ADENOMA [B]		0	0	0	0	1					
Infiltration by histiocytic cells		0	0	0	0	1					
Only one examined		0	1	0	0	0					
Tubular atrophy		9	3	3	1	10					
Sperm granuloma		1	0	1	0	0					
Granuloma(ta)		1	0	0	0	0					
Perivasculitis		2	0	0	0	1					

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
TESTES:		(50)	(25)	(19)	(21)	(50)					
Mineralisation		0	1	0	1	1					
Autolysed, diagnosis difficult		1	1	1	0	1					
THORAX:						(1)					
MESOTHELIOMA [M]						1					
THYMUS:		(48)	(23)	(19)	(18)	(44)	(48)	(27)	(26)	(28)	(46)
No abnormality detected		40	21	19	16	37	35	20	19	17	26
THYMOMA [B]		1	0	0	0	0	0	0	0	0	0
Infiltration by histiocytic cells		0	0	0	1	2	0	0	0	1	0
Infiltration by leukaemic cells		0	0	0	0	1	0	0	0	0	0
Infiltration by lymphoma cells		0	1	0	1	1	0	0	0	0	1
Focal lymphoid hyperplasia		0	0	0	0	1	0	0	0	0	0
Epithelial hyperplasia		2	0	0	0	0	3	0	0	0	3
Haemorrhage(s)		0	0	0	0	0	0	0	0	2	0
Perivascular fibrosis		1	0	0	0	0	0	0	0	0	0
Cyst(s)		5	1	0	0	1	12	7	7	7	18
Congestion		2	0	0	0	1	0	0	0	0	0
Autolysed, diagnosis difficult		2	0	0	0	1	3	1	1	1	1

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)	(50)	(27)	(29)	(29)	(49)
No abnormality detected		35	19	15	16	33	34	21	18	22	31
Unilateral FOLLICULAR CARCINOMA [M]		0	0	0	1	0	0	0	0	0	0
Unilateral FOLLICULAR ADENOMA [B]		0	0	0	1	2	0	0	0	0	0
Unilateral focal follicular-cell hyperplasia		0	0	0	0	0	0	0	0	0	1
Unilateral C-CELL CARCINOMA [M]		0	0	0	0	1	0	0	0	0	0
Bilateral metastasising C-CELL CARCINOMA [M]		0	0	0	1	0	0	0	0	0	0
Unilateral C-CELL ADENOMA MULTIPLE [B]		0	0	0	0	0	0	0	0	1	1
Unilateral C-CELL ADENOMA [B]		9	1	1	2	7	6	1	1	1	6
Bilateral C-CELL ADENOMA [B]		0	0	0	0	1	2	0	0	0	0
Unilateral ADENOMA [B]		0	0	0	0	1	0	0	0	0	0
Unilateral focal c-cell hyperplasia		2	1	0	0	4	9	4	1	0	5
Bilateral focal c-cell hyperplasia		1	0	0	0	2	1	1	0	1	0
Dilated/cystic follicle(s)		2	0	0	0	2	1	0	3	4	6
Only one examined		0	0	0	1	0	0	0	0	0	0
Diffuse c-cell hyperplasia		1	0	1	0	0	2	0	6	1	5
Lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0
Perivasculitis		0	0	0	0	1	0	0	0	0	0
Bilateral diffuse follicular-cell hyperplasia		0	0	0	0	0	0	0	1	0	0
Autolysed, diagnosis difficult		7	10	7	8	5	5	1	5	0	5

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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)	(49)	(50)	(27)	(29)	(29)	(49)
Extra section(s) examined		0	0	0	2	1	1	0	0	0	0
TONGUE:								(1)			
Epithelial hyperplasia								1			
TRACHEA:		(50)	(23)	(18)	(21)	(50)	(50)	(27)	(29)	(30)	(49)
No abnormality detected		49	23	18	20	50	50	27	29	30	49
Inflammatory cell infiltrate		1	0	0	0	0	0	0	0	0	0
Autolysed, diagnosis difficult		1	0	0	0	0	2	0	1	0	1
Infiltration by thyroid tumour		0	0	0	1	0	0	0	0	0	0
URETER:					(1)						
Infiltration by lymphoma cells					1						
URINARY BLADDER:		(49)	(25)	(19)	(20)	(49)	(50)	(28)	(29)	(30)	(49)
No abnormality detected		47	23	15	15	45	50	27	29	30	49
Urothelial hyperplasia (Grade +)		0	0	0	0	1	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 51 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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
URINARY BLADDER:		(49)	(25)	(19)	(20)	(49)	(50)	(28)	(29)	(30)	(49)
Urothelial hyperplasia (Grade ++)		0	0	0	2	0	0	0	0	0	0
Total incidence for score expanded finding		0	0	0	2	1	0	0	0	0	0
Infiltration by lymphoma cells		0	0	0	1	0	0	0	0	0	0
Eosinophilic contents		0	2	0	1	3	0	0	0	0	0
Perivasculitis		0	0	0	0	1	0	0	0	0	0
Inflammation		2	0	1	3	0	0	0	0	0	0
Haemorrhage(s)		1	0	0	1	0	0	0	0	0	0
Dilatation		0	0	3	0	0	0	0	0	0	0
Autolysed, diagnosis difficult		0	8	2	1	0	4	1	0	0	2
Infiltration by uterus tumour		0	0	0	0	0	0	1	0	0	0
UTERUS:							(49)	(28)	(29)	(30)	(49)
No abnormality detected							38	26	19	20	39
STROMAL SARCOMA [M]							0	0	0	1	0
Metastasising endometrial CARCINOMA [M]							0	1	0	0	0
Endometrial CARCINOMA [M]							0	0	0	2	0
Endometrial ADENOMA [B]							1	0	0	0	0
POLYP MULTIPLE [B]							1	0	0	0	0
POLYP [B]							2	1	1	1	3

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)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)									
		MALES					FEMALES				
		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:							(49)	(28)	(29)	(30)	(49)
Infiltration by histiocytic cells							1	0	0	1	0
Dilated/cystic gland(s)							6	0	8	4	4
Pyometra							0	0	1	0	0
Myometrial hypertrophy							0	0	0	0	1
Dilatation							1	0	2	3	3
Autolysed, diagnosis difficult							3	0	0	1	1
VAGINA:									(1)		
No abnormality detected									1		
VASCULAR SYSTEM:		(1)	(1)	(1)		(1)			(1)		
HAEMANGIOMA [B]		1	1	1		0			1		
HAEMANGIOSARCOMA [M]		0	0	0		1			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

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

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)		(1)
No abnormality detected		2	3	1	6	3			1		0
Basophilic focus(i)											
	(Grade +/-)	0	2	2	3	0			0		0
Total incidence for score expanded finding		0	2	2	3	0			0		0
Pale cell focus(i)											
	(Grade +/-)	1	4	1	0	3			0		0
	(Grade +++)	0	0	1	0	0			0		0
Total incidence for score expanded finding		1	4	2	0	3			0		0
Clear cell focus(i)											
	(Grade +/-)	3	1	2	1	1			0		0
	(Grade +)	0	0	1	1	0			0		0
Total incidence for score expanded finding		3	1	3	2	1			0		0
Periportal hepatocyte hypertrophy		0	0	0	0	0			1		0
Spongiosis hepatis		0	0	0	1	0			0		0
Focus(i) of angiectasis		1	0	0	0	0			0		0
Focal cellular change with vascular changes		1	0	0	0	0			0		0
Foamy hepatocytes (bifurcation of median lobe)		3	0	0	2	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 (continued)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)		(1)
Bile duct hyperplasia		4	1	3	2	4			0		0
Vacuolation		3	6	3	1	3			0		0
Increased Kupffer-cell pigmentation		0	0	1	0	0			0		0
Necrosis		0	0	1	1	0			1		0
Inflammatory change(s)		8	5	7	4	7			0		1
Congestion		0	0	0	0	0			0		1
HEART:		(15)				(15)			(2)		(1)
No abnormality detected		3				7			1		1
Cardiomyopathy		12				8			1		0
KIDNEYS:		(15)	(15)	(15)	(15)	(15)			(1)		(1)
No abnormality detected		2	1	9*	5	6			0		1
Nephropathy											
	(Grade +/-)	10	4	1**	3*	4			0		0
	(Grade +)	2	3	0	1	1			0		0
	(Grade ++)	0	0	1	0	0			1		0
Total incidence for score expanded finding		12	7	2***	4**	5*			1		0
Basophilic tubules											
	(Grade +/-)	1	3	4	4	2			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 (continued)

FINDINGS / TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
	SURVIVORS					DECEDENTS				
	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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
KIDNEYS:	(15)	(15)	(15)	(15)	(15)			(1)		(1)
Total incidence for score expanded finding	1	3	4	4	2			0		0
Tubular dilatation (Grade +/-)	0	1	0	0	1			0		0
Total incidence for score expanded finding	0	1	0	0	1			0		0
Urothelial hyperplasia	1	1	1	0	2			0		0
Mineral deposit(s)	0	0	0	0	1			0		0
Pyelitis	3	5	0	2	1			0		0
Focus(i) of inflammation	0	1	0	0	0			0		0
Cyst(s)	0	0	0	1	2			0		0
LUNGS:	(15)	(15)	(15)	(15)	(15)			(2)		(1)
No abnormality detected	8	9	8	4	6			1		1
Alveolitis	2	1	1	4	0			0		0
Area(s) of interstitial pneumonitis	2	0	3	1	4			1		0
Focus(i) of increased alveolar macrophages	3	6	5	5	3			0		0
Focal inflammation	0	0	0	0	2			0		0
Lymphoid tissue increase	1	0	0	2	2			1		0
Medial hypertrophy	0	0	2	1	2			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 (continued)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)		(1)
Focal mineral deposit(s)		1	0	1	2	0			0		0
Agonal congestion		0	0	0	0	0			1		0
SPLEEN:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
ADRENALS:		(15)				(15)			(2)		(1)
No abnormality detected		8				6			2		1
Unilateral medullary hyperplasia		0				2			0		0
Unilateral cellular change (cortex)		3				3			0		0
Unilateral cellular change with degeneration/vascular dilatation		1				0			0		0
Subcapsular pale cell focus(i)		2				5			0		0
Focal subcapsular cellular change		1				0			0		0
THYMUS:		(15)				(13)			(1)		(1)
No abnormality detected		13				11			0		0
THYMOMA(TA) [B]		0				0			1		0
Increased atrophy		2				2			0		1

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)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
TESTES:		(15)				(15)			(2)		(1)
No abnormality detected		12				12			2		1
Interstitial-cell ADENOMA [B]		0				1			0		0
Tubular atrophy		3				2			0		0
PROSTATE:		(15)				(15)			(2)		(1)
No abnormality detected		15				13			1		1
Inflammation		0				2			1		0
SEMINAL VESICLES:											(1)
Secretion decreased											1
BRAIN:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
Fore-brain not available for examination		7				8			0		0
SPINAL CORD:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1

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)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
SKELETAL MUSCLE:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
PANCREAS:		(15)				(15)			(2)		(1)
No abnormality detected		10				13			1		1
Acinar atrophy		3				0			1		0
Focal inflammation		2				1			0		0
Pigment deposit(s)		0				1			0		0
SALIVARY GLAND:		(15)	(15)	(15)	(15)	(15)			(2)		(1)
MANDIBULAR: NAD		15	15	14	10*	3***			2		0
MANDIBULAR: cellular alteration (Grade +)		0	0	1	5*	12***			0		1
Total incidence for score expanded finding		0	0	1	5*	12***			0		1
PAROTID: NAD		14	15	6**	3***	0***			1		1
PAROTID: cellular alteration (Grade +)		0	0	8**	8**	4			1		0
(Grade ++)		0	0	1	4	7**			0		0
(Grade +++)		0	0	0	0	4			0		0
Total incidence for score expanded finding		0	0	9***	12***	15***			1		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 (continued)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 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)		(1)
PAROTID: inflammation		0	0	0	1	0			0		0
PAROTID: not examined histologically		1	0	0	0	0			0		0
SUBLINGUAL: NAD		15	15	15	13	15			2		1
SUBLINGUAL: not examined histologically		0	0	0	2	0			0		0
SUBMANDIBULAR LYMPH NODE:		(1)									
Plasmacytosis		1									
PITUITARY:		(15)				(15)			(1)		(1)
No abnormality detected		14				13			1		0
GLIOMA [M]		0				0			0		1
Hyperplasia		1				2			0		0
SKIN/SUBCUTIS:		(15)				(15)			(2)		(1)
No abnormality detected		14				15			2		1
Area of ulceration with chronic, active inflammation		1				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 (continued)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
MAMMARY GLANDS:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
URINARY BLADDER:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
AORTA:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
MESENTERIC LYMPH NODE:		(15)				(15)			(2)		(1)
No abnormality detected		15				14			1		1
Increased macrophage aggregation		0				0			1		0
Contains lymphosarcoma		0				1			0		0
THYROIDS:		(15)				(15)					(1)
No abnormality detected		9				11					1
FOLLICULAR ADENOMA [B]		1				0					0
C-CELL ADENOMA [B]		2				1					0
Diffuse c-cell hyperplasia		1				2					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 (continued)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)					(1)
Dilated/cystic follicle(s)		2				1					0
PARATHYROIDS:		(14)				(14)			(2)		(1)
No abnormality detected		13				14			2		1
Pale cell focus(i)		1				0			0		0
TRACHEA:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
OESOPHAGUS:		(15)				(15)			(2)		(1)
No abnormality detected		15				15			2		1
STOMACH:		(15)				(15)			(2)		(1)
No abnormality detected		8				11			2		0
Dilated/cystic gland(s)		7				4			0		0
Ulceration with inflammation/necrosis		0				0			0		1

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)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
DUODENUM:		(15)				(15)			(1)		(1)
No abnormality detected		15				15			1		1
JEJUNUM:		(15)				(15)					(1)
No abnormality detected		15				15					1
ILEUM:		(15)				(15)					(1)
No abnormality detected		15				15					1
CAECUM:		(15)				(15)					(1)
No abnormality detected		15				15					1
COLON:		(15)				(15)					(1)
No abnormality detected		15				15					1
RECTUM:		(15)				(15)			(1)		(1)
No abnormality detected		15				15			1		1

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)

FINDINGS	TREATMENT	MALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)		(1)
No abnormality detected		15				15			2		1
STERNUM:		(15)				(15)			(2)		(1)
No abnormality detected		14				14			0		1
Fat vacuolation absent		0				1			0		0
Bone marrow reactive		0				0			1		0
Localised depressed haemopoiesis		1				0			0		0
Contains histiocytic sarcoma		0				0			1		0
LYMPHORETICULAR/HAEMOPOIETIC TISSUE:						(1)			(1)		
Metastasising HISTIOCYTIC SARCOMA(TA) [M]						0			1		
LYMPHOSARCOMA [M]						1			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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)	
No abnormality detected		1	1	2	1	3				1	
HEPATOCELLULAR ADENOMA [B]		1	0	0	0	0				0	
Basophilic focus(i)											
	(Grade +/-)	6	7	7	6	7				0	
	(Grade +)	4	1	3	3	2				0	
	(Grade ++)	2	2	0	2	0				0	
	(Grade +++)	1	1	1	0	0				0	
Total incidence for score expanded finding		13	11	11	11	9				0	
Pale cell focus(i)											
	(Grade +/-)	3	1	2	4	1				0	
Total incidence for score expanded finding		3	1	2	4	1				0	
Clear cell focus(i)											
	(Grade +/-)	1	0	0	2	1				0	
Total incidence for score expanded finding		1	0	0	2	1				0	
Focal hepatocellular hypertrophy		1	1	0	0	0				0	
Periportal hepatocyte hypertrophy		0	0	0	1	0				0	
Spongiosis hepatis		0	0	1	1	0				0	
Subcapsular dilated sinusoids		0	2	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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)	
Foamy hepatocytes (bifurcation of median lobe)		3	3	4	2	1				0	
Increased Kupffer-cell pigmentation		1	0	0	0	0				0	
Necrosis		2	0	2	0	0				1	
Inflammatory change(s)		5	2	3	5	6				0	
Hepatocytes contain red blood cells (a few)		2	0	0	0	0				0	
Diffuse mitotic increase		0	1	0	0	0				0	
Increased multinucleate giant-cell(s)		0	0	0	0	1				0	
Focal fibrosis		0	1	0	0	0				0	
HEART:		(15)				(15)				(1)	
No abnormality detected		6				10				0	
Cardiomyopathy		9				5				1	
KIDNEYS:		(15)	(15)	(15)	(15)	(15)				(1)	
No abnormality detected		3	4	5	6	8				1	
Nephropathy											
	(Grade +/-)	5	5	5	4	4				0	
	(Grade +)	1	1	0	1	2				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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
KIDNEYS:		(15)	(15)	(15)	(15)	(15)				(1)	
Nephropathy (Grade ++)		0	0	0	0	1				0	
Total incidence for score expanded finding		6	6	5	5	7				0	
Basophilic tubules (Grade +/-)		0	0	1	2	0				0	
Total incidence for score expanded finding		0	0	1	2	0				0	
Tubular dilatation (Grade +/-)		0	1	1	0	0				0	
Total incidence for score expanded finding		0	1	1	0	0				0	
Urothelial hyperplasia		8	5	5	2	0**				0	
Unilateral pelvic dilatation		1	0	0	0	0				0	
Mineral deposit(s)		4	4	2	1	0				0	
Increased tubular pigment deposit(s)		1	0	0	0	2				0	
Cyst(s)		1	0	0	0	0				0	
LUNGS:		(15)	(15)	(15)	(15)	(15)				(1)	
No abnormality detected		8	9	8	7	11				1	
Alveolitis		2	0	1	1	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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)				(1)	
Area(s) of interstitial pneumonitis		2	4	1	1	3				0	
Focus(i) of increased alveolar macrophages		4	1	5	7	1				0	
Focal inflammation		0	1	0	1	0				0	
Focal epithelialisation		0	1	0	0	0				0	
Lymphoid tissue increase		0	0	1	0	0				0	
Medial hypertrophy		0	0	0	1	1				0	
Focal mineral deposit(s)		0	0	1	0	0				0	
SPLEEN:		(15)				(15)				(1)	
No abnormality detected		15				13				0	
Increased haemosiderin		0				2				0	
Increased extramedullary haemopoiesis		0				0				1	
ADRENALS:		(15)				(15)				(1)	
No abnormality detected		5				4				1	
PHAEOCHROMOCYTOMA [B]		1				0				0	
Cortical CARCINOMA [M]		1				0				0	
Unilateral cellular change (cortex)		1				2				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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
ADRENALS:		(15)				(15)				(1)	
Unilateral cellular change with degeneration/vascular dilatation		0				2				0	
Subcapsular pale cell focus(i)		0				1				0	
Haemorrhagic degeneration		8				9				0	
THYMUS:		(15)				(15)				(1)	
No abnormality detected		8				12				1	
Epithelial hyperplasia		1				0				0	
Cystic duct(s)		5				2				0	
Increased atrophy		1				1				0	
OVARIES:		(15)				(15)				(1)	
No abnormality detected		4				4				0	
Absence of recent corpus luteum		11				11				0	
Interstitial tissue increased		0				1				0	
Follicular cyst(s)		10				7				1	
Cyst(s)		1				1				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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
UTERUS:		(15)				(15)				(2)	
No abnormality detected		8				9				2	
Dilated/cystic gland(s)		4				5				0	
Dilatation in both horns		1				0				0	
Focal squamous metaplasia		0				1				0	
Glandular epithelial hyperplasia		1				0				0	
Focal endometrial hyperplasia		0				1				0	
Glandular abscess(es)		1				0				0	
BRAIN:		(15)				(15)				(2)	
No abnormality detected		15				14				2	
Compression by pituitary		0				1				0	
Fore-brain not available for examination		10				0***				0	
SPINAL CORD:		(15)				(15)				(2)	
No abnormality detected		15				15				2	
SKELETAL MUSCLE:		(15)				(15)				(2)	
No abnormality detected		15				15				2	

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)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
PANCREAS:		(15)				(15)				(1)	
No abnormality detected		15				13				1	
Acinar atrophy		0				2				0	
SALIVARY GLAND:		(15)	(15)	(15)	(15)	(15)				(1)	
MANDIBULAR: NAD		15	15	15	15	8**				1	
MANDIBULAR: cellular alteration											
(Grade +)		0	0	0	0	7**				0	
Total incidence for score expanded finding		0	0	0	0	7**				0	
PAROTID: NAD		15	14	13	7**	1***				1	
PAROTID: cellular alteration											
(Grade +)		0	0	2	5*	8**				0	
(Grade ++)		0	0	0	3	5*				0	
(Grade +++)		0	0	0	0	1				0	
Total incidence for score expanded finding		0	0	2	8**	14***				0	
PAROTID: not examined histologically		0	1	0	0	0				0	
SUBLINGUAL: NAD		15	13	13	13	15				1	
SUBLINGUAL: not examined histologically		0	2	2	2	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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg 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)	
Reactive										1	
PITUITARY:		(15)				(14)				(2)	
No abnormality detected		10				10				2	
Anterior lobe ADENOMA [B]		3				2				0	
Hyperplasia		2				2				0	
Focal mineral deposit(s)		0				1				0	
Intermediate lobe cyst(s)		0				1				0	
SKIN/SUBCUTIS:		(15)				(15)				(2)	
No abnormality detected		15				15				1	
Large abscess(es)		0				0				1	
MAMMARY GLANDS:		(15)				(15)				(2)	
No abnormality detected		6				12				2	
Intraductal CARCINOMA [M]		1				0				0	
Focal hyperplasia		1				0				0	
Dilated/cystic duct(s)		4				3				0	
Secretion present		8				3				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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg kg/day	Grp 4 300mg kg/day	Grp 5 1000mg kg/day
MAMMARY GLANDS:		(15)				(15)				(2)	
Alveolar development		1				0				0	
URINARY BLADDER:		(15)				(15)				(1)	
No abnormality detected		15				15				1	
AORTA:		(15)				(15)				(2)	
No abnormality detected		15				15				2	
MESENTERIC LYMPH NODE:		(15)				(15)				(2)	
No abnormality detected		14				15				2	
Congestion		1				0				0	
THYROIDS:		(15)				(15)				(1)	
No abnormality detected		11				10				1	
C-CELL ADENOMA [B]		1				0				0	
Unilateral focal c-cell hyperplasia		1				0				0	
Diffuse c-cell hyperplasia		2				4				0	
Dilated/cystic follicle(s)		1				2				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 (continued)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg kg/day	Grp 3 100mg 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)				(1)	
No abnormality detected		15				15				1	
OESOPHAGUS:		(15)				(15)				(2)	
No abnormality detected		15				15				2	
STOMACH:		(15)				(15)				(1)	
No abnormality detected		9				11				1	
Dilated/cystic gland(s)		6				4				0	
DUODENUM:		(15)				(15)				(1)	
No abnormality detected		15				15				1	
JEJUNUM:		(15)				(15)				(1)	
No abnormality detected		15				15				1	

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)

FINDINGS	TREATMENT	FEMALES : INCIDENCE OF LESIONS (NUMERIC)									
		SURVIVORS					DECEDENTS				
		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 1 0mg kg/day	Grp 2 10mg 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				1	
CAECUM:		(15)				(15)				(1)	
No abnormality detected		15				15				1	
COLON:		(15)				(15)				(1)	
No abnormality detected		15				15				1	
RECTUM:		(15)				(15)				(1)	
No abnormality detected		15				15				1	
SCIATIC NERVE:		(15)				(15)				(2)	
No abnormality detected		15				15				2	
STERNUM:		(15)				(15)				(2)	
No abnormality detected		15				15				2	

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 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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
1. SALIVARY GLAND		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
2. ESOPHAGUS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
3. STOMACH		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Adenocarcinoma		0	0	1	0	0	0	0	0
4. DUODENUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
5. ILEUM		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
6. COLON		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(28)
7. PANCREAS		(28)	(30)	(32)	(20)	(26)	(23)	(16)	(28)
Islet cell adenoma		1	0	0	0	0	0	0	0
Cholangio-carcinoma-metastatic		0	1	0	0	1	0	0	0
Undifferentiated Sacrcoma metastatic		0	0	1	0	0	0	0	0
Histiocytic sarcoma metastatic		0	0	0	0	1	0	0	0
8. LIVER		(30)	(30)	(32)	(21)	(26)	(23)	(17)	(29)
Cholangiocarcinoma		0	2	2	2	1	0	0	0
Hepatocellular adenoma		9	9	6	6	2	8	3	5

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
8. LIVER contd.		(30)	(30)	(32)	(21)	(26)	(23)	(17)	(29)
Hepatocellular carcinoma		12	12	9	5	4	4	2	5
Intrahepatic bile duct adenoma		1	1	0	0	0	0	0	0
Histiocytic sarcoma		2	0	2	1	1	0	0	0
Tumour emboli		0	0	1	1	0	0	0	0
Fibrosarcoma		0	1	0	0	0	0	0	0
9. LUNGS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Adenoma		0	0	0	0	0	1	0	0
Histiocytic sarcoma-metastatic		1	0	1	1	1	0	0	0
Cholangiocarcinoma-metastatic		0	1	0	0	0	0	0	0
Hepatocellular carcinoma- metastatic		0	1	0	1	0	0	0	0
Bronchio alveolar adenoma		0	0	0	0	0	0	1	0
Squamous cell carcinoma-metastatic		1	0	0	0	0	0	0	0
Giant cell tumour		0	0	0	1	0	0	0	0
Fibroma		0	0	0	0	0	1	0	0
Round cell sarcoma metastatic		0	0	0	0	0	0	1	0
10. TRACHEA		(29)	(30)	(32)	(21)	(26)	(24)	(17)	(29)

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
11. HEART		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Histiocytic sarcoma-metastatic		1	0	1	1	0	0	0	0
Round cell sarcoma of pericardium		0	0	0	0	0	0	1	0
12. AORTA		(16)	(30)	(32)	(21)	(20)	(24)	(17)	(12)
13. SPLEEN		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Cholangiocarcinoma-metastatic		0	1	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)	(29)
Histiocytic sarcoma-metastatic		1	0	1	0	1	0	0	0
Cholangiocarcinoma-metastatic		0	1	0	0	1	0	0	0
Hepatocellular carcinoma-metastatic		0	1	0	0	0	0	0	0
Giant cell tumour		0	0	0	1	0	0	0	0
Histiocyctic sarcoma		0	0	0	1	0	0	0	0
16. MANDIBULAR LYMPH NODE		(29)	(29)	(32)	(21)	(26)	(24)	(17)	(29)

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
17. KIDNEYS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Cholangio carcinoma-metastatic		0	1	0	0	0	0	0	0
Histiosarcoma metastatic		0	0	1	0	0	0	0	0
18. URINARY BLADDER		(27)	(30)	(32)	(20)	(26)	(24)	(16)	(28)
Transitional cell Carcinoma		0	0	0	0	0	0	0	1
19. TESTES		(30)	(30)	(31)	(21)	NA	NA	NA	NA
Leydig cell tumour		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	NA
Undifferentiated sarcoma		0	0	1	0	NA	NA	NA	NA
21. PROSTATE		(28)	(30)	(31)	(21)	NA	NA	NA	NA
22. SEMINAL VESICLES		(29)	(30)	(31)	(21)	NA	NA	NA	NA
23. COAGULATING GLANDS		(28)	(26)	(31)	(21)	NA	NA	NA	NA
24. OVARIES		NA	NA	NA	NA	(25)	(24)	(17)	(29)

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
25. UTERUS		NA	NA	NA	NA	(26)	(24)	(17)	(29)
Adenocarcinoma		NA	NA	NA	NA	0	0	1	0
Anaplastic carcinoma		NA	NA	NA	NA	0	1	0	0
Leiomyosarcoma		NA	NA	NA	NA	0	0	0	1
26. VAGINA		NA	NA	NA	NA	(26)	(24)	(17)	(29)
27. BRAIN		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Squamous cell carcinoma-metastatic		0	0	0	1	0	0	0	0
28. THYROIDS		(26)	(26)	(29)	(21)	(26)	(24)	(17)	(27)
'C' cell adenoma		0	0	1	0	0	0	1	0
29. PARATHYROIDS		(4)	(2)	(2)	(7)	(3)	(2)	(3)	(1)
30. PITUITARY		(29)	(27)	(30)	(20)	(25)	(22)	(16)	(29)
Adenocarcinoma		0	1	0	0	0	0	0	0
Adenoma		2	2	3	1	5	8	3	5

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
31. ADRENALS		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
Cortical cell adenoma		2	0	0	0	0	0	1	0
Pheochromocytoma		7	3	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		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
36. TONGUE		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
37. THYMUS		(28)	(29)	(31)	(20)	(24)	(24)	(16)	(28)
Thymoma		0	0	0	0	0	1	0	0
38. MUSCLE FEMORAL		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
39. SPINAL CORD		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
40. SCIATIC NERVES		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
41. PREPUTIAL GLANDS		(30)	(30)	(32)	(21)	NA	NA	NA	NA
42. MAMMARY GLAND		NA	NA	NA	NA	(23)	(22)	(16)	(28)
Adenoma		NA	NA	NA	NA	1	1	3	3
Adenocarcinoma		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		(30)	(30)	(31)	(21)	(26)	(24)	(17)	(29)
Squamous cell carcinoma		0	0	1	0	0	0	0	0
Histiocytic sarcoma-metastatic		0	0	0	1	1	0	0	0
Cholangiocarcinoma-metastatic		0	2	0	0	1	0	0	0
Giant cell tumour		0	0	0	1	0	0	0	0

contd.

TABLE 48 contd.

