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TOXICOLOGY DEPARTMENT  
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October 27, 1992

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Document Processing Center (TS-790)  
Office of Toxic Substances  
US Environmental Protection Agency  
401 M Street, SW  
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID No.: 8ECAP - 0004

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN 5266, Princeton, NJ 08543-5266) and its subsidiary Rhône-Poulenc Ag Company (RPAC), the attached study report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for a TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA.

The enclosed study report provides information on M&B 46030. Its CAS number and chemical index name are 120068-37-3 and 5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1H-pyrazole-3-carbonitrile. This chemical is manufactured in Europe and imported by RPAC for pesticide research and development.

No claims of confidentiality are made for this submission. Please note that RPAC released previous confidentiality claims for the subject chemical on September 8, 1992. The title of the enclosed report is "Acute Oral Toxicity to Rats of M&B 46030". The following is a summary of the adverse effects observed in this study.

This study is being submitted under Section 8(e) because signs of toxicity were observed within 5 hours of dosing and included piloerection, hunched posture, waddling, and diarrhea. The doses investigated in the study were 50, 80, 126, and 200 mg/kg. The oral LD50 was 97 mg/kg. Other clinical signs observed shortly after dosing or later in the study were lethargy, decreased respiratory rate, pallor of the extremities, and ptosis. Clonic convulsions were observed at 200 mg/kg but only preceding death. There were no deaths at the lowest dose tested. Surviving animals recovered by Day 3 at 50 mg/kg and by Day 6 at 80, 126, and 200 mg/kg.

Seven previous TSCA Section 8(e) notices were submitted on this chemical. The EPA Document Control Numbers for these submissions are 8EHQ-0191-1162S, 8EHQ-0391-1199S, 8EHQ-

uc  
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11/26/95

0591-1232S, 8EHQ-0791-1284S, 8EHQ-0791-1285S and 8EHQ-0891-1315S, and 8EHQ-0392-2540S. Also several Section 8(e) notices will be submitted on this compound under the CAP.

In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,



Glenn S. Simon, PhD, DABT  
Director of Toxicology

2

881300D/M&B 290/AC

030-TP-28-0000

ACUTE ORAL TOXICITY

TO RATS OF

M&B 46,030

Addressee:

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Report issued: 17 October 1988

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

HRC Report No. 881300D/M&B 290/AC

To the best of my knowledge and belief the study described in this report was conducted in compliance with the following appropriate Good Laboratory Practice Standards:

United States Environmental Protection Agency, (FIFRA)  
Title 40 Code of Federal Regulations Part 160, Federal  
Register, 29 November 1983.

United States Environmental Protection Agency, (TSCA)  
Title 40 Code of Federal Regulations Part 792, Federal  
Register, 29 November 1983

Japan Ministry of Agriculture, Forestry and Fisheries,  
59 NohSan, Notification No. 3850, Agricultural Production  
Bureau, 10 August 1984.

Organisation for Economic Co-operation and Development,  
ISBN 92-64-12367-9, Paris 1982.

United States Food and Drug Administration, Title 21 Code  
of Federal Regulations Part 58, Federal Register,  
22 December 1978 and subsequent Amendments.

Japanese Ministry of Health and Welfare and Ministry of  
International Trade and Industry, Directive 31 March 1984  
(Kanpogyo No. 39. Environmental Agency, Yakuhatsu No. 229,  
MOHW, Kikyoku No. 85 MITI)

Good Laboratory Practice, The United Kingdom Compliance  
Programme, Department of Health and Social Security 1986.



John R. Gardner, B.Sc., C.Biol., M.I.Biol.,  
Study Director,  
Huntingdon Research Centre Ltd.

17 October 1988

Date

QUALITY ASSURANCE STATEMENT

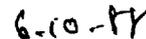
Acute studies are conducted at HRC in a setting which involves frequent repetition of similar or identical procedures. At or about the time the study described in this report was in progress, 'process-based' inspections were made by the Quality Assurance Unit of critical procedures relevant to this study type. For the inspection of any given procedure, at least one study was selected without bias. The findings of these inspections were reported promptly to the Study Director and to HRC Management.

This report has been audited by the HRC Quality Assurance Department. It is considered to be an accurate presentation of the procedures and practices employed during the course of the study and an accurate presentation of the findings.



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Peter H.C.V. Richold, B.Sc.,  
Systems Compliance Auditor,  
Quality Assurance Department,  
Huntingdon Research Centre Ltd.



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Date

Sample designation: M&B 46,030.

Chemical identity: 5-Amino-1-(2,6-dichloro-4-trifluoromethyl phenyl)-3-cyano-4-trifluoromethyl sulphinylpyrazole.

Batch Lot no.: IGB444.

