

Skin Sensitization
in Guinea Pigs (*Cavia porcellus*) of
NES FUNGICIDA, ACARICIDA E
INSECTICIDA SELECTIVO - LIQUIDO

Buehler Test

Guideline OECD N° 406

Test number:

BIBR 6 – 30395

Ref. 6-2151/M

Date:

May 23th, 2010

Sponsor:

AJIM S.R.L Y JORGE NATALIO FELIPE PEISAJOVICH
GALANTE - AGROSERVICIOS NES - MEXICO

Av. Borrini 225

Resistencia, CP (3500), Chaco

Argentina

Study conducted by

MICROQUIM S.A.

Department of Biological Studies

- Biomicro Division -

1MIC5100101300a



Study N° BIBR 6 – 30395

Page 1 of 20

MICROQUIM S.A.
Department of
Biological Studies

Index

| | Pages |
|---|-------|
| Title page | 1 |
| Index | 2 |
| A. Statement of Compliance with Good Laboratory Practices | 3 |
| B. Preface | 4 |
| C. Summary | 8 |
| D. Purpose | 9 |
| E. Test System and Materials | 9 |
| F. Test Procedure | 11 |
| G. Results | 14 |
| H. Conclusion | 14 |
| I. References | 14 |

Tables

| | |
|--|----|
| 1. Body Weight of the Animals during the Test | 15 |
| 2. Evaluation of the Induction and Challenge Test | 16 |
| 3. Evaluation of the Induction and Challenge Test of Control | 17 |
| 4. Challenge Test for Positive Control | 18 |

Annex

| | |
|--|----|
| I –Reference to the Toxicological Classification | 19 |
| II- GLP certificate | 20 |

Quality Assurance Unit Statement

A) STATEMENT OF COMPLIANCE WITH GOOD LABORATORY PRACTICES

TITLE: SKIN SENSITIZATION IN GUINEA PIGS (*Cavia Porcellus*) OF NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO BUEHLER TEST

TEST SUBSTANCE: NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

STUDY NUMBER: BIBR 6 – 30395

This study was conducted according to the OECD series on principles of Good Laboratory Practices and compliance monitoring, N°1, ENV/MC/CHEM (98) 17 OECD and pursuant to the written study plan, authorized by the Sponsor and the Technical Management of MICROQUIM. S.A. following the Standard Operating Procedures (SOP) stated in the Procedures of MICROQUIM S. A.

This report is a true and accurate record of the results obtained, and there were no known circumstances that could have affected the quality and integrity of the data. This certificate can only be reproduced with the approval of the laboratory.

The results obtained, as well as any storage medium for electronically recorded data, all documentation, study plan and final report are retained in the corresponding archives at MICROQUIM S.A.



Ximena Alvarado
Biology Technician
Study Director

Date: 08.07.10

Study N° BIBR 6 – 30395

Page 3 of 20

MICROQUIM S.A.
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B) PREFACE

B.1) GENERAL

Title: Skin Sensitization in Guinea pigs (*Cavia porcellus*) of NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO. Buehler Test.

Sponsor: AJIM S.R.L Y JORGE NATALIO FELIPE PEISAJOVICH GALANTE - AGROSERVICIOS NES – MEXICO, Av. Borrini 225, Resistencia, CP (3500), Chaco, Argentina

Test number: BIBR 6 – 30395

Test substance: NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

Test system: Albino Guinea Pig (*Cavia porcellus*).

Testing Institution: MICROQUIM S.A., Av. Triunvirato 3447, (1427) Buenos Aires, Argentina.

Test facility: BIOMICRO S.A., Costa Rica 4776, Malvinas Argentinas.

Address of the Study Director: BIOMICRO S.A., Costa Rica 4776, Malvinas Argentinas.

B.2) STAFF

Technical Director:

Dr. Alejandro Lucini
Chemistry Degree

Study Director:

Ximena Alvarado
Biology Technician

Animal Health
Responsible

Dr. Juan Manuel Catoyra
Veterinarian

Test Performance:

Dr. Juan Manuel Catoyra
Veterinarian

Final Report
Confection:

Gisele Keim
Romina Nostrala

Archive Responsible:

Silvina López

Study N° BIBR 6 – 30395

Page 4 of 20

MICROQUIM S.A.
Department of
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B.3) SCHEDULE

Date of entrance of the sample: 11.10.09

Start of the experimental phase (beginning of the acclimatization) : 03.19.10

Date of the First dose: 03.29.10

Observation period: 48 hours after the challenge

Date of the end of the experimental phase: 05.06.10

B.4) TEST GUIDELINE

This test was performed in agreement with the following method: Guideline for Chemical Tests N° 406: "Skin Sensitization Buehler Test" by the Organization for Economic Cooperation and Development (OECD), in Guinea Pigs. Adopted on 17.07.92. y SOP : "Sensitization Index" (POE 114-BM/05).