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

Ref.App. 160-167

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	30	30	32	21	26	24	17	29
47. OPTIC NERVES		(27)	(27)	(25)	(20)	(22)	(21)	(16)	(27)
48. BONE (FEMUR) WITH JOINT		(29)	(30)	(31)	(21)	(26)	(24)	(17)	(28)
Histiocytic sarcoma-metastatic		1	0	0	0	0	0	0	0
49. TAIL		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
50. MESENTRY		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
51. STERNUM		(29)	(29)	(30)	(21)	(26)	(24)	(17)	(29)
Histiocytic sarcoma-metastatic		1	0	0	0	0	0	0	0
52. LYMPH NODE (OTHERS)		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)
53. PELVIC CAVITY		(30)	(30)	(32)	(21)	(26)	(24)	(17)	(29)

TABLE 49

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
1. SALIVARY GLAND		(20)	-	-	(29)	(24)	(1)	-	(21)
Duct papilloma		1	-	-	0	0	0	-	0
2. ESOPHAGUS		(20)	-	-	(29)	(24)	-	-	(21)
3. STOMACH		(20)	(1)	-	(29)	(24)	-	-	(21)
Papilloma-forestomach		0	1	-	0	0	-	-	1
4. DUODENUM		(20)	-	-	(29)	(24)	-	-	(21)
5. ILEUM		(20)	-	-	(29)	(24)	(1)	-	(21)
6. COLON		(20)	-	-	(29)	(24)	-	-	(21)
7. PANCREAS		(20)	-	-	(29)	(24)	-	-	(21)
Islet cell adenoma		2	-	-	1	0	-	-	1
Lymphosarcoma metastatic		1	-	-	0	0	-	-	0
8. LIVER		(20)	(20)	(16)	(29)	(24)	(25)	(32)	(21)
Cholangiocarcinoma		1	1	0	1	0	0	0	0
Hepatocellular adenoma		15	13	4	15	16	10	16	8

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
8. LIVER contd.		(20)	(20)	(16)	(29)	(24)	(25)	(32)	(21)
Hepatocellular carcinoma		9	16	9	19	6	11	12	4
Intrahepatic bile duct adenoma		1	0	0	0	0	1	0	0
Histiocytic sarcoma		0	1	1	0	0	0	3	0
Tumour emboli		1	0	1	0	0	0	0	0
Lymphosarcoma		1	0	0	0	0	0	0	0
Benign mixed intra-hepatic bile duct adenoma		0	0	1	0	0	0	0	0
9. LUNGS		(20)	(4)	(3)	(29)	(24)	(4)	(5)	(21)
Bronchio-alveolar adenocarcinoma		0	0	1	0	0	0	0	0
Hepatocellular carcinoma- metastatic		0	0	1	0	0	0	0	0
Bronchio alveolar adenoma		0	0	0	0	1	0	0	1
Histiocytic sarcoma		0	0	0	0	0	0	1	0
10. TRACHEA		(20)	-	-	(29)	(24)	(1)	-	(21)
Histiocytic sarcoma-metastatic		0	-	-	0	0	1	-	0
11. HEART		(20)	-	-	(29)	(24)	(1)	(1)	(21)
Histiocytic sarcoma-metastatic		0	-	-	0	0	1	1	0

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
12. AORTA		(20)	-	-	(29)	(24)	-	-	(21)
13. SPLEEN		(20)	-	(3)	(29)	(24)	-	(2)	(21)
14. MESENTERIC LYMPH NODES		(20)	-	-	(29)	(22)	-	-	(21)
Histiocyctic sarcoma		1	-	-	0	0	-	-	0
15. MEDIASTINAL LYMPH NODE		(19)	(1)	-	(29)	(22)	(1)	-	(21)
Histiocyctic sarcoma		0	0	-	0	0	1	-	0
16. MANDIBULAR LYMPH NODE		(19)	(6)	(5)	(29)	(24)	(9)	(6)	(21)
Lymphoma		0	0	0	2	0	0	0	0
17. KIDNEYS		(20)	(3)	(2)	(29)	(24)	-	(1)	(21)
Lymphosarcoma		0	0	0	0	0	-	1	0
18. URINARY BLADDER		(20)	-	-	(29)	(23)	-	-	(20)

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
19. TESTES		(20)	(7)	(1)	(29)	NA	NA	NA	NA
Leydig cell tumour		2	0	0	3	NA	NA	NA	NA
20. EPIDIDYMES		(19)	(1)	(1)	(29)	NA	NA	NA	NA
21. PROSTATE		(19)	-	-	(29)	NA	NA	NA	NA
22. SEMINAL VESICLES		(18)	-	(1)	(29)	NA	NA	NA	NA
23. COAGULATING GLANDS		(17)	-	-	(28)	NA	NA	NA	NA
24. OVARIES		NA	NA	NA	NA	(24)	(10)	(11)	(21)
25. UTERUS		NA	NA	NA	NA	(24)	(10)	(22)	(21)
Adenoma		NA	NA	NA	NA	0	0	0	1
Adenocarcinoma		NA	NA	NA	NA	0	0	2	0
Adenoma papillary		NA	NA	NA	NA	0	1	0	0
Hemangioma		NA	NA	NA	NA	0	0	1	0

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
26. BRAIN		(20)	-	-	(29)	(24)	-	-	(21)
Pituitary adenocarcinoma metastatic		0	-	-	0	1	-	-	0
27. THYROIDS		(19)	-	-	(29)	(24)	-	-	(20)
'C' cell adenoma		2	-	-	1	2	-	-	1
28. PARATHYROIDS		(5)	-	-	(29)	(6)	-	-	(3)
29. PITUITARY		(20)	(3)	(1)	(29)	(24)	(11)	(7)	(21)
Adenocarcinoma		0	0	0	0	1	0	0	0
Adenoma		1	2	0	4	2	5	4	1
30. ADRENALS		(20)	(3)	(4)	(29)	(24)	(4)	(7)	(21)
Cortical cell adenoma		1	0	1	0	0	0	2	1
Pheochromocytoma		6	2	2	12	1	0	4	2
Malignant Pheochromocytoma		0	0	1	1	0	0	0	0
31. EYES		(20)	(3)	(4)	(29)	(24)	(3)	(7)	(21)
32. BONE MARROW (SMEAR)		(19)	-	-	(29)	(21)	-	-	(19)
33. SKIN		(20)	-	-	(29)	(24)	(4)	(2)	(21)

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
34. THYMUS		(20)	-	-	(29)	(24)	-	-	(21)
Thymoma		0	-	-	0	1	-	-	0
35. MUSCLE FEMORAL		(20)	-	-	(29)	(24)	-	-	(21)
36. SPINAL CORD		(20)	-	-	(29)	(24)	-	-	(21)
37. SCIATIC NERVES		(20)	-	-	(29)	(23)	-	-	(20)
38. PREPUTIAL GLANDS		(20)	-	-	(29)	NA	NA	NA	NA
39. MAMMARY GLAND		NA	NA	NA	NA	(17)	(8)	(17)	(20)
Adenoma		NA	NA	NA	NA	1	2	5	2
Adenocarcinoma		NA	NA	NA	NA	1	0	0	0
40. JEJUNUM		(20)	-	-	(29)	(24)	-	-	(21)
41. CECUM		(20)	(1)	-	(29)	(24)	-	-	(21)
Histiocytic sarcoma		0	1	-	0	0	-	-	0
42. RECTUM		(20)	-	-	(29)	(24)	-	-	(21)

contd.

TABLE 49 contd.

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

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS FOR TERMINALLY SACRIFICED ANIMALS

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

Ref.App. 168-175

TISSUE AND OBSERVATION	Sex	MALE				FEMALE			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No.of rats	50	50	50	50	50	50	50	50
	No.of rats examined	20	20	18	29	24	26	32	21
43. TUMOUR/MASS		(20)	(2)	(3)	(29)	(24)	(4)	(1)	(21)
Fibroma		0	1	1	0	1	0	0	0
Undifferentiated sarcoma		0	0	0	0	1	0	0	0
44. OPTIC NERVES		(16)	-	-	(29)	(23)	(1)	-	(18)
45. BONE (FEMUR) WITH JOINT		(20)	-	-	(29)	(24)	-	-	(21)
46. MESENTERY		(20)	-	-	(29)	(24)	-	(1)	(21)
47. STERNUM		(20)	-	-	(29)	(24)	-	-	(21)
48. LYMPH NODE (OTHERS)		(20)	(1)	-	(29)	(24)	-	-	(21)
49. PELVIC CAVITY		(20)	-	-	(29)	(24)	(1)	-	(21)

Tumor Incidence

PROJECT ID: 1231 GROUP: 0ppm SEX: MALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4029	727	TESTES	B	SEMINOMA	1
4043	681	MAMMARY GLAND	B	FIBROADENOMA	1

Total Animals/Group:	50
Total Primary Tumors:	2
Total Animals with Tumors:	2
Total Animals with Multiple Tumors:	0
Total Benign:	2
Total Malignant:	0
Total Malignant with Metastasis:	0
Avg. DAYS on Test for Animals with Tumors:	704

Tumor Incidence

PROJECT ID: 1231 GROUP: 0ppm SEX: MALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4029	727	TESTES	B	SEMINOMA	1
4043	681	MAMMARY GLAND	B	FIBROADENOMA	1

Total Animals/Group:	50
Total Primary Tumors:	2
Total Animals with Tumors:	2
Total Animals with Multiple Tumors:	0
Total Benign:	2
Total Malignant:	0
Total Malignant with Metastasis:	0
Avg. DAYS on Test for Animals with Tumors:	704

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Tumor Incidence

PROJECT ID: 1231 GROUP: 0ppm SEX: FEMALE DAYS: ALL
FATES: ALL

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,HARD	1
4070	550	SKIN	B	SUBCUT.TISSUE,FIBROMA,HARD	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 GROUP: 0ppm SEX: FEMALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN	TUMOR TYPE	PETO

Total Animals/Group:	50
Total Primary Tumors:	13
Total Animals with Tumors:	13
Total Animals with Multiple Tumors:	0
Total Benign:	12
Total Malignant:	1
Total Malignant with Metastasis:	0
Avg. DAYS on Test for Animals with Tumors:	626

Tumor Incidence

PROJECT ID: 1231 GROUP: 3000ppm SEX: MALE DAYS: ALL
FATES: 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
4150	275	LIVER	C	HEPATOCELLULAR CARCINOMA	4
		SPLEEN	+	LYMPHOMA MALIGNANT LYMPHOCYTIC	
		LUNGS	+	LYMPHOMA MALIGNANT LYMPHOCYTIC	
		MES. LYMPH NODE	+	LYMPHOMA MALIGNANT LYMPHOCYTIC	

Total Animals/Group:	50
Total Primary Tumors:	5
Total Animals with Tumors:	5
Total Animals with Multiple Tumors:	0
Total Benign:	4
Total Malignant:	1
Total Malignant with Metastasis:	1
Avg. DAYS on Test for Animals with Tumors:	590

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Tumor Incidence

PROJECT ID: 1231 GROUP: 3000ppm SEX: FEMALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4161	577	MAMMARY GLAND	B	FIBROADENOMA	2
4165	730	MAMMARY GLAND	B	ADENOMA	2
4170	730	MAMMARY GLAND	B	ADENOMA	1
4178	450	MAMMARY GLAND	B	PAPILLARY ADENOMA	1
4179	637	MAMMARY GLAND	B	ADENOMA	1
4181	730	OVARIES	B	ADENOMA	1
4183	556	MAMMARY GLAND	B	ADENOMA	2
4188	686	MAMMARY GLAND	B	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

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Tumor Incidence

PROJECT ID: 1231 GROUP: 15000ppm SEX: MALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4221	731	MAMMARY GLAND	B	ADENOMA	1
4241	733	TESTES	B	INTERSTITIAL CELL TUMOUR	1
4242	733	SKIN	B	SUBCUT. TISSUE, LIPOMA	2
4244	733	TESTES	B	INTERSTITIAL CELL TUMOUR	1
4245	627	SKIN	B	SUBCUT. TISSUE, FIBROMA	1

Total Animals/Group:	50
Total Primary Tumors:	5
Total Animals with Tumors:	5
Total Animals with Multiple Tumors:	0
Total Benign:	5
Total Malignant:	0
Total Malignant with Metastasis:	0
Avg. DAYS on Test for Animals with Tumors:	711

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Tumor Incidence

PROJECT ID: 1231 GROUP: 15000ppm SEX: FEMALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4257	582	MAMMARY GLAND	B	FIBROADENOMA	1
4262	590	MAMMARY GLAND	B	FIBROADENOMA	1
4273	733	SKIN	B	SUBCUT. TISSUE, FIBROMA	2
4281	372	MAMMARY GLAND	B	ADENOMA	1
4285	733	MAMMARY GLAND	B	FIBROADENOMA	1
4290	493	MAMMARY GLAND	B	ADENOMA	1
4296	734	MAMMARY GLAND	B	FIBROADENOMA	2
4300	734	MAMMARY GLAND	B	FIBROADENOMA	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:	621

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Tumor Incidence

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

ID	DAYS	TISSUE OF ORIGIN	TUMOR TYPE	PETO

Total Animals/Group:	50
Total Primary Tumors:	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

461

Tumor Incidence

PROJECT ID: 1231 GROUP: 25000ppm SEX: FEMALE DAYS: ALL
FATES: ALL

ID	DAYS	TISSUE OF ORIGIN		TUMOR TYPE	PETO
4351	735	MAMMARY GLAND	B	FIBROADENOMA	1
4352	735	MAMMARY GLAND	B	FIBROADENOMA	2
4354	402	MAMMARY GLAND	B	FIBROADENOMA	1
4378	468	SKIN	B	ACANTHOMA	1
4392	708	MAMMARY GLAND	B	FIBROADENOMA	1
4393	500	MAMMARY GLAND	B	FIBROADENOMA	1

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:	0
Avg. DAYS on Test for Animals with Tumors:	591

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Summary Tumor Incidence

PROJECT ID: 1231 FATES: ALL
DAYS: 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 Tumors	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

PROJECT ID: 1231 FATES: ALL
DAYS: ALL SEX: FEMALE

GROUP:	0ppm	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

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Selected Animals

PROJECT ID: 1231

DAYS : ALL
FINDINGS : * Selected

GROUP :	0ppm	3000ppm	15000ppm	25000ppm
SEX :	MALE	MALE	MALE	MALE
No. of ANIMALS :	50	50	50	50
	4029	4107	4221	------
	4043	4108	4241	------
	------	4115	4242	------
	------	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

LUNGS:
LYMPHOMA MALIGNANT LYMPHOCYTIC

MES. LYMPH NODE:
LYMPHOMA MALIGNANT LYMPHOCYTIC

TESTES:
INTERSTITIAL CELL TUMOUR
SEMINOMA

SKIN:
SUBCUT. TISSUE, FIBROMA
SUBCUT. TISSUE, LIPOMA

MAMMARY GLAND:
ADENOMA
FIBROADENOMA

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Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : LIVER FATES : ALL
FINDING : HEPATOCELLULAR CARCINOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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

T Value : -7713.542

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	47	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	%25000.00	0	0.00	0.00

T Value : 0

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%15000.00	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

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GLYPHOSATE TECHNICAL
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Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : SPLEEN FATES : ALL
FINDING : LYMPHOMA MALIGNANT LYMPHOCYTIC

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%25000.00	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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Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : LUNGS FATES : ALL
FINDING : LYMPHOMA MALIGNANT LYMPHOCYTIC

FATAL TUMORS

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

T Value : 0

NON-FATAL TUMORS

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

T Value : 0

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%15000.00	0	0.00	0.00	1.00
4M: 25000ppm	47	%25000.00	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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GLYPHOSATE TECHNICAL
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Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MES. LYMPH NODE FATES : ALL
FINDING : LYMPHOMA MALIGNANT LYMPHOCYTIC

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%25000.00	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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GLYPHOSATE TECHNICAL
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Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : TESTES FATES : ALL
FINDING : INTERSTITIAL CELL TUMOUR

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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	%25000.00	0	0.00	0.00

T Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	48	0.00	0	0.00	0.00
2M: 3000ppm	49	3000.00	1	0.36	0.64
3M: 15000ppm	49	%15000.00	2	0.89	1.11
4M: 25000ppm	47	%25000.00	0	1.75	-1.75

T Value : -25225.03

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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

T Value : %-25225.02730
Variance : %117651824.00000
Z Value : -2.32559
One Tailed Probability: 0.01500

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : TESTES FATES : ALL
FINDING : SEMINOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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	%25000.00	0	0.00	0.00

T Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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

T Value : -9952.381

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%15000.00	0	0.25	-0.25	0.00
4M: 25000ppm	47	%25000.00	0	0.21	-0.21	0.00

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

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : SKIN FATES : ALL
FINDING : SUBCUT. TISSUE, FIBROMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

NON-FATAL TUMORS

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

T Value : 3375

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : SKIN FATES : ALL
FINDING : SUBCUT. TISSUE, LIPOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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 Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	48	0.00	0	0.00	0.00
2M: 3000ppm	18	3000.00	0	0.00	0.00
3M: 15000ppm	21	%15000.00	1	0.10	0.90
4M: 25000ppm	47	%25000.00	0	0.90	-0.90

T Value : -9000

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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

T Value : %-9000.00000
Variance : %8999936.00000
Z Value : -3.00001
One Tailed Probability: 0.00200

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : ADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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	%25000.00	0	0.00	0.00

T Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	1	0.00	0	0.20	-0.20
2M: 3000ppm	3	3000.00	1	0.60	0.40
3M: 15000ppm	1	%15000.00	1	1.20	-0.20
4M: 25000ppm	0	%25000.00	0	0.00	0.00

T Value : -1800.001

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%25000.00	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 INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : FIBROADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	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	%25000.00	0	0.00	0.00

T Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1M: 0ppm	1	0.00	1	0.58	0.42
2M: 3000ppm	3	3000.00	2	1.33	0.67
3M: 15000ppm	1	%15000.00	0	1.08	-1.08
4M: 25000ppm	0	%25000.00	0	0.00	0.00

T Value : -14250

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1M: 0ppm	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	%15000.00	0	1.08	-1.08	0.00
4M: 25000ppm	0	%25000.00	0	0.00	0.00	1.00

T Value : %-14250.00100
Variance : %111187504.00000
Z Value : -1.35141
One Tailed Probability: 0.09000

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

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

FINDING : HEPATOCELLULAR CARCINOMA

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
1M*	0	47	47								
2M	1	48	49	0.51042	1.00000	0.51042	1.02083	1.00000	?	0.969280	0.000439
3M	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	

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : SPLEEN 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		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
3M	0	21	21	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	

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
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		CHI 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 Chi Square	
4M	0	47	47	1.00000	1.00000	1.00000	2.00000	1.00000		Zero Values - No Chi Square	

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MES. LYMPH NODE 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		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
3M	0	21	21	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	

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
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
1M*	0	48	48								
2M	1	48	49	0.50515	1.00000	0.50515	1.01031	1.00000	?	0.989796	0.000107
3M	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		Zero Values - No Chi Square	

FINDING : SEMINOMA

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
1M*	1	47	48								
2M	0	49	49	0.49485	0.49485	1.00000	0.98969	0.49485	?	1.031467	0.000107
3M	0	49	49	0.49485	0.49485	1.00000	0.98969	0.49485	?	1.031467	0.000107
4M	0	47	47	0.50526	0.50526	1.00000	1.01053	1.00000	?	0.989583	0.000112

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

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

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
1M*	0	48	48								
2M	0	18	18	1.00000	1.00000	1.00000	2.00000	1.00000		Zero Values - No Chi Square	
3M	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

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
1M*	0	48	48								
2M	0	18	18	1.00000	1.00000	1.00000	2.00000	1.00000		Zero Values - No Chi Square	
3M	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	

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL

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
1M*	0	1	1								
2M	1	2	3	0.75000	1.00000	0.75000	1.50000	1.00000	?	0.444444	0.444444
3M	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		Zero Values - No Chi Square	

FINDING : FIBROADENOMA

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
1M*	1	0	1								
2M	2	1	3	0.75000	0.75000	1.00000	1.50000	1.00000	?	0.444444	0.444444
3M	0	1	1	0.50000	0.50000	1.00000	1.00000	1.00000	?	2.000000	0.000000
4M	0	0	0	1.00000	1.00000	1.00000	2.00000	1.00000		Zero Values - No Chi Square	

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GLYPHOSATE TECHNICAL
TABLE - Z

Selected Animals

PROJECT ID: 1231

DAYS : ALL
FINDINGS : * Selected

GROUP :	0ppm	3000ppm	15000ppm	25000ppm
SEX :	FEMALE	FEMALE	FEMALE	FEMALE
No. of ANIMALS :	50	50	50	50
	4054	4161	4257	4351
	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	------
	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
CYSTADENOMA

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : OVARIES FATES : ALL
FINDING : ADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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

T Value : 0

NON-FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	49	0.00	0	0.00	0.00
2F: 3000ppm	49	3000.00	1	0.35	0.65
3F: 15000ppm	48	%15000.00	0	0.35	-0.35
4F: 25000ppm	50	%25000.00	0	0.29	-0.29

T Value : -10705.88

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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

T Value : %-10705.88280
Variance : %78560560.00000
Z Value : -1.20787
One Tailed Probability: 0.15000

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

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

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	48	0.00	0	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

T Value : 13448.82

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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	%25000.00	1	0.35	0.65	2.82

T Value : %13448.81930
Variance : %123034800.00000
Z Value : 1.21247
One Tailed Probability: 0.15000

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : SKIN FATES : ALL
FINDING : SUBCUT. TISSUE, FIBROMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	48	0.00	0	0.00	0.00
2F: 3000ppm	22	3000.00	0	0.00	0.00
3F: 15000ppm	22	%15000.00	1	0.14	0.86
4F: 25000ppm	50	%25000.00	0	0.86	-0.86

T Value : -8620.69

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	48	0.00	0	0.00	0.00	1.00
2F: 3000ppm	22	3000.00	0	0.00	0.00	1.00
3F: 15000ppm	22	%15000.00	1	0.14	0.86	7.25
4F: 25000ppm	50	%25000.00	0	0.86	-0.86	0.00

T Value : %-8620.69040
Variance : %11890624.00000
Z Value : -2.50000
One Tailed Probability: 0.00700

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EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : ADENOCARCINOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	48	0.00	1	0.41	0.59
2F: 3000ppm	22	3000.00	0	0.07	-0.07
3F: 15000ppm	22	%15000.00	0	0.09	-0.09
4F: 25000ppm	50	%25000.00	0	0.43	-0.43

T Value : -12320.99

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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	%25000.00	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
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : ADENOMA

FATAL TUMORS

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

T Value : -110799.1

TOTAL TUMORS

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

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

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : PAPILLARY ADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	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

T Value : -20849.08

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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	%15000.00	0	0.23	-0.23	0.00
4F: 25000ppm	50	%25000.00	0	0.79	-0.79	0.00

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

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : FIBROADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	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

T Value : -37904.6

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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	%15000.00	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

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Peto Score Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL
FINDING : CYSTADENOMA

FATAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected
1F: 0ppm	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: 0ppm	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

T Value : -11015.87

TOTAL TUMORS

Group	Number of Animals	Dose Level	Observed	Expected	Observed - Expected	ML Value
1F: 0ppm	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.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

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

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*	0	49	49								
2F	1	48	49	0.50000	1.00000	0.50000	1.00000	1.00000	?	1.010309	0.000000
3F	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	

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

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

FINDING : ACANTHOMA

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	
3F	0	22	22	1.00000	1.00000	1.00000	2.00000	1.00000		Zero Values - No Chi Square	
4F	1	49	50	0.51020	1.00000	0.51020	1.02041	1.00000	?	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	
3F	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

Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL

FINDING : ADENOCARCINOMA

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*	1	47	48								
2F	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
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 : 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
3F	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
1F*	1	47	48								
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

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	1	21	22	0.35369	0.49517	0.85852	0.99034	1.35369	?	0.326340	0.005099
3F	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

15-FEB-1997
EXCEL INDUSTRIES LTD.
GLYPHOSATE TECHNICAL
TABLE - Z

Fisher's Exact Statistics

PROJECT ID: 1231 DAYS : ALL
TISSUE : MAMMARY GLAND FATES : ALL

FINDING : CYSTADENOMA

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*	1	47	48								
2F	0	22	22	0.68571	0.68571	1.00000	1.37143	1.00000	?	0.464976	0.162357
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

Table 25 - 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
	No. of animals examined	10	10	10	10
Cardiovascular System					
Heart:	(N=)	(10)	(10)	(10)	(10)
Aorta:	(N=)	(10)	(10)	(10)	(10)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (vertebra):	(N=)	(10)	(10)	(10)	(10)
Thymus:	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (cervical):	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (mesenteric):	(N=)	(10)	(10)	(10)	(10)
Spleen:	(N=)	(10)	(10)	(10)	(10)
Respiratory System					
Trachea:	(N=)	(10)	(10)	(10)	(10)
Lung:	(N=)	(10)	(10)	(10)	(10)
Digestive System					
Submaxillary gland:	(N=)	(10)	(10)	(10)	(10)
Sublingular gland:	(N=)	(10)	(10)	(10)	(10)
Esophagus:	(N=)	(10)	(10)	(10)	(10)
Stomach (non-glandular portion):	(N=)	(10)	(10)	(10)	(10)
Stomach (glandular portion):	(N=)	(10)	(10)	(10)	(10)
Small intestine:	(N=)	(10)	(10)	(10)	(10)
Large intestine:	(N=)	(10)	(10)	(10)	(10)
Liver:	(N=)	(10)	(10)	(10)	(10)
Pancreas:	(N=)	(10)	(10)	(10)	(10)
Urinary System					
Kidney:	(N=)	(10)	(10)	(10)	(10)
Urinary bladder:	(N=)	(10)	(10)	(10)	(10)
Genital System					
Testis:	(N=)	(10)	(10)	(10)	(10)
Epididymis:	(N=)	(10)	(10)	(10)	(10)
Seminal vesicle:	(N=)	(10)	(10)	(10)	(10)
Coagulating gland:	(N=)	(10)	(10)	(10)	(10)
Prostate:	(N=)	(10)	(10)	(10)	(10)
Endocrine System					
Pituitary:	(N=)	(10)	(10)	(10)	(10)
Thyroid:	(N=)	(10)	(10)	(10)	(10)
Parathyroid:	(N=)	(10)	(10)	(10)	(10)
Adrenal:	(N=)	(10)	(10)	(10)	(10)
Nervous System					
Cerebrum:	(N=)	(10)	(10)	(10)	(10)
Cerebellum:	(N=)	(10)	(10)	(10)	(10)
Brain stem:	(N=)	(10)	(10)	(10)	(10)
Spinal cord (cervical):	(N=)	(10)	(10)	(10)	(10)
Spinal cord (thoracic):	(N=)	(9)	(10)	(10)	(10)
Spinal cord (lumbar):	(N=)	(10)	(10)	(9)	(10)
Sciatic nerve:	(N=)	(10)	(10)	(10)	(10)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone (femur):	(N=)	(10)	(10)	(10)	(10)
Bone (vertebra):	(N=)	(10)	(10)	(10)	(10)

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

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
	No. of animals examined	10	10	10	10
Musculo-Skeletal System《cont.》					
Bone (vertebra) 《cont.》:	(N=)	(10)	(10)	(10)	(10)
Tibio-femoral joint:	(N=)	(10)	(10)	(10)	(10)
Skeletal muscle (m. triceps surae):	(N=)	(10)	(10)	(10)	(10)
Sense Organs					
Eye:	(N=)	(10)	(10)	(10)	(10)
Harderian gland:	(N=)	(10)	(10)	(10)	(10)
Integumentary System					
Skin:	(N=)	(10)	(10)	(10)	(10)
No. of benign neoplasms		0	0	0	0
No. of malignant neoplasms		0	0	0	0
No. of benign & malignant neoplasms		0	0	0	0
No. of animals with benign neoplasm(s)		0	0	0	0
No. of animals with malignant neoplasm(s)		0	0	0	0
No. of animals with 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	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	10	10	10	10
Cardiovascular System					
Heart:	(N=)	(10)	(10)	(10)	(10)
Aorta:	(N=)	(10)	(10)	(10)	(10)
Hematopoietic & Lymphatic System					
Bone marrow (femur) :	(N=)	(10)	(10)	(10)	(10)
Bone marrow (sternum) :	(N=)	(10)	(10)	(10)	(10)
Bone marrow (vertebra) :	(N=)	(10)	(10)	(10)	(10)
Thymus:	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (cervical) :	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (mesenteric) :	(N=)	(10)	(10)	(10)	(10)
Spleen:	(N=)	(10)	(10)	(10)	(10)
Respiratory System					
Trachea:	(N=)	(10)	(10)	(10)	(10)
Lung:	(N=)	(10)	(10)	(10)	(10)
Digestive System					
Submaxillary gland:	(N=)	(10)	(10)	(10)	(10)
Sublingular gland:	(N=)	(10)	(10)	(10)	(10)
Esophagus:	(N=)	(10)	(10)	(10)	(10)
Stomach (non-glandular portion) :	(N=)	(10)	(10)	(10)	(10)
Stomach (glandular portion) :	(N=)	(10)	(10)	(10)	(10)
Small intestine:	(N=)	(10)	(10)	(10)	(10)
Large intestine:	(N=)	(10)	(10)	(10)	(10)
Liver:	(N=)	(10)	(10)	(10)	(10)
Pancreas:	(N=)	(10)	(10)	(10)	(10)
Urinary System					
Kidney:	(N=)	(10)	(10)	(10)	(10)
Urinary bladder:	(N=)	(10)	(10)	(10)	(10)
Genital System					
Testis:	(N=)	(10)	(10)	(10)	(10)
Epididymis:	(N=)	(10)	(10)	(10)	(10)
Seminal vesicle:	(N=)	(10)	(10)	(10)	(10)
Coagulating gland:	(N=)	(10)	(10)	(10)	(10)
Prostate:	(N=)	(10)	(10)	(10)	(10)
Endocrine System					
Pituitary:	(N=)	(10)	(10)	(10)	(10)
(B) Anterior adenoma		0	1	2	0
Thyroid:	(N=)	(10)	(10)	(10)	(10)
(B) Follicular adenoma		0	1	0	0
(B) C-cell adenoma		0	0	1	0
Parathyroid:	(N=)	(10)	(10)	(10)	(10)
Adrenal:	(N=)	(10)	(10)	(10)	(10)
Nervous System					
Cerebrum:	(N=)	(10)	(10)	(10)	(10)
Cerebellum:	(N=)	(10)	(10)	(10)	(10)
Brain stem:	(N=)	(10)	(10)	(10)	(10)
Spinal cord (cervical) :	(N=)	(10)	(10)	(10)	(10)
Spinal cord (thoracic) :	(N=)	(10)	(10)	(10)	(10)
Spinal cord (lumbar) :	(N=)	(10)	(10)	(10)	(9)
Sciatic nerve:	(N=)	(10)	(10)	(10)	(10)

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

Table 25 - 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
	No. of animals examined	10	10	10	10
Musculo-Skeletal System					
Bone (sternum) :	(N=)	(10)	(10)	(10)	(10)
Bone (femur) :	(N=)	(10)	(10)	(10)	(10)
Bone (vertebra) :	(N=)	(10)	(10)	(10)	(10)
Tibio-femoral joint:	(N=)	(10)	(10)	(10)	(10)
Skeletal muscle (m. triceps surae) :	(N=)	(10)	(10)	(10)	(10)
Sense Organs					
Eye:	(N=)	(10)	(10)	(10)	(10)
Harderian gland:	(N=)	(10)	(10)	(10)	(10)
Integumentary System					
Skin:	(N=)	(10)	(10)	(10)	(10)
(B) Papilloma		1	0	0	0
(B) Fibroma		0	1	0	0
No. of benign neoplasms		1	3	3	0
No. of malignant neoplasms		0	0	0	0
No. of benign & malignant neoplasms		1	3	3	0
No. of animals with benign neoplasm(s)		1	3	3	0
No. of animals with malignant neoplasm(s)		0	0	0	0
No. of animals with neoplasm(s)		1	3	3	0

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

Table 25 - 5 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	30000
	No. of animals examined	6	5	10	8
Cardiovascular System					
Heart:	(N=)	(6)	(5)	(10)	(8)
Aorta:	(N=)	(6)	(5)	(10)	(8)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(6)	(5)	(10)	(8)
Bone marrow (sternum):	(N=)	(6)	(5)	(10)	(8)
Bone marrow (vertebra):	(N=)	(6)	(5)	(10)	(8)
Thymus:	(N=)	(6)	(5)	(10)	(8)
Lymph nodes (cervical):	(N=)	(6)	(5)	(10)	(8)
Lymph nodes (mesenteric):	(N=)	(6)	(5)	(10)	(8)
Spleen:	(N=)	(6)	(5)	(10)	(8)
Respiratory System					
Trachea:	(N=)	(6)	(5)	(10)	(8)
Lung:	(N=)	(6)	(5)	(10)	(8)
(B) Adenoma		2	0	0	0
Digestive System					
Submaxillary gland:	(N=)	(6)	(5)	(10)	(8)
Sublingular gland:	(N=)	(6)	(5)	(10)	(8)
Esophagus:	(N=)	(6)	(5)	(10)	(8)
Stomach (non-glandular portion):	(N=)	(6)	(5)	(10)	(8)
Stomach (glandular portion):	(N=)	(6)	(5)	(10)	(8)
Small intestine:	(N=)	(6)	(5)	(10)	(8)
Large intestine:	(N=)	(6)	(5)	(10)	(8)
Liver:	(N=)	(6)	(5)	(10)	(8)
(B) Hepatocellular adenoma		1	0	1	1
Pancreas:	(N=)	(6)	(5)	(10)	(8)
Urinary System					
Urinary bladder:	(N=)	(6)	(5)	(10)	(8)
Genital System					
Testis:	(N=)	(6)	(5)	(10)	(8)
Epididymis:	(N=)	(6)	(5)	(10)	(8)
Seminal vesicle:	(N=)	(6)	(5)	(10)	(8)
Coagulating gland:	(N=)	(6)	(5)	(10)	(8)
Prostate:	(N=)	(6)	(5)	(10)	(8)
Endocrine System					
Pituitary:	(N=)	(6)	(5)	(10)	(8)
(B) Anterior adenoma		3	4	4	3
Thyroid:	(N=)	(6)	(5)	(10)	(8)
(B) C-cell adenoma		2	1	2	1
Parathyroid:	(N=)	(6)	(5)	(10)	(8)
Adrenal:	(N=)	(6)	(5)	(10)	(8)
(B) Cortical adenoma		0	0	1	0
(B) Pheochromocytoma		0	1	0	0
Nervous System					
Cerebrum:	(N=)	(6)	(5)	(10)	(8)
Cerebellum:	(N=)	(6)	(5)	(10)	(8)
Brain stem:	(N=)	(6)	(5)	(10)	(8)
Spinal cord (cervical):	(N=)	(6)	(5)	(10)	(8)
Spinal cord (thoracic):	(N=)	(6)	(5)	(10)	(8)
Spinal cord (lumbar):	(N=)	(6)	(5)	(10)	(8)

(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	30000
	No. of animals examined	6	5	10	8
Nervous System《cont.》					
Spinal cord (lumbar) 《cont.》:	(N=)	(6)	(5)	(10)	(8)
Sciatic nerve:	(N=)	(6)	(5)	(10)	(8)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(6)	(5)	(10)	(8)
Bone (femur):	(N=)	(6)	(5)	(10)	(8)
Bone (vertebra):	(N=)	(6)	(5)	(10)	(8)
Tibio-femoral joint:	(N=)	(6)	(5)	(10)	(8)
Skeletal muscle (m. triceps surae):	(N=)	(6)	(5)	(10)	(8)
Sense Organs					
Eye:	(N=)	(6)	(5)	(10)	(8)
Harderian gland:	(N=)	(6)	(5)	(10)	(8)
Integumentary System					
Skin:	(N=)	(6)	(5)	(10)	(8)
(B) Keratoacanthoma		1	0	0	0
(B) Fibroma		0	0	1	0
No. of benign neoplasms		9	6	9	5
No. of malignant neoplasms		0	0	0	0
No. of benign & malignant neoplasms		9	6	9	5
No. of animals with benign neoplasm(s)		6	4	7	4
No. of animals with malignant neoplasm(s)		0	0	0	0
No. of animals with neoplasm(s)		6	4	7	4