Purity: 93% by g.c.

Examination for: Acute oral toxicity to rats.

## 1. INTRODUCTION

- 1.1. The study was designed to assess the toxicity following a single oral dose. The test substance may be ingested accidentally.
- 1.2. The rat has been shown to be a suitable model for this type of study and is the animal recommended in the test guidelines.
- 1.3. The study plan of the main study was first agreed by the Study Director on 28 June 1988 and the main study was undertaken between 29 June and 20 July 1988.

## 2. TEST SUBSTANCE

- 2.1. M&B 46,030, a green solid, was received on 17 June 1988 and stored in the original container and in ambient conditions of humidity and temperature in the dark.
- 2.2. M&B 46,030 was prepared at various (w/v) concentrations in corn oil and administered at a volume of 10.0 ml/kg.
- 2.3. The test substance was prepared on the day of dosing.
- 2.4. The absorption of the test substance was not determined.
- 2.5. The homogeneity, stability and purity of the test substance were the responsibility of the Sponsor.

### 3. EXPERIMENTAL PROCEDURE

#### 3.1. Protocol

The experimental procedure was based on that recommended under (1) Annex V of the EEC directive 79/831/EEC, Part B Methods for determination of toxicity. Method B1 Acute Oral Toxicity, and (2) the OECD guideline for Testing of Chemicals No. 401 "Acute Oral Toxicity".

#### 3.2. Animal management

3.2.1. Equal numbers of male and female CD rats [CrI:CD (SD) BR] were obtained from Charles River U.K. Limited, Margate, Kent, England. They were in a weight range of 100 to 138 g prior to dosing (Day 1) in the main study and approximately four to six weeks of age. All the rats were acclimated to the experimental environment for a period of 7 days prior to the start of the main study.

3.2.2. The rats were allocated to cages within the treatment groups. They were housed in groups of up to five rats of the same sex in metal cages with wire mesh floors. Each cage was identified by a coloured label displaying the dose level, study schedule number and the initials of the Study Director. Each animal was identified by cage number and ear punching.

3.2.3. A standard laboratory rodent diet (Labsure LAD 1) and domestic quality potable water were provided ad libitum. Access to food only was prevented overnight prior to and for approximately 4 hours after dosing. The batch of diet used for the study was analysed for certain chemical and microbiological contaminants (Appendix 1).

Results of routine chemical examination of water at source (Grafham Final Water) as conducted by the Anglian Water Authority, are made available to Huntingdon Research Centre (Appendix 2).

3.2.4. The mean daily minimum and maximum temperatures of the animal room were 24°C and 28°C respectively and the mean daily relative humidity value was 61% R.H. The rate of air exchange was maintained at approximately 15 air changes/hour. Lighting was controlled by means of a time switch to provide 12 hours artificial light in each 24-hour period.

#### 3.3. Experimental design

##### 3.3.1. Preliminary study

A trial test was carried out to establish a dosing regimen for the main study. Groups of two male and two female rats were dosed at 25 and 100 mg/kg bodyweight.

## 3.3.2. Main study

Based on the preliminary study, further groups of rats were dosed in order to establish the acute toxicity of the test substance more precisely.

The treatment regime and constitution of the groups are shown below:

| Dose<br>(mg/kg) | Concentration<br>(% w/v) | No. of rats |   |
|-----------------|--------------------------|-------------|---|
|                 |                          | ♂           | ♀ |
| 50              | 0.50                     | 5           | 5 |
| 80              | 0.80                     | 5           | 5 |
| 126             | 1.26                     | 5           | 5 |
| 200             | 2.00                     | 5           | 5 |

3.4. Treatment procedure

The appropriate dose volume of the test substance was administered to each rat using a syringe and plastic catheter (8 choke).

The day of dosing was designated Day 1.

3.5. Observation

3.5.1. Animals were observed soon after dosing and at frequent intervals for the remainder of Day 1 (a period of five hours). On subsequent days the animals were observed once in the morning and again at the end of the experimental day. This latter observation was at approximately 16.30 hours on week days or 11.30 hours on public holidays, including Saturday and Sunday. Clinical signs were recorded at each observation.

3.5.2. The animals surviving treatment on the preliminary and main studies were observed for 5 and 14 days respectively, after dosing.

3.5.3. The following were recorded on the main study:

3.5.3.1. Approximate time of death of individual rats.

3.5.3.2. The nature, severity, approximate time of onset and duration of each toxic sign.

3.5.3.3. Individual bodyweights of rats on Days 1 (day of dosing), 8 and 15 and at death.

### 3.6. Post mortem examination

Surviving animals on the main study were killed on Day 15 by carbon dioxide asphyxiation. All animals that died during the study and those killed on Day 15 were subjected to a macroscopic post mortem examination which consisted of opening the cranial, abdominal and thoracic cavities. The macroscopic appearance of all examined tissues was recorded.