B.5 GOOD LABORATORY PRACTICES

This study will assure the performance of the standard operation procedures. The Quality Assurance Unit will periodically inspect test procedures and inspection dates will be included in the report.

This study will be performed according to the OECD principles of good laboratory practices, 1998. Established by SENASA Resolution No. 230/2000.

B.6) CERTIFICATIONS, REGISTRATION, ACCREDITATIONS AND REGISTERS

- Certification in accordance with principles of Good Laboratory Practices (1998), issued by OAA.
- **GLP** Certification in accordance with: EPA 40 CFR PART 160 "Principles of Good Laboratory Practice and Compliance Monitoring" ENV/MC/CHEM (98) 17 OECD. SENASA 230/2000 Resolution. Commission Directive 2004/10/EC of de European Parliament. Issued by **Bureau Veritas Certification**.
- **ISO 9001:2000** Certification for the Quality Management System, issued by **Bureau Veritas Certification** with accreditation of:

OAA (Argentina)

ANAB (U.S.A.)

Study N° BIBR 6 – 30395

Page 5 of 20

MICROQUIM S.A.
Department of
Biological Studies

UKAS (United Kingdom)

INMETRO (Brazil)

- **COFILAB** (Laboratories Control Committee)
- **CALIBA** (Argentine Chamber of Independent Laboratories of Bromatological, Environmental and Other Related Analysis)
- **SENASA** Accreditation (National Health Service and agro food quality) LR 0060 as laboratory of agrochemicals analysis to perform physicochemical, toxicological studies and determination of pesticide residues in vegetal matrixes.
- Animal facility subscribed at **SENASA** (National Health Service and agro food quality) according to regulations of Resolution 617/02 for the production of toxicological and ecotoxicological data.
- **AACyTAL** (Argentinian Asociation of Science and Technology of Laboratory animals) No. 09-0076
- **Colombian Agricultural Institute (ICA)**, part of the Treaty of the Andean Pact, Resolution No. 03431 as a Quality Control Laboratory of chemical pesticides for agricultural use.
- **EPA** (Environmental Protection Agency) assigned laboratory code number 955079.
- **Environment Aptitude certificate** issued by the Government of the Autonomous City of Buenos Aires Res. 077 A.A. 123/2000 Law.
- **Provincial Agency for Sustainable** Development Accreditation as Laboratory of Industrial Analysis according to the provisions of Resolution No. 504/01. Registration No. 31.
- **SEDRONAR** (Secretaryship of Programs to prevent the drug addiction and fight against the drug trafficking) N° RN 858 PQ

B.7) AMENDMENT PROCEDURE

This final report can be amended by the Study Director and the Sponsor by the Sponsor in the event that his request. The Study Director will sign detailed descriptions of all amendments. The amendment will be effective at the time of Study Director's signature.

B.8) ARCHIVES

The laboratory will preserve the following data at least for 6 years: study plan, report and original data, in the general archive situated at Triunvirato 3447, (1427) Buenos Aires, Argentina. During that period no data will be discarded without the Sponsor's consent.

B.9) COMMITMENT OF CONFIDENTIALITY

The signatories of this final report are committed to safeguarding the confidentiality of all information involved in this study, both delivered by the Sponsor as that generated by this laboratory.

B.10) SAFETY PRECAUTIONS

Gloves, cap, mask with filters and protective goggles (if required) will be used to ensure proper safety and personal health and avoid inhalation and skin contact with the substance of test. In case of contact with eyes, wash them thoroughly with water and will seek medical treatment. In case of contact with skin, wash with soap and water with subsequent medical help.

C) SUMMARY

Test system: Skin Sensitization in Guinea Pigs (*Cavia porcellus*) of NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO Buehler Test.

Test substance: NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

The purpose of this test is to assess the skin sensitization potential of NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO according to Buehler method

Dose levels Pre-Test:

0.5 ml of 100% NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO, 0.5 ml of 75% v/w NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO suspensión, 0.5 ml of 50% v/w NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO suspensión.

Dose induction stage:

0.5 ml of 100% NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

Dose challenge stage:

0.5 ml of 100% NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

Positive control Benzocaine (Cas N° 94-09-7) 100% w/v.