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

Table 25 - 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
	No. of animals examined	18	20	18	29
Cardiovascular System					
Heart:	(N=)	(18)	(20)	(18)	(29)
(B) Schwannoma		0	0	0	1
Aorta:	(N=)	(18)	(20)	(18)	(29)
Hematopoietic & Lymphatic System					
General:	(N=)	(18)	(20)	(18)	(29)
(M) Mononuclear cell leukemia		0	1	0	0
Bone marrow (femur):	(N=)	(18)	(20)	(18)	(29)
Bone marrow (sternum):	(N=)	(18)	(20)	(18)	(29)
Bone marrow (vertebra):	(N=)	(18)	(20)	(18)	(29)
Thymus:	(N=)	(18)	(20)	(18)	(29)
Lymph nodes (cervical):	(N=)	(18)	(20)	(18)	(29)
Lymph nodes (mesenteric):	(N=)	(18)	(20)	(18)	(29)
Spleen:	(N=)	(18)	(20)	(18)	(29)
Respiratory System					
Trachea:	(N=)	(18)	(20)	(18)	(29)
Lung:	(N=)	(18)	(20)	(18)	(29)
(B) Adenoma		0	2	1	3
(M) Squamous cell carcinoma		0	0	1	0
Digestive System					
Submaxillary gland:	(N=)	(18)	(20)	(18)	(29)
Sublingular gland:	(N=)	(18)	(20)	(18)	(29)
Esophagus:	(N=)	(18)	(20)	(18)	(29)
Stomach (non-glandular portion):	(N=)	(18)	(20)	(18)	(29)
Stomach (glandular portion):	(N=)	(18)	(20)	(18)	(29)
(M) Leiomyosarcoma		0	0	1	0
Small intestine:	(N=)	(18)	(20)	(18)	(29)
(B) Leiomyoma		0	0	0	1
(M) Adenocarcinoma		0	0	1	0
Large intestine:	(N=)	(18)	(20)	(18)	(29)
Liver:	(N=)	(18)	(20)	(18)	(29)
(M) Hepatocellular carcinoma		0	0	0	1
Pancreas:	(N=)	(18)	(20)	(18)	(29)
(B) Acinar cell adenoma		0	1	0	1
(B) Islet cell adenoma		3	1	1	0
(M) Islet cell carcinoma		0	0	1	0
Urinary System					
Kidney:	(N=)	(18)	(20)	(18)	(29)
(B) Adenoma		0	0	0	1
(B) Lipoma		0	0	0	1
Urinary bladder:	(N=)	(18)	(20)	(18)	(29)
Genital System					
Testis:	(N=)	(18)	(20)	(18)	(29)
(B) Interstitial cell tumor		1	1	0	2
Epididymis:	(N=)	(18)	(20)	(18)	(29)
Seminal vesicle:	(N=)	(18)	(20)	(18)	(29)
Coagulating gland:	(N=)	(18)	(20)	(18)	(29)
(B) Adenoma		0	0	0	1
Prostate:	(N=)	(18)	(20)	(18)	(29)

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

Table 25 - 8 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
	No. of animals examined	18	20	18	29
Endocrine System					
Pituitary:	(N=)	(18)	(20)	(18)	(29)
(B) Anterior adenoma		13	14	13	21
(B) Adenoma in intermediate part		0	1	0	0
< Mass not in section >		0	0	0	1
Thyroid:	(N=)	(18)	(20)	(18)	(29)
(B) Follicular adenoma		2	1	0	0
(B) C-cell adenoma		2	5	0	1
(M) C-cell carcinoma		0	0	1	0
Parathyroid:	(N=)	(18)	(20)	(18)	(29)
Adrenal:	(N=)	(18)	(20)	(18)	(29)
(B) Pheochromocytoma		8	4	3	4*
Nervous System					
Cerebrum:	(N=)	(18)	(20)	(18)	(29)
(B) Glioma		0	0	0	1
Cerebellum:	(N=)	(18)	(20)	(18)	(29)
(B) Granular cell tumor		0	0	1	0
Brain stem:	(N=)	(18)	(20)	(18)	(29)
Spinal cord (cervical):	(N=)	(18)	(20)	(18)	(29)
Spinal cord (thoracic):	(N=)	(18)	(20)	(18)	(29)
Spinal cord (lumbar):	(N=)	(18)	(20)	(18)	(29)
Sciatic nerve:	(N=)	(18)	(20)	(18)	(29)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(18)	(20)	(18)	(29)
Bone (femur):	(N=)	(18)	(20)	(18)	(29)
Bone (vertebra):	(N=)	(18)	(20)	(18)	(29)
Tibio-femoral joint:	(N=)	(18)	(20)	(18)	(29)
Skeletal muscle (m. triceps surae):	(N=)	(18)	(20)	(18)	(29)
Sense Organs					
Eye:	(N=)	(18)	(20)	(18)	(29)
(B) Schwannoma		1	0	0	0
Harderian gland:	(N=)	(18)	(20)	(18)	(29)
Auricle:	(N=)	(3)	(0)	(0)	(2)
(B) Papilloma		1	-	-	0
(M) Malignant schwannoma		0	-	-	1
Integumentary System					
Skin:	(N=)	(18)	(20)	(18)	(29)
(B) Papilloma		1	3	2	0
(B) Keratoacanthoma		1	2	0	6
(B) Trichoepithelioma		0	1	0	0
(B) Sebaceous gland adenoma		0	1	0	0
(B) Basal cell adenoma		0	0	0	1
(B) Fibroma		1	0	3	2
(B) Lipoma		2	1	2	1
(M) Basal cell carcinoma		0	0	0	1
(M) Fibrosarcoma		0	1	1	0
(M) Malignant schwannoma		0	0	0	1
Mammary gland:	(N=)	(1)	(3)	(1)	(1)
(B) Fibroadenoma		1	2	0	0
(M) Adenocarcinoma		0	0	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.

Table 25 - 9 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
	No. of animals examined	18	20	18	29
No. of benign neoplasms		37	40	26	48
No. of malignant neoplasms		0	2	7	5
No. of benign & malignant neoplasms		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 animals with neoplasm(s)		18	19	18	27

Table 25 - 10 Histopathology - Incidence of microscopic neoplastic lesions in male rats (Main group)
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	32	30	32	21
General Organs					
(M) Systemic histiocytic sarcoma		0	0	1	0
(M) Systemic malignant fibrous histiocytoma		2	0	0	0
Cardiovascular System					
Heart:	(N=)	(32)	(30)	(32)	(21)
(B) Schwannoma		0	1	1	0
Aorta:	(N=)	(32)	(30)	(32)	(21)
Hematopoietic & Lymphatic System					
General:	(N=)	(32)	(30)	(32)	(21)
(M) Myelogenic leukemia		1	0	0	0
(M) Malignant lymphoma		0	2	1	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)	(29)	(32)	(21)
Lymph nodes (cervical):	(N=)	(32)	(29)	(30)	(21)
Lymph nodes (mesenteric):	(N=)	(32)	(30)	(32)	(21)
Spleen:	(N=)	(32)	(30)	(32)	(21)
(M) Histiocytic sarcoma		0	1	0	0
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	0
(M) Adenocarcinoma		0	0	0	1
Digestive System					
Submaxillary gland:	(N=)	(32)	(29)	(30)	(21)
Sublingular 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)
Small intestine:	(N=)	(32)	(30)	(32)	(21)
(M) Malignant schwannoma		0	1	0	0
Large intestine:	(N=)	(32)	(30)	(32)	(21)
Liver:	(N=)	(32)	(30)	(32)	(21)
(B) Hepatocellular adenoma		0	0	1	0
(M) Hepatocellular carcinoma		0	1	2	0
Pancreas:	(N=)	(32)	(30)	(32)	(21)
(B) Acinar cell adenoma		0	0	1	1
(B) Islet cell adenoma		1	0	0	1
Urinary System					
Kidney:	(N=)	(32)	(30)	(32)	(21)
(B) Adenoma		0	0	0	3
Urinary bladder:	(N=)	(32)	(30)	(32)	(21)
Genital System					
Testis:	(N=)	(31)	(30)	(32)	(21)
(B) Interstitial cell tumor		2	1	0	0
Epididymis:	(N=)	(31)	(30)	(32)	(21)
Seminal vesicle:	(N=)	(32)	(30)	(32)	(21)

(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 (ppm)	0	3000	10000	30000
	No. of animals examined	32	30	32	21
Genital System《cont.》					
Seminal vesicle《cont.》:	(N=)	(32)	(30)	(32)	(21)
Coagulating gland:	(N=)	(32)	(30)	(32)	(21)
Prostate:	(N=)	(32)	(30)	(32)	(21)
Penis:	(N=)	(1)	(0)	(0)	(0)
Endocrine System					
Pituitary:	(N=)	(32)	(30)	(32)	(21)
(B) Anterior adenoma		22	21	14*	18
Thyroid:	(N=)	(32)	(29)	(31)	(21)
(B) Follicular adenoma		1	0	1	0
(B) C-cell adenoma		2	4	2	4
(M) Follicular adenocarcinoma		1	0	0	0
(M) C-cell carcinoma		2	0	0	1
Parathyroid:	(N=)	(32)	(28)	(31)	(21)
Adrenal:	(N=)	(32)	(30)	(32)	(21)
(B) Cortical adenoma		1	2	0	0
(B) Pheochromocytoma		6	4	2	6
(M) Cortical adenocarcinoma		0	0	1	0
Nervous System					
Cerebrum:	(N=)	(32)	(30)	(32)	(21)
(B) Glioma		1	0	1	0
(M) Malignant reticulosis		1	0	0	0
Cerebellum:	(N=)	(32)	(30)	(32)	(21)
Brain stem:	(N=)	(32)	(30)	(32)	(21)
Spinal cord (cervical):	(N=)	(32)	(30)	(32)	(21)
Spinal cord (thoracic):	(N=)	(32)	(30)	(32)	(21)
Spinal cord (lumbar):	(N=)	(32)	(30)	(32)	(21)
Sciatic nerve:	(N=)	(31)	(30)	(31)	(20)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(32)	(30)	(32)	(21)
Bone (femur):	(N=)	(32)	(30)	(31)	(21)
(B) Osteochondroma		0	0	1	0
Bone (vertebra):	(N=)	(32)	(30)	(32)	(21)
Bone (others):	(N=)	(3)	(3)	(8)	(3)
(M) Osteosarcoma		0	0	1	0
Tibio-femoral joint:	(N=)	(32)	(30)	(31)	(21)
Skeletal muscle (m. triceps surae):	(N=)	(32)	(30)	(32)	(21)
Sense Organs					
Eye:	(N=)	(32)	(29)	(30)	(21)
Harderian gland:	(N=)	(32)	(29)	(30)	(21)
Ear:	(N=)	(0)	(1)	(1)	(0)
(M) Zymbal's gland carcinoma		-	0	1	-
Integumentary System					
Skin:	(N=)	(32)	(30)	(32)	(21)
(B) Papilloma		0	2	1	0
(B) Keratoacanthoma		2	1	0	1
(B) Basal cell adenoma		0	0	0	2
(B) Fibroma		3	3	0	3
(B) Lipoma		2	1	0	0
(M) Squamous cell carcinoma		0	0	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.

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

Site & Lesion	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	32	30	32	21
Integumentary System《cont.》					
Skin《cont.》:	(N=)	(32)	(30)	(32)	(21)
(M) Liposarcoma		1	0	0	0
(M) Hemangiosarcoma		0	0	1	0
(M) Malignant hemangiopericytoma		0	0	0	1
(M) Osteosarcoma		0	1	0	1
(M) Histiocytic sarcoma		0	0	1	0
Mammary gland:	(N=)	(2)	(2)	(1)	(1)
(B) Adenoma		1	0	0	0
(B) Fibroadenoma		1	1	1	0
(M) Adenocarcinoma		0	0	0	1
Body Cavities					
Thoracic cavity:	(N=)	(0)	(0)	(1)	(0)
(M) Malignant mesothelioma		-	-	1	-
Abdominal cavity:	(N=)	(1)	(4)	(3)	(1)
(M) Malignant schwannoma		0	0	1	0
(M) Malignant mesothelioma		0	1	0	0
No. of benign neoplasms		45	42	26	39
No. of malignant neoplasms		8	7	12	6
No. of benign & malignant neoplasms		53	49	38	45
No. of animals with benign neoplasm(s)		26	28	18	20
No. of animals with malignant neoplasm(s)		8	7	12	4
No. of animals with neoplasm(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	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	76	75	80	78
General Organs					
(M) Systemic histiocytic sarcoma		0	0	1	0
(M) Systemic malignant fibrous histiocytoma		2	0	0	0
Cardiovascular System					
Heart:	(N=)	(76)	(75)	(80)	(78)
(B) Schwannoma		0	1	1	1
Aorta:	(N=)	(76)	(75)	(80)	(78)
Hematopoietic & Lymphatic System					
General:	(N=)	(76)	(75)	(80)	(78)
(M) Myelogenic leukemia		1	0	0	0
(M) Malignant lymphoma		0	2	1	0
(M) Mononuclear cell leukemia		0	1	0	0
Bone marrow (femur):	(N=)	(76)	(75)	(79)	(78)
Bone marrow (sternum):	(N=)	(76)	(75)	(80)	(78)
Bone marrow (vertebra):	(N=)	(76)	(75)	(80)	(78)
Thymus:	(N=)	(76)	(74)	(80)	(78)
Lymph nodes (cervical):	(N=)	(76)	(74)	(78)	(78)
Lymph nodes (mesenteric):	(N=)	(76)	(75)	(80)	(78)
Spleen:	(N=)	(76)	(75)	(80)	(78)
(M) Histiocytic sarcoma		0	1	0	0
Respiratory System					
Nasal cavity:	(N=)	(0)	(2)	(0)	(3)
Trachea:	(N=)	(76)	(75)	(80)	(78)
Lung:	(N=)	(76)	(75)	(80)	(78)
(B) Adenoma		2	3	1	3
(M) Squamous cell carcinoma		0	0	1	0
(M) Adenocarcinoma		0	0	0	1
Digestive System					
Submaxillary gland:	(N=)	(76)	(74)	(78)	(78)
Sublingular gland:	(N=)	(76)	(74)	(78)	(78)
Esophagus:	(N=)	(76)	(75)	(80)	(78)
Stomach (non-glandular portion):	(N=)	(76)	(75)	(80)	(78)
Stomach (glandular portion):	(N=)	(76)	(75)	(80)	(78)
(M) Leiomyosarcoma		0	0	1	0
Small intestine:	(N=)	(76)	(75)	(80)	(78)
(B) Leiomyoma		0	0	0	1
(M) Adenocarcinoma		0	0	1	0
(M) Malignant schwannoma		0	1	0	0
Large intestine:	(N=)	(76)	(75)	(80)	(78)
Liver:	(N=)	(76)	(75)	(80)	(78)
(B) Hepatocellular adenoma		1	0	2	1
(M) Hepatocellular carcinoma		0	1	2	1
Pancreas:	(N=)	(76)	(75)	(80)	(78)
(B) Acinar cell adenoma		0	1	1	2
(B) Islet cell adenoma		4	1	1	1
(M) Islet cell carcinoma		0	0	1	0
Urinary System					
Kidney:	(N=)	(76)	(75)	(80)	(78)
(B) Adenoma		0	0	0	4

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

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

Site & Lesion	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	76	75	80	78
Urinary System《cont.》					
Kidney《cont.》:	(N=)	(76)	(75)	(80)	(78)
(B) Lipoma		0	0	0	1
Urinary bladder:	(N=)	(76)	(75)	(80)	(78)
Genital System					
Testis:	(N=)	(75)	(75)	(80)	(78)
(B) Interstitial cell tumor		3	2	0	2
Epididymis:	(N=)	(75)	(75)	(80)	(78)
Seminal vesicle:	(N=)	(76)	(75)	(80)	(78)
Coagulating gland:	(N=)	(76)	(75)	(80)	(78)
(B) Adenoma		0	0	0	1
Prostate:	(N=)	(76)	(75)	(80)	(78)
Penis:	(N=)	(1)	(0)	(0)	(0)
Endocrine System					
Pituitary:	(N=)	(76)	(75)	(80)	(78)
(B) Anterior adenoma		38	40	33	42
(B) Adenoma in intermediate part		0	1	0	0
< Mass not in section >		0	0	0	1
Thyroid:	(N=)	(76)	(74)	(79)	(78)
(B) Follicular adenoma		3	2	1	0
(B) C-cell adenoma		6	10	5	6
(M) Follicular adenocarcinoma		1	0	0	0
(M) C-cell carcinoma		2	0	1	1
Parathyroid:	(N=)	(76)	(73)	(79)	(78)
Adrenal:	(N=)	(76)	(75)	(80)	(78)
(B) Cortical adenoma		1	2	1	0
(B) Pheochromocytoma		14	9	5*	10
(M) Cortical adenocarcinoma		0	0	1	0
Nervous System					
Cerebrum:	(N=)	(76)	(75)	(80)	(78)
(B) Glioma		1	0	1	1
(M) Malignant reticulosis		1	0	0	0
Cerebellum:	(N=)	(76)	(75)	(80)	(78)
(B) Granular cell tumor		0	0	1	0
Brain stem:	(N=)	(76)	(75)	(80)	(78)
Spinal cord (cervical):	(N=)	(76)	(75)	(80)	(78)
Spinal cord (thoracic):	(N=)	(75)	(75)	(80)	(78)
Spinal cord (lumbar):	(N=)	(76)	(75)	(79)	(77)
Sciatic nerve:	(N=)	(75)	(75)	(79)	(77)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(76)	(75)	(80)	(78)
Bone (femur):	(N=)	(76)	(75)	(79)	(78)
(B) Osteochondroma		0	0	1	0
Bone (vertebra):	(N=)	(76)	(75)	(80)	(78)
Bone (others):	(N=)	(6)	(4)	(10)	(9)
(M) Osteosarcoma		0	0	1	0
Tibio-femoral joint:	(N=)	(76)	(75)	(79)	(78)
Skeletal muscle (m. triceps 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	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	76	75	80	78
Sense Organs					
Eye:	(N=)	(76)	(74)	(78)	(78)
(B) Schwannoma		1	0	0	0
Harderian gland:	(N=)	(76)	(74)	(78)	(78)
Ear:	(N=)	(0)	(1)	(1)	(0)
(M) Zymbal's gland carcinoma		-	0	1	-
Auricle:	(N=)	(3)	(1)	(0)	(2)
(B) Papilloma		1	0	-	0
(M) Malignant schwannoma		0	0	-	1
Integumentary System					
Skin:	(N=)	(76)	(75)	(80)	(78)
(B) Papilloma		2	5	3	0
(B) Keratoacanthoma		4	3	0	7
(B) Trichoepithelioma		0	1	0	0
(B) Sebaceous gland adenoma		0	1	0	0
(B) Basal cell adenoma		0	0	0	3
(B) Fibroma		4	4	4	5
(B) Lipoma		4	2	2	1
(M) Squamous cell carcinoma		0	0	1	1
(M) Basal cell carcinoma		0	0	0	1
(M) Fibrosarcoma		0	1	1	0
(M) Liposarcoma		1	0	0	0
(M) Hemangiosarcoma		0	0	1	0
(M) Malignant hemangiopericytoma		0	0	0	1
(M) Osteosarcoma		0	1	0	1
(M) Malignant schwannoma		0	0	0	1
(M) Histiocytic sarcoma		0	0	1	0
Mammary gland:	(N=)	(4)	(5)	(2)	(2)
(B) Adenoma		1	0	0	0
(B) Fibroadenoma		2	3	1	0
(M) Adenocarcinoma		0	0	1	2
Body Cavities					
Thoracic cavity:	(N=)	(0)	(0)	(1)	(0)
(M) Malignant mesothelioma		-	-	1	-
Abdominal cavity:	(N=)	(1)	(5)	(4)	(2)
(M) Malignant schwannoma		0	0	1	0
(M) Malignant mesothelioma		0	1	0	0
No. of benign neoplasms		92	91	64	92
No. of malignant neoplasms		8	9	19	11
No. of benign & malignant neoplasms		100	100	83	103
No. of animals with benign neoplasm(s)		51	54	43	51
No. of animals with malignant neoplasm(s)		8	9	19	9
No. of animals with neoplasm(s)		55	54	52	51

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

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

Site & Lesion	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	10	10	10	10
Cardiovascular System					
Heart:	(N=)	(10)	(10)	(10)	(10)
Aorta:	(N=)	(10)	(10)	(10)	(10)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (vertebra):	(N=)	(10)	(10)	(10)	(10)
Thymus:	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (cervical):	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (mesenteric):	(N=)	(10)	(10)	(10)	(10)
Spleen:	(N=)	(10)	(10)	(10)	(10)
Respiratory System					
Trachea:	(N=)	(10)	(10)	(10)	(10)
Lung:	(N=)	(10)	(10)	(10)	(10)
Digestive System					
Submaxillary gland:	(N=)	(10)	(10)	(10)	(10)
Sublingular gland:	(N=)	(10)	(10)	(10)	(10)
Esophagus:	(N=)	(10)	(10)	(10)	(10)
Stomach (non-glandular portion):	(N=)	(10)	(10)	(10)	(10)
Stomach (glandular portion):	(N=)	(10)	(10)	(10)	(10)
Small intestine:	(N=)	(10)	(10)	(10)	(10)
Large intestine:	(N=)	(10)	(10)	(10)	(10)
Liver:	(N=)	(10)	(10)	(10)	(10)
Pancreas:	(N=)	(10)	(10)	(10)	(10)
Urinary System					
Kidney:	(N=)	(10)	(10)	(10)	(10)
Urinary bladder:	(N=)	(10)	(10)	(10)	(10)
Genital System					
Ovary:	(N=)	(10)	(10)	(10)	(10)
Uterus:	(N=)	(10)	(10)	(10)	(10)
(B) Polyp/endometrial stromal polyp		1	0	0	0
Vagina:	(N=)	(10)	(10)	(10)	(10)
Endocrine System					
Pituitary:	(N=)	(10)	(10)	(10)	(10)
(B) Anterior adenoma		1	0	0	0
Thyroid:	(N=)	(10)	(10)	(10)	(10)
Parathyroid:	(N=)	(10)	(10)	(10)	(10)
Adrenal:	(N=)	(10)	(10)	(10)	(10)
Nervous System					
Cerebrum:	(N=)	(10)	(10)	(10)	(10)
Cerebellum:	(N=)	(10)	(10)	(10)	(10)
Brain stem:	(N=)	(10)	(10)	(10)	(10)
Spinal cord (cervical):	(N=)	(10)	(10)	(10)	(10)
Spinal cord (thoracic):	(N=)	(10)	(10)	(10)	(10)
Spinal cord (lumbar):	(N=)	(10)	(10)	(10)	(10)
Sciatic nerve:	(N=)	(10)	(10)	(10)	(10)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone (femur):	(N=)	(10)	(10)	(10)	(10)
Bone (vertebra):	(N=)	(10)	(10)	(10)	(10)

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

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

Site & Lesion	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	10	10	10	10
Musculo-Skeletal System《cont.》					
Bone (vertebra) 《cont.》:	(N=)	(10)	(10)	(10)	(10)
Tibio-femoral joint:	(N=)	(10)	(10)	(10)	(10)
Skeletal muscle (m. triceps surae):	(N=)	(10)	(10)	(10)	(10)
Sense Organs					
Eye:	(N=)	(10)	(10)	(10)	(10)
Harderian gland:	(N=)	(10)	(10)	(10)	(10)
Integumentary System					
Skin:	(N=)	(10)	(10)	(10)	(10)
Mammary gland:	(N=)	(10)	(10)	(9)	(10)
No. of benign neoplasms		2	0	0	0
No. of malignant neoplasms		0	0	0	0
No. of benign & malignant neoplasms		2	0	0	0
No. of animals with benign neoplasm(s)		2	0	0	0
No. of animals with malignant neoplasm(s)		0	0	0	0
No. of animals with neoplasm(s)		2	0	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	Dose (ppm)	0	3000	10000	30000
	No. of animals examined	10	10	10	10
Cardiovascular System					
Heart:	(N=)	(10)	(10)	(10)	(10)
Aorta:	(N=)	(10)	(10)	(10)	(10)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone marrow (vertebra):	(N=)	(10)	(10)	(10)	(10)
Thymus:	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (cervical):	(N=)	(10)	(10)	(10)	(10)
Lymph nodes (mesenteric):	(N=)	(10)	(10)	(10)	(10)
Spleen:	(N=)	(10)	(10)	(10)	(10)
Respiratory System					
Trachea:	(N=)	(10)	(10)	(10)	(10)
Lung:	(N=)	(10)	(10)	(10)	(10)
Digestive System					
Submaxillary gland:	(N=)	(10)	(10)	(10)	(10)
Sublingular gland:	(N=)	(10)	(10)	(10)	(10)
Esophagus:	(N=)	(10)	(10)	(10)	(10)
Stomach (non-glandular portion):	(N=)	(10)	(10)	(10)	(10)
Stomach (glandular portion):	(N=)	(10)	(10)	(10)	(10)
Small intestine:	(N=)	(10)	(10)	(10)	(10)
Large intestine:	(N=)	(10)	(10)	(10)	(10)
Liver:	(N=)	(10)	(10)	(10)	(10)
Pancreas:	(N=)	(10)	(10)	(10)	(10)
Urinary System					
Kidney:	(N=)	(10)	(10)	(10)	(10)
Urinary bladder:	(N=)	(10)	(10)	(10)	(10)
Genital System					
Ovary:	(N=)	(10)	(10)	(10)	(10)
Uterus:	(N=)	(10)	(10)	(10)	(10)
(B) Polyp/endometrial stromal polyp		0	1	1	1
Vagina:	(N=)	(10)	(10)	(10)	(10)
(B) Polyp		0	0	1	0
Endocrine System					
Pituitary:	(N=)	(10)	(10)	(10)	(10)
(B) Anterior adenoma		1	1	3	1
Thyroid:	(N=)	(10)	(10)	(10)	(10)
Parathyroid:	(N=)	(10)	(10)	(10)	(10)
Adrenal:	(N=)	(10)	(10)	(10)	(10)
Nervous System					
Cerebrum:	(N=)	(10)	(10)	(10)	(10)
Cerebellum:	(N=)	(10)	(10)	(10)	(10)
Brain stem:	(N=)	(10)	(10)	(10)	(10)
Spinal cord (cervical):	(N=)	(10)	(10)	(10)	(10)
Spinal cord (thoracic):	(N=)	(10)	(10)	(10)	(10)
Spinal cord (lumbar):	(N=)	(10)	(10)	(10)	(10)
Sciatic nerve:	(N=)	(10)	(10)	(10)	(10)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(10)	(10)	(10)	(10)
Bone (femur):	(N=)	(10)	(10)	(10)	(10)

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

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 animals examined	10	10	10	10
Musculo-Skeletal System《cont.》					
Bone (femur) 《cont.》:	(N=)	(10)	(10)	(10)	(10)
(B) Osteochondroma		0	0	0	1
Bone (vertebra):	(N=)	(10)	(10)	(10)	(10)
Tibio-femoral joint:	(N=)	(10)	(10)	(10)	(10)
Skeletal muscle (m. triceps surae):	(N=)	(10)	(10)	(10)	(10)
Sense Organs					
Eye:	(N=)	(10)	(10)	(10)	(10)
Harderian gland:	(N=)	(10)	(10)	(10)	(10)
Integumentary System					
Skin:	(N=)	(10)	(10)	(10)	(10)
Mammary gland:	(N=)	(10)	(10)	(10)	(10)
(B) Fibroadenoma		1	0	1	0
No. of benign neoplasms		2	2	6	3
No. of malignant neoplasms		0	0	0	0
No. of benign & malignant neoplasms		2	2	6	3
No. of animals with benign neoplasm(s)		2	2	4	2
No. of animals with malignant neoplasm(s)		0	0	0	0
No. of animals with neoplasm(s)		2	2	4	2

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

Table 26 - 5 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
	No. of animals examined	8	9	8	8
Cardiovascular System					
Heart:	(N=)	(8)	(9)	(8)	(8)
Aorta:	(N=)	(8)	(9)	(8)	(8)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(8)	(9)	(8)	(8)
Bone marrow (sternum):	(N=)	(8)	(9)	(8)	(8)
Bone marrow (vertebra):	(N=)	(8)	(9)	(8)	(8)
Thymus:	(N=)	(8)	(9)	(8)	(8)
Lymph nodes (cervical):	(N=)	(8)	(9)	(8)	(8)
Lymph nodes (mesenteric):	(N=)	(8)	(9)	(8)	(8)
Spleen:	(N=)	(8)	(9)	(8)	(8)
Respiratory System					
Trachea:	(N=)	(8)	(9)	(8)	(8)
Lung:	(N=)	(8)	(9)	(8)	(8)
Digestive System					
Submaxillary gland:	(N=)	(8)	(9)	(8)	(8)
Sublingual gland:	(N=)	(8)	(9)	(8)	(8)
Esophagus:	(N=)	(8)	(9)	(8)	(8)
Stomach (non-glandular portion):	(N=)	(8)	(9)	(8)	(8)
Stomach (glandular portion):	(N=)	(8)	(9)	(8)	(8)
Small intestine:	(N=)	(8)	(9)	(8)	(8)
Large intestine:	(N=)	(8)	(9)	(8)	(8)
Liver:	(N=)	(8)	(9)	(8)	(8)
Pancreas:	(N=)	(8)	(9)	(8)	(8)
Urinary System					
Kidney:	(N=)	(8)	(9)	(8)	(8)
Urinary bladder:	(N=)	(8)	(9)	(8)	(8)
Genital System					
Ovary:	(N=)	(8)	(9)	(8)	(8)
Uterus:	(N=)	(8)	(9)	(8)	(8)
(M) Adenocarcinoma		0	1	0	0
Vagina:	(N=)	(8)	(9)	(8)	(8)
(B) Polyp		0	0	0	1
Endocrine System					
Pituitary:	(N=)	(8)	(9)	(8)	(8)
(B) Anterior adenoma		6	5	4	7
Thyroid:	(N=)	(8)	(9)	(8)	(8)
(B) C-cell adenoma		0	0	1	2
Parathyroid:	(N=)	(8)	(9)	(8)	(8)
Adrenal:	(N=)	(8)	(9)	(8)	(8)
Nervous System					
Cerebrum:	(N=)	(8)	(9)	(8)	(8)
Cerebellum:	(N=)	(8)	(9)	(8)	(8)
Brain stem:	(N=)	(8)	(9)	(8)	(8)
Spinal cord (cervical):	(N=)	(8)	(9)	(8)	(8)
Spinal cord (thoracic):	(N=)	(8)	(9)	(8)	(8)
Spinal cord (lumbar):	(N=)	(8)	(9)	(8)	(8)
Sciatic nerve:	(N=)	(8)	(9)	(8)	(8)

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

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
	No. of animals examined	8	9	8	8
Musculo-Skeletal System					
Bone (sternum) :	(N=)	(8)	(9)	(8)	(8)
Bone (femur) :	(N=)	(8)	(9)	(8)	(8)
Bone (vertebra) :	(N=)	(8)	(9)	(8)	(8)
Tibio-femoral joint:	(N=)	(8)	(9)	(8)	(8)
Skeletal muscle (m. triceps surae) :	(N=)	(8)	(9)	(8)	(8)
Sense Organs					
Eye:	(N=)	(8)	(9)	(8)	(8)
Harderian gland:	(N=)	(8)	(9)	(8)	(8)
Auricle:	(N=)	(0)	(0)	(1)	(0)
(B) Papilloma		-	-	1	-
Integumentary System					
Skin:	(N=)	(8)	(9)	(8)	(8)
(B) Lipoma		0	1	0	0
Mammary gland:	(N=)	(8)	(9)	(8)	(8)
(B) Adenoma		0	1	1	0
(B) Fibroadenoma		1	3	2	0
(M) Adenocarcinoma		1	1	0	0
No. of benign neoplasms		7	10	9	10
No. of malignant neoplasms		1	2	0	0
No. of benign & malignant neoplasms		8	12	9	10
No. of animals with benign neoplasm(s)		7	5	4	8
No. of animals with malignant neoplasm(s)		1	2	0	0
No. of animals with neoplasm(s)		7	6	4	8