## 4. STATISTICAL ANALYSIS

The acute median lethal oral dose ( $LD_{50}$ ) to male and female rats was calculated using the method of:

Finney (1971) Probit Analysis (3rd Edition) Cambridge University Press.

Separate  $LD_{50}$  values for males and females were estimated by undertaking probit analysis on the mortality data by fitting two parallel lines on the data (males only and females only) using the technique described by Finney (1978, Statistical Method in Biological Assay, 3rd Edition, Charles Griffin, London). A chi-squared test was carried out to check that the data did not contain any evidence for non-parallelism.

## 5. ARCHIVES

All specimens, raw data and other documents generated at HRC during the course of this study, together with a copy of this Final Report, have been lodged in the Huntingdon Research Centre Archives, Huntingdon, England.

## 6. RESULTS

### Preliminary study (Table 1)

The results of the preliminary study indicated that the acute median lethal oral dose to male and female rats of M&B 46,030 was approximately 100 mg/kg bodyweight.

Groups of ten rats (five males and five females) were dosed at 50, 80, 126 and 200 mg/kg bodyweight to determine the acute toxicity of the test substance more precisely.

Main studyMortality (Table 2)

There were deaths amongst rats of both sexes treated at 80 mg/kg and above. Deaths occurred from within four hours of dosing until Day 3.

Autopsy of rats that died revealed no macroscopic abnormalities.

Bodyweight losses or in one case, no change in bodyweight, were recorded for rats that died.

Clinical signs (Table 3)

Common signs of reaction to treatment observed within five hours of dosing were pilo-erection, abnormal body carriage (hunched posture), abnormal gait (waddling) and diarrhoea. Other clinical signs apparent at the same time or at later intervals were:

- lethargy amongst rats treated at 80 mg/kg and above,
- decreased respiratory rate, pallor of the extremities and/or ptosis for a single male dosed at 80 mg/kg and for all rats treated at the high dose level,
- clonic convulsions and prostration, preceding death, for two males and one female respectively dosed at 200 mg/kg.

Recovery of rats surviving treatment, as judged by external appearance and behaviour, was complete by Day 3 (50 mg/kg) or by Day 6 (all other dose levels).

Bodyweight (Table 4)

Low bodyweight gains were recorded on Day 8 for up to two females at each dose level and for all males surviving treatment. With the exception of a single female dosed at 50 mg/kg which showed a slightly low bodyweight gain, all rats achieved anticipated bodyweight gains during the second week of the study.

Terminal autopsy

Terminal autopsy findings were commonly found to be normal. However, hydronephrosis was apparent in single male and female rats dosed at 80 mg/kg. As a low incidence of this abnormality occurs spontaneously amongst untreated rats of this strain at this laboratory, the finding was not considered to be related to treatment.

Estimation of LD<sub>50</sub> values (Figure 1)

## (i) Combined sexes

The acute median lethal oral dose of M&B 46,030 and its 95% confidence limits were estimated to be:

Males and females combined: 97 (76 to 122) mg/kg bodyweight.

The slope of the probit line was 5.4 with a standard error of 1.4 using log. transformation of dose. The heterogeneity factor was not significant.

## (ii) Separate sexes

When probit analysis was carried out by fitting two parallel lines the values were:

Males only: 92 (64 to 128) mg/kg bodyweight.

Females only: 103 (73 to 141) mg/kg bodyweight.

The slope of the parallel probit lines was 5.5 with a standard error of 1.4 using log. transformation of dose. The heterogeneity factor was not significant.

The mortality response curves are presented in Figure 1.

The chi-squared test for parallelism gave no evidence of non-parallelism.

7. CONCLUSION

The acute median lethal oral doses (LD<sub>50</sub>) and their 95% confidence limits to rats of M&B 46,030 were estimated to be:

Males and females combined: 97 (76 to 122) mg/kg bodyweight

Males only: 92 (64 to 128) mg/kg bodyweight

Females only: 103 (73 to 141) mg/kg bodyweight

FIGURE 1

Mortality response curve for male and female rats  
dosed with M&B 46,030

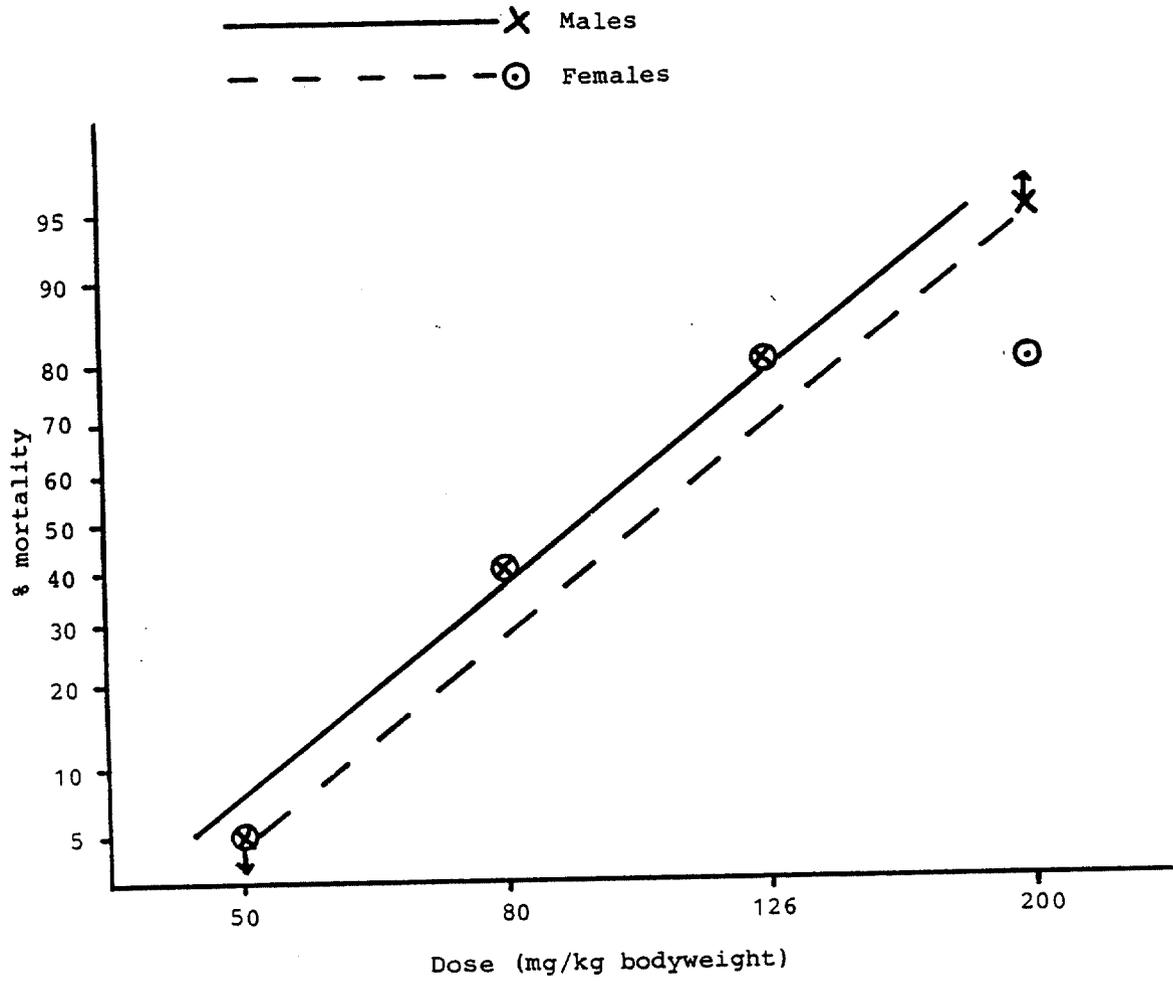


TABLE 1

Mortality data for groups of rats dosed orally  
with M&B 46,030

## Preliminary study

| Dose<br>(mg/kg) | Mortality ratio (No. of deaths)<br>(No. dosed) |     |          | Time of death<br>after dosing<br>(hours) |
|-----------------|--|-----|----------|--|
|                 | ♂  | ♀   | Combined |  |
| 25              | 0/2  | 0/2 | 0/4      | -  |
| 100             | 2/2  | 0/2 | 2/4      | <22 - <29                                |