Animals behaved normally and their external appearance was not influenced by the treatment.

Conclusion

Under the test conditions the test substance **NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO** in albino Guinea pigs **did not present sensitization reactions**. At 24 hrs, 0% of the animals (0/20) presented skin reaction and at 48 hours 0% of the animals (0/20) presented skin reaction.

D) PURPOSE

The aim of the sensitization study was the assessment of the allergenic potential of NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO, when it is administered to the skin of Guinea pigs.

This test provided a rational basis for the hazard evaluation of the sensitization potential of NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO in human beings.

E) TEST SYSTEM AND MATERIALS

E.1) TEST ANIMALS

Test system: Albino Guinea Pig

Source: Distribuidora Izaguirre. Antonia Ribero 2352 - 1708 Morón – Pcia. de Buenos Aires. Argentina.

Animal Lot Number: Cb 08/10

Number and sex of the test animals: 33 animals, 18 females y 15 males.

Age and weight at the start of the test: Young adult animals.

Identification: By cage number and labels in the ears.

Selection: Animals were chosen at random at the time of the assay.

Acclimatization: 10 days under the test conditions after the clinical exam.

Distribution: Animals were assigned to groups as follows:

| Number of group | Group | Number of animals per group |
|-----------------|---------------|-----------------------------|
| 1 | Pre-test | 3 |
| 2 | Control group | 10 |
| 3 | Test group | 20 |

E.2) HOUSING AND FEEDING CONDITIONS

Animals were housed under standard laboratory conditions. The animals' test room was provided with conditioned air by HEPA filters, carrying out 10 to 15 air changes per

hour. The temperature of the animals' room was $20 \pm 3^{\circ}\text{C}$ and the relative humidity 30-70 per cent, although the upper relative humidity range may have exceeded during the cleaning of the room.

Animals were provided with photoperiods of 12 hours light- 12 hours darkness and placed into individual cages made of steel with litter of autoclaved wood shavings. Lot Number: 41 al 50/26.10.09, 01 al 13/ 25.01.10.

The following diet was provided *ad libitum*: Maintenance food supplied by Distribuidora Horacio Izaguirre. Lot Number: 10013-13-09, 10013-05-10, 10003-45-09. Well water was used *ad libitum*.

The diet was enriched daily with fresh vegetables.

E.3) IDENTIFICATION AND CHARACTERISTICS OF THE TEST SUBSTANCE

(According to information provided by the Sponsor)

- Label: NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO
- Valuation of the active principle: AZUFRE: 13.68 % w/w; 14.91 % w/v, Batch N°: 025/2009
- Product description: Yellow-greens liquit
- Storage conditions: Room temperature.
- Container: Plastic bottle

The sampling was made by the sponsor

E.4) PREPARATION OF THE TEST SUBSTANCE

- Physical state of the test substance: Liquid.
- Solvent used: Induction: None.
Challenge: None.
- Preparation: A solution was performed inside a glass container, with an exact quantity of the weighed test substance before each dosage.

E.5) DOSE LEVELS

Dose levels were selected through a Pre-Test.

Study N° BIBR 6 – 30395

Page 10 of 20

MICROQUIM S.A.
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E.6) EXPOSURE/OBSERVATION PERIOD

During the induction period, skin observation is carried out for irritation effects. After challenge exposure, skin reaction is recorded 24 and 48 hrs after the patch removal, i.e. 30 and 54 hrs after beginning of application.

F) TEST PROCEDURE

F.1) DOSAGE

F.1.1) PREPARATION OF THE ANIMALS

Animals were shaved in the shoulder region (approximately 5 cm × 4 cm) avoiding skin abrasion.

F.1.2) PRE-TEST

It was performed using 3 animals with the following doses: 100% , 75% w/v y 50% w/v.

In the dose 100% it was saturated a filter paper 2.5 x 2.5 cm, with approximately 0.5 ml of the sample homogenized with the vehicle, the patch was held firmly for 6 hours with a hypoallergenic adhesive bandage. In the dose 75% w/v and 50% w/v It was saturated a filter paper 2.5 x 2.5 cm, with approximately 0.5 ml of suspension, The patch was held firmly for 6 hours with a hypoallergenic adhesive bandage.

The selected concentrations of the test substance used for each induction exposure were well tolerated systemically and were the highest to cause mild to moderate skin irritation.

Topical challenge concentration:

The test substance concentration used for the topical challenge was the highest technically possible as no skin irritation was observed.

