scantox

TEST REPORT

STUDY TITLE:	Mutagenicity test: Micronucleus test with Glyphosate, batch 206-JaK-25-1.
DATA REQUIREMENT:	FIFRA 84-2 OECD 474
AUTHOR:	[redacted]
REPORT DATE:	12.09.1991
PERFORMING LABORATORY:	Scantox A/S
LABORATORY NO.:	12324
CLIENT:	Cheminova Agro A/S P.O. Box 9 DK-7620 Lemvig Denmark

CONFIDENTIAL
PROPERTY OF
CHEMINOVA
DK-7620 LEMVIG
DENMARK

The testing is subjected to the conditions stated overleaf.

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These conditions shall apply to the performance of the testing and to the preparation of this present test report:

1. In respect of tests made and reports thereon, the laboratory shall as against the party ordering be liable in damages under the Danish general rules on liability in tort, subject to the limitations set out in paras. 2-6 of these present conditions.

2. The test and report have been made by the laboratory on the basis of the knowledge and facilities available to the laboratory at the time of execution of the test. The laboratory shall not be held liable where later developments may indicate that laboratory knowledge or facilities are insufficient or incorrect.

3. The laboratory shall not be held liable for damage caused by a product manufactured by the party ordering the test where

   - the tort is referable to the party ordering prior to the laboratory report having been submitted by the laboratory,

   -the specific product causing the damage has not been tested by the laboratory, save where the party ordering proves that the product causing the damage is identical with a specific product tested by the laboratory, and

   - the damage is due to a characteristic of the product, or an application of the product, that either has not been tested and described in the test report or that varies from the laboratory test report description of product characteristics and possible applications of the product.

4. The laboratory shall not be held liable for damage referable to use made of any opinion given by the laboratory where such opinion is stated to be based on estimated judgment or assessment.

5. In instances other than those set out in paras. 2-4 above, the laboratory may be held liable where damage is proved to be caused by default or negligence on the part of the laboratory. However, laboratory liability in respect of material damage shall not, unless otherwise expressly agreed, exceed DKK 1.500.000 for each individual claim. The laboratory shall not be liable for loss of production, consequential loss, loss of profit, or any other indirect loss. The laboratory shall be liable to pay damages only where the claim is made in writing within three years from the date of this present test report.

6. Where in a legal action against the laboratory, the claim set up goes beyond the limitations to laboratory liability stated in paras. 2-5 above, the client shall at the request of the laboratory take on himself the conduct of such action.

   The client shall indemnify the laboratory to the extend that the laboratory may be held liable - or may otherwise have defrayed any expenses - in excess of the limitations to laboratory liability stated in paras. 2-5 above.

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claims of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA § 10(d) (1)(A), (B) or (C).

Company: Cheminova Agro A/S

Company Agent: [redacted]

Date: _____

Signature: _____

AUTHENTICATION

The investigation described in this report (Micronucleus test with Glyphosate, batch 206-JaK-25-1) was carried out under my supervision and in accordance with the principles of Good Laboratory Practice (GLP) according to OECD codes of GLP, May 1981, Doc C (81) 30 (Final) Annex 2. The study was conducted according to the procedures herein described and the report is a complete and accurate account of the methods employed and the data obtained. The experimental work was carried out between January 24, 1991 and February 1, 1991.

12.09.1991

[redacted]

Study Director

QUALITY ASSURANCE STATEMENT

Study number: 12324

The quality of non-clinical safety studies performed at Scantox A/S is secured by an independent Quality Assurance Unit.

Short term routine studies such as are reported here, are inspected by the Quality Assurance Unit in a process based manner, i.e. critical phases in the actual study type are inspected regularly. In addition, the test system facilities are inspected approximately once a week. Documented inspection reports are communicated to the study director and to the facility management.

All reports are audited before release.

Date of audit:	13.06.1991
Date of report to study director:	13.06.1991

This report accurately describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The Quality Assurance of this study complies with OECD codes of GLP and, in general, also with the FIFRA Good Laboratory Practice Standards (40 CFR part 160) with the exception that the above mentioned inspections are conducted regularly and not on an individual basis.

12.09.1991

Quality Assurance Manager

PERSONNEL RESPONSIBLE FOR THE STUDY

Study Director	[redacted]
Quality Assurance	
Sponsor Monitor	

SUMMARY

"Glyphosate, batch 206-JaK-25-1" was tested in the Mouse Micronucleus test.