TABLE 2

Time and number of deaths of rats dosed orally  
with M&B 46,030

## Main study

| Sex | Dose<br>(mg/kg) | Number<br>of<br>deaths<br>in a<br>group<br>of 5 | Day                |   |   |   |   |   |   |               |   |   |   |   |  |  |  |  |
|-----|-----------------|---|--------------------|---|---|---|---|---|---|---------------|---|---|---|---|--|--|--|--|
|     |                 |   | 1                  |   |   |   |   | 2 | 3 | 4<br>to<br>15 |   |   |   |   |  |  |  |  |
|     |                 |   | Hours after dosing |   |   |   |   |   |   |               |   |   |   |   |  |  |  |  |
|     |                 |   | <½                 | 1 | 2 | 3 | 4 | 5 | a | b             | a | b | a | b |  |  |  |  |
| ♂   | 50              | 0   |                    |   |   |   |   |   |   |               |   |   |   |   |  |  |  |  |
|     | 80              | 2   |                    |   |   |   |   |   |   |               | 2 |   |   |   |  |  |  |  |
|     | 126             | 4   |                    |   |   |   |   |   |   |               | 2 | 1 |   | 1 |  |  |  |  |
|     | 200             | 5   |                    |   |   |   |   | 2 |   |               | 2 | 1 |   |   |  |  |  |  |
| ♀   | 50              | 0   |                    |   |   |   |   |   |   |               |   |   |   |   |  |  |  |  |
|     | 80              | 2   |                    |   |   |   |   |   |   |               |   | 2 |   |   |  |  |  |  |
|     | 126             | 4   |                    |   |   |   |   |   |   |               |   | 4 |   |   |  |  |  |  |
|     | 200             | 4   |                    |   |   |   |   |   |   | 2             | 2 |   |   |   |  |  |  |  |

The hour/day indicated is the time that the animal was  
observed to die or found dead

a First observation  
b Second observation

TABLE 3

Signs of reaction to treatment observed in rats dosed orally with M&B 46,030

## Main study

| Signs                                       | No. of rats in group of 5 showing signs |   |    |   |     |   |     |   |
|---|---|---|----|---|-----|---|-----|---|
|   | Dose (mg/kg)                            |   |    |   |     |   |     |   |
|   | 50                                      |   | 80 |   | 126 |   | 200 |   |
|   | ♂                                       | ♀ | ♂  | ♀ | ♂   | ♀ | ♂   | ♀ |
| Pilo-erection                               | 5                                       | 5 | 5  | 5 | 5   | 5 | 5   | 5 |
| Diarrhoea                                   | 5                                       | 5 | 5  | 5 | 5   | 5 | 5   | 5 |
| Abnormal body carriage<br>(hunched posture) | 5                                       | 5 | 5  | 5 | 5   | 5 | 3   | 5 |
| Abnormal gait (waddling)                    | 5                                       | 5 | 5  | 5 | 5   | 5 | 3   | 5 |
| Lethargy                                    | 0                                       | 0 | 5  | 5 | 5   | 5 | 3   | 5 |
| Decreased respiratory rate                  | 0                                       | 0 | 1  | 0 | 0   | 0 | 5   | 5 |
| Ptosis                                      | 0                                       | 0 | 0  | 0 | 0   | 0 | 5   | 5 |
| Pallor of extremities                       | 0                                       | 0 | 1  | 0 | 0   | 0 | 5   | 5 |
| Clonic convulsions                          | 0                                       | 0 | 0  | 0 | 0   | 0 | 2   | 0 |
| Prostrate                                   | 0                                       | 0 | 0  | 0 | 0   | 0 | 0   | 1 |