MAGNUSSON-KLIGMAN SCALE

- 0 = Without visible change
- 1 = Slight erythema
- 2 = Moderate erythema
- 3 = Intensive erythema and secretions

Study N° BIBR 6 – 30395

Page 11 of 20

MICROQUIM S.A.
Department of
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Independently of the result, any difference in the reactions in comparison with the control group will be considered as a positive result for that animal.

The incidence index is equal to the number of animals with positive score for erythema.

PRE-TEST- Determination of concentrations for induction tests and challenge of the test product NES FUNGICIDA, ACARÍCIDA E INSECTICIDA SELECTIVO - LIQUIDO

| PRE-TEST | ANIMAL N° | DOSES | READING | |
|----------|-----------|----------|----------|----------|
| | | | 24 HOURS | 48 HOURS |
| | | | ERYTHEMA | ERYTHEMA |
| Topical | 1 | 100 % | 0 | 0 |
| | 2 | 75 % w/v | 0 | 0 |
| | 3 | 50 % w/v | 0 | 0 |

Determined dose levels for the induction test: topical: 100%

Determined dose levels for the challenge test: topical: 100%

F.1.3) HISTORICAL POSITIVE CONTROL VALIDITY STUDY

The procedures used in this study were validated using Benzocaine (Cas N° 94-09-7). The study has been completed recently. This test was conducted using guinea pigs of the same strain as the one in the study, following induction and challenge procedures similar to those described in it.

F.1.4) INDUCTION

The induction application was made over a three week period using the following procedures:

Topical applications:

Day 0

- Treated group: A filter paper (2 x 4 cm) loaded with approximately 0.5 ml of suspension sample was applied on the shaved area of the left flank and held in contact with the skin for 6 hours, by a hypoallergenic adhesive bandage.

- Control Group: No applications were performed.

Day 7

- Treated group: A filter paper (2 x 4 cm) loaded with approximately 0.5 ml of suspension sample was applied on the shaved area of the left flank and held in contact with the skin for 6 hours, by an hypoallergenic adhesive bandage.
- Control Group: No applications were performed.

Day 14

- Treated group: A filter paper (2 x 4 cm) loaded with approximately 0.5 ml of suspension sample was applied on the shaved area of the left flank and held in contact with the skin for 6 hours, by an hypoallergenic adhesive bandage.
- Control Group: No applications were performed.

Challenge

Day 28

- Treated group and Control Group: The filter paper loaded with approximately 0.5 ml of suspension sample was applied on the right flank. Patches were held in contact with the skin for 6 hours, by a hypoallergenic adhesive bandage.

F.2) CLINICAL EXAMINATION

Mortality/Viability: Animals were observed daily, from the start of the pre-test to the finalization of the test. Evidence of systemic intoxication was observed but there were no deaths.

F.3) ANATOMY -PATHOLOGY

Deaths were not recorded during the observation period. Therefore the animals necropsy was not necessary.

G) RESULTS

Dermal reactions were summarized in a tabular form, showing for each animal the sensitization score observed at different reading times. The results were compared with the findings obtained during challenge application in control animals.

The body weight of the animals wasn't within the physiological variability range of the test system, so it was observed an increase in the body weight curve. (TABLE 1).

According to the Magnusson-Kligman scale, skin reaction grades were recorded (TABLES 2 and 3).

Positive Control with Benzocaina (TABLE 4).

H) CONCLUSION

Under the test conditions the test substance **NES FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO** in albino Guinea pigs **did not present sensitization reactions**. At 24 hrs, 0% of the animals (0/20) presented skin reaction and at 48 hours 0% of the animals (0/20) presented skin reaction.

I) REFERENCES

Good Laboratory Practice – ENV/MC/CHEM (98) 17 OECD.

Guideline for Chemical Tests N° 406: “Skin Sensitization Buehler Test” by the Organization for Economic Cooperation and Development (OECD), in Guinea Pigs. Adopted on 17.07.92. y SOP : “Sensitization Index” (POE 114-BM/05).

The data contained in this report as well as the conclusion are the accurate reproduction of the raw data registered on the logbook **4.Cob** page 002885 to 002889.