The test was performed in accordance with the guideline recommended by OECD "Micronucleus Test" No. 474, 1983, (4) as well as US CFR part 700 (F) § 798.5395 (1987).

Glyphosate, batch 206-JaK-25-1 was tested as follows: Three groups of 5 male and 5 female mice were given a single oral dose of 5.0 g/kg b.w. Bone marrow samples were taken 24, 48 and 72 hours after dosing. A negative control group was dosed orally with an equivalent volume of the vehicle and a positive control group was dosed orally with 30 mg/kg b.w. cyclophosphamide.

It is concluded that the test article induced no increase in the number of micronuclei in the polychromatic erythrocytes as compared to the control level. Thus, Glyphosate, batch 206-JaK-25-1 was found non-mutagenic in the Mouse Micronucleus test.

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1. PURPOSE

The Mouse Micronucleus test is designed to provide an evaluation of the mutagenic (clastogenic) potential of chemicals using the frequency of micronuclei in polychromatic erythrocytes from the bone marrow as a measure of chromosome damage.

2. TEST ARTICLE

Scantox A/S received on 24.01.1991 a sample of the test article, Glyphosate, batch 206-JaK-25-1 which was a white powder. According to Sponsor the Glyphosate was of 98.6% purity. The sample was labelled with Scantox Lab. No. 12324 and stored at room temperature in the dark until use.

No analyses on the test solution or solvent has been performed by Scantox Ltd.

3. TEST SYSTEM

3.1 Principle

The micronucleus test, as described by Schmid (1), is based on the observation that erythroblasts in the bone marrow expulse their nucleus in the last stage of the erythropoiesis, thereby becoming polychromatic (immature) erythrocytes (PCE). Acentric chromosome fragments (and possibly also single chromosomes detached from the spindle) will stay in the cell, thereby giving rise to micronuclei which can be observed in the microscope after staining.

A measure of the chromosome damaging effect of the test chemical is obtained by comparing the frequency of micronuclei in PCE in treated versus control animals.

3.2 Experimental conditions

The experiment was performed using NMRI SPF mice of the strain Bom:NMRI from Gl. Bomholtgård Ltd, DK-8680 Ry. At the start of the experiment the mice weighed 26 - 31 g and were approximately 10 weeks of age. They were divided randomly into 5 groups with 5 males and 5 females in each group.

	Female mice	Male mice
Control group	1 - 5	6 - 10
24-hour test group	11 - 15	16 - 20
48-hour test group	21 - 25	26 - 30
72-hour test group	31 - 35	36 - 40
Positive control group	41 - 45	46 - 50

The mice were kept in type III Macrolone cages (420 x 260 x 150 mm), 5 in each cage, males and females separately. The bedding used was softwood sawdust "Spanvall Special White" from Spanvall Ltd, DK-4490 Jerslev. The mice were fed ad libitum a complete rodent diet "Altromin 1314" from Chr. Petersen Ltd, DK-4100 Ringsted, and had free access to drinking water acidified with hydrochloric acid to pH 2.5 in order to prevent microbial growth. The temperature in the animal room was 21 +/-3°C and the relative humidity 55 +/-15%. Air change about 10 times an hour and lights on from 6 to 18 h.

4. TEST PROCEDURES

4.1 Dosing

According to Sponsor the oral route is the most likely route of exposure for humans. Thus, the oral route was chosen for the assay. All mice used in the assay were dosed orally by gavage using the dose volume of 10 ml/kg b.w. As vehicle was used distilled water with 0.5% carboxymethyl-cellulose.

4.2. Preliminary toxicity test

The Glyphosate was expected to be of very low toxicity. Since 5.0 g/kg b.w. is generally considered the highest relevant dose to include in the assay this dose was first given to 9 mice (5 ♀ and 4 ♂) and the vehicle to another three mice (2 ♂ and 1 ♀) in order to examine if this dose could be used for the main assay.

Three groups of three mice were killed 24, 48 and 72 hours after dosing and the control group 48 hours after dosing. Bone marrow samples were prepared from each mouse and the per cent PCE in 200 erythrocytes were determined (see 4.6).

Between 34 and 43 per cent PCE were found with no clear difference between the test groups or between the test groups and the control group.

4.3 Dosing in the main study

On the basis of the preliminary toxicity test the dose of 5.0 g/kg body weight was chosen for the main study.