TABLE 4

Individual and group mean bodyweights (g) of rats dosed orally  
with M&B 46,030

## Main study

| Sex  | Dose<br>(mg/kg) | Animal<br>number<br>& ear mark | Bodyweight (g) at |       |        |       |
|------|-----------------|--------------------------------|-------------------|-------|--------|-------|
|      |                 |                                | Day 1             | Day 8 | Day 15 | Death |
| ♂    | 50              | 21 RP                          | 126               | 182   | 238    | -     |
|      |                 | 22 LP                          | 132               | 196   | 270    | -     |
|      |                 | 23 RPLP                        | 118               | 183   | 242    | -     |
|      |                 | 24 RIRO                        | 134               | 201   | 258    | -     |
|      |                 | 25 LILO                        | 130               | 196   | 263    | -     |
|      | Mean            |                                | 128               | 192   | 254    |       |
|      | 80              | 1 RP                           | 118               | 184   | 250    | -     |
|      |                 | 2 LP                           | 121               | -     | -      | 118   |
|      |                 | 3 RPLP                         | 112               | 152   | 208    | -     |
|      |                 | 4 RIRO                         | 123               | -     | -      | 112   |
|      |                 | 5 LILO                         | 138               | 196   | 270    | -     |
|      | Mean            |                                | 122               | 177   | 243    |       |
| 126  | 11 RP           | 127                            | -                 | -     | 120    |       |
|      | 12 LP           | 110                            | -                 | -     | 107    |       |
|      | 13 RPLP         | 138                            | 186               | 260   | -      |       |
|      | 14 RIRO         | 136                            | -                 | -     | 128    |       |
|      | 15 LILO         | 134                            | -                 | -     | 124    |       |
| Mean |                 | 129                            | -                 | -     |        |       |
| 200  | 31 RP           | 122                            | -                 | -     | 113    |       |
|      | 32 LP           | 136                            | -                 | -     | 134    |       |
|      | 33 RPLP         | 121                            | -                 | -     | 116    |       |
|      | 34 RIRO         | 125                            | -                 | -     | 119    |       |
|      | 35 LILO         | 130                            | -                 | -     | 130    |       |
| Mean |                 | 127                            | -                 | -     |        |       |
| ♀    | 50              | 26 RP                          | 112               | 164   | 192    | -     |
|      |                 | 27 LP                          | 110               | 152   | 180    | -     |
|      |                 | 28 RPLP                        | 108               | 162   | 186    | -     |
|      |                 | 29 RIRO                        | 122               | 172   | 204    | -     |
|      |                 | 30 LILO                        | 100               | 138   | 156    | -     |
|      | Mean            |                                | 110               | 158   | 184    |       |
|      | 80              | 6 RP                           | 110               | 154   | 182    | -     |
|      |                 | 7 LP                           | 116               | -     | -      | 110   |
|      |                 | 8 RPLP                         | 110               | -     | -      | 106   |
|      |                 | 9 RIRO                         | 106               | 144   | 174    | -     |
|      |                 | 10 LILO                        | 120               | 180   | 218    | -     |
|      | Mean            |                                | 112               | 159   | 191    |       |
| 126  | 16 RP           | 120                            | -                 | -     | 110    |       |
|      | 17 LP           | 110                            | 142               | 168   | -      |       |
|      | 18 RPLP         | 122                            | -                 | -     | 114    |       |
|      | 19 RIRO         | 108                            | -                 | -     | 104    |       |
|      | 20 LILO         | 102                            | -                 | -     | 94     |       |
| Mean |                 | 112                            | -                 | -     |        |       |
| 200  | 36 RP           | 111                            | -                 | -     | 109    |       |
|      | 37 LP           | 110                            | -                 | -     | 105    |       |
|      | 38 RPLP         | 104                            | -                 | -     | 102    |       |
|      | 39 RIRO         | 126                            | 152               | 194   | -      |       |
|      | 40 LILO         | 104                            | -                 | -     | 100    |       |
| Mean |                 | 111                            | -                 | -     |        |       |

## APPENDIX 1

Composition and quality assurance aspects of rodent diet

Labsure LAD is a closed formula diet suitable for normal health, growth and reproduction of laboratory rats and mice. The standards of production adopted by the manufacturers have been approved by the HRC Department of Quality Assurance.

Analyses have been made of all batches of diet for most nutrients and for specified substances and micro-organisms likely to be present in feed ingredients or the finished diet and which, if in excess of specified amounts, might have an undesirable effect on the test system. Although occasional slight deviation may have been permitted, batches of diet conformed with the acceptable standards agreed by the Study Director and Quality Assurance HRC as detailed below.

(A) Nutrients

|               |         | <u>Target level</u>             | <u>Maximum Tolerance (%)</u> |
|---------------|---------|---------------------------------|------------------------------|
| Crude fat     | %       | 3.7                             | ±15                          |
| Crude protein | %       | 21.5                            | ±10                          |
| Crude fibre   | %       | 2.0                             | ±40                          |
| Ash           | %       | 5.5                             | ±15                          |
| Moisture      | %       | 9.5                             | +10.5                        |
| Calcium       | %       | 1.0                             | ±20                          |
| Phosphorus    | %       | 0.9                             | ±20                          |
| Sodium        | %       | 0.3                             | +100-50                      |
| Chlorine      | %       | 0.5                             | +100-50                      |
| Potassium     | %       | 0.8                             | +100-50                      |
| Magnesium     | %       | 0.15                            | ±50                          |
| Manganese     | mg/kg   | 70                              | ±50                          |
| Iron          | mg/kg   | 220                             | ±50                          |
| Copper        | mg/kg   | 15                              | ±50                          |
| Zinc          | mg/kg   | 60                              | ±50                          |
| Vitamin A     | i.u./kg | 12000                           | +50-20                       |
| Vitamin E     |         | acceptable range 28 to 88 mg/kg |                              |

(B) Contaminants

|   | <u>Maximum allowable concentration</u><br>(mg/kg except where stated) |
|---|---|
| Lead  | 2.5   |
| Cadmium   | 0.5   |
| Arsenic   | 1.5   |
| Mercury   | 0.1   |
| Selenium  | 0.6   |
| Fluorine  | 40  |
| Nitrates (as sodium nitrate)  | 200   |
| Nitrites (as sodium nitrite)  | 10  |
| PCBs  | 0.05  |
| Total DDT   | 0.15  |
| Dieldrin  | 0.05  |
| Lindane   | 0.15  |
| Heptachlor  | 0.05  |
| Malathion   | 5.0   |
| Total aflatoxins (B <sub>1</sub> , B <sub>2</sub> , G <sub>1</sub> , G <sub>2</sub> ) µg/kg | 5.0   |