MICROQUIM S.A.
XIMENA ALVARADO
Téc. Bióloga
Director de Estudio
Study Director

MICROQUIM S.A.
Dr. ALEJANDRO D. LUCINI
Director Técnico
Technical Director
M.N.7174/M.P. 4765

Study N° BIBR 6 – 30395

Page 14 of 20

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TABLE 1:
BODY WEIGHT OF THE ANIMALS DURING THE TEST OF : NES FUNGICIDA,
ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

| Number | Sex | Body weight during the test (gr) | |
|------------------|--------|----------------------------------|------------------------------------|
| | | At the start of Acclimatization | At the conclusion of the Challenge |
| Pre-test animals | | | |
| 1 | Female | 325 | 328 |
| 2 | Female | 321 | 324 |
| 3 | Female | 325 | 327 |
| Test animals | | | |
| 4 | Female | 327 | 429 |
| 5 | Female | 324 | 427 |
| 6 | Female | 323 | 425 |
| 7 | Female | 325 | 428 |
| 8 | Female | 321 | 425 |
| 9 | Female | 324 | 427 |
| 10 | Female | 323 | 425 |
| 11 | Female | 325 | 429 |
| 12 | Female | 328 | 431 |
| 13 | Female | 330 | 433 |
| 14 | Male | 345 | 457 |
| 15 | Male | 339 | 452 |
| 16 | Male | 341 | 453 |
| 17 | Male | 340 | 452 |
| 18 | Male | 342 | 455 |
| 19 | Male | 340 | 453 |
| 20 | Male | 347 | 459 |

| | | | |
|-----------------|--------|-----|-----|
| 21 | Male | 342 | 455 |
| 22 | Male | 340 | 453 |
| 23 | Male | 338 | 450 |
| Control animals | | | |
| 24 | Female | 323 | 427 |
| 25 | Female | 327 | 429 |
| 26 | Female | 322 | 425 |
| 27 | Female | 328 | 431 |
| 28 | Female | 325 | 428 |
| 29 | Male | 345 | 457 |
| 30 | Male | 343 | 455 |
| 31 | Male | 340 | 452 |
| 32 | Male | 338 | 450 |
| 33 | Male | 339 | 451 |

TABLE 2:
EVALUATION OF THE INDUCTION AND CHALLENGE TEST OF NES
FUNGICIDA, ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO

| Animal N° | Challenge | |
|-----------|-------------|----------|
| | Right flank | |
| | 24 hours | 48 hours |
| | Erythema | Erythema |
| 4 | 0 | 0 |
| 5 | 0 | 0 |
| 6 | 0 | 0 |
| 7 | 0 | 0 |
| 8 | 0 | 0 |
| 9 | 0 | 0 |
| 10 | 0 | 0 |
| 11 | 0 | 0 |
| 12 | 0 | 0 |
| 13 | 0 | 0 |

| | | |
|----------------------|----|----|
| 14 | 0 | 0 |
| 15 | 0 | 0 |
| 16 | 0 | 0 |
| 17 | 0 | 0 |
| 18 | 0 | 0 |
| 19 | 0 | 0 |
| 20 | 0 | 0 |
| 21 | 0 | 0 |
| 22 | 0 | 0 |
| 23 | 0 | 0 |
| Affected animals (%) | 0% | 0% |

TABLE 3:
EVALUATION OF THE INDUCTION AND CHALLENGE TEST OF CONTROL

| Animal N° | Challenge | |
|-----------|-------------|----------|
| | Right flank | |
| | 24 hours | 48 hours |
| | Erythema | Erythema |
| 24 | 0 | 0 |
| 25 | 0 | 0 |
| 26 | 0 | 0 |
| 27 | 0 | 0 |
| 28 | 0 | 0 |
| 29 | 0 | 0 |
| 30 | 0 | 0 |
| 31 | 0 | 0 |
| 32 | 0 | 0 |
| 33 | 0 | 0 |

TABLE 4:

CHALLENGE TEST FOR POSITIVE CONTROL: Benzocaine (Cas N° 94-09-7),

Semestral Control Period: January-June 2010

Selected dose levels for the induction test: topical: 100% w/w

Selected dose levels for the challenge test: topical: 100% w/w

| Animal N° | Challenge | |
|----------------------|-------------|----------|
| | Right flank | |
| | 24 hours | 48 hours |
| | Erythema | Erythema |
| 4 | 0 | 0 |
| 5 | 0 | 0 |
| 6 | 1 | 1 |
| 7 | 0 | 0 |
| 8 | 0 | 0 |
| 9 | 1 | 1 |
| 10 | 1 | 0 |
| 11 | 1 | 1 |
| 12 | 1 | 1 |
| 13 | 0 | 0 |
| 14 | 0 | 0 |
| 15 | 1 | 1 |
| 16 | 1 | 0 |
| 17 | 0 | 0 |
| 18 | 0 | 0 |
| 19 | 0 | 0 |
| 20 | 1 | 1 |
| 21 | 0 | 0 |
| 22 | 0 | 0 |
| 23 | 1 | 1 |
| Affected animals (%) | 45% | 35% |

