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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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APR 8 - 1993

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: HWG 1608 (Tebuconazole) technical. Upgrade of metabolism study.
Tox Chem No. 463P
MRID No. 425083-01
PC Code: 128997
DP Barcode: D184304, D184310, D184311, D184312, D184318, D184319,
and D184320
Submission Nos.: S428527, S428531, S428535, S428544, S428598,
S428600, and S428601
Action: 116, 101, 231, and 251,

From: Alberto Protzel, Ph.D.
Review Section III
Toxicology Branch II
Health Effects Division (H7509C)

Alberto Protzel 4/6/93

To: Mr. Benjamin Chambliss/Ms. Susan Lewis (PM-21)
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: James N. Rowe, Ph.D., Head
Review Section III
Toxicology Branch II
Health Effects Division (H7509C)

James N. Rowe 4/6/93

and

Marcia van Gemert, Ph.D., Chief
Toxicology Branch II
Health Effects Division (H7509C)

Marcia van Gemert 4/7/93

ACTION: Review of the following study on the chemical HWG 1608 (Tebuconazole) Technical submitted by Miles Inc.:

Addendum I. [Phenyl-U-¹⁴C] HWG 1608: Study of Biokinetic Behavior in the Rat. Response to EPA Requests and Inquiries. [Report 97439-1; MRID 425083-01].

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CONCLUSIONS:

It is recommended that the tebuconazole metabolism study in rats that was initially submitted in the following two volumes:

1. Study of Biokinetic Behavior in the Rat (Mobay Report No. 97439, MRID 409959-11)
2. FOLICUR[®]: Metabolism Part of the General Metabolism Study in the Rat. (Mobay Report No. 97439, MRID 409959-12),

be upgraded from Supplementary to Minimum

DETAILED CONSIDERATIONS

A rat metabolism study of tebuconazole by Mobay was initially reviewed in a DER dated 12/19/90 (Microfiche 008241). The metabolism study was submitted in the following two volumes:

1. Study of Biokinetic Behavior in the Rat (Mobay Report No. 97439, MRID 409959-11)
2. FOLICUR[®]: Metabolism Part of the General Metabolism Study in the Rat. (Mobay Report No. 97439, MRID 409959-12).

The study was initially classified as supplementary pending submission of additional data.

In response to the classification of Supplementary, Miles, Inc. initially submitted the following additional study:

Addendum I. FOLICUR[®]: Metabolism Part of the General Metabolism Study in the Rat. Additional Information requested by the EPA. [Report 97438-1; MRID 421762-02].

Based on the review of the additional data submitted as Report 97438-1 (MRID 421762-02) it was concluded in the TB-II Memorandum from A. Protzel to B. Chambliss/S. Lewis, dated 8/8/92 that

- o The additional information submitted by the Registrant had adequate responses to items 1,2,3 and 5 listed in the DER.
- o The subject metabolism study may be upgraded from supplementary to minimum if the following information (item 4 in the DER) is submitted and is deemed acceptable:
 - a. A clarification as to why it is stated (in Report 97439) that GLP requirements do not apply to the portion of the study in Mobay Report No. 97439 (Pharmacokinetics) [MRID 409959-12].
 - b. A signed and dated GLP compliance statement for the portion of the study in Mobay Report No. 97439 (MRID 409959-12).

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Mobay, Inc. has now submitted the required information:

Concerning above item (a), Mobay, Inc. stated that "The pharmacokinetics study (Miles Report No. 97439) always had an appropriate GLP statement on page 86, but Miles mistakenly claimed on page 3 that there was no need for a GLP statement. An appropriate GLP statement is included as page 3 of this addendum".

Concerning above item (b), Mobay, Inc. stated that "A copy of the signed and dated Statement of Compliance with GLP Standards is now included as Figure 2 of this addendum".

Agency's Response:

Concerning item (a), Mobay has submitted a suitable clarification. Concerning item (b), the submitted GLP statement is included as Attachment 1. It is noted that although "requirements for recording raw data were not consequently met in all cases", the work appears to be scientifically sound.

It is recommended that the tebuconazole metabolism study in rats that was submitted in the following two volumes:

1. Study of Biokinetic Behavior in the Rat (Mobay Report No. 97439, MRID 409959-11)
2. FOLICUR[®]: Metabolism Part of the General Metabolism Study in the Rat. (Mobay Report No. 97439, MRID 409959-12),

be upgraded from Supplementary to Minimum

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Attachment 1

Statement of GLP Compliance
From p.8 of Study 97439-1, MRID 425083-01

97439-1

STATEMENT OF COMPLIANCE

Oct-02-1987

To the best of our knowledge and belief we declare that this study was conducted in compliance with GLP Standards (USA, EPA, 40 CFR Part 166, November 29, 1983; OECD, C (81) 30 (Final), May 12, 1981) with the exception in the following respect:

- Although this study was conducted according to standard operating procedures, not all of the procedures concerning the combustion and radioactivity measurement techniques of biological material were formally designated as S.O.P.'s.
- The requirements for recording raw data were not consequently met in all cases.

Notwithstanding this departure from the current GLP-regulations, we believe the quality and integrity of the data submitted was not affected and the study is valid to support the conclusions drawn.

Signatures:

(Study Director)

W. Weber 2.10.87
.....
(Dr. W. Weber) Date

(Responsibility for radioactivity measurement)

U. Neukamp 5.10.87
.....
(Dr. U. Neukamp) Date

(Head of Institute)

Kaufmann 7.10.87
.....
(Dr. E.U. Kaufmann) Date



Figure 2. A copy of the statement of compliance with GLP standards from page 11 of the "[Phenyl-U-14C] HMG 1608: study of biokinetic behavior in the rat" (Miles Report No. 97439; MRID 409959-12).

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