The Glyphosate was dissolved/suspended in distilled water with 0.5% carboxymethyl-cellulose at the concentration of 0.5 g/ml. The 30 test mice were each dosed orally by gavage with 10 ml/kg body weight of the test solution equal to 5.0 g Glyphosate per kg body weight.

The control mice were dosed orally with 10 ml/kg b.w. 0.5% carboxymethyl-cellulose in distilled water, and the positive control compound, cyclophosphamide, was given orally in a dose of 30 mg/kg b.w.

4.4 Bone marrow samples

The three test groups were killed by dislocation of the neck 24, 48 and 72 hours after dosing, respectively. Bone marrow smears were made as described below.

The control group was killed 48 hours after dosing, and the positive control group was killed 24 hours after dosing.

4.5 Preparation of smears

Immediately after a mouse was killed, the right femoral bone was dissected free. The proximal end of the femur was cut. A 1 ml syringe with needle containing 1 ml foetal calf serum was gently inserted into the bone marrow canal and the bone marrow was flushed out into 1.5 ml foetal calf serum. After whirl mixing, the suspension was centrifuged for 10 minutes at 1000 rpm. Smears were made after removal of the supernatant. The specimens were fixed in methanol and stained with May-Grünwald/Giemsa, as described in (1).

4.6 Microscopic analysis

Prior to microscopic analysis, all slides were coded in order to perform a blind counting.

The following counts were made:

Per cent polychromatic erythrocytes (PCE) in 200 erythrocytes, (% PCE).
Number of micronuclei (MN) observed in 2000 polychromatic erythrocytes, (MN/PCE).
Number of micronuclei (MN) in normochromatic erythrocytes (NCE) observed during the counting of 2000 PCE, (MN/NCE).

4.7 Statistical analysis

The control and test group data were analysed statistically using one-way Analysis of Variance performed on the values transformed to normal scores according to Blom's method (3).

5. RESULTS

The individual counts made at the microscopic analysis are presented in table 1.

The ratio of PCE to NCE was in the range 37.7 to 42.2 per cent PCE which is within our normal range. No statistically significant differences between any control or test groups were found, thus indicating, that no significant bone marrow toxicity occurred.

In table 3 is shown the frequency of micronuclei in PCE. The frequency of micronuclei in the positive and negative control groups were in accordance with our historical data. The frequency of micronuclei in PCE was similar in the control group and the test groups, and the statistical analysis revealed no significant increase in micronuclei in any of the test groups.

6. CONCLUSION

Glyphosate, batch 206-JaK-25-1 was found non-mutagenic in the Mouse Micronucleus test.

7. REFERENCES

(1) W. Schmid, The micronucleus test, Mut. Res. 31, pp. 9-15 (1975).

(2) U. Kliesch, et al., Micronucleus test and bone-marrow chromosome analysis - a comparison of 2 methods in vivo for evaluating chemically induced chromosomal alterations, Mut. Res. 80, pp. 321-332 (1981).

(3) G. Blom, Statistical Estimates and Transformed Beta Variables, New York: John Wiley and Sons, Inc. (1958).

(4) OECD Guidelines for Testing of Chemicals, (No. 474), OECD Publication Office, 2 rue André-Pascal, F-75775 Paris Cedex 16, France, (1983).

TABLE 1. INDIVIDUAL COUNTS.

NEGATIVE CONTROL GROUP

SEX	NO	N	MN/NCE	% PCE	MN/PCE
FEMALE	1	2000	0	39	2
FEMALE	2	2000	0	41	2
FEMALE	3	2000	0	41	2
FEMALE	4	2000	0	40	3
FEMALE	5	2000	1	38	3
MALE	6	2000	2	29	4
MALE	7	2000	1	34	2
MALE	8	2000	2	36	4
MALE	9	2000	1	40	4
MALE	10	2000	1	42	1

POSITIVE CONTROL GROUP

SEX	NO	N	MN/NCE	% PCE	MN/PCE
FEMALE	41	2000	3	38	32
FEMALE	42	2000	2	37	54
FEMALE	43	2000	0	46	49
FEMALE	44	2000	1	44	58
FEMALE	45	2000	0	51	46
MALE	46	2000	1	39	54
MALE	47	2000	2	43	48
MALE	48	2000	0	37	52
MALE	49	2000	2	44	41
MALE	50	2000	0	43	48