ANNEX I
Reference to the Toxicological Classification

Kligman's modified classification, to discriminate between non-sensitizer products and weak sensitizer products. ASTM F 720-81.

| Sensibility rate | Grade | Class |
|------------------|-------|---------------------|
| 0 | 1 | Non Sensitizer |
| 1 – 8 | 2 | Weak Sensitizer |
| 9 – 28 | 3 | Mild Sensitizer |
| 29 – 64 | 4 | Moderate Sensitizer |
| 65 – 80 | 5 | Strong Sensitizer |
| 81 – 100 | 6 | Extreme Sensitizer |

GHS (Harmonized Classification System for Chemicals Substances and Mixtures). By OECD, UN Comité Experts on Transport of Dangerous Goods, ILO and IOMC

Contact Sensitiser: is a substance tht will induce an allergic response following skin contact.

Substances shall be classified as **contact sensitizers (Category 1)** in accordance with the following criteria:

- There is evidence that the substance can induce sensitization by skin contact in a substantial number of humans, or
- Positive results are obtained from appropriate animal tests.

ANNEX II
GLP Certificate

Página 1 de 1

OAA ✓

Organismo
Argentino de
Acreditación

Reconocido
internacionalmente
por los organismos
de ILAC, IAAP y APAC

Av. Julio A. Roca 651 5° Sec. 8 y 9
(C1067AB6) Bs. As. Argentina
Teléfono: 54-11 4349-3962 / 3 / 4
info@oaa.org.ar | www.oaa.org.ar

OAA- Organismo Argentino de Acreditación
F13-(PRO-BPL)v2, F.e.V.= 01-diciembre-2009

**CERTIFICATE OF COMPLIANCE WITH OECD
PRINCIPLES OF GOOD LABORATORY
PRACTICE**

Granted to the Testing Facility

MICROQUIM S.A.

División Biomicro

The Argentine Accreditation Body -OAA- declares that according to the requirements of its Good Laboratory Practice Monitoring Program, the Test Facility MICROQUIM S.A. DIVISIÓN BIOMICRO carries out the non-clinical studies mentioned in this certificate in compliance with the Principles of Good Laboratory Practice of the Organisation for Economic Co-operation and Development -OECD- (1998).

REGISTRATION OF COMPLIANCE WITH GPL No 02

AUTHORIZED REPRESENTATIVE: Lic. Alejandro LUCINI

Area of expertise:

- 2- toxicity testing
- 4- environmental toxicity studies on aquatic and terrestrial organisms

These types of non-clinical studies are performed in AGROCHEMICAL.

Carried out in: MICROQUIM S.A., DIVISIÓN BIOMICRO

Address of the Facility: Costa Rica 4776 – Partido de Malvinas Argentinas

Inspection Date:

October 5 and 6, 2009

Inspection and study audit

President
Higinio B. Ridolfi

This certificate was issued in Buenos Aires on January 4, 2010.

QUALITY ASSURANCE UNIT STATEMENT

TITLE: Skin Sensitization in Guinea Pigs (*Cavia porcellus*) of NES FUNGICIDA,
ACARICIDA E INSECTICIDA SELECTIVO - LIQUIDO – Buehler Test

TEST SUBSTANCE: NES FUNGICIDA, ACARICIDA E INSECTICIDA
SELECTIVO - LIQUIDO

STUDY NUMBER: BIBR 6 – 30395

This study was audited during its different stages. The final report was compared with the Standard Operating Procedures (SOP) for this study.

The report is in accordance with the obtained data.

The audit was carried out according to the Standard Operating Procedures (SOP) established in the Procedures of MICROQUIM S.A.

Findings resulting from the audit were reported to the Direction and the Study Director. A copy of this report is kept in the archive “Internal Audits” of the Quality Assurance Unit of MICROQUIM S.A.

| Audit N° | Audited area / Details | Audit Date |
|-----------------|--|-------------------|
| 8644.a | Audit's Study Plan | 03.18.10 |
| 8644.b | Audit's Study | 04.01.10 |
| 8644.c | Final report revision. | 07.16.10 |
| 8644.d | Audit's Report to Direction and the Study Director | 07.19.10 |

Dr. Ana Inés Chanfreau
Veterinarian
GLP Quality Assurance Unit