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

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 System					
Heart:	(N=)	(15)	(19)	(16)	(14)
Aorta:	(N=)	(15)	(19)	(16)	(14)
Hematopoietic & Lymphatic System					
Bone marrow (femur):	(N=)	(15)	(19)	(16)	(14)
Bone marrow (sternum):	(N=)	(15)	(19)	(16)	(14)
Bone marrow (vertebra):	(N=)	(15)	(19)	(16)	(14)
Thymus:	(N=)	(15)	(19)	(16)	(14)
Lymph nodes (cervical):	(N=)	(15)	(19)	(16)	(14)
Lymph nodes (mesenteric):	(N=)	(15)	(19)	(16)	(14)
Spleen:	(N=)	(15)	(19)	(16)	(14)
Respiratory System					
Trachea:	(N=)	(15)	(19)	(16)	(14)
Lung:	(N=)	(15)	(19)	(16)	(14)
Digestive System					
Submaxillary gland:	(N=)	(15)	(19)	(16)	(14)
Sublingual gland:	(N=)	(15)	(19)	(16)	(14)
Esophagus:	(N=)	(15)	(19)	(16)	(14)
Stomach (non-glandular portion):	(N=)	(15)	(19)	(16)	(14)
Stomach (glandular portion):	(N=)	(15)	(19)	(16)	(14)
Small intestine:	(N=)	(15)	(19)	(16)	(14)
(B) Leiomyoma		0	0	1	0
Large intestine:	(N=)	(15)	(19)	(16)	(14)
(M) Malignant histiocytoma		1	0	0	0
Liver:	(N=)	(15)	(19)	(16)	(14)
(B) Hepatocellular adenoma		1	1	0	0
Pancreas:	(N=)	(15)	(19)	(16)	(14)
(B) Islet cell adenoma		1	1	0	0
Urinary System					
Kidney:	(N=)	(15)	(19)	(16)	(14)
(B) Lipoma		0	1	0	0
Urinary bladder:	(N=)	(15)	(19)	(16)	(14)
Genital System					
Ovary:	(N=)	(15)	(19)	(16)	(14)
(B) Granulosa cell tumor		1	0	0	0
(B) Luteoma		0	0	1	0
Uterus:	(N=)	(15)	(19)	(16)	(14)
(B) Polyp/endometrial stromal polyp		3	3	1	2
(B) Granular cell tumor		1	0	0	0
(M) Adenocarcinoma		1	0	0	0
Vagina:	(N=)	(15)	(19)	(16)	(14)
Endocrine System					
Pituitary:	(N=)	(15)	(19)	(16)	(14)
(B) Anterior adenoma		12	19	12	13
(M) Anterior adenocarcinoma		1	0	0	0
Thyroid:	(N=)	(15)	(18)	(16)	(14)
(B) Follicular adenoma		0	0	1	0
(B) C-cell adenoma		1	4	2	1
Parathyroid:	(N=)	(15)	(19)	(16)	(14)
Adrenal:	(N=)	(15)	(19)	(16)	(14)

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

Table 26 - 8 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
Endocrine System《cont.》					
Adrenal《cont.》:	(N=)	(15)	(19)	(16)	(14)
(B) Cortical adenoma		0	0	1	0
(B) Pheochromocytoma		1	0	2	1
Nervous System					
Cerebrum:	(N=)	(15)	(19)	(16)	(14)
(M) Malignant reticulosis		0	1	0	0
Cerebellum:	(N=)	(15)	(19)	(16)	(14)
Brain stem:	(N=)	(15)	(19)	(16)	(14)
Spinal cord (cervical):	(N=)	(15)	(19)	(16)	(14)
Spinal cord (thoracic):	(N=)	(15)	(19)	(16)	(14)
Spinal cord (lumbar):	(N=)	(15)	(19)	(16)	(14)
Sciatic nerve:	(N=)	(15)	(19)	(16)	(14)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(15)	(19)	(16)	(14)
Bone (femur):	(N=)	(15)	(19)	(16)	(14)
Bone (vertebra):	(N=)	(15)	(19)	(16)	(14)
(B) Chordoma		1	0	0	0
Bone (others):	(N=)	(4)	(1)	(0)	(1)
(B) Osteochondroma		2	0	-	1
Tibio-femoral joint:	(N=)	(15)	(19)	(16)	(14)
Skeletal muscle (m. triceps surae):	(N=)	(15)	(19)	(16)	(14)
Sense Organs					
Eye:	(N=)	(15)	(19)	(16)	(14)
Harderian gland:	(N=)	(15)	(19)	(16)	(14)
Ear:	(N=)	(0)	(1)	(0)	(1)
Integumentary System					
Skin:	(N=)	(15)	(19)	(16)	(14)
(B) Papilloma		0	0	1	0
(B) Fibroma		2	2	0	1
(B) Lipoma		2	0	1	0
Mammary gland:	(N=)	(15)	(19)	(16)	(14)
(B) Adenoma		0	1	0	0
(B) Fibroadenoma		10	13	12	10
(M) Adenocarcinoma		2	2	5	1
Body Cavities					
Abdominal cavity:	(N=)	(1)	(0)	(1)	(0)
(B) Lipoma		0	-	1	-
(M) Malignant schwannoma		1	-	0	-
No. of benign neoplasms		38	45	36	29
No. of malignant neoplasms		6	3	5	1
No. of benign & malignant neoplasms		44	48	41	30
No. of animals with benign neoplasm(s)		15	19	15	14
No. of animals with malignant neoplasm(s)		4	3	5	1
No. of animals with neoplasm(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 sarcoma		1	0	0	0
Cardiovascular System					
Heart:	(N=)	(35)	(31)	(34)	(36)
(B) Schwannoma		0	0	0	1
Aorta:	(N=)	(35)	(31)	(34)	(36)
Hematopoietic & Lymphatic System					
General:	(N=)	(35)	(31)	(34)	(36)
(M) Malignant lymphoma		1	1	1	2
Bone marrow (femur):	(N=)	(35)	(31)	(34)	(36)
Bone marrow (sternum):	(N=)	(35)	(31)	(34)	(36)
Bone marrow (vertebra):	(N=)	(35)	(31)	(34)	(36)
Thymus:	(N=)	(35)	(31)	(34)	(36)
Lymph nodes (cervical):	(N=)	(35)	(31)	(32)	(36)
Lymph nodes (mesenteric):	(N=)	(35)	(31)	(34)	(36)
Spleen:	(N=)	(35)	(30)	(34)	(36)
Respiratory System					
Nasal cavity:	(N=)	(2)	(0)	(3)	(1)
(M) Squamous cell carcinoma		1	-	0	0
Trachea:	(N=)	(35)	(31)	(34)	(36)
Lung:	(N=)	(35)	(31)	(34)	(36)
Digestive System					
Submaxillary gland:	(N=)	(35)	(31)	(32)	(36)
Sublingular gland:	(N=)	(35)	(31)	(32)	(36)
Esophagus:	(N=)	(35)	(31)	(34)	(36)
Stomach (non-glandular portion):	(N=)	(35)	(30)	(34)	(36)
Stomach (glandular portion):	(N=)	(35)	(30)	(34)	(36)
Small intestine:	(N=)	(35)	(31)	(34)	(36)
Large intestine:	(N=)	(35)	(31)	(34)	(36)
Liver:	(N=)	(35)	(31)	(34)	(36)
Pancreas:	(N=)	(35)	(31)	(34)	(36)
(B) Islet cell adenoma		2	1	1	1
(M) Islet cell carcinoma		0	1	0	0
Urinary System					
Kidney:	(N=)	(35)	(31)	(34)	(36)
(M) Transitional cell carcinoma		1	0	0	0
Urinary bladder:	(N=)	(35)	(31)	(34)	(36)
(B) Papilloma		0	1	0	0
Genital System					
Ovary:	(N=)	(35)	(31)	(34)	(36)
Uterus:	(N=)	(35)	(31)	(34)	(36)
(B) Polyp/endometrial stromal polyp		1	4	0	2
(M) Malignant schwannoma		0	0	0	1
< Mass not in section >		1	0	0	0
Vagina:	(N=)	(35)	(31)	(34)	(36)
(B) Polyp		1	0	0	0
(M) Leiomyosarcoma		0	0	0	1
Clitoral gland:	(N=)	(1)	(0)	(0)	(0)
(M) Squamous cell carcinoma		1	-	-	-

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

Table 26 - 10 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
Endocrine System					
Pituitary:	(N=)	(35)	(31)	(33)	(36)
(B) Anterior adenoma		34	29	28	31
Thyroid:	(N=)	(35)	(31)	(32)	(36)
(B) Follicular adenoma		0	2	0	0
(B) C-cell adenoma		3	3	5	1
Parathyroid:	(N=)	(33)	(31)	(32)	(36)
Adrenal:	(N=)	(35)	(31)	(34)	(36)
(B) Cortical adenoma		0	1	0	0
(B) Ganglioneuroma		0	1	0	0
(B) Pheochromocytoma		1	0	0	0
Nervous System					
Cerebrum:	(N=)	(35)	(31)	(33)	(36)
(B) Meningioma		0	1	0	0
(M) Malignant reticulosis		1	0	0	0
Cerebellum:	(N=)	(35)	(31)	(33)	(36)
(B) Granular cell tumor		0	0	1	0
Brain stem:	(N=)	(35)	(31)	(33)	(36)
Spinal cord (cervical):	(N=)	(35)	(31)	(34)	(36)
Spinal cord (thoracic):	(N=)	(35)	(31)	(34)	(36)
Spinal cord (lumbar):	(N=)	(35)	(31)	(34)	(36)
Sciatic nerve:	(N=)	(35)	(31)	(34)	(36)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(35)	(31)	(34)	(36)
Bone (femur):	(N=)	(35)	(31)	(34)	(36)
Bone (vertebra):	(N=)	(35)	(31)	(34)	(36)
Bone (others):	(N=)	(2)	(2)	(2)	(4)
(B) Osteochondroma		0	0	0	2
Tibio-femoral joint:	(N=)	(35)	(31)	(34)	(36)
Skeletal muscle (m. triceps surae):	(N=)	(35)	(31)	(34)	(36)
Sense Organs					
Eye:	(N=)	(35)	(31)	(32)	(36)
Harderian gland:	(N=)	(35)	(31)	(33)	(36)
Ear:	(N=)	(3)	(1)	(1)	(2)
Auricle:	(N=)	(1)	(1)	(1)	(2)
(B) Fibroma		1	0	0	0
Integumentary System					
Skin:	(N=)	(35)	(31)	(34)	(36)
(B) Papilloma		0	1	0	0
(B) Keratoacanthoma		0	0	0	1
(B) Fibroma		2	1	2	3
(B) Lipoma		2	0	2	0
< Mass not in section >		0	0	3	0
Mammary gland:	(N=)	(35)	(31)	(34)	(36)
(B) Adenoma		1	0	0	0
(B) Fibroadenoma		13	14	12	20
(M) Adenocarcinoma		8	5	6	7

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

Table 26 - 11 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
No. of benign neoplasms		61	59	51	62
No. of malignant neoplasms		14	7	7	11
No. of benign & malignant neoplasms		75	66	58	73
No. of animals with benign neoplasm(s)		34	29	31	35
No. of animals with malignant neoplasm(s)		12	7	7	11
No. of animals with neoplasm(s)		34	31	31	36

Table 26 - 12 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 animals examined	78	79	78	78
General Organs					
(M) Systemic histiocytic sarcoma		1	0	0	0
Cardiovascular System					
Heart:	(N=)	(78)	(79)	(78)	(78)
(B) Schwannoma		0	0	0	1
Aorta:	(N=)	(78)	(79)	(78)	(78)
Hematopoietic & Lymphatic System					
General:	(N=)	(78)	(79)	(78)	(78)
(M) Malignant lymphoma		1	1	1	2
Bone marrow (femur):	(N=)	(78)	(79)	(78)	(78)
Bone marrow (sternum):	(N=)	(78)	(79)	(78)	(78)
Bone marrow (vertebra):	(N=)	(78)	(79)	(78)	(78)
Thymus:	(N=)	(78)	(79)	(78)	(78)
Lymph nodes (cervical):	(N=)	(78)	(79)	(76)	(78)
Lymph nodes (mesenteric):	(N=)	(78)	(79)	(78)	(78)
Spleen:	(N=)	(78)	(78)	(78)	(78)
Respiratory System					
Nasal cavity:	(N=)	(2)	(0)	(3)	(1)
(M) Squamous cell carcinoma		1	-	0	0
Trachea:	(N=)	(78)	(79)	(78)	(78)
Lung:	(N=)	(78)	(79)	(78)	(78)
Digestive System					
Submaxillary gland:	(N=)	(78)	(79)	(76)	(78)
Sublingular gland:	(N=)	(78)	(79)	(76)	(78)
Esophagus:	(N=)	(78)	(79)	(78)	(78)
Stomach (non-glandular portion):	(N=)	(78)	(78)	(78)	(78)
Stomach (glandular portion):	(N=)	(78)	(78)	(78)	(78)
Small intestine:	(N=)	(78)	(79)	(78)	(78)
(B) Leiomyoma		0	0	1	0
Large intestine:	(N=)	(78)	(79)	(78)	(78)
(M) Malignant histiocytoma		1	0	0	0
Liver:	(N=)	(78)	(79)	(78)	(78)
(B) Hepatocellular adenoma		1	1	0	0
Pancreas:	(N=)	(78)	(79)	(78)	(78)
(B) Islet cell adenoma		3	2	1	1
(M) Islet cell carcinoma		0	1	0	0
Urinary System					
Kidney:	(N=)	(78)	(79)	(78)	(78)
(B) Lipoma		0	1	0	0
(M) Transitional cell carcinoma		1	0	0	0
Urinary bladder:	(N=)	(78)	(79)	(78)	(78)
(B) Papilloma		0	1	0	0
Genital System					
Ovary:	(N=)	(78)	(79)	(78)	(78)
(B) Granulosa cell tumor		1	0	0	0
(B) Luteoma		0	0	1	0
Uterus:	(N=)	(78)	(79)	(78)	(78)
(B) Polyp/endometrial stromal polyp		5	8	2	5
(B) Granular cell tumor		1	0	0	0
(M) Adenocarcinoma		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 (ppm)	0	3000	10000	30000
	No. of animals examined	78	79	78	78
Genital System《cont.》					
Uterus《cont.》:	(N=)	(78)	(79)	(78)	(78)
(M) Malignant schwannoma		0	0	0	1
< Mass not in section >		1	0	0	0
Vagina:	(N=)	(78)	(79)	(78)	(78)
(B) Polyp		1	0	1	1
(M) Leiomyosarcoma		0	0	0	1
Clitoral gland:	(N=)	(1)	(0)	(0)	(1)
(M) Squamous cell carcinoma		1	-	-	0
Endocrine System					
Pituitary:	(N=)	(78)	(79)	(77)	(78)
(B) Anterior adenoma		54	54	47	52
(M) Anterior adenocarcinoma		1	0	0	0
Thyroid:	(N=)	(78)	(78)	(76)	(78)
(B) Follicular adenoma		0	2	1	0
(B) C-cell adenoma		4	7	8	4
Parathyroid:	(N=)	(76)	(79)	(76)	(78)
Adrenal:	(N=)	(78)	(79)	(78)	(78)
(B) Cortical adenoma		0	1	1	0
(B) Ganglioneuroma		0	1	0	0
(B) Pheochromocytoma		2	0	2	1
Nervous System					
Cerebrum:	(N=)	(78)	(79)	(77)	(78)
(B) Meningioma		0	1	0	0
(M) Malignant reticulosis		1	1	0	0
Cerebellum:	(N=)	(78)	(79)	(77)	(78)
(B) Granular cell tumor		0	0	1	0
Brain stem:	(N=)	(78)	(79)	(77)	(78)
Spinal cord (cervical):	(N=)	(78)	(79)	(78)	(78)
Spinal cord (thoracic):	(N=)	(78)	(79)	(78)	(78)
Spinal cord (lumbar):	(N=)	(78)	(79)	(78)	(78)
Sciatic nerve:	(N=)	(78)	(79)	(78)	(78)
Musculo-Skeletal System					
Bone (sternum):	(N=)	(78)	(79)	(78)	(78)
Bone (femur):	(N=)	(78)	(79)	(78)	(78)
(B) Osteochondroma		0	0	0	1
Bone (vertebra):	(N=)	(78)	(79)	(78)	(78)
(B) Chordoma		1	0	0	0
Bone (others):	(N=)	(6)	(3)	(2)	(5)
(B) Osteochondroma		2	0	0	3
Tibio-femoral joint:	(N=)	(78)	(79)	(78)	(78)
Skeletal muscle (m. triceps surae):	(N=)	(78)	(79)	(78)	(78)
Sense Organs					
Eye:	(N=)	(78)	(79)	(76)	(78)
Harderian gland:	(N=)	(78)	(79)	(77)	(78)
Ear:	(N=)	(3)	(2)	(1)	(3)
Auricle:	(N=)	(3)	(1)	(2)	(3)
(B) Papilloma		0	0	1	0
(B) Fibroma		1	0	0	0

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

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 animals examined	78	79	78	78
Integumentary System					
Skin:	(N=)	(78)	(79)	(78)	(78)
(B) Papilloma		0	1	1	0
(B) Keratoacanthoma		0	0	0	1
(B) Fibroma		4	3	2	4
(B) Lipoma		4	1	3	0
< Mass not in section >		0	0	3	0
Mammary gland:	(N=)	(78)	(79)	(77)	(78)
(B) Adenoma		1	2	1	0
(B) Fibroadenoma		25	30	27	30
(M) Adenocarcinoma		11	8	11	8
Body Cavities					
Abdominal cavity:	(N=)	(1)	(2)	(1)	(0)
(B) Lipoma		0	0	1	-
(M) Malignant schwannoma		1	0	0	-
No. of benign neoplasms		110	116	102	104
No. of malignant neoplasms		21	12	12	12
No. of benign & malignant neoplasms		131	128	114	116
No. of animals with benign neoplasm(s)		60	55	54	59
No. of animals with malignant neoplasm(s)		17	12	12	12
No. of animals with neoplasm(s)		60	58	54	60

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

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
ABDOMINAL CAVITY								
EXAMINED	0	1	2	0	4	3	0	0
Lipoma..(BENIGN)	0	0	0	0	1	0	0	0
ADRENAL GLAND								
EXAMINED	37	36	34	26	20	24	13	23
MISSING	0	0	1	0	0	0	0	0
Benign ganglioneuroma..(BENIGN)	0	0	0	0	0	1	0	0
Benign phaeochromocytoma..(BENIGN)	4	2	3	3	0	0	0	0
Cortical adenoma..(BENIGN)	0	0	0	1	0	0	0	0
Malignant phaeochromocytoma (MALIGNANT)	0	1	0	0	0	0	0	0
BRAIN								
EXAMINED	37	36	35	26	20	24	13	23
Astrocytoma..(MALIGNANT)	0	0	2	0	0	0	1	1
Benign meningioma..(BENIGN)	0	1	0	1	0	0	0	0
Benign ependymoma..(BENIGN)	0	0	1	0	0	0	0	0
Pineal gland tumour..(BENIGN)	0	0	0	0	0	0	1	0
CERVIX								
EXAMINED	-	-	-	-	19	20	12	22
MISSING	-	-	-	-	1	4	1	1
Adenocarcinoma..(MALIGNANT)	-	-	-	-	1	0	0	1
Stromal cell sarcoma..(MALIGNANT)	-	-	-	-	0	0	0	2
Haemangiosarcoma..(MALIGNANT)	-	-	-	-	0	0	1	0
DUODENUM								
EXAMINED	36	32	34	25	17	21	13	20
MISSING	1	4	1	1	3	3	0	3
Leiomyoma..(BENIGN)	0	0	0	0	0	1	0	0
EAR/ZYMBALS GLAND								
EXAMINED	0	0	1	0	0	0	0	0

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
EAR/ZYMBALS GLAND (CONTINUED)								
Squamous cell carcinoma..(MALIGNANT)..	0	0	1	0	0	0	0	0
HARDERIAN GLAND								
EXAMINED	36	34	35	26	20	23	13	23
MISSING	1	2	0	0	0	1	0	0
Anaplastic sarcoma..(MALIGNANT)	0	0	0	0	0	1	0	0
HEART								
EXAMINED	37	36	35	26	20	24	13	23
Malignant endocardial schwannoma (MALIGNANT)	1	0	0	0	0	0	0	0
KIDNEY								
EXAMINED	37	36	35	26	20	24	13	23
Haemangioma..(BENIGN)	0	0	0	1	0	0	0	0
LACRIMAL GLAND								
EXAMINED	36	34	35	26	19	23	13	22
MISSING	1	2	0	0	1	1	0	1
Neurofibrosarcoma..(MALIGNANT)	1	0	0	0	0	0	0	0
LIMB								
EXAMINED	9	10	3	4	2	1	0	1
MISSING	0	1	0	0	0	0	0	0
Squamous papilloma..(BENIGN)	0	1	0	1	0	0	0	0
Benign histiocytoma..(BENIGN)	0	0	0	0	1	0	0	0
LIVER								
EXAMINED	37	36	35	26	20	24	13	23
Hepatocellular adenoma..(BENIGN)	0	2	0	3	0	0	0	0
Liposarcoma..(MALIGNANT)	0	0	1	0	0	0	0	0
LUNG								
EXAMINED	37	36	35	26	20	24	13	23

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
LUNG (CONTINUED)								
Adenocarcinoma..(MALIGNANT).....	0	1	0	0	0	0	0	0
LYMPH NODE-MESENTERIC								
EXAMINED.....	37	34	35	26	20	22	13	21
MISSING.....	0	2	0	0	0	2	0	2
Haemangioma..(BENIGN).....	5	4	3	1	2	1	0	0
Haemangiosarcoma..(MALIGNANT).....	1	0	0	0	0	0	0	0
LYMPHORETICULAR SYSTEM								
EXAMINED.....	5	1	1	1	6	6	3	4
Lymphosarcoma..(MALIGNANT).....	1	0	0	0	1	0	0	0
Large granular lymphocyte leukemia (MALIGNANT).....	3	1	0	1	5	5	3	4
Myeloid leukaemia..(MALIGNANT).....	0	0	1	0	0	0	0	0
Histiocytic/Granulocytic cell tumour (MALIGNANT).....	1	0	0	0	0	1	0	0
MAMMARY GLAND								
EXAMINED.....	-	-	-	-	20	23	13	23
MISSING.....	-	-	-	-	0	1	0	0
Adenoma..(BENIGN).....	-	-	-	-	1	0	0	0
Cystadenoma..(BENIGN).....	-	-	-	-	0	0	1	1
Fibroadenoma..(BENIGN).....	-	-	-	-	2	3	1	1
NASAL CAVITY								
EXAMINED.....	37	36	35	26	20	24	13	23
Fibrosarcoma..(MALIGNANT).....	0	0	1	0	0	0	0	0
Papilloma/s nasolachrymal duct (BENIGN).....	0	0	1	0	0	0	1	0
Ameloblastoma..(MALIGNANT).....	0	1	0	0	0	0	0	0
ORAL CAVITY								
EXAMINED.....	6	3	4	2	1	5	1	2
MISSING.....	0	0	0	1	0	0	0	0

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
ORAL CAVITY	(CONTINUED)							
Squamous cell carcinoma..(MALIGNANT)..	0	1	1	0	1	1	0	0
Fibrosarcoma..(MALIGNANT).....	0	0	0	1	0	0	0	0
PANCREAS								
EXAMINED.....	37	36	35	26	19	23	13	23
MISSING.....	0	0	0	0	1	1	0	0
Exocrine adenoma..(BENIGN).....	2	1	3	3	0	0	0	0
Exocrine adenocarcinoma..(MALIGNANT)..	0	1	0	0	0	0	0	0
Islet cell adenoma..(BENIGN).....	0	1	0	0	0	0	0	0
PARATHYROID GLAND								
EXAMINED.....	32	33	32	26	19	18	13	22
MISSING.....	5	3	3	0	1	6	0	1
Adenoma..(BENIGN).....	0	1	0	0	0	0	0	0
PHARYNX								
EXAMINED.....	36	36	35	26	20	24	13	23
MISSING.....	1	0	0	0	0	0	0	0
Squamous cell carcinoma..(MALIGNANT)..	1	0	0	0	0	0	0	0
PITUITARY GLAND								
EXAMINED.....	37	35	35	26	20	23	13	23
MISSING.....	0	1	0	0	0	1	0	0
Adenoma pars distalis..(BENIGN).....	11	7	11	6	17	16	8	17
Adenoma pars intermedia..(BENIGN).....	0	1	0	0	0	0	0	0
SALIVARY GLAND								
EXAMINED.....	35	34	35	26	19	22	13	23
MISSING.....	2	2	0	0	1	2	0	0
Adenoma..(BENIGN).....	0	0	0	0	1	0	0	0
SKIN								
EXAMINED.....	37	36	35	25	20	24	13	23
MISSING.....	0	0	0	1	0	0	0	0

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
SKIN	(CONTINUED)							
Squamous papilloma..(BENIGN).....	0	0	1	0	0	0	0	0
Squamous carcinoma..(MALIGNANT).....	0	0	0	0	0	1	0	0
Benign basal cell tumour..(BENIGN)....	1	0	0	1	0	0	0	0
Basal cell carcinoma..(MALIGNANT).....	0	0	1	0	0	0	0	0
Pilomatrixoma..(BENIGN).....	5	0	0	3	0	0	0	0
Keratoacanthoma..(BENIGN).....	0	0	1	0	0	0	0	0
Sebaceous adenoma..(BENIGN).....	0	1	0	0	0	0	0	0
Trichofolliculoma..(BENIGN).....	0	1	0	0	0	0	0	0
Histiocytic sarcoma..(MALIGNANT).....	1	0	0	0	0	0	0	0
STOMACH								
EXAMINED.....	37	36	35	26	20	23	13	23
MISSING.....	0	0	0	0	0	1	0	0
Squamous papilloma..(BENIGN).....	0	0	0	0	0	0	1	0
SUBCUTANEOUS TISSUE								
EXAMINED.....	8	2	5	6	4	4	2	1
Fibroma..(BENIGN).....	0	1	0	1	0	1	0	0
Fibrosarcoma..(MALIGNANT).....	1	0	2	1	0	0	0	0
Haemangioma..(BENIGN).....	0	0	1	0	0	0	0	0
Lipoma..(BENIGN).....	0	0	0	0	1	0	0	0
TAIL								
EXAMINED.....	21	26	24	17	3	2	3	7
MISSING.....	1	0	0	0	0	0	0	1
Fibrosarcoma..(MALIGNANT).....	0	0	0	0	0	0	0	1
TESTIS								
EXAMINED.....	36	35	34	26	-	-	-	-
MISSING.....	1	1	1	0	-	-	-	-
Benign Leydig cell tumour..(BENIGN)...	1	1	1	0	-	-	-	-

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

REMOVAL REASON: INTERCURRENT	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	37	36	35	26	20	24	13	23
TESTIS	(CONTINUED)							
Malignant mesothelioma..(MALIGNANT)...	0	1	0	0	-	-	-	-
THYMUS								
EXAMINED.....	34	33	30	23	20	22	12	22
MISSING.....	3	3	5	3	0	2	1	1
Benign thymoma..(BENIGN).....	1	1	0	1	1	0	0	0
Malignant thymoma..(MALIGNANT).....	0	0	0	0	1	0	1	0
Not otherwise specified sarcoma (MALIGNANT).....	0	0	0	0	0	0	0	1
THYROID GLAND								
EXAMINED.....	36	35	35	26	19	23	13	23
MISSING.....	1	1	0	0	1	1	0	0
Follicular cell adenoma..(BENIGN).....	1	0	0	0	0	1	0	0
Parafollicular cell adenoma..(BENIGN).	1	0	0	0	0	0	0	2
UTERUS								
EXAMINED.....	-	-	-	-	20	24	13	23
Stromal cell polyp..(BENIGN).....	-	-	-	-	1	1	1	1
Adenocarcinoma..(MALIGNANT).....	-	-	-	-	2	8	0	2
Squamous cell carcinoma..(MALIGNANT)..	-	-	-	-	0	1	1	1
Haemangiosarcoma..(MALIGNANT).....	-	-	-	-	1	0	1	0

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

REMOVAL REASON: INTERIM	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	11	11	11	12	12	12	12	11
PITUITARY GLAND								
EXAMINED	11	11	11	11	12	12	11	11
MISSING	0	0	0	1	0	0	1	0
Adenoma pars distalis..(BENIGN)	2	2	0	1	5	4	4	4
THYROID GLAND								
EXAMINED	11	11	10	12	12	12	12	11
MISSING	0	0	1	0	0	0	0	0
Parafollicular cell adenoma..(BENIGN)	0	0	0	0	1	0	0	0
UTERUS								
EXAMINED	-	-	-	-	12	12	12	11
Stromal cell polyp..(BENIGN)	-	-	-	-	1	1	1	0

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

REMOVAL REASON: TERMINAL	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	16	17	18	26	32	28	39	30
ADRENAL GLAND								
EXAMINED	16	17	18	26	32	28	38	30
MISSING	0	0	0	0	0	0	1	0
Benign phaeochromocytoma..(BENIGN)	4	2	4	1	1	2	0	0
Cortical adenoma..(BENIGN)	0	1	0	0	0	0	0	0
Malignant phaeochromocytoma (MALIGNANT)	0	0	0	1	0	0	0	0
BRAIN								
EXAMINED	16	17	18	26	32	28	39	30
Astrocytoma..(MALIGNANT)	0	0	0	0	0	0	1	0
Benign meningioma..(BENIGN)	0	0	0	0	0	0	0	1
CERVIX								
EXAMINED	-	-	-	-	32	28	39	30
Stromal cell polyp..(BENIGN)	-	-	-	-	0	0	1	0
Stromal cell sarcoma..(MALIGNANT)	-	-	-	-	0	0	1	0
DUODENUM								
EXAMINED	16	17	18	26	32	28	39	30
Adenocarcinoma..(MALIGNANT)	0	0	0	0	0	1	0	0
EPIDIDYMIS								
EXAMINED	16	17	18	26	-	-	-	-
Benign mesothelioma..(BENIGN)	0	1	0	1	-	-	-	-
Malignant mesothelioma..(MALIGNANT)	0	1	0	0	-	-	-	-
ILEUM								
EXAMINED	16	17	18	26	30	27	39	30
MISSING	0	0	0	0	2	1	0	0
Leiomyosarcoma..(MALIGNANT)	0	0	0	0	0	1	0	0
KIDNEY								
EXAMINED	16	17	18	26	32	28	39	30

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

REMOVAL REASON: TERMINAL	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	16	17	18	26	32	28	39	30
KIDNEY (CONTINUED)								
Liposarcoma..(MALIGNANT).....	0	0	0	0	0	0	1	0
Mixed mesenchymal tumour..(MALIGNANT).	0	0	0	1	0	0	0	0
LIVER								
EXAMINED.....	16	17	18	26	32	28	39	30
Hepatocellular adenoma..(BENIGN).....	0	0	0	2	0	0	1	0
LYMPH NODE-MESENTERIC								
EXAMINED.....	16	17	18	26	32	28	39	30
Haemangioma..(BENIGN).....	2	2	1	4	2	5	6	3
Haemangiosarcoma..(MALIGNANT).....	0	1	0	0	1	0	0	1
LYMPH NODE-PANCREATIC								
EXAMINED.....	1	0	1	1	0	1	1	0
Haemangioma..(BENIGN).....	1	0	0	0	0	0	0	0
LYMPHORETICULAR SYSTEM								
EXAMINED.....	1	3	0	2	5	7	11	4
Lymphosarcoma..(MALIGNANT).....	0	0	0	0	0	0	1	0
Large granular lymphocyte leukemia (MALIGNANT).....	1	3	0	2	4	7	10	4
Histiocytic/Granulocytic cell tumour (MALIGNANT).....	0	0	0	0	1	0	0	0
MAMMARY GLAND								
EXAMINED.....	-	-	-	-	31	28	39	30
MISSING.....	-	-	-	-	1	0	0	0
Adenocarcinoma..(MALIGNANT).....	-	-	-	-	2	0	0	2
Adenoma..(BENIGN).....	-	-	-	-	0	2	0	0
Cystadenoma..(BENIGN).....	-	-	-	-	2	0	0	0
Fibroadenoma..(BENIGN).....	-	-	-	-	2	1	5	4
NASAL CAVITY								
EXAMINED.....	16	17	18	26	32	28	39	30