NCE : NORMOCHROMATIC ERYTHROCYTES
PCE : POLYCHROMATIC ERYTHROCYTES
MN/NCE : NUMBER OF MICRONUCLEI OBSERVED IN NCE DURING THE SCORING OF 2000 PCE
% PCE : PCE IN PERCENT OF TOTAL ERYTHROCYTES
MN/PCE : NUMBER OF MICRONUCLEI OBSERVED IN 2000 PCE

24 HOUR TEST GROUP

SEX	NO	N	MN/NCE	% PCE	MN/PCE
FEMALE	11	2000	0	37	1
FEMALE	12	2000	1	45	4
FEMALE	13	2000	1	40	4
FEMALE	14	2000	1	41	2
FEMALE	15	2000	0	37	4
MALE	16	2000	1	35	3
MALE	17	2000	2	37	5
MALE	18	2000	1	36	2
MALE	19	2000	1	31	4
MALE	20	2000	2	29	3

48 HOUR TEST GROUP

SEX	NO	N	MN/NCE	% PCE	MN/PCE
FEMALE	21	2000	0	37	2
FEMALE	22	2000	0	41	2
FEMALE	23	2000	0	42	4
FEMALE	24	2000	0	41	6
FEMALE	25	2000	0	41	3
MALE	26	2000	1	37	3
MALE	27	2000	0	34	2
MALE	28	2000	0	40	2
MALE	29	2000	0	38	3
MALE	30	2000	0	36	1

72 HOUR TEST GROUP

SEX	NO	N	MN/NCE	% PCE	MN/PCE
FEMALE	31	2000	0	42	3
FEMALE	32	2000	1	39	2
FEMALE	33	2000	1	32	2
FEMALE	34	2000	1	38	0
FEMALE	35	2000	0	38	1
MALE	36	2000	1	36	1
MALE	37	2000	1	35	1
MALE	38	2000	0	34	4
MALE	39	2000	1	42	2
MALE	40	2000	0	40	1

TABLE 2. PCE IN PERCENT OF TOTAL ERYTRODYTES, BAR CHART OF MEANS

GROUP		N	% PCE MEAN
NEG. CONTROL	**********	10	39.0
TEST 24 HOUR	**********	10	38.0
TEST 48 HOUR	**********	10	38.7
TEST 72 HOUR	**********	10	37.7
POS. CONTROL	**********	10	42.2

2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42

NO STATISTICALLY SIGNIFICANT DIFFERENCE WAS FOUND BETWEEN THE TEST GROUPS AND THE NEGATIVE CONTROL GROUP.

TABLE 3. MICRONUCLEI PER 2000 PCE, BAR CHART OF MEANS

GROUP		N	MN/PCE MEAN
NEG. CONTROL	*****	10	2.7
TEST 24 HOUR	******	10	3.2
TEST 48 HOUR	******	10	2.8
TEST 72 HOUR	***	10	1.7
POS. CONTROL	**********	10	48.2

2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48

NO STATISTICALLY SIGNIFICANT INCREASE WAS FOUND IN ANY OF THE TEST GROUPS AS COMPARED TO THE NEGATIVE CONTROL GROUP.
THE LEVEL OF MICRONUCLEI IN THE 72-HOUR TEST GROUP WAS SIGNIFICANTLY LOWER THAN THE CONTROL GROUP AND THE TWO OTHER TEST GROUPS.

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Authorization no. 145

Lab. No. 12324

MICRONUCLEUS TEST

Protocol

Test article: Glyphosate

Sponsor: Cheminova Agro A/S
P.O. Box 9
DK-7620 Lemvig
Denmark

Study performance: Scantox A/S
40, Tornbjergvej, Ejby
DK-4623 Lille Skensved
Denmark

Date: 11.01.1991

Management of study:

Study director: [redacted]

Head, QAU:

Sponsor contact:

MICRONUCLEUS TEST

Test article: Glyphosate

Sponsor: Cheminova Agro A/S

Protocol approval

Scantox A/S:

Issued by: [redacted] Date: 18.01.1991
(Head of Genetic Toxicology Unit)

Sponsor:

This protocol is accepted without revision and my signature authorises the study to proceed as described in this document.

Approved by: [redacted] Date 22/1-1991

Details concerning the experiment are described in the following protocol:

MICRONUCLEUS TEST

Protocol

1. INTRODUCTION

The micronucleus test is a short term in vivo mutagenicity test for the evaluation of possible mutagenic (clastogenic) effects of chemicals.