## APPENDIX 1

(continued)

(C) Microbiological content

Maximum count/g diet (at time of manufacture)

|                            |              |
|----------------------------|--------------|
|                            | <u>LAD 1</u> |
| Total viable organisms     | 10,000       |
| Mesophilic spores          | 30,000       |
| Presumptive <u>E. coli</u> | 0            |
| <u>E. coli</u> Type 1      | 0            |
| <u>Salmonella</u> spp.     | 0            |
| Fungal units               | 1,000        |
| Antibiotic activity        | 0            |

## APPENDIX 2

Quality assurance aspects of water

Results of the routine physical and chemical examination of drinking water at source (Grafham Final Water) as conducted usually weekly by the supplier, Anglian Water Authority, have been made available to HRC as quarterly summaries. Additionally, levels of specified substances known to be present from time to time in local water and which, if in excess of the maxima recommended (for humans) might have undesirable effects on the test system, have been determined in HRC tap water at approximately 6-monthly intervals.

Quarterly summary analyses of source water normally include levels of nitrites, nitrates, Ca, Mg, Na, K, P, Cl, Si, Fe.

Six-monthly analyses of HRC tap water currently include levels of As, Se, Ba, Ag, Sb, organophosphorus, organochlorine and other pesticides, haloforms, chlorophenols, polychlorinated biphenyls and polycyclic aromatic hydrocarbons.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

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Research Triangle Park, North Carolina 27709

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)  
Attn: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

*Terry R. O'Bryan*  
Terry R. O'Bryan  
Risk Analysis Branch

Enclosure

12208A



Recycled/Recyclable  
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**Triage of 8(e) Submissions**

AUG 24 1985

Date sent to triage: \_\_\_\_\_

NON-CAP

CAP

Submission number: 12208A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): \_\_\_\_\_

Notes:

**THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY**

**For Contractor Use Only**

entire document: 0 1 2 pages 1/2 pages 1/2, 7/11/95

Notes:

Contractor reviewer: POZ Date: 3/21/95

CECATS DATA: Submission # BEHQ-1192-12208 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE:  
 0501 NO INFO REQUESTED  
 0502 INFO REQUESTED (TECH)  
 0503 INFO REQUESTED (VOL ACTIONS)  
 0504 INFO REQUESTED (REPORTING RATIONALE)  
 DISPOSITION:  
 0639 REFER TO CHEMICAL SCREENING  
 0678 CAP NOTICE

VOLUNTARY ACTIONS:  
 0401 NO ACTION REPORTED  
 0402 STUDIES PLANNED/IN PROGRESS  
 0403 MITIGATION IN WORK/PLANNED  
 0404 LARPI/MSDS CHANGES  
 0405 PROCESS/AND/OR CHANGES  
 0406 APPEASE DISCONTINUED  
 0407 PRODUCTION DISCONTINUED  
 0408 CONFIDENTIAL

SUB. DATE: 10/27/92 OIS DATE: 11/2/92 CSRAD DATE: 01/25/95

CHEMICAL NAME

M-B 46030

CASE

120068-37-3

5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-  
4-[(trifluoromethyl)sulfonyl]pyrazole-3-carbonitrile