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

REMOVAL REASON: TERMINAL	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	16	17	18	26	32	28	39	30
NASAL CAVITY	(CONTINUED)							
Papilloma/s nasolachrymal duct (BENIGN)	0	0	0	0	0	0	0	1
Adenoma nasolachrymal duct..(BENIGN)..	0	0	0	0	0	1	0	0
ORAL CAVITY								
EXAMINED	2	1	3	2	3	2	4	1
Squamous cell carcinoma..(MALIGNANT)..	0	1	1	2	0	1	0	0
Squamous cell papilloma..(BENIGN).....	0	0	0	0	0	0	1	0
PANCREAS								
EXAMINED	16	17	18	26	32	28	39	30
Exocrine adenoma..(BENIGN).....	2	1	4	4	0	0	0	0
Islet cell adenoma..(BENIGN).....	1	1	0	1	0	0	1	0
Islet cell adenocarcinoma (MALIGNANT)	0	0	0	0	0	1	0	0
PITUITARY GLAND								
EXAMINED	16	17	18	26	31	28	39	30
MISSING	0	0	0	0	1	0	0	0
Adenoma pars distalis..(BENIGN).....	5	7	4	11	25	24	34	28
Adenoma pars intermedia..(BENIGN).....	0	0	3	1	0	0	0	0
SALIVARY GLAND								
EXAMINED	16	17	18	26	32	28	39	30
Neurofibrosarcoma..(MALIGNANT).....	0	0	0	1	0	0	0	0
SKIN								
EXAMINED	16	17	18	26	32	28	39	30
Squamous carcinoma..(MALIGNANT).....	0	0	0	0	0	0	0	1
Benign basal cell tumour..(BENIGN)....	0	0	1	0	0	0	0	1
Pilomatrixoma..(BENIGN).....	0	3	0	1	1	0	0	1

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

REMOVAL REASON: TERMINAL	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	16	17	18	26	32	28	39	30
SKIN	(CONTINUED)							
Keratoacanthoma..(BENIGN).....	1	0	0	1	0	0	0	0
Sebaceous adenoma..(BENIGN).....	0	0	1	0	0	0	0	0
SPLEEN								
EXAMINED.....	16	17	18	26	32	28	39	30
Haemangiosarcoma..(MALIGNANT).....	0	0	0	0	0	0	1	0
Not otherwise specified sarcoma (MALIGNANT).....	0	1	0	0	0	0	0	0
SUBCUTANEOUS TISSUE								
EXAMINED.....	3	4	5	2	4	3	7	6
Fibroma..(BENIGN).....	2	1	0	0	1	0	1	0
Haemangioma..(BENIGN).....	1	0	0	0	0	0	0	1
Haemangiosarcoma..(MALIGNANT).....	0	1	0	0	0	0	0	0
Lipoma..(BENIGN).....	0	0	1	1	0	0	2	0
TESTIS								
EXAMINED.....	16	17	18	26	-	-	-	-
Benign Leydig cell tumour..(BENIGN)...	4	1	1	2	-	-	-	-
Benign mesothelioma..(BENIGN).....	0	1	0	0	-	-	-	-
THYMUS								
EXAMINED.....	16	16	18	25	31	28	38	30
MISSING.....	0	1	0	1	1	0	1	0
Benign thymoma..(BENIGN).....	0	0	0	1	1	1	0	1
THYROID GLAND								
EXAMINED.....	16	17	18	26	32	28	39	30
Follicular cell adenoma..(BENIGN).....	0	0	2	3	1	1	1	0
Parafollicular cell adenoma..(BENIGN).	1	1	1	0	3	0	0	0
Parafollicular cell carcinoma (MALIGNANT).....	0	1	0	0	0	0	0	1
UTERUS								
EXAMINED.....	-	-	-	-	32	28	39	30

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

REMOVAL REASON: TERMINAL	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	16	17	18	26	32	28	39	30
UTERUS	(CONTINUED)							
Stromal cell polyp..(BENIGN).....	-	-	-	-	5	3	5	1
Adenocarcinoma..(MALIGNANT).....	-	-	-	-	4	2	9	3
Leiomyoma..(BENIGN).....	-	-	-	-	0	0	2	0
Haemangioma..(BENIGN).....	-	-	-	-	0	0	1	0
VOLUNTARY MUSCLE								
EXAMINED.....	16	17	17	26	32	28	38	30
MISSING.....	0	0	1	0	0	0	1	0
Haemangioma..(BENIGN).....	0	0	1	0	0	0	0	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
ABDOMINAL CAVITY								
EXAMINED	0	1	3	0	5	5	0	2
Lipoma..(BENIGN)	0	0	0	0	1	0	0	0
ADRENAL GLAND								
EXAMINED	64	64	63	64	64	64	63	64
MISSING	0	0	1	0	0	0	1	0
Benign ganglioneuroma..(BENIGN)	0	0	0	0	0	1	0	0
Benign phaeochromocytoma..(BENIGN)	8	4	7	4	1	2	0	0
Cortical adenoma..(BENIGN)	0	1	0	1	0	0	0	0
Malignant phaeochromocytoma (MALIGNANT)	0	1	0	1	0	0	0	0
BRAIN								
EXAMINED	64	64	64	64	64	64	64	64
Astrocytoma..(MALIGNANT)	0	0	2	0	0	0	2	1
Benign meningioma..(BENIGN)	0	1	0	1	0	0	0	1
Benign ependymoma..(BENIGN)	0	0	1	0	0	0	0	0
Pineal gland tumour..(BENIGN)	0	0	0	0	0	0	1	0
CERVIX								
EXAMINED	-	-	-	-	63	60	63	62
MISSING	-	-	-	-	1	4	1	2
Stromal cell polyp..(BENIGN)	-	-	-	-	0	0	1	0
Adenocarcinoma..(MALIGNANT)	-	-	-	-	1	0	0	1
Stromal cell sarcoma..(MALIGNANT)	-	-	-	-	0	0	1	2
Haemangiosarcoma..(MALIGNANT)	-	-	-	-	0	0	1	0
DUODENUM								
EXAMINED	63	60	62	63	61	61	64	61
MISSING	1	4	2	1	3	3	0	3
Adenocarcinoma..(MALIGNANT)	0	0	0	0	0	1	0	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
DUODENUM (CONTINUED)								
Leiomyoma..(BENIGN)	0	0	0	0	0	1	0	0
EAR/ZYMBALS GLAND								
EXAMINED	0	0	1	0	0	0	0	0
MISSING	2	1	0	0	0	0	0	0
Squamous cell carcinoma..(MALIGNANT)	0	0	1	0	0	0	0	0
EPIDIDYMIS								
EXAMINED	63	63	63	64	-	-	-	-
MISSING	1	1	1	0	-	-	-	-
Benign mesothelioma..(BENIGN)	0	1	0	1	-	-	-	-
Malignant mesothelioma..(MALIGNANT)	0	1	0	0	-	-	-	-
HARDERIAN GLAND								
EXAMINED	63	62	64	64	64	63	64	64
MISSING	1	2	0	0	0	1	0	0
Anaplastic sarcoma..(MALIGNANT)	0	0	0	0	0	1	0	0
HEART								
EXAMINED	64	64	64	64	64	64	64	64
Malignant endocardial schwannoma (MALIGNANT)	1	0	0	0	0	0	0	0
ILEUM								
EXAMINED	57	57	61	62	56	59	63	61
MISSING	7	7	3	2	8	5	1	3
Leiomyosarcoma..(MALIGNANT)	0	0	0	0	0	1	0	0
KIDNEY								
EXAMINED	64	64	64	64	64	64	64	64
Haemangioma..(BENIGN)	0	0	0	1	0	0	0	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
KIDNEY (CONTINUED)								
Liposarcoma..(MALIGNANT)	0	0	0	0	0	0	1	0
Mixed mesenchymal tumour..(MALIGNANT)	0	0	0	1	0	0	0	0
LACRIMAL GLAND								
EXAMINED	63	62	64	63	63	63	64	63
MISSING	1	2	0	1	1	1	0	1
Neurofibrosarcoma..(MALIGNANT)	1	0	0	0	0	0	0	0
LIMB								
EXAMINED	13	14	9	12	2	5	3	6
MISSING	0	1	0	0	0	0	0	0
Squamous papilloma..(BENIGN)	0	1	0	1	0	0	0	0
Benign histiocytoma..(BENIGN)	0	0	0	0	1	0	0	0
LIVER								
EXAMINED	64	64	64	64	64	64	64	64
Hepatocellular adenoma..(BENIGN)	0	2	0	5	0	0	1	0
Liposarcoma..(MALIGNANT)	0	0	1	0	0	0	0	0
LUNG								
EXAMINED	64	64	64	64	64	64	64	64
Adenocarcinoma..(MALIGNANT)	0	1	0	0	0	0	0	0
LYMPH NODE-MESENTERIC								
EXAMINED	64	62	64	64	64	62	64	62
MISSING	0	2	0	0	0	2	0	2
Haemangioma..(BENIGN)	7	6	4	5	4	6	6	3
Haemangiosarcoma..(MALIGNANT)	1	1	0	0	1	0	0	1
LYMPH NODE-PANCREATIC								
EXAMINED	1	0	1	1	0	1	1	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
LYMPH NODE-PANCREATIC (CONTINUED)								
Haemangioma..(BENIGN)	1	0	0	0	0	0	0	0
LYMPHORETICULAR SYSTEM								
EXAMINED	6	4	1	3	11	13	14	8
Lymphosarcoma..(MALIGNANT)	1	0	0	0	1	0	1	0
Large granular lymphocyte leukemia (MALIGNANT)	4	4	0	3	9	12	13	8
Myeloid leukaemia..(MALIGNANT)	0	0	1	0	0	0	0	0
Histiocytic/Granulocytic cell tumour (MALIGNANT)	1	0	0	0	1	1	0	0
MAMMARY GLAND								
EXAMINED	-	-	-	-	63	63	64	64
MISSING	-	-	-	-	1	1	0	0
Adenocarcinoma..(MALIGNANT)	-	-	-	-	2	0	0	2
Adenoma..(BENIGN)	-	-	-	-	1	2	0	0
Cystadenoma..(BENIGN)	-	-	-	-	2	0	1	1
Fibroadenoma..(BENIGN)	-	-	-	-	4	4	6	5
NASAL CAVITY								
EXAMINED	64	64	64	64	64	64	64	64
Fibrosarcoma..(MALIGNANT)	0	0	1	0	0	0	0	0
Papilloma/s nasolachrymal duct (BENIGN)	0	0	1	0	0	0	1	1
Adenoma nasolachrymal duct..(BENIGN)	0	0	0	0	0	1	0	0
Ameloblastoma..(MALIGNANT)	0	1	0	0	0	0	0	0
ORAL CAVITY								
EXAMINED	8	4	7	4	4	7	5	4
MISSING	0	0	0	1	0	0	0	0
Squamous cell carcinoma..(MALIGNANT)	0	2	2	2	1	2	0	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
ORAL CAVITY	(CONTINUED)							
Fibrosarcoma..(MALIGNANT)	0	0	0	1	0	0	0	0
Squamous cell papilloma..(BENIGN)	0	0	0	0	0	0	1	0
PANCREAS								
EXAMINED	64	64	64	64	63	63	64	64
MISSING	0	0	0	0	1	1	0	0
Exocrine adenoma..(BENIGN)	4	2	7	7	0	0	0	0
Exocrine adenocarcinoma..(MALIGNANT)	0	1	0	0	0	0	0	0
Islet cell adenoma..(BENIGN)	1	2	0	1	0	0	1	0
Islet cell adenocarcinoma (MALIGNANT)	0	0	0	0	0	1	0	0
PARATHYROID GLAND								
EXAMINED	57	60	58	59	59	52	57	58
MISSING	7	4	6	5	5	12	7	6
Adenoma..(BENIGN)	0	1	0	0	0	0	0	0
PHARYNX								
EXAMINED	63	64	64	64	64	64	64	64
MISSING	1	0	0	0	0	0	0	0
Squamous cell carcinoma..(MALIGNANT)	1	0	0	0	0	0	0	0
PITUITARY GLAND								
EXAMINED	64	63	64	63	63	63	63	64
MISSING	0	1	0	1	1	1	1	0
Adenoma pars distalis..(BENIGN)	18	16	15	18	47	44	46	49
Adenoma pars intermedia..(BENIGN)	0	1	3	1	0	0	0	0
SALIVARY GLAND								
EXAMINED	62	62	64	64	63	62	64	64
MISSING	2	2	0	0	1	2	0	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
SALIVARY GLAND (CONTINUED)								
Adenoma..(BENIGN)	0	0	0	0	1	0	0	0
Neurofibrosarcoma..(MALIGNANT)	0	0	0	1	0	0	0	0
SKIN								
EXAMINED	64	64	64	63	64	64	64	64
MISSING	0	0	0	1	0	0	0	0
Squamous papilloma..(BENIGN)	0	0	1	0	0	0	0	0
Squamous carcinoma..(MALIGNANT)	0	0	0	0	0	1	0	1
Benign basal cell tumour..(BENIGN)	1	0	1	1	0	0	0	1
Basal cell carcinoma..(MALIGNANT)	0	0	1	0	0	0	0	0
Pilomatrixoma..(BENIGN)	5	3	0	4	1	0	0	1
Keratoacanthoma..(BENIGN)	1	0	1	1	0	0	0	0
Sebaceous adenoma..(BENIGN)	0	1	1	0	0	0	0	0
Trichofolliculoma..(BENIGN)	0	1	0	0	0	0	0	0
Histiocytic sarcoma..(MALIGNANT)	1	0	0	0	0	0	0	0
SPLEEN								
EXAMINED	64	64	64	64	64	63	64	64
MISSING	0	0	0	0	0	1	0	0
Haemangiosarcoma..(MALIGNANT)	0	0	0	0	0	0	1	0
Not otherwise specified sarcoma (MALIGNANT)	0	1	0	0	0	0	0	0
STOMACH								
EXAMINED	64	64	64	64	64	63	64	64
MISSING	0	0	0	0	0	1	0	0
Squamous papilloma..(BENIGN)	0	0	0	0	0	0	1	0
SUBCUTANEOUS TISSUE								
EXAMINED	11	6	10	8	8	7	9	7
Fibroma..(BENIGN)	2	2	0	1	1	1	1	0

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
SUBCUTANEOUS TISSUE	(CONTINUED)							
Fibrosarcoma..(MALIGNANT).....	1	0	2	1	0	0	0	0
Haemangioma..(BENIGN).....	1	0	1	0	0	0	0	1
Haemangiosarcoma..(MALIGNANT).....	0	1	0	0	0	0	0	0
Lipoma..(BENIGN).....	0	0	1	1	1	0	2	0
TAIL								
EXAMINED.....	37	40	36	41	18	10	14	18
MISSING.....	1	2	0	0	0	0	0	3
Fibrosarcoma..(MALIGNANT).....	0	0	0	0	0	0	0	1
TESTIS								
EXAMINED.....	63	63	63	64	-	-	-	-
MISSING.....	1	1	1	0	-	-	-	-
Benign Leydig cell tumour..(BENIGN)...	5	2	2	2	-	-	-	-
Benign mesothelioma..(BENIGN).....	0	1	0	0	-	-	-	-
Malignant mesothelioma..(MALIGNANT)...	0	1	0	0	-	-	-	-
THYMUS								
EXAMINED.....	59	59	57	60	63	62	62	63
MISSING.....	5	5	7	4	1	2	2	1
Benign thymoma..(BENIGN).....	1	1	0	2	2	1	0	1
Malignant thymoma..(MALIGNANT).....	0	0	0	0	1	0	1	0
Not otherwise specified sarcoma (MALIGNANT).....	0	0	0	0	0	0	0	1
THYROID GLAND								
EXAMINED.....	63	63	63	64	63	63	64	64
MISSING.....	1	1	1	0	1	1	0	0
Follicular cell adenoma..(BENIGN).....	1	0	2	3	1	2	1	0
Parafollicular cell adenoma..(BENIGN).	2	1	1	0	4	0	0	2
Parafollicular cell carcinoma (MALIGNANT).....	0	1	0	0	0	0	0	1
UTERUS								
EXAMINED.....	-	-	-	-	64	64	64	64

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

	MALES				FEMALES			
	0 ppm	2000 ppm	6000 ppm	20000 ppm	0 ppm	2000 ppm	6000 ppm	20000 ppm
ANIMALS ON STUDY	64	64	64	64	64	64	64	64
ANIMALS COMPLETED	64	64	64	64	64	64	64	64
UTERUS	(CONTINUED)							
Stromal cell polyp..(BENIGN).....	-	-	-	-	7	5	7	2
Adenocarcinoma..(MALIGNANT).....	-	-	-	-	6	10	9	5
Leiomyoma..(BENIGN).....	-	-	-	-	0	0	2	0
Squamous cell carcinoma..(MALIGNANT)..	-	-	-	-	0	1	1	1
Haemangiosarcoma..(MALIGNANT).....	-	-	-	-	1	0	1	0
Haemangioma..(BENIGN).....	-	-	-	-	0	0	1	0
VOLUNTARY MUSCLE								
EXAMINED.....	64	64	63	64	64	64	63	64
MISSING.....	0	0	1	0	0	0	1	0
Haemangioma..(BENIGN).....	0	0	1	0	0	0	0	0

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

	MALES								FEMALES							
	0ppm		1500ppm		5000ppm		15000ppm		0ppm		1500ppm		5000ppm		15000ppm	
Number of Rats	51		51		51		51		51		51		51		51	
CONDITION	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ADRENAL GLAND																
Cortical adenoma b	1	2	1	2	0	0	0	0	1	2	1	2	0	0	0	0
Cortical carcinoma m	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Phaeochromocytoma b	0	0	0	0	0	0	2	4	0	0	0	0	0	0	0	0
Phaeochromocytoma m	2	4	0	0	3	6	0	0	0	0	0	0	0	0	0	0
Ganglioneuroma b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
BONE																
Osteoma b	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
BRAIN/SPINAL CORD																
Astrocytoma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Granular cell tumour b	1	2	1	2	0	0	0	0	0	0	0	0	0	0	0	0
Granular cell tumour m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Oligodendroglioma b	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
Ependymoma m	0	0	0	0	0	0	0	0	1	2	1	2	0	0	0	0
INTESTINAL TRACT																
Leiomyoma b	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
Leiomyosarcoma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
EPIDIDYMIS																
Mesothelioma b	1	2	0	0	0	0	0	0								
Mesothelioma m	0	0	2	4	0	0	0	0								
HEART																
Schwannoma m	0	0	1	2	0	0	0	0	2	4	0	0	0	0	0	0
KIDNEY																
Lipoma b	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Tubular carcinoma m	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Clear cell carcinoma m	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0
LIVER																
Hepatocellular adenoma b	0	0	2	4	1	2	1	2	1	2	0	0	1	2	1	2
Hepatocellular carcinoma m	1	2	0	0	0	0	0	0	0	0	0	0	1	2	0	0
Cholangioma b	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
LYMPH NODE																
Angioma b	7	14	4	8	1	2	6	12	3	6	1	2	0	0	1	2
Angiosarcoma m	4	8	0	0	2	4	0	0	0	0	0	0	0	0	0	0

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

	MALES								FEMALES							
	0ppm		1500ppm		5000ppm		15000ppm		0ppm		1500ppm		5000ppm		15000ppm	
Number of Rats	51		51		51		51		51		51		51		51	
CONDITION	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
MAMMARY GLAND																
Fibroadenoma b									7	14	9	18	7	14	5	10
Adenoma b									0	0	0	0	0	0	2	4
Adenocarcinoma m									2	4	3	6	1	2	6	12
Total									9	18	12	24	8	16	13	26
NASAL CAVITIES																
Polypoid adenoma b	2	4	1	2	0	0	0	0	0	0	0	0	0	0	0	0
OVARY																
Granulosa cell tumour b									3	6	0	0	1	2	0	0
Granulosa-theca cell tumour b									1	2	3	6	0	0	0	0
Anaplastic sarcoma m									1	2	0	0	0	0	0	0
PANCREAS																
Islet cell adenoma b	4	8	1	2	2	4	1	2	0	0	0	0	0	0	0	0
Islet cell adenocarcinoma m	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0
PARATHYROID																
Adenoma b	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PAROTID SALIVARY GLAND																
Acinar adenoma b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PHARYNX																
Squamous papilloma b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
PITUITARY																
Adenoma b	16	31	11	22	10	20	20	39	24	47	23	45	16	31	32	63
Adenocarcinoma m	1	2	0	0	0	0	0	0	0	0	1	2	0	0	0	0
SKIN - SUBCUTANEOUS																
Fibroma b	0	0	1	2	2	4	0	0	0	0	0	0	1	2	0	0
Fibrosarcoma m	2	4	2	4	3	6	0	0	0	0	0	0	0	0	0	0
Histiocytic sarcoma m	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
Lipoma b	0	0	0	0	1	2	0	0	0	0	1	2	0	0	1	2
Leiomyosarcoma m	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
Angioma b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	4

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

	MALES								FEMALES							
	0ppm		1500ppm		5000ppm		15000ppm		0ppm		1500ppm		5000ppm		15000ppm	
Number of Rats	51		51		51		51		51		51		51		51	
CONDITION	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
SKIN - CUTANEOUS																
Basal cell tumour b	1	2	0	0	0	0	0	0	1	2	0	0	0	0	0	0
Squamous cell carcinoma m	3	6	0	0	0	0	1	2	0	0	0	0	1	2	0	0
Keratoacanthoma b	2	4	3	6	0	0	6	12	0	0	0	0	0	0	0	0
Sebaceous adenoma b	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
Sebaceous adenocarcinoma m	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
Trichoepithelioma b	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
Squamous papilloma b	0	0	0	0	0	0	1	2	0	0	1	2	0	0	0	0
*Sebaceous-squamous carcinoma m	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
SPLEEN																
Angioma b	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
Angiosarcoma m	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
STOMACH																
Squamous papilloma b	1	2	0	0	2	4	1	2	0	0	1	2	0	0	0	0
TESTIS																
Interstitial cell tumour b	2	4	3	6	1	2	1	2								
THYMUS																
Lymphocytic thymoma b	0	0	0	0	1	2	1	2	7	14	2	4	4	8	3	6
Lymphocytic thymoma m	0	0	1	2	0	0	1	2	0	0	0	0	0	0	0	0
Carcinoma m	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
THYROID																
Follicular adenoma b	5	10	1	2	0	0	6	12	3	6	0	0	0	0	2	4
Follicular adenocarcinoma m	0	0	0	0	1	2	0	0	1	2	1	2	0	0	0	0
Parafollicular adenoma b	9	18	1	2	0	0	3	6	6	12	1	2	1	2	0	0
Parafollicular adenocarcinoma m	2	4	1	2	0	0	0	0	0	0	1	2	0	0	0	0
Hibernoma m	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0
TONGUE																
Granular cell tumour b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
URINARY BLADDER																
Transitional cell papilloma b	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0

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

	MALES								FEMALES							
	0ppm		1500ppm		5000ppm		15000ppm		0ppm		1500ppm		5000ppm		15000ppm	
Number of Rats	51		51		51		51		51		51		51		51	
CONDITION	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
UTERUS																
Endometrial stromal polyp b									7	14	5	10	4	8	8	16
Adenocarcinoma m									6	12	6	12	4	8	5	10
Stromal sarcoma m									1	2	0	0	0	0	1	2
Leiomyoma b									2	4	0	0	1	2	1	2
Angiosarcoma m									0	0	1	2	0	0	0	0
ABDOMINAL																
Adenocarcinoma m	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0
Anaplastic carcinoma m	0	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0
LYMPHOID/HAEMOPOIETIC																
Malignant lymphoma m	0	0	1	2	1	2	0	0	2	4	0	0	1	2	0	0
OVERALL TUMOUR INCIDENCE																
Primary benign tumours	27	53	17	33	17	33	29	57	28	55	22	43	20	39	32	63
Primary malignant tumours	14	28	10	20	11	22	5	10	15	29	11	22	10	20	12	24
Multiple benign tumours	17	33	9	18	4	8	17	33	28	55	13	26	14	28	21	41
Multiple malignant tumours	4	8	2	4	1	2	0	0	1	2	3	6	0	0	1	2

Pestycydy, 2000, (3-4), 11-20.
ISSN 0208-8703

Glyphosate
Evaluation of chronic activity and possible far – reaching effects
Part 1. Studies on chronic toxicity*)

Krystyna CHRUŚCIELSKA[1], Jacek BRZEZIŃSKI[2], Kazimierz KITA[3], Dorota KALHORN[1], Izabela KITA[3], Barbara GRAFFSTEIN[1] and Piotr KORZENIOWSKI[1]

[1]Institute of Industrial Organic Chemistry, 6 Annopol Str., 03-236 Warszawa
[2]Chair and Department of Toxicology, Medical Academy in Warsaw, 1 Banacha Str., 02-097 Warszawa
[3]Institute of Industrial Organic Chemistry, Department at Pszczyna

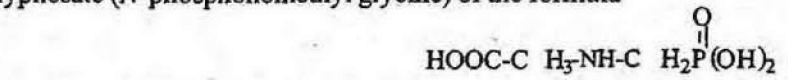
Abstract: The combined test of chronic toxicity and carcinogenicity of glyphosate was performed on Wistar-RIZ rats. The herbicide was administered in water at concentrations: 0, 300, 900, 2700 mg/L. The examination of the peripheral blood parameters and the smears of bone marrow did not reveal harmful 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



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_{50} *per os* for rats > 5600 mg/kg b.w.
LD_{50} inhalation > 12.2 mg/l air
LD_{50} *per os* for mouse 1100 mg/kg b.w.
LD_{50} 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

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).

⇒ 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

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.

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).

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.

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

Examined organ	Kind of neoplasm	Group			
		0	1	2	3
Lungs	*Lymphoma*	2	2	1	3
	Adenocarcicioma	1	-	-	-
	Histocytoma malignum	-	-	1	-
Spleen	*Leucemia*	0	2	0	1
Kidneys	*Fibrohistiocytoma*	-	-	-	1
Pituitary gland	*Adenoma*	4	5	2	0
	Adenoma malignum	0	0	1	1
	Carcinoma	0	0	1	0
Thyroid	*Adenoma*	1	1	0	3
	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 2. Localization, kind and frequency of neoplasms occurrence in female rats chronically exposed to glyphosate

Examined organ	Kind of neoplasm	Group			
		0	1	2	3
Lungs	*Lymphoma*	-	-	-	1
	Histiocytoma	-	-	-	1
	Histocytoma malignum	1	-	-	-
Pituitary gland	*Adenoma*	10	6	8	3
	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
Mammary gland	*Fibroma*	0	0	1	0
	Fibroadenoma pericanaliculare	3	2	3	3
Subcutaneous tissue	*Fibroma*	1	2	-	-
	Lipoma	-	-	-	1
	Cystadenoma	1	-	-	-
Lymph nodes	*Lymphoma*	1	-	1	-
	Lymphoma malignum	1	-	-	-
Total:		**25**	**18**	**17**	**21**

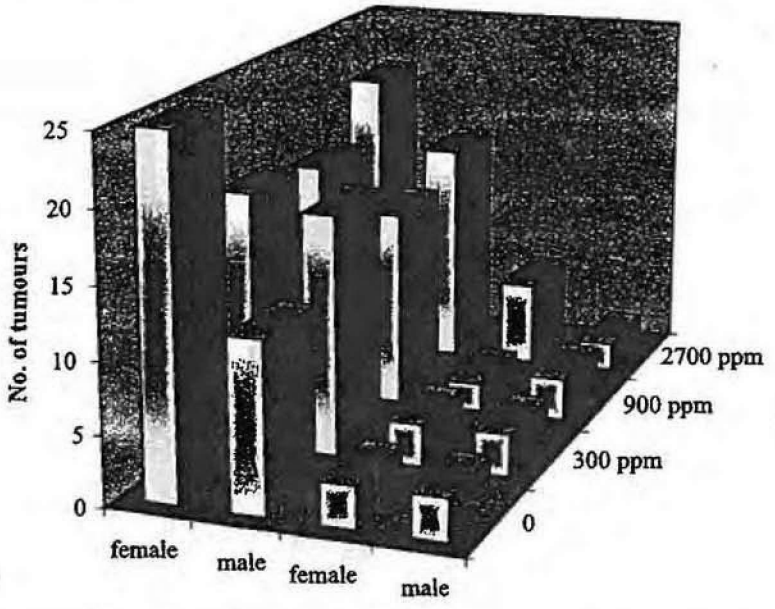


Fig. 1. Total number of tumours and malignant tumours during chronic exposure to glyphosat.

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

Glifosat
Ocena działania przewlekłego 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 wykazywały 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.