This outline protocol describes the test performed with mice. The test is performed in accordance with the guideline recommended by OECD "Micronucleus Test", No. 474, 1983, (4) as well as US CFR part 700 (F) § 798.5395 (1987).

2. PRINCIPLE

The micronucleus test, as described by Schmid (1), is based on the observation that erythroblasts in the bone marrow expulse their nucleus in the last stage of the erythropoiesis, thereby becoming polychromatic (immature) erythrocytes (PCE). Acentric chromosome fragments (and possibly also single chromosomes detached from the spindle) will stay in the cell, thereby giving rise to micronuclei which can be observed in the microscope after staining.

A measure of the chromosome damaging effect of the test chemical is obtained by comparing the frequency of micronuclei in PCE in treated versus control animals.

3. EXPERIMENTAL ANIMALS

SPF mice of the strain Bom:NMRI are obtained from Gl. Bomholtgaard A/S, DK-8680 Ry. By the start of the experiment the animals are 7 - 10 weeks old, weighing 25 to 40 g.

3.1 Animal groups

A standard test is carried out using five groups of 5 males and 5 females each. The animals are randomly assigned to the groups.

3.2. Animal housing

The mice are kept in Macrolon type III cages, 5 in each cage, males and females separately. As bedding is used softwood sawdust "Spanvall Special White" from Spanwall Ltd, DK-4535 Vallekilde.

The temperature in the animal room is kept at 21 +/- 3°C, the relative humidity is 55 +/- 15% and the air change is about 6 times an hour. Light period from 6 to 18 h.

3.3. Food and drinking water

The mice are fed ad libitum "Altromin 1314" mouse/rat food from Chr. Petersen Ltd, DK-4100 Ringsted. The water is acidified with hydrochloric acid to pH 2.5 and given ad libitum.

3.4. Pre-period

: mice are allowed to aclimate for 5 days after receipt before they are used in assays.

4. TEST METHOD

4.1 Test article

According to Sponsor the present test article, Glyphosate, is soluble in water up to approx. 2%. If the MTD (see 4.3) can be reached using a volume of less than 20 ml/kg b.w., isotonic saline is used as vehicle. If higher concentrations are needed 0.5% carboxymethylcellulose in isotonic saline will be used as vehicle.

4.2. Dosing

According to Sponsor the oral route is the most likely route of exposure for humans. A single high dose is the most widely used procedure. The choice of a single dose has recently been found appropriate on the basis of an extensive comparison of different dosing regimes (ref. 5).

Thus, the test article will be administered as a single oral dose administered by gavage.

4.3. Determination of the Maximum Tolerable Dose (MTD)

The MTD is detemined in a preliminary test. The MTD is defined as the highest dose which can be administered

1. Without completely disturbing the erythropoiesis
2. Without excessive deaths among the animals in the test period

Disturbancy of the erythropoiesis results in a reduction in the ratio of polychromatic erythrocytes (PCE) to normochromatic erythrocytes (NCE). The ratio PCE/NCE should not come below approx. 1:10. MTD should be less than LD_{10}, i.e. maximally 10% of the test animals should die.

The MTD is determined in two steps. Firstly, groups of 1 to 3 mice are dosed with an anticipated lethal dose or with 5.0 mg/kg b.w. which is usually the highest dose that is relevant to include. If deaths occur within 72 hours a lower dose is given to another group of mice which are again observed for up to 72 h. This procedure is followed until a dose is established which allows all three mice to survive for 72 hours and which is at the same time close to a lethal dose. Usually this dose is about 25 - 75 per cent of the lethal dose and usually the mice exhibit clear signs of intoxication.

Secondly, 9 mice are dosed with the selected near-lethal dose and three mice are given an equal volume of the solvent. Three test mice are killed 24, 48 and 72 hours after dosing while the control mice are killed 48 hours after dosing. Bone marrow smears are prepared from all the mice and scored for PCE/NCE ratio in order to determine possible effects on the erythropoiesis.

If one or more of the nine test mice dies or if the erythropoiesis is profoundly disturbed the selected dose may be further adjusted - if possible on the basis of the existing data.

4.4. Performance of the test

mice are divided randomly into 5 groups of 5 males and 5 females and dosed as follows:

Negative control group:	vehicle, same volume as for the test groups.
Positive control group:	30 mg/kg B.W. cyclophosphamide.
Test groups:	All animals are given the test compound in the pre-determined MTD.