BEST COPY AVAILABLE

| INFORMATION TYPE:             | P.F.C.   | INFORMATION TYPE:              | P.F.C.   | INFORMATION TYPE:      | P.F.C.   |
|-------------------------------|----------|--------------------------------|----------|------------------------|----------|
| 0201 ONCO (HUMAN)             | 01 02 04 | 0216 EPICLIN                   | 01 02 04 | 0241 IMMUNO (ANIMAL)   | 01 02 04 |
| 0202 ONCO (ANIMAL)            | 01 02 04 | 0217 HUMAN EXPOS (PROD CONTAM) | 01 02 04 | 0242 IMMUNO (HUMAN)    | 01 02 04 |
| 0203 CELL TRANS (IN VITRO)    | 01 02 04 | 0218 HUMAN EXPOS (ACCIDENTAL)  | 01 02 04 | 0243 CHEMPHYS PROP     | 01 02 04 |
| 0204 MUTA (IN VITRO)          | 01 02 04 | 0219 HUMAN EXPOS (MONITORING)  | 01 02 04 | 0244 CLASTO (IN VITRO) | 01 02 04 |
| 0205 MUTA (IN VIVO)           | 01 02 04 | 0220 BODWATER TOX              | 01 02 04 | 0245 CLASTO (ANIMAL)   | 01 02 04 |
| 0206 REPRO/TERATO (HUMAN)     | 01 02 04 | 0221 ENV. OCCUREL/FATE         | 01 02 04 | 0246 CLASTO (HUMAN)    | 01 02 04 |
| 0207 REPRO/TERATO (ANIMAL)    | 01 02 04 | 0222 EMER INCI OF ENV CONTAM   | 01 02 04 | 0247 DNA DAMREPAIR     | 01 02 04 |
| 0208 NEURO (HUMAN)            | 01 02 04 | 0223 RESPONSE REOBST DELAY     | 01 02 04 | 0248 PRODUCE/PROC      | 01 02 04 |
| 0209 NEURO (ANIMAL)           | 01 02 04 | 0224 PROD/COMP/CHSM ID         | 01 02 04 | 0251 MSDS              | 01 02 04 |
| 0210 ACUTE TOX. (HUMAN)       | 01 02 04 | 0225 REPORTING RATIONALE       | 01 02 04 | 0259 OTHER             | 01 02 04 |
| 0211 CHR. TOX. (HUMAN)        | 01 02 04 | 0226 CONFIDENTIAL              | 01 02 04 |                        |          |
| 0212 ACUTE TOX. (ANIMAL)      | 01 02 04 | 0227 ALLERG (HUMAN)            | 01 02 04 |                        |          |
| 0213 SUB ACUTE TOX (ANIMAL)   | 01 02 04 | 0228 ALLERG (ANIMAL)           | 01 02 04 |                        |          |
| 0214 SUB CHRONIC TOX (ANIMAL) | 01 02 04 | 0229 METABPHARMACO (ANIMAL)    | 01 02 04 |                        |          |
| 0215 CHRONIC TOX (ANIMAL)     | 01 02 04 | 0240 METABPHARMACO (HUMAN)     | 01 02 04 |                        |          |

| IRACLES/MSDS | NON-CBI INVENTORY | ONGOING REVIEW   | SPECIES | TOXICOLOGICAL CONCERN: | USE:      | PRODUCTION: |
|--------------|-------------------|------------------|---------|------------------------|-----------|-------------|
|              | YES               | YES (DROP/REFER) | RAT     | LOW                    | R+D       |             |
| CAS SR       | NO                | NO (CONTINUE)    |         | MED                    | Pesticide |             |
|              | IN TRAINING       | REF-R            |         | HIGH                   |           |             |

IRACLES CBI substantiation claim released on 9/8/92, per cover page.  
 CAP ID NO: 8ECAP-0004

-CPSS-

> <ID NUMBER>  
8(E)-12208A

> <TOX CONCERN>  
M

> <COMMENT>  
ACUTE ORAL TOXICITY IN MALE AND FEMALE CRL:CD RATS IS OF MEDIUM CONCERN. SINGLE ORAL DOSES OF 50, 80, 126 AND 200 MG/KG GAVAGED TO GROUPS OF 5 EACH MALE AND FEMALE RATS WERE ASSOCIATED WITH SIGNS OF NEUROTOXICITY AND MORTALITY AS FOLLOWS: 50 MG/KG (0/5M, 0/5F), 80 MG/KG (2/5M, 2/5F), 126 MG/KG (4/5M, 4/5F), 200 MG/KG (5/5M, 4/5F). ORAL LD50'S FOR MALE AND FEMALE RATS WERE 92 (64 TO 128) MG/KG AND 103 (73 TO 141) MG/KG RESPECTIVELY; A COMBINED LD50 FOR MALE AND FEMALE RATS WAS 97 (76 TO 122) MG/KG. ALL DEATHS OCCURRED WITHIN 3 DAYS OF DOSING. CLINICAL SIGNS OF TOXICITY OF INCREASING SEVERITY WERE DOSE DEPENDENT AND INCLUDED PILOERECTION, DIARRHEA, HUNCHED POSTURE, "WADDLING" GAIT, LETHARGY, DECREASED RESPIRATORY RATE, PTOSIS, PALLOR OF EXTREMITIES, CLONIC CONVULSIONS AND PROSTRATION. ALL TREATMENT GROUPS SHOWED LOW MEAN BODYWEIGHT GAINS IN SURVIVING ANIMALS AT DAY 8 OF POST-DOSING OBSERVATION WITH RESTORED MEAN WEIGHT GAIN BY THE END OF 14-DAY OBSERVATION. IN AN INITIAL TRIAL STUDY, DOSES OF 25 AND 100 MG/KG EACH ADMINISTERED TO GROUPS OF 2 MALE AND 2 FEMALE RATS WERE ASSOCIATED WITH AN APPROXIMATE ORAL LD50 OF 100 MG/KG.

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-CPSS-

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8(E)-12208A

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