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

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		SEX:	MALE			
		GROUP:	-1-	-2-	-3-	-4-
		NUMBER:	50	50	50	50
** TOP OF LIST **						
PITUITARY GLAND (PG)	NUMBER EXAMINED:		32	18	32	32
BRAIN (BN)	NUMBER EXAMINED:		49	50	50	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS, METASTATIC			0	0	1	0
			0%	0%	2%	0%
CERVICAL SC (SC0)	NUMBER EXAMINED:		49	48	50	50
THORACOLUMBAR SC (SC1)	NUMBER EXAMINED:		10	8	10	23
HEART (HT)	NUMBER EXAMINED:		47	49	49	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	1	2	1
			0%	2%	4%	2%
AORTA (AO)	NUMBER EXAMINED:		46	50	50	47
TRACHEA (TR)	NUMBER EXAMINED:		48	50	50	49
ESOPHAGUS (ES)	NUMBER EXAMINED:		48	50	50	48
LUNGS (LU)	NUMBER EXAMINED:		48	50	50	50
--B- BRONCHIOLAR-ALVEOLAR ADENOMA			5	9	9	9
			10%	18%	18%	18%
--M- BRONCHIOLAR-ALVEOLAR ADENOCARCINOMA			4	3	2	1
			8%	6%	4%	2%
--S- GRANULOSA CELL TUMOR			0	0	0	0
			0%	0%	0%	0%
--S- LEIOMYOSARCOMA			0	0	0	0
			0%	0%	0%	0%
--S- LIPOSARCOMA			0	0	0	0
			0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA			0	0	0	0
			0%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
LUNGS (LU)	NUMBER EXAMINED:	48	50	50	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	4	3	1
		2%	8%	6%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	1	0	0
		0%	2%	0%	0%
LIVER (LI)	NUMBER EXAMINED:	49	50	50	50
--M- HEPATOCELLULAR ADENOCARCINOMA		5	6	6	4
		10%	12%	12%	8%
--B- HEPATOCELLULAR ADENOMA		0	0	1	0
		0%	0%	2%	0%
--M- HEPATOCELLULAR CARCINOMA		0	0	0	2
		0%	0%	0%	4%
--M- HEMANGIOENDOTHELIOMA		0	0	0	0
		0%	0%	0%	0%
--S- HISTIOCYTIC SARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- LIPOSARCOMA		0	0	1	1
		0%	0%	2%	2%
--S- HEMANGIOENDOTHELIOMA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%

* CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		MALE			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
LIVER (LI)	NUMBER EXAMINED:	49	50	50	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	4	2	2
		2%	8%	4%	4%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
GALLBLADDER (GB)	NUMBER EXAMINED:	45	32	36	41
MESENTERIC LN (LN0)	NUMBER EXAMINED:	48	50	46	49
--M- HISTIOCYTIC SARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- ENDOMETRIAL ADENOCARCINOMA		0	0	0	0
		0%	0%	0%	0%
--M- COMPOSITE LYMPHOSARCOMA		1	0	1	0
		2%	0%	2%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	2	1	0
		2%	4%	2%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	2
		0%	0%	2%	4%
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	1	0	0
		0%	2%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
MESENTERIC LN (LN0)	NUMBER EXAMINED:	48	50	46	49
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- HEMANGIOENDOTHELIOMA		0	0	0	0
		0%	0%	0%	0%
MEDIASTINAL LN (LN1)	NUMBER EXAMINED:	45	49	41	49
--S- HISTIOCYTIC SARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- LIPOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		1	0	1	0
		2%	0%	2%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	2	1	2
		2%	4%	2%	4%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	2	0
		0%	0%	5%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
SALIVARY GLANDS (SG)	NUMBER EXAMINED:	49	50	49	50
--S- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		SEX:	MALE			
		GROUP:	-1-	-2-	-3-	-4-
		NUMBER:	50	50	50	50
			--- NUMBER OF ANIMALS AFFECTED ---			
** FROM PREVIOUS PAGE **						
SALIVARY GLANDS (SG)	NUMBER EXAMINED:		49	50	49	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	0	1	0
			2%	0%	2%	0%
THYMUS (TM)	NUMBER EXAMINED:		2	0	1	1
PLEEN (SP)	NUMBER EXAMINED:		48	49	50	49
--M- HEMANGIOENDOTHELIOMA			0	0	1	0
			0%	0%	2%	0%
--B- HEMANGIOMA			0	0	0	0
			0%	0%	0%	0%
--S- HISTIOCYTIC SARCOMA			0	1	0	0
			0%	2%	0%	.0%
--M- GRANULOCYTIC LEUKEMIA			0	0	0	0
			0%	0%	0%	0%
--S- ENDOMETRIAL ADENOCARCINOMA			0	0	0	0
			0%	0%	0%	0%
--S- HEMANGIOENDOTHELIOMA			0	0	0	0
			0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA			1	0	1	0
			2%	0%	2%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	2	2	0
			2%	4%	4%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	2	0	1
			0%	4%	0%	2%
--M- COMPOSITE LYMPHOSARCOMA			0	0	0	0
			0%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
SPLEEN (SP)	NUMBER EXAMINED:	48	49	50	49
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
STOMACH (ST)	NUMBER EXAMINED:	49	47	48	49
--M- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--M- GASTRIC ADENOCARCINOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	0	0	0
		2%	0%	0%	0%
DUODENUM (DU)	NUMBER EXAMINED:	46	43	44	48
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
PANCREAS (PA)	NUMBER EXAMINED:	48	48	49	50
--S- HISTIOCYTIC SARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	2%	0%
JEJUNUM (JE)	NUMBER EXAMINED:	46	41	41	47
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		SEX:	MALE			
		GROUP:	-1-	-2-	-3-	-4-
		NUMBER:	50	50	50	50
			--=-	--=-	--=-	--=-
			--- N U M B E R - O F - A N I M A L S - A F F E C T E D ---			
** FROM PREVIOUS PAGE **						
ILEUM (IL)	NUMBER EXAMINED:		47	41	40	48
--S- COMPOSITE LYMPHOSARCOMA			1	0	0	0
			2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	0	0	0
			2%	0%	0%	0%
CECUM (CE)	NUMBER EXAMINED:		45	43	47	47
--S- COMPOSITE LYMPHOSARCOMA			0	0	0	0
			0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	0	0	0
			2%	0%	0%	0%
COLON (CO)	NUMBER EXAMINED:		46	47	47	48
--S- COMPOSITE LYMPHOSARCOMA			1	0	0	0
			2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	0	0	0
			0%	0%	0%	0%
KIDNEYS (KD)	NUMBER EXAMINED:		49	49	50	50
--B- RENAL TUBULE ADENOMA			0	0	1	3
			0%	0%	2%	6%
--S- B/ HISTIOCYTIC SARCOMA			0	1	0	0
			0%	2%	0%	0%
--S- B/ LEIOMYOSARCOMA			0	0	0	0
			0%	0%	0%	0%
--S- B/ GRANULOCYTIC LEUKEMIA			0	0	0	0
			0%	0%	0%	0%
--S- B/ COMPOSITE LYMPHOSARCOMA			1	0	0	0
			2%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

RGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
IDNEYS (KD)	NUMBER EXAMINED:	49	49	50	50
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	3	2	2
		2%	6%	4%	4%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
TESTES (TE)	NUMBER EXAMINED:	49	48	50	50
--B- U/ INTERSTITIAL CELL TUMOR		1	0	2	0
		2%	0%	4%	0%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	0	0
		0%	2%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	2%	0%
EPIDIDYMIDES (EP)	NUMBER EXAMINED:	49	48	50	50
--M- U/ LEIOMYOSARCOMA		0	1	0	1
		0%	2%	0%	2%
PROSTATE (PR)	NUMBER EXAMINED:	49	47	50	49
URINARY BLADDER (UB)	NUMBER EXAMINED:	48	46	47	47
--S-HISTIOCYTICSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	1	0	0
		2%	2%	0%	0%

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
OVARIES (OV)	NUMBER EXAMINED:	0	0	0	0
--B- U/ LUTEOMA		0	0	0	0
		0%	0%	0%	0%
--M- B/ MALIGNANT TERATOMA		0	0	0	0
		0%	0%	0%	0%
--M- B/ GRANULOSA CELL TUMOR		0	0	0	0
		0%	0%	0%	0%
--S- B/ LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--I- B/ ENDOMETRIAL ADENOCARCINOMA		0	0	0	0
		0%	0%	0%	0%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
--S- B/ COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0
--B- LIEOMYOMA		0	0	0	0
		0%	0%	0%	0%
--M- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--M- ENDOMETRIAL STROMAL CELL SARCOMA		0	0	0	0
		0%	0%	0%	0%
--B- HEMANGIOMA		0	0	0	0
		0%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		--------MALE--------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
UTERUS (UT)	NUMBER EXAMINED:	0	0	0	0
--M- ENDOMETRIAL ADENOCARCINOMA		0	0	0	0
		0%	0%	0%	0%
--M- HEMANGIOENDOTHELIOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
ROID GLAND (TH)	NUMBER EXAMINED:	40	40	50	48
--B- FOLLICULAR ADENOMA		0	0	0	0
		0%	0%	0%	0%
PARATHYROID GLS. (PT)	NUMBER EXAMINED:	17	23	22	15
ENAL GLANDS (AD)	NUMBER EXAMINED:	48	49	50	48
--B- U/ CORTICAL ADENOMA		1	2	0	1
		2%	4%	0%	2%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	0	0
		0%	2%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	2%	0%
N/SUBQ/EARS (SK)	NUMBER EXAMINED:	49	48	48	47
--M- FIBROSARCOMA		0	0	1	0
		0%	0%	2%	0%
--M- LIPOSARCOMA		0	0	0	1
		0%	0%	0%	2%
--M- RHABDOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%

CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED --- SEX: MALE			
	GROUP:	-1-	-2-	-3-	-4-
	NUMBER:	50	50	50	50
** FROM PREVIOUS PAGE **					
SKIN/SUBQ/EARS (SK)	NUMBER EXAMINED:	49	48	48	47
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	2%	0%
MAMMARY (MG)	NUMBER EXAMINED:	1	0	2	2
--M- DUCTAL ADENOCARCINOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
MUSCLE (SM)	NUMBER EXAMINED:	49	50	50	49
--S- LIPOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
NERVE (NE)	NUMBER EXAMINED:	39	49	48	42
EYES (EY)	NUMBER EXAMINED:	41	41	44	44
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	0	1	0
		2%	0%	2%	0%
HARDERIAN GLAND (HG)	NUMBER EXAMINED:	47	48	45	48
--B- ADENOMA		1	0	0	0
		2%	0%	0%	0%
--M- LIPOSARCOMA		0	0	1	0
		0%	0%	2%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
BONE (BO)	NUMBER EXAMINED:	43	45	45	48

BLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

CAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		-------MALE-------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
FROM PREVIOUS PAGE **					
NE MARROW (BM)	NUMBER EXAMINED:	48	45	47	49
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	2	1	1
		2%	4%	2%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
MINAL VESICLES (SV)	NUMBER EXAMINED:	14	8	13	13
IL (TA)	NUMBER EXAMINED:	14	9	6	19
AGULAT. GLAND (CG)	NUMBER EXAMINED:	1	0	0	0
DOMEN (AB)	NUMBER EXAMINED:	0	0	0	0
ALL INTESTINES (SI)	NUMBER EXAMINED:	0	0	0	0
EPUTIAL GLAND (PP)	NUMBER EXAMINED:	2	2	3	0
SENTERY (ME)	NUMBER EXAMINED:	0	2	0	0
--B- HEMANGIOMA		0	1	0	0
		0%	50%	0%	0%
--S- TERATOMA		0	0	0	0
		0%	0%	0%	0%
NERAL COMMENTS (GC)	NUMBER EXAMINED:	0	0	0	0

BLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		MALE			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
GINA (VA)	NUMBER EXAMINED:	0	0	0	0
--M- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
MPH NODE (LN)	NUMBER EXAMINED:	0	3	2	2
--S- HISTIOCYTIC SARCOMA		0	1	0	0
		0%	33%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	0	0	0
		0%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		0	0	1	0
		0%	0%	50%	0%
--M- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	1	0
		0%	33%	50%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	1
		0%	0%	0%	50%
PENIS (PE)	NUMBER EXAMINED:	1	5	7	0
OMINAL CAVITY (AC)	NUMBER EXAMINED:	0	0	0	0
'ITY (CA)	NUMBER EXAMINED:	0	0	0	0
NAL CORD (SC)	NUMBER EXAMINED:	0	0	0	0
GASTROINTESTINES (GI)	NUMBER EXAMINED:	0	0	0	0
TERS (UR)	NUMBER EXAMINED:	0	0	1	0
ADIPOSE TISSUE (AT)	NUMBER EXAMINED:	0	0	1	0
--M- LIPOSARCOMA		0	0	1	0
		0%	0%	100%	0%

TABLE INCLUDES: SEX=M;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		-------MALE-------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
HEAD SECTIONS (NT)	NUMBER EXAMINED:	10	8	10	10
--B- DENTINOMA		0	0	0	0
		0%	0%	0%	0%
JUNCTION (JU)	NUMBER EXAMINED:	0	0	0	0
CORRELATE #1 (G1)	NUMBER EXAMINED:	0	0	0	0
CERVIX (CV)	NUMBER EXAMINED:	0	0	0	0
--M- LEIOMYOSARCOMA		0	0	0	0
		0%	0%	0%	0%
MUSCLE OTHER (MU)	NUMBER EXAMINED:	0	0	0	0
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	0
		0%	0%	0%	0%
CORRELATE #2 (G2)	NUMBER EXAMINED:	0	0	0	0

** END OF LIST **

Table 18 C

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

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

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL.
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
	SEX:	-------FEMALE-------			
	GROUP:	-1-	-2-	-3-	-4-
	NUMBER:	50	50	50	50
** TOP OF LIST **					
PITUITARY GLAND (PG)	NUMBER EXAMINED:	32	21	44	37
BRAIN (BN)	NUMBER EXAMINED:	50	49	50	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS, METASTATIC		0 0%	0 0%	1 2%	0 0%
CERVICAL SC (SC0)	NUMBER EXAMINED:	48	49	49	49
THORACOLUMBAR SC (SC1)	NUMBER EXAMINED:	10	9	8	12
HEART (HT)	NUMBER EXAMINED:	50	50	50	49
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0 0%	0 0%	2 4%	0 0%
AORTA (AO)	NUMBER EXAMINED:	47	49	49	47
TRACHEA (TR)	NUMBER EXAMINED:	47	50	50	48
ESOPHAGUS (ES)	NUMBER EXAMINED:	48	50	50	50
LUNGS (LU)	NUMBER EXAMINED:	49	50	49	50
--B- BRONCHIOLAR-ALVEOLAR ADENOMA		10 20%	9 18%	10 20%	1 2%
--M- BRONCHIOLAR-ALVEOLAR ADENOCARCINOMA		1 2%	3 6%	4 8%	4 8%
--S- GRANULOSA CELL TUMOR		0 0%	1 2%	0 0%	0 0%
--S- LEIOMYOSARCOMA		0 0%	1 2%	0 0%	0 0%
--S- LIPOSARCOMA		1 2%	0 0%	0 0%	0 0%
--S- COMPOSITE LYMPHOSARCOMA		1 2%	0 0%	0 0%	1 2%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
LUNGS (LU)	NUMBER EXAMINED:	49	50	49	50
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	2	5	1
		2%	4%	10%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
LIVER (LI)	NUMBER EXAMINED:	49	50	49	49
--M- HEPATOCELLULAR ADENOCARCINOMA		1	2	1	0
		2%	4%	2%	0%
--B- HEPATOCELLULAR ADENOMA		0	1	0	0
		0%	2%	0%	0%
--M- HEPATOCELLULAR CARCINOMA		0	0	0	0
		0%	0%	0%	0%
--M- HEMANGIOENDOTHELIOMA		0	0	1	0
		0%	0%	2%	0%
--S- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LEIOMYOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	3	0	0
		0%	6%	0%	0%
--S- LIPOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- HEMANGIOENDOTHELIOMA		0	0	2	0
		0%	0%	4%	0%
--S- COMPOSITE LYMPHOSARCOMA		2	1	0	4
		4%	2%	0%	8%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		-------FEMALE-------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
LIVER (LI)	NUMBER EXAMINED:	49	50	49	49
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	4	4	1
		2%	8%	8%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	2
		0%	0%	0%	4%
GALLBLADDER (GB)	NUMBER EXAMINED:	36	42	41	44
MESENTERIC LN (LNO)	NUMBER EXAMINED:	49	49	48	48
--M- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LEIOMYOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	1	0	0
		0%	2%	0%	0%
--S- ENDOMETRIAL ADENOCARCINOMA		1	0	0	0
		2%	0%	0%	0%
--M- COMPOSITE LYMPHOSARCOMA		2	0	0	1
		4%	0%	0%	2%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	3	1	1
		0%	6%	2%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	1	3	0
		2%	2%	6%	0%
--S- COMPOSITE LYMPHOSARCOMA		1	1	1	3
		2%	2%	2%	6%
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	2
		0%	0%	0%	4%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
MESENTERIC LN (LN0)	NUMBER EXAMINED:	49	49	48	48
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
--S- HEMANGIOENDOTHELIOMA		0	0	0	1
		0%	0%	0%	2%
MEDIASTINAL LN (LN1)	NUMBER EXAMINED:	42	48	39	47
--S- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LEIOMYOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	1	0	0
		0%	2%	0%	0%
--S- LIPOSARCOMA		1	0	0	0
		2%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		1	1	0	2
		2%	2%	0%	4%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	3	0
		0%	2%	8%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	1	2	0
		2%	2%	5%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
SALIVARY GLANDS (SG)	NUMBER EXAMINED:	50	50	50	47
--S- LEIOMYOSARCOMA		0	0	1	0
		0%	0%	2%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
SALIVARY GLANDS (SG)	NUMBER EXAMINED:	50	50	50	47
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	1	0
		0%	2%	2%	0%
THYMUS (TM)	NUMBER EXAMINED:	2	2	2	1
SPLEEN (SP)	NUMBER EXAMINED:	50	48	49	49
--M- HEMANGIOENDOTHELIOMA		1	0	2	1
		2%	0%	4%	2%
--B- HEMANGIOMA		0	0	1	0
		0%	0%	2%	0%
--S- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--M- GRANULOCYTIC LEUKEMIA		0	3	0	0
		0%	6%	0%	0%
--S- ENDOMETRIAL ADENOCARCINOMA		1	0	0	0
		2%	0%	0%	0%
--S- HEMANGIOENDOTHELIOMA		0	0	0	1
		0%	0%	0%	2%
--S- COMPOSITE LYMPHOSARCOMA		2	0	0	1
		4%	0%	0%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	2	2	0
		2%	4%	4%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	2	0
		0%	0%	4%	0%
--M- COMPOSITE LYMPHOSARCOMA		1	1	1	5
		2%	2%	2%	10%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER-OF-ANIMALS-AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
SPLEEN (SP)	NUMBER EXAMINED:	50	48	49	49
--M- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
STOMACH (ST)	NUMBER EXAMINED:	48	49	50	50
--M- LEIOMYOSARCOMA		0	0	1	0
		0%	0%	2%	0%
--M- GASTRIC ADENOCARCINOMA		0	0	1	0
		0%	0%	2%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
DUODENUM (DU)	NUMBER EXAMINED:	43	47	48	49
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%
PANCREAS (PA)	NUMBER EXAMINED:	47	49	49	50
--S- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	1	0	0
		0%	2%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		2	1	0	1
		4%	2%	0%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	1	1	0
		2%	2%	2%	0%
JEJUNUM (JE)	NUMBER EXAMINED:	42	47	44	48
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL.
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL.

		--- NUMBER-OF-ANIMALS-AFFECTED			
SEX:		-------FEMALE-------			
GROUP:		-1-	-2-	-3-	-4-
ORGAN AND FINDING DESCRIPTION	NUMBER:	50	50	50	50
** FROM PREVIOUS PAGE **					
ILEUM (IL)	NUMBER EXAMINED:	43	43	43	49
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
CECUM (CE)	NUMBER EXAMINED:	44	45	49	50
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
COLON (CO)	NUMBER EXAMINED:	49	44	48	50
--S- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	0	0	0
		2%	0%	0%	0%
KIDNEYS (KD)	NUMBER EXAMINED:	50	50	50	50
--B- RENAL TUBULE ADENOMA		0	0	0	0
		0%	0%	0%	0%
--S- B/ HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- B/ LEIOMYOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--S- B/ GRANULOCYTIC LEUKEMIA		0	1	0	0
		0%	2%	0%	0%
--S- B/ COMPOSITE LYMPHOSARCOMA		2	1	1	2
		4%	2%	2%	4%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		SEX:	FEMALE			
		GROUP:	-1-	-2-	-3-	-4-
		NUMBER:	50	50	50	50
** FROM PREVIOUS PAGE **						
KIDNEYS (KD)	NUMBER EXAMINED:		50	50	50	50
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	2	3	1
			2%	4%	6%	2%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA			0	0	0	1
			0%	0%	0%	2%
TESTES (TE)	NUMBER EXAMINED:		0	0	0	0
--B- U/ INTERSTITIAL CELL TUMOR			0	0	0	0
			0%	0%	0%	0%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	0	0	0
			0%	0%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	0	0	0
			0%	0%	0%	0%
EPIDIDYMIDES (EP)	NUMBER EXAMINED:		0	0	0	0
--M- U/ LEIOMYOSARCOMA			0	0	0	0
			0%	0%	0%	0%
PROSTATE (PR)	NUMBER EXAMINED:		0	0	0	0
URINARY BLADDER (UB)	NUMBER EXAMINED:		47	43	49	48
--S-HISTIOCYTICSARCOMA			0	0	0	0
			0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA			0	1	0	0
			0%	2%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA			1	1	0	0
			2%	2%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			1	2	2	0
			2%	5%	4%	0%

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL.
DEATH=ALL ;FIND=M,B,X,I,S;SUBSET=ALL

		--- NUMBER-OF-ANIMALS-AFFECTED --			
	SEX:	------FEMALE------			
	GROUP:	-1-	-2-	-3-	-4-
ORGAN AND FINDING DESCRIPTION	NUMBER:	50	50	50	50
** FROM PREVIOUS PAGE **					
OVARIES (OV) ..... NUMBER EXAMINED:		47	47	50	47
--B- U/ LUTEOMA		0	0	1	0
		0%	0%	2%	0%
--M- B/ MALIGNANT TERATOMA		0	1	0	0
		0%	2%	0%	0%
--M- B/ GRANULOSA CELL TUMOR		0	1	0	0
		0%	2%	0%	0%
--S- B/ LEIOMYOSARCOMA		0	1	0	0
		0%	2%	0%	0%
--I- B/ ENDOMETRIAL ADENOCARCINOMA		1	0	0	0
		2%	0%	0%	0%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	0	0
		0%	2%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	0	2	0
		2%	0%	4%	0%
--S- B/ COMPOSITE LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
UTERUS (UT) ..... NUMBER EXAMINED:		49	48	49	50
--B- LEIOMYOMA		2	1	1	1
		4%	2%	2%	2%
--M- LEIOMYOSARCOMA		2	3	2	3
		4%	6%	4%	6%
--M- ENDOMETRIAL STROMAL CELL SARCOMA		0	1	0	0
		0%	2%	0%	0%
--B- HEMANGIOMA		0	1	0	0
		0%	2%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		SEX:	FEMALE			
		GROUP:	-1-	-2-	-3-	-4-
		NUMBER:	50	50	50	50
** FROM PREVIOUS PAGE **						
UTERUS (UT)	NUMBER EXAMINED:		49	48	49	50
--M- ENDOMETRIAL ADENOCARCINOMA			2	1	0	0
			4%	2%	0%	0%
--M- HEMANGIOENDOTHELIOMA			0	0	0	1
			0%	0%	0%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	3	1	0
			0%	6%	2%	0%
THYROID GLAND (TH)	NUMBER EXAMINED:		43	37	49	48
--B- FOLLICULAR ADENOMA			0	0	1	0
			0%	0%	2%	0%
PARATHYROID GLS. (PT)	NUMBER EXAMINED:		11	18	27	15
ADRENAL GLANDS (AD)	NUMBER EXAMINED:		50	47	49	49
--B- U/ CORTICAL ADENOMA			0	0	0	0
			0%	0%	0%	0%
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	0	0	0
			0%	0%	0%	0%
--S- B/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS			0	0	0	0
			0%	0%	0%	0%
SKIN/SUBQ/FARS (SK)	NUMBER EXAMINED:		45	45	49	48
--M- FIBROSARCOMA			0	1	1	0
			0%	2%	2%	0%
--M- LIPOSARCOMA			1	0	0	0
			2%	0%	0%	0%
--M- RHABDOMYOSARCOMA			1	0	0	0
			2%	0%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA			0	0	0	0
			0%	0%	0%	0%

** CONTINUED ON NEXT PAGE **

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
SKIN/SUBQ/FARS (SK)	NUMBER EXAMINED:	45	45	49	48
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	3	0
		0%	0%	6%	0%
MAMMARY (MG)	NUMBER EXAMINED:	38	36	40	38
--M- DUCTAL ADENOCARCINOMA		2	4	2	1
		5%	11%	5%	3%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	3%	0%
MUSCLE (SM)	NUMBER EXAMINED:	50	50	50	49
--S- LIPOSARCOMA		1	0	0	0
		2%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	0	1	0
		2%	0%	2%	0%
NERVE (NE)	NUMBER EXAMINED:	41	45	49	47
EYES (EY)	NUMBER EXAMINED:	41	37	41	42
--S- U/ LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
HARDERIAN GLAND (HG)	NUMBER EXAMINED:	45	48	49	44
--B- ADENOMA		2	0	1	0
		4%	0%	2%	0%
--M- LIPOSARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	1	0
		0%	0%	2%	0%
BONE (BO)	NUMBER EXAMINED:	47	48	49	41

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
** FROM PREVIOUS PAGE **					
BONE MARROW (BM)	NUMBER EXAMINED:	46	49	47	49
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	1	3	1
		0%	2%	6%	2%
--S- LYMPHOBLASTIC LYMPHOSARCOMA		0	0	0	2
		0%	0%	0%	4%
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	2%
SEMINAL VESICLES (SV)	NUMBER EXAMINED:	0	0	0	0
TAIL (TA)	NUMBER EXAMINED:	13	10	10	11
COAGULAT. GLAND (CG)	NUMBER EXAMINED:	0	0	0	0
ABDOMEN (AB)	NUMBER EXAMINED:	0	0	0	0
SMALL INTESTINES (SI)	NUMBER EXAMINED:	0	0	0	0
PREPUTIAL GLAND (PP)	NUMBER EXAMINED:	0	0	1	0
MESENTERY (MF)	NUMBER EXAMINED:	2	1	5	0
--B- HEMANGIOMA		0	0	0	0
		0%	0%	0%	0%
--S- TERATOMA		0	1	0	0
		0%	100%	0%	0%
GENERAL COMMENTS (GC)	NUMBER EXAMINED:	0	0	0	0

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		-------FEMALE-------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
VAGINA (VA)	NUMBER EXAMINED:	1	0	0	0
--M- LEIOMYOSARCOMA		1	0	0	0
		100%	0%	0%	0%
LYMPH NODE (LN)	NUMBER EXAMINED:	5	4	3	1
--S- HISTIOCYTIC SARCOMA		0	0	0	0
		0%	0%	0%	0%
--S- GRANULOCYTIC LEUKEMIA		0	1	0	0
		0%	25%	0%	0%
--S- COMPOSITE LYMPHOSARCOMA		2	1	0	1
		40%	25%	0%	100%
--M- COMPOSITE LYMPHOSARCOMA		1	0	0	0
		20%	0%	0%	0%
--S- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		1	1	0	0
		20%	25%	0%	0%
--M- LYMPHOBLASTIC LYMPHOSARCOMA WITH LEUKEMIC MANIFESTATIONS		0	0	0	0
		0%	0%	0%	0%
PENIS (PE)	NUMBER EXAMINED:	0	0	0	0
ABDOMINAL CAVITY (AC)	NUMBER EXAMINED:	0	0	0	1
CAVITY (CA)	NUMBER EXAMINED:	0	0	1	1
SPINAL CORD (SC)	NUMBER EXAMINED:	0	0	0	0
GASTROINTESTINES (GI)	NUMBER EXAMINED:	0	0	0	0
URETERS (UR)	NUMBER EXAMINED:	0	0	0	0
ADIPOSE TISSUE (AT)	NUMBER EXAMINED:	0	0	0	0
--M- LIPOSARCOMA		0	0	0	0
		0%	0%	0%	0%

TABLE INCLUDES: SEX=F;GROUP=ALL;SCREEN=ALL;WEEKS=ALL
DEATH=ALL;FIND=M,B,X,I,S;SUBSET=ALL

ORGAN AND FINDING DESCRIPTION		--- NUMBER OF ANIMALS AFFECTED ---			
SEX:		------FEMALE------			
GROUP:		-1-	-2-	-3-	-4-
NUMBER:		50	50	50	50
HEAD SECTIONS (NT)	NUMBER EXAMINED:	11	9	8	10
--B- DENTINOMA		1	0	0	0
		9%	0%	0%	0%
JUNCTION (JU)	NUMBER EXAMINED:	0	0	0	0
CORRELATE #1 (G1)	NUMBER EXAMINED:	0	0	0	0
CERVIX (CV)	NUMBER EXAMINED:	0	2	0	1
--M- LEIOMYOSARCOMA		0	2	0	0
		0%	100%	0%	0%
MUSCLE OTHER (MU)	NUMBER EXAMINED:	0	0	0	1
--S- COMPOSITE LYMPHOSARCOMA		0	0	0	1
		0%	0%	0%	100%
CORRELATE #2 (G2)	NUMBER EXAMINED:	0	0	0	0

** END OF LIST **

TABLE 15

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

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
GENERALISED CONDITION:		(11)	(5)	(4)	(9)	(6)	(11)	(3)	(7)
Amyloidosis		6	1	1	7	3	7	1	5
ABDOMEN:			(1)		(2)	(1)			(1)
Haemorrhage(s)			0		1	0			0
Inflammation/fat necrosis			1		1	1			1
ACCESSORY SEX GLAND(S):			(1)	(1)	(1)				
PREPUTIAL GLAND: purulent inflammation/abscess(es)			1	1	1				
ADRENALS:		(50)	(23)	(21)	(48)	(50)	(32)	(24)	(50)
No abnormality detected		14	13	8	25*	4	1	4	6
Unilateral PHAEOCHROMOCYTOMA [M]		0	1	0	0	0	0	0	0
Unilateral subcapsular CORTICAL CARCINOMA [M]		0	1	0	0	0	1	0	0
Unilateral PHAEOCHROMOCYTOMA [B]		0	0	0	1	0	0	0	0
Unilateral CORTICAL ADENOMA [B]		1	0	0	0	0	0	0	0
Unilateral subcapsular CORTICAL ADENOMA [B]		0	1	2	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
ADRENALS:		(50)	(23)	(21)	(48)	(50)	(32)	(24)	(50)
Subcapsular hyperplasia		19	5	4	14	40	29	18	40
(Associated) subcapsular hyperplasia		0	1	1	0	1	0	0	0
Unilateral medullary hyperplasia		1	1	1	1	0	0	0	0
Focal cortical hyperplasia		0	0	0	2	0	1	0	0
Diffuse cortical hyperplasia		0	0	0	0	1	1	0	0
Unilateral focus(i) of subcapsular medullary cell(s)		1	0	0	0	0	0	0	0
Infiltration by lymphoma cells		1	0	0	2	3	2	1	1
Increased corticomedullary pigmented foamy cells		0	0	0	0	3	1	3	6
Unilateral focus(i) of cellular change (cortex)		1	0	0	0	0	0	0	0
Accessory cortical nodule(s)		1	0	0	1	2	4	2	7
Unilateral thrombus		0	0	0	0	1	0	0	0
Unilateral inflammatory cell infiltrate		0	0	0	0	0	0	1	0
Focal/diffuse cortical hypertrophy		14	1	5	6	1	0	0	0
Focal cortical degeneration		0	1	0	2	0	0	0	0
Congestion		0	1	0	0	0	0	0	0
Amyloidosis		6	1	1	2	3	5	1	3

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
AORTA:		(50)	(24)	(20)	(50)	(48)	(32)	(24)	(50)
No abnormality detected		49	24	20	48	45	30	20	48
Lymphoma cells in surrounding tissue		1	0	0	2	3	2	4	2
BONE:						(2)		(1)	
Metastasising OSTEOSARCOMA [M]						0		1	
BRAIN:		(49)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		44	20	14	36*	40	28	18	39
MENINGIOMA [B]		0	0	1	0	0	0	0	0
Compression by pituitary		0	0	0	0	1	0	0	1
Meningeal infiltration by lymphoma cells		1	0	0	0	2	1	2	1
Mineral deposit(s)		4	4	7	13*	4	4	5	8
Meningeal inflammatory cell infiltrate		0	0	1	0	1	0	0	0
Focus(i) of bacterial inflammation		0	0	0	0	0	0	0	1
Cerebral haemorrhage(s)		0	0	0	0	1	0	0	0
Ventricular dilatation		0	0	0	1	0	0	0	0
Cerebral cyst(s)		0	0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(41)	(47)	(33)	(22)	(49)
No abnormality detected		38	18	16	39	43	29	22	45
Mucosal hyperplasia		0	0	0	0	1	0	0	1
Infiltration by lymphoma cells		1	0	0	1	2	0	0	0
Submucosal oedema		3	0	0	0	1	4	0	1
Mucosal necrosis with/without inflammation		0	0	0	1	0	0	0	1
Amyloidosis		0	0	0	0	0	1	0	0
CERVIX:						(2)			(2)
Dilatation/cyst(s)						2			2
COAGULATING GLANDS:		(1)	(1)		(1)				
Dilated		1	1		1				
Inflammation		0	1		1				
COLON:		(47)	(21)	(19)	(48)	(49)	(33)	(23)	(49)
No abnormality detected		44	21	19	48	48	32	23	49
Infiltration by lymphoma cells		1	0	0	0	1	1	0	0
Submucosal oedema		2	0	0	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:			(1)	(1)		(1)		(1)	
Chronic inflammatory cell infiltrate			0	0		1		0	
Contains secondary tumour			1	1		0		1	
DUODENUM:		(45)	(17)	(16)	(44)	(49)	(31)	(19)	(48)
No abnormality detected		39	17	16	39	45	28	18	44
Infiltration by lymphoma cells		1	0	0	1	1	0	1	1
Inflammation in muscle layer		0	0	0	0	0	1	0	0
Amyloidosis		4	0	0	4	3	3	0	3
Submucosal focus of pancreatic tissue		1	0	0	0	0	0	0	0
EYES:		(7)	(1)	(1)	(2)	(3)	(1)	(2)	(2)
No abnormality detected		6	1	1	1	3	1	2	2
Unilateral keratitis		1	0	0	1	0	0	0	0
GALL BLADDER:		(44)	(45)	(43)	(41)	(44)	(43)	(44)	(46)
No abnormality detected		40	42	37	37	30	36	34	37
Mucosal hyperplasia		0	1	0	0	0	0	1	0
Mesothelial hyperplasia		0	0	0	0	1	0	0	0
Infiltration by lymphoma cells		1	0	0	1	2	4	4	2