Bone marrow sampling times

The negative control group is killed 48 hours after dosing.

The positive control group is killed 24 hours after dosing.

The three test groups are killed 24, 48 and 72 hours after dosing, respectively.

Bone marrow preparation

Immediately after a mouse has been killed by dislocation of the neck, the right femur is dissected free and using a 1 ml syringe with needle, the bone marrow is flushed out into 2.5 ml of foetal calf serum. After whirl mixing, the suspension is centrifuged for 10 minutes at 1000 rpm. Smears are made after removal of the supernatant. The specimens are fixed in methanol and stained with May-Grünwald/Giemsa (1).

4.5. Microscopic analysis

Prior to the microscopic analysis all slides are furnished with code numbers, so that the counting is blind.

For each animal the following counts are made:

Number of polychromatic erythrocytes (PCE) per 200 erythrocytes.
Number of micronuclei (MN) in 2000 polychromatic erythrocytes.
Number of micronuclei (MN) in normochromatic erythrocytes observed during scoring of the 2000 PCE.

5. EVALUATION OF RESULTS

The number of micronulei in the test groups are compared to the number found in the control (vehicle) group. Statistical analysis is performed using a one way Analysis of Variances based on rank values (Blom's method (3)), and the result is interpretated.

6. GOOD LABORATORY PRACTICE (GLP)

This study will be conducted in accordance with the principles of Good Laboratory Practice (GLP) according to OECD codes of GLP, May 1981, Doc C(81)30 (Final) Annex 2 and Scantox Standard Operation Procedures.

The Quality Assurance Unit (QAU) will carry out periodic and independent routine inspections on critical phases and repeated processes in this type of study, but necessarily on activities of this study. The report on the study will be audited.

7. REPORT

report is made in English language covering description of the test procedures, tables with the relevant observations, statistical analysis, evaluation and interpretation of results.

8. ARCHIVES

All original data, including copies of correspondance, all reports issued and a sample of the test article will be stored at ambient temperature in the GLP Archives of Scantox Biological Laboratory Ltd. for a period of 5 years. Samples that are unstable may be disposed of before that time or stored under specified conditions after consultation with the Sponsor. At the end of the period Sponsor will be consulted regarding requirements for disposal or further storage.

10. REFERENCES

(1) W. Schmid, The micronucleus test, Mut. Res. 31, pp. 9-15 (1975)

(2) U. Kliesch, et al., Micronucleus test and bone marrow chromosome analysis - a comparison of 2 methods in vivo for evaluating chemically induced chromosomal alterations, Mut. Res. 80, pp. 321-332 (1981)

(3) G. Blom, Statistical Estimates and Transformed Beta Variables, New York: John Wiley and Sons, Inc. (1958)

(4) OECD Guidelines for Testing of Chemicals, (1983), OECD Publication office, 2 rue André-Pascal, F-75775 Paris Cedex 16, France.

(5) J. Ashby, et al., Overview of the study in relation to protocol design for the rodent bone-marrow micronucleus assay, Mut. Res. 234, pp. 223-248 (1990).

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MICRONUCLEUS TEST

Test article: Glyphosate

Sponsor: Cheminova Agro A/S

Ammendment No. 1

to Protocol

1. Regarding the test article "Glyphosate".
   The sample was labelled:
   Glyphosate technical
   Batch 206-JaK-25-1
   Purity: 98.6%

   The same identification appeared in the letter following the test article.

2. The test article is stored at Scantox at room temperature protected from light until use.

3. Page 4, section 4.1: "accroding" should be read "according".

Approved by:

[redacted]

St[redacted] Date 08.02.1991

[redacted]

Sponsor Date 4/2-91

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Authorization no. 145

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MICRONUCLEUS TEST

Test article: Glyphosate

Sponsor: Cheminova Agro A/S

Ammendment No. 2

to Protocol

6. Good Laboratory Practice (GLP).

The sentence: "The Quality Assurance Unit (QAU) will carry out periodic and independent routine inspections on critical phases and repeated processes in this type of study, but necessarily on activities of this study. The report on the study will be audited" is incorrect.

The correct sentence is: "The Quality Assurance Unit (QAU) will carry out periodic and independent routine inspections on critical phases and processes in this type of study, but not necessarily on activities of this study. The report on the study will be audited"

Approved by:

[redacted]

06.09.1991
Date

[redacted]

Sponsor

11/9-91
Date