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(45)	(43)	(41)	(44)	(43)	(44)	(46)
Dilated		2	2	3	3	12	3*	5	7
Inflammation		1	0	1	0	0	0	0	1
Cyst(s)		0	0	1	0	0	0	0	0
Contains secondary tumour		0	0	1	0	0	0	0	0
HARDERIAN GLAND:		(1)	(2)		(2)				
Unilateral ADENOMA [B]		1	1		2				
Unilateral bacterial abscess(es)		0	1		0				
HEART:		(50)	(25)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		27	14	12	27	36	19	12	31
Infiltration by histiocytic cells		0	2	0	0	0	0	1	0
Infiltration by lymphoma cells		2	0	0	4	4	4	5	3
Cardiomyopathy with/without necrosis		17	6	5	14	6	5	0	5
Myocardial mineral deposit(s)		0	0	0	0	0	0	1	0
Widespread myocardial vacuolation		1	0	0	0	0	0	0	0
Atrial thrombosis		2	1	2	0	1	1	2	3
Perivasculitis		5	2	2	2	3	2	1	5
Inflammatory changes		2	0	3	3	0	2	1	5
Haemorrhage(s)		0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
HEART:		(50)	(25)	(21)	(50)	(50)	(33)	(24)	(50)
Focal fibrosis		1	1	1	0	0	0	0	0
Valvular bacterial endocarditis		0	0	0	0	1	0	0	2
Amyloidosis		3	0	0	0	0	0	1	0
Epicardial lymphoid cell(s)		0	0	0	0	1	1	1	0
Contains secondary tumour		0	0	1	1	0	1	0	0
ILEUM:		(43)	(19)	(16)	(41)	(45)	(32)	(22)	(48)
No abnormality detected		36	17	16	35	40	25	21	42
Infiltration by lymphoma cells		1	1	0	0	1	1	0	1
Amyloidosis		6	1	0	6	3	6	1	5
JEJUNUM:		(43)	(19)	(18)	(45)	(48)	(30)	(20)	(48)
No abnormality detected		37	18	18	41	45	26	20	44
Infiltration by lymphoma cells		1	0	0	1	1	1	0	0
Amyloidosis		5	1	0	3	2	3	0	4
KIDNEYS:		(50)	(50)	(50)	(50)	(50)	(49)	(50)	(50)
No abnormality detected		8	2	6	4	11	7	9	2*
Unilateral TUBULAR CARCINOMA [M]		1	1	0	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(50)	(50)	(50)	(50)	(50)	(49)	(50)	(50)
Unilateral TUBULAR ADENOMA [B]		1	1	0	0	0	0	0	0
Unilateral focus(i) of tubular hyperplasia		1	0	0	0	0	1	0	0
Unilateral focal urothelial hyperplasia		1	0	0	0	0	0	0	0
Infiltration by histiocytic cells		0	1	0	1	0	2	3	0
Infiltration by lymphoma cells		2	0	1	4	10	9	8	8
Unilateral focus(i) of fat cell(s)		0	0	0	1	0	0	0	0
Basophilic tubules		5	5	7	3	1	2	4	4
Focal tubular atrophy		2	5	5	5	6	3	3	5
Tubular dilatation		1	0	2	4	1	3	3	0
Pelvic dilatation		1	1	2	1	1	4	2	1
Papillary necrosis		1	0	1	0	0	1	1	0
Focal nephritis		0	2	0	0	0	0	0	1
Mineral deposit(s)		2	4	2	4	0	0	0	0
Cortical tubular pigment deposit(s)		0	1	2	0	0	1	1	1
Cortical tubular-cell vacuolation		0	0	0	0	0	1	0	0
Unilateral thrombus		0	0	0	1	0	0	0	0
Unilateral chronic capsular thickening		0	0	0	1	0	0	0	0
Pyelitis		0	1	0	1	0	0	0	0
Perivasculitis		1	4	1	3	1	0	0	0
Nephropathy		31	34	28	27	26	16	25	27
Unilateral coagulative necrosis		0	0	0	2	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(50)	(50)	(50)	(50)	(50)	(49)	(50)	(50)
Interstitial/perivascular lymphoid focus(i)		3	5	4	6	5	10	3	10
Tubular hypertrophy		0	1	2	0	0	0	0	0
Cortical tubular eosinophilic droplet(s)		0	0	0	0	0	1	2	0
Cyst(s)		11	21	22*	15	5	11	3	9
Congestion		0	0	0	1	0	0	0	0
Amyloidosis		6	2	1	3	3	5	1	3
Contains secondary tumour		0	0	1	1	0	1	0	0
LIVER:		(50)	(50)	(50)	(50)	(50)	(49)	(50)	(50)
No abnormality detected		17	21	16	12	17	12	15	20
HEPATOCELLULAR CARCINOMA(TA) [M]		8	5	6	7	1	0	0	0
HEPATOCELLULAR ADENOMA(TA) [B]		8	12	11	9	1	0	2	0
(Associated) HEPATOCELLULAR ADENOMA(TA) [B]		1	1	4	4	0	0	0	0
Infiltration by histiocytic cells		0	2	0	1	0	3	3	0
Infiltration by lymphoma cells		2	0	1	5	9	8	8	5
Focal oval-cell hyperplasia		0	0	0	1	0	0	0	0
Hepatocyte atypia		0	1	1	1	0	0	0	1
Contains haemangiosarcoma		0	0	0	3	0	0	0	1
Hepatocyte rarefaction		3	1	0	1	0	2	2	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(50)	(50)	(50)	(50)	(50)	(49)	(50)	(50)
Necrosis with inflammation		1	1	0	2	0	1	1	0
Kupffer cell pigmentation		0	0	0	3	1	0	0	0
Pale/clear cell focus(i)		3	2	0	0	0	0	0	0
Basophilic focus(i)		3	0	0	1	0	0	0	0
Focus(i) of lymphoid cell(s)		4	2	6	2	6	5	6	10
Extramedullary haemopoiesis		1	2	0	3	3	6	3	3
Hepatocyte vacuolation		1	5	1	3	2	4	1	1
Thrombus		0	0	0	0	0	1	0	0
Perivasculitis		0	0	0	1	0	0	0	0
Focus(i) of mineralisation		0	0	0	1	0	0	0	0
Centrilobular hepatocyte enlargement		1	0	1	1	0	2	1	1
Area(s) of degeneration/necrosis		1	2	1	5	3	2	3	3
Cyst(s)		0	0	0	0	0	0	1	1
Dilated sinusoids/angiectasis		0	0	2	0	0	1	0	0
Vascular amyloidosis		3	1	0	0	2	3	1	2
Increased cell turnover		2	1	1	4	1	3	2	1
Vascular endothelial pavementing by neutrophils		0	1	0	0	0	0	0	0
Inflammatory changes with/without mineralisation		6	5	9	11	10	9	6	8
Multinucleate hepatocytes		0	0	0	0	0	0	0	1
Contains secondary tumour		0	0	1	1	2	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS / TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
	MALES				FEMALES			
	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)	(50)	(50)	(50)	(49)	(50)	(50)
No abnormality detected	18	17	15	15	15	18	17	12
ALVEOLAR/BRONCHIOLAR CARCINOMA(TA) [M]	10	7	8	9	3	2	1	5
ALVEOLAR/BRONCHIOLAR ADENOMA(TA) [B]	9	15	11	13	7	3	3	6
(Associated) ALVEOLAR/BRONCHIOLAR ADENOMA(TA) [B]	3	0	1	3	0	2	0	3
Infiltration by histiocytic cells	0	2	0	1	0	1	2	0
Infiltration by lymphoma cells	2	1	1	6	10	8	8	10
Alveolar epithelialisation	0	0	2	1	1	0	1	0
Focal adenomatosis	0	0	1	0	0	0	0	0
Interstitial/perivascular lymphoid cells	0	2	1	0	3	7	6	8
Interstitial pneumonitis	3	1	4	3	1	2	2	1
Increased alveolar macrophages	7	10	8	13	6	9	8	9
B.A.L.T. increase	2	1	3	2	2	0	2	0
Alveolitis	4	2	5	2	4	2	1	5
Perivasculitis	0	1	1	0	2	2	1	1
Alveolar oedema	0	0	0	0	0	0	0	2
Inflammatory changes	1	1	0	0	1	1	4	0
Alveolar haemorrhage(s)	0	1	1	1	2	4	1	3
Focal alveolar fibrosis	0	0	1	0	0	0	0	1
Focal pleural eosinophilic deposit(s)	0	0	0	0	0	0	1	0
Congestion	2	3	3	2	1	1	0	1
Bronchopneumonia	1	0	2	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(50)	(50)	(50)	(49)	(50)	(50)
Focal pleural fibrosis/thickening		0	0	1	0	0	1	2	1
Solitary focus of vascular mural thickening		0	0	0	0	0	0	0	1
Contains secondary tumour		1	0	1	1	0	0	2	1
LYMPH NODE(S):		(8)	(12)	(9)	(20)	(18)	(16)	(15)	(13)
One or more has lymphoid hyperplasia		0	0	0	0	0	1	0	0
One or more infiltrated by histiocytic cells		0	0	0	0	0	2	2	1
One or more infiltrated by lymphoma cells		2	0	0	5	8	7	6	4
One or more has vascular medial hypertrophy		0	0	0	0	1	0	0	0
One or more has extramedullary haemopoiesis		0	0	1	0	1	0	0	0
One or more has pigment deposits		0	0	0	0	2	0	0	0
One or more reactive		0	0	0	0	1	2	1	0
One or more has inflammatory cell infiltrate		0	0	1	1	0	0	0	1
One or more has plasmacytosis		1	2	1	3	0	1	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(9)	(20)	(18)	(16)	(15)	(13)
One or more has multinucleate macrophages		0	0	0	1	0	0	0	0
One or more congested		0	0	0	0	0	2	0	0
One or more has amyloidosis		0	0	0	0	0	1	0	0
One or more contains secondary tumour		0	0	0	2	0	1	2	0
LYMPHORETICULAR/HAEMOPOIETIC TISSUE:		(4)	(4)	(1)	(8)	(14)	(15)	(12)	(14)
HISTIOCYTIC SARCOMA [M]		0	2	0	2	0	3	3	1
LYMPHOMA [M]		4	2	1	6	14	12	9	13
MAMMARY GLANDS:		(44)	(14)	(20)	(42)	(49)	(33)	(24)	(50)
No abnormality detected		42	14	20	42	42	28	17	42
CARCINOMA(TA) [M]		0	0	0	0	2	0	1	0
ADENOACANTHOMA MULTIPLE [B]		0	0	0	0	0	0	0	1
Alveolar development		0	0	0	0	2	2	0	5
Infiltration by lymphoma cells		0	0	0	0	3	3	3	0
Dilated/cystic duct(s)		1	0	0	0	1	0	1	0
Increased secretion present		0	0	0	0	1	0	0	3
Thrombosis		0	0	0	0	0	0	1	0
Inflammation		2	0	0	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(44)	(14)	(20)	(42)	(49)	(33)	(24)	(50)
Amyloidosis		0	0	0	0	0	0	1	0
Site only examined		39	12	17	31	0	0	0	1
MEDIASTINUM:							(1)		
Infiltration by lymphoma cells							1		
MESENTERIC LYMPH NODE:		(46)	(20)	(18)	(47)	(48)	(31)	(22)	(49)
No abnormality detected		30	13	11	29	28	10	14	33
Infiltration by histiocytic cells		0	0	0	0	0	1	0	0
Infiltration by lymphoma cells		2	1	0	5	8	7	6	8
Lymphoid hyperplasia		0	0	0	0	0	1	0	0
Extramedullary haemopoiesis		0	1	2	2	1	0	0	0
Increased lymphocytolysis/lymphoid depletion		0	0	2	0	1	1	0	0
Pigmented macrophages		1	1	1	2	3	0	0	1
Reactive		0	0	0	0	1	0	0	0
Plasmacytosis		0	0	0	1	0	1	0	0
Oedema		0	0	0	0	0	2	0	1
Inflammatory changes		2	1	2	1	0	4	0	1
Cyst(s)		0	0	0	0	1	0	0	2

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(46)	(20)	(18)	(47)	(48)	(31)	(22)	(49)
Congestion		7	3	3	4	4	4	1	3
Amyloidosis		5	1	0	3	2	4	1	4
Contains secondary tumour		0	0	0	1	0	0	0	0
MESENTERY:				(2)	(1)	(3)		(1)	(1)
Infiltration by histiocytic cells				0	1	0		0	0
Infiltration by lymphoma cells				0	0	2		0	1
Perivasculitis				0	0	1		0	0
Chronic, active inflammation				1	0	0		0	0
Contains secondary tumour				1	0	0		1	0
NASAL CAVITY:					(1)	(1)			
Mucosal inflammation					0	1			
Haemorrhage(s)					1	0			
OESOPHAGUS:		(50)	(24)	(21)	(50)	(50)	(32)	(24)	(50)
No abnormality detected		50	24	21	50	50	32	24	48
Submucosal inflammation		0	0	0	0	0	0	0	2

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
OVARIES:						(50)	(33)	(24)	(50)
No abnormality detected						8	3	1	6
Unilateral GRANULOSA CELL TUMOUR(S) [M]						1	0	0	0
Unilateral metastasising LUTEAL CELL TUMOUR [M]						0	0	1	0
Unilateral tubulostromal ADENOMA [B]						0	0	0	2
Unilateral focus(i) of tubulostromal hyperplasia						0	0	1	3
(Associated) bilateral tubulostromal hyperplasia						0	0	0	1
Unilateral focus(i) of papillary hyperplasia						0	0	0	2
Bilateral Sertoliform tubular hyperplasia						1	0	0	0
Interstitial cell hyperplasia						2	1	0	3
Infiltration by histiocytic cells						0	0	1	1
Infiltration by lymphoma cells						7	6	5	2
Unilateral mineral deposit(s)						1	0	0	0
Pigment deposit(s)						4	1	1	0
Unilateral thrombus						1	1	0	1
Perivasculitis						3	3	1	3
Absence of recent corpus luteum						4	9	6	6
Cyst(s)						36	27	20	37
Unilateral angiectasis						0	0	0	1

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
OVARIES:						(50)	(33)	(24)	(50)
Amyloidosis						2	3	0	3
Increased luteal tissue						0	1	3	1
Contains secondary tumour						0	0	1	0
PANCREAS:		(50)	(25)	(20)	(49)	(50)	(33)	(24)	(50)
No abnormality detected		41	17	13	39	30	17	15	30
ISLET ADENOMA [B]		0	0	0	1	0	1	0	0
Islet hyperplasia		0	0	1	0	0	0	0	2
Infiltration by histiocytic cells		0	0	0	1	0	0	0	0
Infiltration by lymphoma cells		2	0	0	5	7	5	5	4
Cystic duct(s)		0	1	1	0	1	0	0	0
Localised replacement by fat		0	0	0	0	0	0	0	2
Acinar atrophy		0	0	1	2	0	2	1	0
Focus(i) of lymphoid cell(s)		5	2	2	2	6	1	1	5
Acinar-cell vacuolation		0	0	1	0	2	2	3	2
Perivasculitis		0	0	0	0	1	0	0	1
Interstitial oedema		2	3	0	0	2	8	0	1
Interstitial inflammation with/without necrosis		0	3	1	0	1	2	1	2
Focal acinar hypertrophy		0	0	0	0	1	0	0	0
Interstitial fibrosis		0	0	0	0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(49)	(50)	(33)	(24)	(50)
Decreased islet tissue		0	1	0	0	0	0	0	0
Contains secondary tumour		0	0	0	0	0	0	0	1
PARATHYROIDS:		(44)	(19)	(19)	(45)	(43)	(28)	(21)	(41)
No abnormality detected		39	18	18	42	41	23	20	38
Infiltration by lymphoma cells		1	0	0	1	0	0	0	1
Lymphocytic infiltration		0	0	0	0	1	1	1	1
Unilateral mast-cell infiltration		0	0	0	0	0	1	0	0
Unilateral cyst(s)		0	0	0	0	0	1	0	0
Amyloidosis		4	1	1	2	1	2	0	1
PITUITARY:		(47)	(24)	(20)	(44)	(49)	(32)	(23)	(50)
No abnormality detected		43	23	19	41	41	29	20	43
Anterior lobe ADENOMA [B]		0	0	0	0	1	0	0	2
Intermediate lobe ADENOMA [B]		0	0	0	1	0	0	0	1
Cellular change		3	1	0	1	2	1	2	3
Infiltration by lymphoma cells		0	0	0	0	2	2	0	1
Focal mineral deposit(s)		0	0	0	1	0	0	0	0
Thrombus		0	0	0	0	1	0	0	0
Perivasculitis		0	0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
PITUITARY:		(47)	(24)	(20)	(44)	(49)	(32)	(23)	(50)
Focal haemorrhage(s)		0	0	0	0	1	0	0	0
Anterior lobe cyst(s)		1	0	0	0	0	1	0	0
Congestion		0	0	1	0	0	0	1	1
PROSTATE:		(48)	(24)	(21)	(50)				
No abnormality detected		46	20	20	40*				
Metastasising SARCOMA [M]		0	0	1	0				
Contains haemangiosarcoma		0	0	0	1				
Hyperplasia		2	0	0	2				
Infiltration by histiocytic cells		0	0	0	1				
Infiltration by lymphoma cells		0	0	0	2				
Inflammation		0	4	0	3				
RECTUM:		(46)	(21)	(19)	(48)	(49)	(32)	(23)	(49)
No abnormality detected		45	21	19	48	49	32	23	49
Infiltration by lymphoma cells		1	0	0	0	0	0	0	0
SALIVARY GLAND:		(50)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		32	19	19	31	27	17	17	27

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(50)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
SUBMAXILLARY: infiltration by lymphoma cells		1	0	0	3	8	2	3	3
SUBMAXILLARY: mucous hypertrophy		0	0	0	0	5	5	4	1
SUBMAXILLARY: medial hypertrophy		0	0	0	0	1	0	0	0
SUBMAXILLARY: acinar atrophy		3	0	0	1	1	0	0	0
SUBMAXILLARY: bacterial focus(i)		0	1	0	0	0	0	0	0
SUBMAXILLARY: lymphoid foci		9	3	2	9	9	6	2	16
SUBMAXILLARY: perivasculitis		0	0	0	1	1	0	0	1
SUBMAXILLARY: capsular fibrosis		0	0	0	0	0	0	1	0
SUBMAXILLARY: amyloidosis		0	0	0	0	0	0	1	0
SUBLINGUAL: infiltration by lymphoma cells		0	0	0	1	1	0	1	0
SUBLINGUAL: lymphoid foci		1	0	0	2	1	1	0	0
SUBLINGUAL: acinar-cell enlargement		0	0	0	1	0	0	0	0
SUBLINGUAL: amyloidosis		0	0	0	0	0	0	1	0
PAROTID: infiltration by lymphoma cells		0	0	0	1	3	2	2	0
PAROTID: acinar-cell vacuolation		1	1	0	2	0	0	0	1
PAROTID: acinar atrophy		0	0	0	0	0	1	0	0
PAROTID: lymphoid foci		1	0	0	2	2	1	1	3
PAROTID: inflammation		0	1	0	1	0	0	0	0
PAROTID: amyloidosis		5	1	0	2	2	3	1	2

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
SCIATIC NERVE:		(49)	(24)	(21)	(49)	(50)	(33)	(23)	(50)
No abnormality detected		46	23	21	49	50	33	21	48
Inflammatory changes		3	1	0	0	0	0	1	1
Lymphoma cells in surrounding tissue		0	0	0	0	0	0	1	1
SEMINAL VESICLES:		(24)	(10)	(9)	(24)				
No abnormality detected		0	4	1	0				
Unilateral mucosal hyperplasia		0	0	0	1				
Infiltration by histiocytic cells		0	0	0	1				
Infiltration by lymphoma cells		0	0	0	1				
Dilated with secretion		24	6	5	24				
Inflammation		2	0	1	1				
Haemorrhage(s)		0	0	1	0				
Cellular infiltrate in secretion		1	0	1	0				
Contains secondary tumour		0	0	1	0				
SKELETAL MUSCLE:		(50)	(24)	(21)	(50)	(49)	(33)	(24)	(50)
No abnormality detected		49	24	20	46	47	30	22	47
Infiltration by lymphoma cells		0	0	0	1	2	1	1	2
Mineral deposit(s)		0	0	0	0	0	0	1	0
Lymphocytic infiltration		1	0	0	1	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(24)	(21)	(50)	(49)	(33)	(24)	(50)
Perivasculitis		0	0	0	1	0	0	0	1
Myositis		0	0	0	1	0	1	0	0
Areas of intramuscular haemorrhage(s)		0	0	1	0	0	0	0	0
SKIN/SUBCUTIS:		(50)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		42	18	17	37	40	30	16	46
SQUAMOUS-CELL CARCINOMA [M]		1	0	0	0	0	0	1	1
SARCOMA(TA) of unknown cell origin [M]		1	0	1	0	1	0	1	1
PAPILLOMA(TA) [B]		0	0	0	1	1	0	0	0
LIPOMA [B]		0	0	0	1	0	0	0	0
Focus(i) of epidermal hyperplasia		0	0	0	0	0	0	0	1
Infiltration by histiocytic cells		0	0	0	1	0	0	0	0
Infiltration by lymphoma cells		0	0	0	1	5	1	2	0
Epidermal ulceration with inflammation/necrosis		4	5	3	4	1	0	5	1
Mast-cell accumulation		1	0	0	0	0	1	0	0
Subcutaneous oedema		0	1	0	0	0	0	0	0
Inflammation		1	0	0	2	1	0	0	0
Focus(i) of granulation tissue		0	0	0	1	0	0	0	0
Increased subcutaneous fat		0	0	0	0	0	1	0	0
Subcutaneous squamous epithelial cyst(s)		0	0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
SKIN/SUBCUTIS:		(50)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
Focal subcutaneous congestion		0	0	0	1	0	0	0	0
Subcutaneous sebaceous duct dilatation		0	0	0	0	0	0	0	1
SPINAL CORD:		(50)	(24)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		46	22	21	50	49	32	24	46
LUMBAR : GANGLIONEUROMA [B]		1	0	0	0	0	0	0	0
THORACIC : meningeal hyperplasia		1	0	0	0	0	0	0	0
THORACIC : white matter mineralisation		0	0	0	0	0	0	0	1
Infiltration by lymphoma cells		0	0	0	0	1	1	0	0
Spinal canal dilatation		1	1	0	0	0	0	0	0
Axonal degeneration		0	1	0	0	0	0	0	2
Cyst(s)		1	0	0	0	0	0	0	1
SPLEEN:		(50)	(26)	(21)	(50)	(50)	(33)	(24)	(50)
No abnormality detected		32	8	12	27	21	7	6	28
SARCOMA of unknown cell origin [M]		0	0	0	0	0	0	1	0
Contains haemangiosarcoma		0	0	0	3	0	1	0	0
Infiltration by lymphoma cells		2	1	0	4	9	7	4	6
Lymphoid hyperplasia		0	0	0	1	0	0	0	0
Splenic contraction		2	3	2	1	1	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(21)	(50)	(50)	(33)	(24)	(50)
White pulp depletion		0	1	0	1	0	0	1	0
Increased extramedullary haemopoiesis		9	8	6	11	13	15	11	10
Increased lymphocytolysis		1	3	1	2	0	1	0	1
Increased brown pigment deposit(s)		1	0	0	0	6	0	1	2
Perivasculitis		0	0	0	0	0	0	0	1
Large focus(i) of necrosis		0	0	0	0	1	1	0	0
Congestion in the red pulp		0	1	0	0	0	0	0	0
Amyloidosis		2	1	1	3	2	4	1	2
Abscess(es)		0	0	0	0	1	0	1	0
Increased cellularity of red pulp		1	0	0	0	0	0	0	0
Cell vacuolation in the red pulp		0	0	0	0	1	0	0	0
Chronic inflammatory thickening of the capsule		0	0	0	0	1	0	0	0
Contains secondary tumour		0	0	0	0	0	1	1	0
STERNUM:									
No abnormality detected		45	20	19	37	37	19	15	31
Bone marrow infiltration by lymphoma cells		1	0	0	2	3	4	4	2
Fibrous osteopathy		0	0	0	0	3	3	0	8
Pigment deposit(s)		0	0	0	0	0	0	0	1

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
STERNUM:		(50)	(25)	(21)	(50)	(50)	(32)	(24)	(49)
Focal bone marrow necrosis		0	0	0	0	1	0	0	0
Increased granulocytic haemopoiesis		1	3	2	4	3	1	2	3
Increased haemopoiesis		2	1	0	5	1	0	0	3
Decreased haemopoiesis		1	1	0	0	0	0	0	0
Lymphoid foci in marrow		0	0	0	2	0	0	0	0
Maldevelopment of one rib		0	0	0	1	0	0	0	0
Increased lymphoid cells in marrow		0	0	0	0	1	0	0	3
Increased medullary trabecular bone		1	0	0	0	2	5	3	1
STOMACH:		(50)	(24)	(21)	(49)	(50)	(33)	(24)	(49)
No abnormality detected		39	18	15	31	29	19	13	33
SQUAMOUS-CELL CARCINOMA [M]		0	0	0	1	0	0	0	0
Squamous epithelial hyperplasia		1	0	0	1	1	0	0	0
Focal glandular mucosal hyperplasia		3	0	0	6	2	1	3	5
Diffuse glandular mucosal hyperplasia		5	6	4	9	11	8	2	9
Infiltration by lymphoma cells		1	0	0	1	5	3	3	2
Dilated glands in muscle layer		0	0	0	2	0	0	0	0
Dilated mucosal glands		1	0	1	1	2	2	1	2
Submucosal lymphoid cell(s)		0	0	0	0	2	1	0	0
Perivasculitis		0	0	0	0	2	0	0	0
Submucosal oedema		0	0	0	0	0	1	0	1

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
STOMACH:		(50)	(24)	(21)	(49)	(50)	(33)	(24)	(49)
Inflammation		0	0	0	1	0	0	1	0
Submucosal haemopoiesis		0	0	0	0	0	1	0	0
Amyloidosis		0	0	0	0	0	0	0	1
Contains secondary tumour		0	0	1	0	0	0	1	0
SUBMANDIBULAR LYMPH NODE:		(5)	(2)		(5)	(8)	(1)	(1)	(4)
No abnormality detected		0	0		0	1	0	0	0
Infiltration by lymphoma cells		2	0		3	6	1	1	2
Lymphoid hyperplasia		0	0		0	1	0	0	0
Pigment deposit(s)		1	0		0	0	0	0	0
Reactive		0	0		1	0	0	0	0
Plasmacytosis		2	2		1	0	0	0	1
Cyst(s)		0	0		0	0	0	0	1
Congestion		0	0		0	0	1	0	1
TESTES:		(50)	(24)	(21)	(50)				
No abnormality detected		21	14	14	27				
INTERSTITIAL-CELL ADENOMA(TA) [B]		3	0	0	2				
Unilateral focal interstitial-cell hyperplasia		0	0	0	1				

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(24)	(21)	(50)				
Diffuse interstitial cell hyperplasia		6	2	1	5				
Unilateral rete testis hyperplasia		1	0	0	1				
Infiltration by histiocytic cells		0	0	0	1				
Unilateral infiltration by lymphoma cells		0	0	0	1				
Tubular atrophy/mineralisation		18	5	5	11				
Depressed spermatogenesis		2	0	0	1				
Sperm accumulation		8	1	2	4				
Unilateral coagulative necrosis		0	0	0	2				
Unilateral rete testis inflammation		1	0	0	0				
Interstitial congestion		1	0	0	0				
Amyloidosis		1	0	1	0				
EPIDIDYMIS: infiltration by histiocytic cells		0	2	0	1				
EPIDIDYMIS: infiltration by lymphoma cells		1	0	0	1				
EPIDIDYMIS: spermatocoele(s)		2	0	1	1				
EPIDIDYMIS: inflammation		2	0	0	2				
EPIDIDYMIS: tubular dilatation		1	0	0	0				
EPIDIDYMIS: vascular endothelial pavementing by neutrophils		0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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)	(1)		(1)		
PLEURA: inflammation				0	0		1		
Infiltration by lymphoma cells				0	1		0		
Contains secondary tumour				1	0		0		
THYMUS:		(42)	(21)	(16)	(41)	(46)	(31)	(23)	(44)
No abnormality detected		32	16	11	25	27	15	13	17
Infiltration by lymphoma cells		3	0	0	5	10	10	6	10
Lymphoid hyperplasia		1	0	0	1	6	1	2	12
Epithelial hyperplasia		0	0	1	0	0	0	0	0
Increased lymphocytolysis		0	1	0	0	1	0	1	2
Focal foamy cell accumulation		0	0	0	0	0	0	0	1
Thrombus		0	0	0	0	1	0	1	0
Focus(i) of necrosis		0	0	0	0	0	0	0	1
Mast-cell infiltration		0	0	0	0	0	1	0	0
Chronic inflammatory cell infiltrate		0	0	0	0	0	1	0	0
Hassall's corpuscle enlargement		0	0	0	0	0	0	0	1
Cyst(s)		3	1	2	5	2	1	0	1
Vascular mural thickening		0	0	0	0	0	1	0	2
Congestion		0	1	0	0	0	0	2	2
Atrophy		3	2	1	5	1	0	0	0
Focus(i) of hyaline change		0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
THYMUS:		(42)	(21)	(16)	(41)	(46)	(31)	(23)	(44)
Contains secondary tumour		0	0	1	0	0	1	0	1
Germinal centre development		0	0	0	0	0	0	0	1
THYROIDS:		(50)	(24)	(21)	(50)	(50)	(32)	(24)	(50)
No abnormality detected		24	17	13	28	30	26	15	28
Unilateral FOLLICULAR ADENOMA [B]		0	0	1	0	0	0	0	1
Unilateral focus(i) of follicular-cell hyperplasia		1	0	0	0	0	0	0	0
Unilateral focus(i) of c-cell hyperplasia		0	0	0	0	0	0	1	0
Infiltration by lymphoma cells		0	0	0	2	2	0	0	2
Dilated/cystic follicle(s)		20	6	5	19	12	4	6	17
Focus(i) of lymphoid cell(s)		2	0	0	0	4	0	2	1
Perivasculitis		1	0	0	0	1	0	0	0
Unilateral inflammatory cell infiltrate		0	0	1	1	0	0	0	0
Amyloidosis		6	1	1	1	2	2	1	1
TRACHEA:		(50)	(24)	(21)	(50)	(50)	(32)	(24)	(50)
No abnormality detected		50	24	21	50	50	32	23	50
Infiltration by lymphoma cells in lamina propria		0	0	0	0	0	0	1	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: * P<0.05, ** P<0.01, *** P<0.001

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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
URETER:						(1)			
Infiltration by lymphoma cells						1			
URINARY BLADDER:		(49)	(23)	(19)	(50)	(49)	(32)	(23)	(49)
No abnormality detected		36	10	10	29	30	24	16	27
Infiltration by histiocytic cells		0	0	0	1	0	0	1	0
Infiltration by lymphoma cells		1	0	0	4	7	4	3	5
Submucosal lymphoid focus(i)		6	3	3	6	12	2	3	16
Perivasculitis		0	0	0	1	0	0	0	1
Inflammation		4	6	4	3	0	0	0	0
Focal transitional-cell hypertrophy		0	0	0	0	0	0	0	1
Submucosal haemorrhage(s)		0	1	0	1	0	0	0	0
Dilatation		4	8	6	6	0	2	0	1
Large plug of seminal fluid in lumen		0	1	0	0	0	0	0	0
UTERUS:						(50)	(33)	(24)	(50)
No abnormality detected						7	1	5	6
STROMAL SARCOMA [M]						2	0	1	2
STROMAL TUMOUR [B]						0	0	0	1
POLYP(S) [B]						1	3	1	2
LEIOMYOMA(TA) [B]						0	1	0	2

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:						(50)	(33)	(24)	(50)
Cystic endometrial hyperplasia						32	21	12	33
Endometrial hyperplasia						1	2	0	1
Contains haemangiosarcoma						0	1	0	0
Infiltration by histiocytic cells						0	3	3	0
Infiltration by lymphoma cells						4	1	2	2
Dilated/cystic gland(s)						7	6	3	5
Mesothelial hyperplasia						1	0	0	0
Extramedullary haemopoiesis						0	0	0	1
Adenomyosis						2	0	1	2
Thrombosis						1	3	0	4
Perivasculitis						2	1	0	4
Myometrial inflammation						0	0	1	0
Mural haemorrhage(s)						1	0	0	0
Fat necrosis						0	0	1	0
Dilatation						0	3	2	2
Angiectasis						2	1	0	0
Pigmented macrophages in muscle layer						1	0	0	0
VAGINA:									(1)
POLYP [B]									1

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

TABLE 15 (continued)

FINDINGS	TREATMENT	INCIDENCE OF LESIONS (NUMERIC)							
		MALES				FEMALES			
		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:		(5)	(6)	(3)	(9)	(6)	(7)	(2)	(9)
HAEMANGIOSARCOMA [M]		0	0	0	4	0	2	0	1
Perivasculitis		5	6	3	5	6	5	2	9
Vascular endothelial pavementing by neutrophils		0	1	0	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: * P<0.05, ** P<0.01, *** P<0.001

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	26	34	27	29
Hematopoietic & Lymphatic System					
General:	(N=)	(26)	(34)	(27)	(29)
(M) Malignant lymphoma		0	0	0	2
Respiratory System					
Lung:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		5	13	10	7
(M) Adenocarcinoma		0	0	4	1
Digestive System					
Liver:	(N=)	(26)	(34)	(27)	(29)
(B) Hepatocellular adenoma		8	13	9	5
(B) Hemangioma		1	0	0	0
(M) Hepatocellular carcinoma		0	0	2	0
Urinary System					
Kidney:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		0	0	0	2
Urinary bladder:	(N=)	(26)	(34)	(27)	(29)
(B) Transitional cell papilloma		0	2	0	0
Genital System					
Testis:	(N=)	(26)	(34)	(27)	(29)
(B) Interstitial cell tumor		0	1	0	0
Endocrine System					
Thyroid:	(N=)	(26)	(34)	(27)	(29)
(B) Follicular adenoma		0	1	0	0
Nervous System					
Cerebrum:	(N=)	(26)	(34)	(27)	(29)
(B) Lipoma		0	1	0	0
Musculo-Skeletal System					
Bone (others):	(N=)	(3)	(1)	(4)	(1)
(B) Osteoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(26)	(34)	(27)	(29)
(B) Adenoma		2	4	0	2
Integumentary System					
Skin:	(N=)	(26)	(34)	(27)	(29)
(B) Papilloma		1	1	0	0
(M) Hemangiosarcoma		0	0	0	1
No. of benign neoplasms		17	36	20	16
No. of malignant neoplasms		0	0	6	4
No. of benign & malignant neoplasms		17	36	26	20
No. of animals with benign neoplasm(s)		13	25	17	14
No. of animals with malignant neoplasm(s)		0	0	6	4
No. of animals with neoplasm(s)		13	25	20	15

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

Table 20 - 2 Histopathology - Incidence of microscopic neoplastic lesions in male mice
Killed in extremis or found dead

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	24	16	23	21
Hematopoietic & Lymphatic System					
General:	(N=)	(24)	(16)	(23)	(21)
(M) Malignant lymphoma		2	2	0	4
Lymph nodes (mesenteric):	(N=)	(24)	(16)	(23)	(21)
(M) Malignant lymphoma		0	1	0	0
Spleen:	(N=)	(24)	(16)	(23)	(21)
(M) Histiocytic sarcoma		1	0	0	0
Respiratory System					
Nasal cavity:	(N=)	(0)	(0)	(0)	(1)
(M) Adenocarcinoma		-	-	-	1
Lung:	(N=)	(24)	(16)	(23)	(21)
(B) Adenoma		3	1	3	4
(M) Adenocarcinoma		1	1	2	3
Digestive System					
Small intestine:	(N=)	(24)	(16)	(23)	(21)
(B) Papillary adenoma		0	1	0	0
(M) Adenocarcinoma		0	0	0	1
Liver:	(N=)	(24)	(16)	(23)	(21)
(B) Hepatocellular adenoma		6	2	6	2
(M) Histiocytic sarcoma		1	0	0	0
(M) Hepatocellular carcinoma		0	1	1	1
Genital System					
Testis:	(N=)	(24)	(16)	(23)	(21)
(B) Hemangioma		1	0	0	0
Endocrine System					
Thyroid:	(N=)	(24)	(16)	(23)	(21)
(B) Follicular adenoma		0	1	0	0
Adrenal:	(N=)	(24)	(16)	(23)	(21)
(B) Benign B cell tumor		0	1	0	0
Musculo-Skeletal System					
Bone (others):	(N=)	(6)	(1)	(2)	(1)
(B) Osteoma		1	0	0	0
(M) Osteosarcoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(23)	(16)	(23)	(21)
(B) Adenoma		1	0	1	1
Integumentary System					
Skin:	(N=)	(24)	(16)	(23)	(21)
(M) Hemangiosarcoma		0	0	0	1
(M) Leiomyosarcoma		0	0	1	1
(M) Osteosarcoma		0	0	0	1

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

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	24	16	23	21
No. of benign neoplasms		12	6	10	7
No. of malignant neoplasms		5	5	5	13
No. of benign & malignant neoplasms		17	11	15	20
No. of animals with benign neoplasm(s)		10	5	8	6
No. of animals with malignant neoplasm(s)		5	5	5	12
No. of animals with neoplasm(s)		12	9	10	15

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Hematopoietic & Lymphatic System					
General:	(N=)	(50)	(50)	(50)	(50)
(M) Malignant lymphoma		2	2	0	6
Lymph nodes (mesenteric):	(N=)	(50)	(50)	(50)	(50)
(M) Malignant lymphoma		0	1	0	0
Spleen:	(N=)	(50)	(50)	(50)	(50)
(M) Histiocytic sarcoma		1	0	0	0
Respiratory System					
Nasal cavity:	(N=)	(0)	(0)	(0)	(1)
(M) Adenocarcinoma		-	-	-	1
Lung:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		8	14	13	11
(M) Adenocarcinoma		1	1	6	4
Digestive System					
Small intestine:	(N=)	(50)	(50)	(50)	(50)
(B) Papillary adenoma		0	1	0	0
(M) Adenocarcinoma		0	0	0	1
Liver:	(N=)	(50)	(50)	(50)	(50)
(B) Hepatocellular adenoma		14	15	15	7
(B) Hemangioma		1	0	0	0
(M) Histiocytic sarcoma		1	0	0	0
(M) Hepatocellular carcinoma		0	1	3	1
Urinary System					
Kidney:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	0	0	2
Urinary bladder:	(N=)	(50)	(50)	(50)	(50)
(B) Transitional cell papilloma		0	2	0	0
Genital System					
Testis:	(N=)	(50)	(50)	(50)	(50)
(B) Interstitial cell tumor		0	1	0	0
(B) Hemangioma		1	0	0	0
Endocrine System					
Thyroid:	(N=)	(50)	(50)	(50)	(50)
(B) Follicular adenoma		0	2	0	0
Adrenal:	(N=)	(50)	(50)	(50)	(50)
(B) Benign B cell tumor		0	1	0	0
Nervous System					
Cerebrum:	(N=)	(50)	(50)	(50)	(50)
(B) Lipoma		0	1	0	0
Musculo-Skeletal System					
Bone (others):	(N=)	(9)	(2)	(6)	(2)
(B) Osteoma		1	0	1	0
(M) Osteosarcoma		0	0	1	0
Sense Organs					
Harderian gland:	(N=)	(49)	(50)	(50)	(50)
(B) Adenoma		3	4	1	3
Integumentary System					
Skin:	(N=)	(50)	(50)	(50)	(50)
(B) Papilloma		1	1	0	0
(M) Hemangiosarcoma		0	0	0	2

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

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Integumentary System《cont.》					
Skin《cont.》:	(N=)	(50)	(50)	(50)	(50)
(M) Leiomyosarcoma		0	0	1	1
(M) Osteosarcoma		0	0	0	1
No. of benign neoplasms		29	42	30	23
No. of malignant neoplasms		5	5	11	17
No. of benign & malignant neoplasms		34	47	41	40
No. of animals with benign neoplasm(s)		23	30	25	20
No. of animals with malignant neoplasm(s)		5	5	11	16
No. of animals with neoplasm(s)		25	34	30	30

Malignancy: (M), malignant neoplasm.

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	32	36	40	35
Hematopoietic & Lymphatic System					
General:	(N=)	(32)	(36)	(40)	(35)
(M) Malignant lymphoma		4	0*	5	3
Thymus:	(N=)	(32)	(35)	(40)	(35)
(M) Malignant lymphoma		0	0	1	0
Spleen:	(N=)	(32)	(36)	(40)	(35)
(B) Hemangioma		0	0	1	0
Respiratory System					
Lung:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		7	4	12	4
(M) Adenocarcinoma		1	1	3	0
Digestive System					
Small intestine:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		0	0	1	0
Liver:	(N=)	(32)	(36)	(40)	(35)
(B) Hepatocellular adenoma		1	1	1	0
Urinary System					
Urinary bladder:	(N=)	(32)	(36)	(40)	(35)
(B) Leiomyoma		0	0	1	1
Genital System					
Uterus:	(N=)	(32)	(36)	(40)	(35)
(B) Endometrial stromal polyp		0	2	0	0
(B) Hemangioma		0	0	1	2
(B) Leiomyoma		1	0	2	1
(M) Histiocytic sarcoma		0	1	0	0
(M) Leiomyosarcoma		2	1	0	0
Endocrine System					
Pituitary:	(N=)	(32)	(36)	(40)	(35)
(B) Anterior adenoma		0	1	0	0
Thyroid:	(N=)	(32)	(36)	(40)	(35)
(B) Follicular adenoma		0	1	0	0
Adrenal:	(N=)	(32)	(36)	(40)	(35)
(B) Benign A cell tumor		0	1	2	0
(B) Pheochromocytoma		0	2	0	0
Sense Organs					
Harderian gland:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		1	3	0	3
Integumentary System					
Skin:	(N=)	(32)	(36)	(40)	(35)
(B) Papilloma		1	0	0	0
(B) Lipoma		1	0	1	0
(M) Liposarcoma		0	0	0	1
Mammary gland:	(N=)	(32)	(36)	(40)	(35)
(B) Adenoma		0	1	0	0
(M) Adenocarcinoma		0	2	0	0
Body Cavities					
Abdominal cavity:	(N=)	(5)	(4)	(3)	(4)
(B) Hemangioma		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.

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	32	36	40	35
No. of benign neoplasms		12	16	22	12
No. of malignant neoplasms		7	5	9	4
No. of benign & malignant neoplasms		19	21	31	16
No. of animals with benign neoplasm(s)		11	12	18	11
No. of animals with malignant neoplasm(s)		7	5	9	4
No. of animals with neoplasm(s)		16	16	21	12

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	18	14	10	15
Hematopoietic & Lymphatic System					
General:	(N=)	(18)	(14)	(10)	(15)
(M) Myeloid leukemia		0	0	0	1
(M) Malignant lymphoma		2	4	3	4
Spleen:	(N=)	(18)	(14)	(10)	(15)
(M) Hemangiosarcoma		0	0	1	0
(M) Histiocytic sarcoma		0	0	0	1
Respiratory System					
Lung:	(N=)	(18)	(14)	(10)	(15)
(B) Adenoma		1	1	0	1
(M) Adenocarcinoma		0	1	0	1
< Nodule/mass not in section >		0	0	1	0
Digestive System					
Liver:	(N=)	(18)	(14)	(10)	(15)
(B) Hemangioma		0	0	0	1
Genital System					
Ovary:	(N=)	(18)	(14)	(10)	(15)
(B) Hemangioma		0	0	0	1
Uterus:	(N=)	(18)	(14)	(10)	(15)
(M) Leiomyosarcoma		0	0	0	1
Endocrine System					
Thyroid:	(N=)	(18)	(14)	(10)	(15)
(B) Follicular adenoma		0	1	0	0
Musculo-Skeletal System					
Bone (femur):	(N=)	(18)	(14)	(10)	(15)
(B) Osteoma		0	0	0	1
Skeletal muscle (others):	(N=)	(0)	(3)	(3)	(1)
(M) Rhabdomyosarcoma		-	1	2	0
Sense Organs					
Harderian gland:	(N=)	(18)	(14)	(10)	(15)
(B) 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	0
Mammary gland:	(N=)	(18)	(14)	(10)	(15)
(M) Adenocarcinoma		0	1	1	0
Body Cavities					
Thoracic cavity:	(N=)	(2)	(4)	(4)	(7)
(M) Osteosarcoma		0	0	0	1
Abdominal cavity:	(N=)	(3)	(5)	(6)	(5)
(M) Osteosarcoma		0	0	0	1

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

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	18	14	10	15
No. of benign neoplasms		1	2	0	6
No. of malignant neoplasms		2	8	8	10
No. of benign & malignant neoplasms		3	10	8	16
No. of animals with benign neoplasm(s)		1	1	0	5
No. of animals with malignant neoplasm(s)		2	8	7	9
No. of animals with neoplasm(s)		3	8	7	11

Table 21 - 5 Histopathology - Incidence of microscopic neoplastic lesions in female mice
All animals examined

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Hematopoietic & Lymphatic System					
General:	(N=)	(50)	(50)	(50)	(50)
(M) Myeloid leukemia		0	0	0	1
(M) Malignant lymphoma		6	4	8	7
Thymus:	(N=)	(49)	(49)	(50)	(50)
(M) Malignant lymphoma		0	0	1	0
Spleen:	(N=)	(50)	(50)	(50)	(50)
(B) Hemangioma		0	0	1	0
(M) Hemangiosarcoma		0	0	1	0
(M) Histiocytic sarcoma		0	0	0	1
Respiratory System					
Lung:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		8	5	12	5
(M) Adenocarcinoma		1	2	3	1
< Nodule/mass not in section >		0	0	1	0
Digestive System					
Small intestine:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	0	1	0
Liver:	(N=)	(50)	(50)	(50)	(50)
(B) Hepatocellular adenoma		1	1	1	0
(B) Hemangioma		0	0	0	1
Urinary System					
Urinary bladder:	(N=)	(50)	(50)	(50)	(50)
(B) Leiomyoma		0	0	1	1
Genital System					
Ovary:	(N=)	(50)	(50)	(50)	(50)
(B) Hemangioma		0	0	0	1
Uterus:	(N=)	(50)	(50)	(50)	(50)
(B) Endometrial stromal polyp		0	2	0	0
(B) Hemangioma		0	0	1	2
(B) Leiomyoma		1	0	2	1
(M) Histiocytic sarcoma		0	1	0	0
(M) Leiomyosarcoma		2	1	0	1
Endocrine System					
Pituitary:	(N=)	(50)	(50)	(50)	(50)
(B) Anterior adenoma		0	1	0	0
Thyroid:	(N=)	(50)	(50)	(50)	(50)
(B) Follicular adenoma		0	2	0	0
Adrenal:	(N=)	(50)	(50)	(50)	(50)
(B) Benign A cell tumor		0	1	2	0
(B) Pheochromocytoma		0	2	0	0
Musculo-Skeletal System					
Bone (femur):	(N=)	(50)	(50)	(50)	(50)
(B) Osteoma		0	0	0	1
Skeletal muscle (others):	(N=)	(0)	(3)	(4)	(3)
(M) Rhabdomyosarcoma		-	1	2	0
Sense Organs					
Harderian gland:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		1	3	0	5

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

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

Site & Lesion	Dose (ppm)	0	1600	8000	40000
	No. of animals examined	50	50	50	50
Integumentary System					
Skin:	(N=)	(50)	(50)	(50)	(50)
(B) Papilloma		1	0	0	0
(B) Lipoma		1	0	1	0
(M) Basal cell carcinoma		0	1	0	0
(M) Liposarcoma		0	0	0	1
(M) Hemangiosarcoma		0	0	1	0
Mammary gland:	(N=)	(50)	(50)	(50)	(50)
(B) Adenoma		0	1	0	0
(M) Adenocarcinoma		0	3	1	0
Body Cavities					
Thoracic cavity:	(N=)	(4)	(6)	(5)	(10)
(M) Osteosarcoma		0	0	0	1
Abdominal cavity:	(N=)	(8)	(9)	(9)	(9)
(B) Hemangioma		0	0	0	1
(M) Osteosarcoma		0	0	0	1
No. of benign neoplasms		13	18	22	18
No. of malignant neoplasms		9	13	17	14
No. of benign & malignant neoplasms		22	31	39	32
No. of animals with benign neoplasm(s)		12	13	18	16
No. of animals with malignant neoplasm(s)		9	13	16	13
No. of animals with neoplasm(s)		19	24	28	23

(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.

TABLE 20

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
1. SALIVARY GLAND		(22)	(20)	(20)	(27)	(16)	(16)	(20)	(20)
2. ESOPHAGUS		(22)	(20)	(22)	(26)	(16)	(16)	(19)	(20)
3. STOMACH		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	1 [6]	0	0
4. DUODENUM		(22)	(20)	(22)	(27)	(15)	(15)	(20)	(20)
5. JEJUNUM		(22)	(19)	(22)	(27)	(16)	(13)	(20)	(20)
6. ILEUM		(22)	(20)	(20)	(26)	(16)	(16)	(19)	(20)
7. CECUM		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Adenoma(B)		1 [5]	0	0	0	0	0	0	0
8. COLON		(21)	(20)	(22)	(26)	(16)	(16)	(20)	(20)
9. RECTUM		(21)	(19)	(20)	(26)	(16)	(16)	(19)	(19)

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
10. PANCREAS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	1 [6]	0	0
11. LIVER		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Hemangiosarcoma(M)		0	0	1 [5]	0	0	0	0	0
Endometrial stromal sarcoma -metastatic(MM)		0	0	0	0	0	2 [13]	1 [5]	0
Hepatocellular adenoma(B)		0	1 [5]	0	1 [4]	0	0	0	0
Hepatocellular carcinoma(M)		0	0	0	1 [4]	0	0	0	0
12. GALL BLADDER		(22)	(18)	(20)	(24)	(13)	(14)	(16)	(17)
13. LUNGS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Squamous cell carcinoma-metastatic(MM)		0	1 [5]	0	0	0	0	0	0

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
13. LUNGS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -metastatic(MM)		0	0	0	0	0	0	1 [5]	0
Bronchio-alveolar carcinoma(M)		0	0	0	1 [4]	1 [6]	0	0	0
Bronchio-alveolar adenoma(B)		0	0	0	1 [4]	0	0	1 [5]	2 [10]
14. TRACHEA		(22)	(20)	(22)	(26)	(16)	(16)	(19)	(20)
15. HEART		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
16. SPLEEN		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
17. MESENTERIC LYMPH NODES		(22)	(20)	(22)	(25)	(16)	(16)	(20)	(20)
Hemangioma(B)		0	0	0	0	1 [6]	0	0	2 [10]
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	1 [6]	0	0

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
18. MEDIASTINAL LYMPH NODE		(-)	(-)	(2)	(2)	(1)	(-)	(1)	(1)
Endometrial stromal sarcoma -metastatic(MM)		-	-	0	0	0	-	1 [100]	0
19. MANDIBULAR LYMPH NODE		(22)	(18)	(21)	(27)	(16)	(15)	(20)	(19)
20. KIDNEYS		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	1 [6]	0	0
Renal cell adenoma(B)		0	0	0	2 [7]	0	0	0	0
21. URINARY BLADDER		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	0	1 [5]	0
22. TESTES		(22)	(20)	(22)	(27)	NA	NA	NA	NA
Leydig cell tumour(B)		0	0	0	1 [4]	NA	NA	NA	NA
						NA	NA	NA	NA

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
23. EPIDIDYMES		(22)	(20)	(22)	(27)	NA	NA	NA	NA
24. PROSTATE		(22)	(20)	(20)	(27)	NA	NA	NA	NA
25. SEMINAL VESICLES		(22)	(20)	(22)	(27)	NA	NA	NA	NA
26. COAGULATING GLANDS		(22)	(20)	(22)	(27)	NA	NA	NA	NA
27. OVARIES		NA	NA	NA	NA	(16)	(16)	(20)	(20)
Hemangioma(B)		NA	NA	NA	NA	0	0	0	1
		NA	NA	NA	NA				[5]
Endometrial stromal sarcoma -infiltrative(I)		NA	NA	NA	NA	0	2	1	0
		NA	NA	NA	NA		[13]	[5]	
28. UTERUS		NA	NA	NA	NA	(16)	(16)	(20)	(20)
Leiomyosarcoma(M)		NA	NA	NA	NA	0	0	0	1
		NA	NA	NA	NA				[5]
Endometrial stromal sarcoma(M)		NA	NA	NA	NA	1	2	1	0
		NA	NA	NA	NA	[6]	[13]	[5]	
29. VAGINA		NA	NA	NA	NA	(-)	(1)	(1)	(-)

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

contd.

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 evaluated/group

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

Sex	MALES				FEMALES			
Group No.	G1	G2	G3	G4	G1	G2	G3	G4
TISSUE AND OBSERVATION: Dose (ppm)	0	100	1000	10000	0	100	1000	10000
No. of mice	22	20	22	27	16	16	20	20
No. of mice examined	22	20	22	27	16	16	20	20
30. THYROIDS	(22)	(20)	(22)	(25)	(16)	(16)	(19)	(20)
31. PARATHYROIDS	(19)	(19)	(22)	(23)	(15)	(16)	(13)	(19)
32. PITUITARY	(22)	(20)	(21)	(27)	(14)	(16)	(17)	(18)
Adenoma(B)	0	0	0	0	0	0	0	1 [6]
33. ADRENALS	(22)	(19)	(22)	(27)	(16)	(16)	(20)	(20)
Endometrial stromal sarcoma -infiltrative(I)	0	0	0	0	0	1 [6]	0	0
34. EYES WITH OPTIC NERVE	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
35. BONE MARROW (SMEAR)	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(19)
36. SKIN	(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Squamous cell carcinoma(M)	1 [5]	1 [5]	0	0	0	0	0	0
37. THYMUS	(20)	(18)	(17)	(19)	(13)	(14)	(17)	(17)

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	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)		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Hemangiosarcoma(M)		0	0	0	0	0	1 [6]	0	0
43. BONE (FEMUR) WITH JOINT		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Osteoma(B)		1 [5]	0	0	1 [4]	1 [6]	0	0	0
44. TAIL		(1)	(-)	(-)	(-)	(1)	(-)	(-)	(-)
Hemangioma(B)		1 [100]	-	-	-	0	-	-	-
Hemangiosarcoma(M)		0	-	-	-	1 [100]	-	-	-

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
45. MESENTERY		(2)	(2)	(1)	(1)	(3)	(5)	(5)	(4)
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	1 [20]	0	0
46. STERNUM WITH MARROW		(22)	(19)	(22)	(27)	(15)	(16)	(20)	(19)
47. LYMPH NODE (OTHERS)		(3)	(5)	(4)	(3)	(5)	(5)	(5)	(1)
Endometrial stromal sarcoma -metastatic(MM)		0	0	0	0	0	0	1 [20]	0
Endometrial stromal sarcoma -infiltrative(I)		0	0	0	0	0	0	1 [20]	0
48. BRAIN-CEREBRUM		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
49. BRAIN-CEREBELLUM		(21)	(20)	(22)	(27)	(16)	(16)	(19)	(18)
50. BRAIN-MEDULLA		(22)	(20)	(22)	(27)	(15)	(16)	(20)	(19)
51. SUPERFICIAL.ING.L.NODE		(22)	(20)	(21)	(27)	(16)	(16)	(19)	(19)

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

contd.

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 evaluated/group

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

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	Dose (ppm)	0	100	1000	10000	0	100	1000	10000
	No. of mice	22	20	22	27	16	16	20	20
	No. of mice examined	22	20	22	27	16	16	20	20
52. HEMOLYMPHORETICULAR SYSTEM		(22)	(20)	(22)	(27)	(16)	(16)	(20)	(20)
Histiocytic sarcoma(M)		1	1	0	1	0	2	1	1
		[5]	[5]		[4]		[13]	[5]	[5]
Malignant lymphoma(M)		9	12	13	13	9	10	13	12
		[41]	[60]	[59]	[48]	[56]	[63]	[65]	[60]
Myeloid leukemia(M)		2	1	1	1	2	1	2	1
		[9]	[5]	[5]	[4]	[13]	[6]	[10]	[5]

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

TABLE 21

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
1. SALIVARY GLAND		(28)	(1)	(1)	(23)	(34)	(1)	(-)	(30)
2. ESOPHAGUS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
3. STOMACH		(28)	(30)	(28)	(23)	(34)	(-)	(-)	(30)
4. DUODENUM		(28)	(30)	(28)	(23)	(34)	(-)	(-)	(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. PANCREAS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

	Sex	MALES				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)	(6)	(23)	(34)	(4)	(2)	(30)
Hepatocellular adenoma(B)		4	4	3	2	2	1	2	2
		[14]	[80]	[50]	[9]	[6]	[25]	[100]	[7]
Hepatocellular carcinoma(M)		1	0	0	1	0	0	0	0
		[4]			[4]				
12. GALL BLADDER		(27)	(-)	(-)	(22)	(32)	(-)	(-)	(30)
13. LUNGS		(28)	(2)	(-)	(23)	(34)	(-)	(1)	(30)
Bronchio-alveolar adenoma(B)		0	2	-	0	1	-	1	1
			[100]			[3]		[100]	[3]
14. TRACHEA		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
15. HEART		(28)	(2)	(-)	(23)	(34)	(-)	(-)	(30)
16. SPLEEN		(28)	(30)	(27)	(23)	(34)	(33)	(27)	(30)
17. MESENTERIC LYMPH NODES		(28)	(29)	(27)	(23)	(34)	(32)	(28)	(30)
Hemangioma(B)		1	0	0	1	0	0	0	2
		[4]			[4]				[7]
Hemangiosarcoma(M)		0	0	1	0	0	0	0	0
				[4]					

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
18. MEDIASTINAL LYMPH NODE		(-)	(-)	(-)	(1)	(1)	(-)	(-)	(-)
19. MANDIBULAR LYMPH NODE		(28)	(30)	(28)	(23)	(34)	(33)	(28)	(30)
20. KIDNEYS		(28)	(6)	(4)	(23)	(34)	(2)	(1)	(30)
	Malignant hybernoma-infiltrative(I)	1 [4]	0	0	0	0	0	0	0
	Renal cell adenoma(B)	0	0	1 [25]	0	0	0	0	0
21. URINARY BLADDER		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
22. TESTES		(28)	(1)	(1)	(23)	NA	NA	NA	NA
	Leydig cell tumour(B)	1 [4]	1 [100]	0	1 [4]	NA NA	NA NA	NA NA	NA NA
23. EPIDIDYMES		(28)	(1)	(-)	(23)	NA	NA	NA	NA
	Leiomyoma(B)	0	1 [100]	-	0	NA NA	NA NA	NA NA	NA NA
24. PROSTATE		(28)	(-)	(-)	(23)	NA	NA	NA	NA

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
25. SEMINAL VESICLES		(28)	(18)	(10)	(23)	NA	NA	NA	NA
26. COAGULATING GLANDS		(27)	(-)	(-)	(22)	NA	NA	NA	NA
27. OVARIES		NA	NA	NA	NA	(34)	(13)	(13)	(29)
Granulosa cell tumour(B)		NA	NA	NA	NA	0	0	0	1
		NA	NA	NA	NA				[3]
Luteoma(B)		NA	NA	NA	NA	0	0	0	1
		NA	NA	NA	NA				[3]
28. UTERUS		NA	NA	NA	NA	(34)	(15)	(10)	(30)
Leiomyoma(B)		NA	NA	NA	NA	0	0	1	0
		NA	NA	NA	NA			[10]	
Endometrial stromal sarcoma(M)		NA	NA	NA	NA	1	0	2	1
		NA	NA	NA	NA	[3]		[20]	[3]
29. VAGINA		NA	NA	NA	NA	(2)	(-)	(-)	(2)
30. THYROIDS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
31. PARATHYROIDS		(25)	(-)	(-)	(22)	(30)	(-)	(-)	(29)

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
32. PITUITARY		(27)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
33. ADRENALS		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(29)
Subcapsular cell adenoma(B)		0	-	-	0	0	-	-	1 [3]
Pheochromocytoma(B)		0	-	-	0	0	-	-	1 [3]
34. EYES WITH OPTIC NERVE		(28)	(-)	(1)	(23)	(34)	(2)	(1)	(30)
35. BONE MARROW (SMEAR)		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
36. SKIN		(28)	(8)	(9)	(23)	(34)	(8)	(4)	(30)
Squamous cell carcinoma(M)		0	0	0	0	0	1 [13]	1 [25]	0
37. THYMUS		(24)	(-)	(-)	(19)	(33)	(-)	(-)	(30)
Lymphoma(B)		0	-	-	0	1 [3]	-	-	0
38. MUSCLE FEMORAL		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
39. SPINAL CORD		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
40. SCIATIC NERVES		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
41. MAMMARY GLAND		NA	NA	NA	NA	(34)	(1)	(-)	(30)
Adenocarcinoma(M)		NA	NA	NA	NA	1	0	-	1
		NA	NA	NA	NA	[3]			[3]
42. TUMOUR/MASS		(-)	(-)	(-)	(1)	(-)	(-)	(-)	(1)
Hemangioma(B)		-	-	-	1	-	-	-	0
					[100]				
43. BONE (FEMUR) WITH JOINT		(28)	(-)	(-)	(23)	(34)	(2)	(1)	(30)
Osteoma(B)		0	-	-	0	0	2	1	3
							[100]	[100]	[10]
44. MESENTERY		(-)	(-)	(-)	(1)	(2)	(1)	(1)	(2)
Lipoma(B)		-	-	-	1	1	0	1	0
					[100]	[50]		[100]	
Endometrial stromal sarcoma -infiltrative(I)		-	-	-	0	0	0	0	1
									[50]

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

TISSUE AND OBSERVATION	Sex	MALES				FEMALES			
	Group No.	G1	G2	G3	G4	G1	G2	G3	G4
	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
45. STERNUM WITH MARROW		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
46. LYMPH NODE (OTHERS)		(5)	(3)	(5)	(2)	(3)	(9)	(3)	(6)
47. BRAIN-CEREBRUM		(28)	(-)	(-)	(23)	(34)	(-)	(-)	(30)
48. BRAIN-CEREBELLUM		(28)	(-)	(-)	(23)	(33)	(-)	(-)	(29)
49. BRAIN-MEDULLA		(28)	(-)	(-)	(23)	(33)	(-)	(-)	(30)
50. SNOUT		(2)	(5)	(5)	(2)	(1)	(4)	(1)	(-)
51. SUPERFICIAL.ING.L.NODE		(28)	(1)	(2)	(23)	(34)	(4)	(1)	(30)
52. HEMOLYMPHORETICULAR SYSTEM		(28)	(30)	(28)	(23)	(34)	(34)	(30)	(30)
Histiocytic sarcoma(M)		1 [4]	0	0	0	0	0	0	1 [3]
Malignant lymphoma(M)		1 [4]	3 [10]	3 [11]	6 [26]	9 [26]	10 [29]	6 [20]	13 [43]
Myeloid leukemia(M)		1 [4]	0	0	0	0	0	0	0

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

contd.

TABLE 21 contd.

CARCINOGENICITY STUDY WITH GLYPHOSATE TECHNICAL IN SWISS ALBINO MICE

SUMMARY OF HISTOPATHOLOGICAL (NEOPLASTIC) FINDINGS OF TERMINALLY SACRIFICED MICE

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

Ref.App.: 47-50 & 51-54

	Sex	MALES				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
53. BONE (OTHERS)		(-)	(-)	(-)	(-)	(-)	(-)	(1)	(1)
Osteoma(B)		-	-	-	-	-	-	1	1
								[100]	[100]

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

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

	MALES								FEMALES							
	0ppm		500ppm		1500ppm		5000ppm		0ppm		500ppm		1500ppm		5000ppm	
Number of Mice	51		51		51		51		51		51		51		51	
CONDITION	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
ADRENAL GLAND*																
Cortical adenoma b	3	6	0	0	0	0	3	6	0	0	0	0	0	0	0	0
Cortical carcinoma m	1	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
Histiocytic sarcoma m	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
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 m	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	6	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	1	2	1	2	1	2	0	0	0	0	1	2	0	0
LUNG*																
Adenoma b	9	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	6
Combined	14	28	12	24	16	32	15	30	7	14	6	12	4	8	5	10
MAMMARY GLAND																
Adenocarcinoma m	0	0	0	0	0	0	0	0	0	0	1	2	3	6	1	2
Adenosquamous carcinoma m	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0

* Group 1 male % based on 50 animals ** Group 1 male % based on 49 animals

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

	MALES								FEMALES							
	0ppm		500ppm		1500ppm		5000ppm		0ppm		500ppm		1500ppm		5000ppm	
Number of Mice	51		51		51		51		51		51		51		51	
CONDITION	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
MESENTERIC LYMPH NODE																
Histiocytic sarcoma m	0	0	0	0	0	0	0	0	2	4	0	0	0	0	1	2
OVARY																
Luteoma b									1	2	1	2	1	2	1	2
Haemangioma b									0	0	0	0	0	0	1	2
Sertoli cell tumour b									0	0	0	0	0	0	1	2
Cystadenoma b									0	0	0	0	0	0	2	4
Anaplastic sarcoma m									0	0	1	2	0	0	0	0
PANCREAS																
Islet cell adenocarcinoma m	0	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	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	0	0
Haemangiosarcoma m	0	0	0	0	0	0	0	0	1	2	0	0	0	0	1	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	0	0	1	2	0	0
UTERUS																
Endometrial stromal polyp b									2	4	2	4	3	6	4	8
Haemangioma b									0	0	1	2	0	0	0	0
Leiomyoma b									0	0	0	0	1	2	0	0
Squamous cell carcinoma m									1	2	0	0	0	0	0	0
Histiocytic sarcoma m									2	4	2	4	0	0	1	2
Leiomyosarcoma m									1	2	0	0	0	0	0	0

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

	MALES								FEMALES							
	0ppm		500ppm		1500ppm		5000ppm		0ppm		500ppm		1500ppm		5000ppm	
Number of Mice	51		51		51		51		51		51		51		51	
CONDITION	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
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	6
Combined	0	0	2	4	2	4	5	10	15	29	10	20	12	24	14	28
OVERALL TUMOUR INCIDENCE																
Primary benign tumours	15	29	6	12	9	18	7	14	5	10	6	12	6	12	9	18
Primary malignant tumours	14	28	20	39	17	33	20	39	23	45	15	29	17	33	18	35
Multiple benign tumours	6	12	2	4	4	8	1	2	4	8	4	8	1	2	7	14
Multiple malignant tumours	1	2	2	4	3	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