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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

December 13, 2001

MEMORANDUM

Subject: D277659 – T344, EPA File Symbol 72992-E
D277653 – T427, EPA File Symbol 72992-G
D277645 – T345, EPA File Symbol 72992-L
D277651 – T430, EPA File Symbol 72992-A
D277649 – T428, EPA File Symbol 72992-T
D277647 – T333, EPA File Symbol 72992-I
D277656 – T426, EPA File Symbol 72992-O

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BACKGROUND

In response to agency letters of 06/06/01 and 06/07/01, the applicant – Pokon & Chrysal B.V. (as represented by an agent) – has submitted papers in support of the acute toxicity data requirements (mammalian) for registration of the subject products: T344, T427, T345, T430, T428, T333, and T426. The papers included:

- Details of a previously cited particle attrition test for T344 (as possible support for acute inhalation data waivers for T344, T345, and T333);
- Procedure confirmation and eye-effects grading system, to supplement the previously submitted eye irritation studies (conducted on T427 and T344 and cited to support most of the other products);
- Treatment volumes, induction reactions, and skin-effects grading system, to supplement the previously submitted skin sensitization studies (conducted on T344 and cited to support T345 and T333).

Each of the subject products is meant to provide conditioning for ornamental cut flowers by controlling microbial growth, activating water uptake, and preventing premature wilting. Each product contains the following active ingredients:

- 2-bromo-2-nitropropane-1,3-diol (i.e., Bronopol), EPA code 216400
- Poly(iminoimidocarbonyliminoimidocarbonyliminohexamethylene)hydrochloride (i.e., polymeric biguanide), EPA code 111801.

RECOMMENDATION

Upon review of the supplemental information listed above, PSB considers the product-specific acute toxicity data requirements for the subject products to be fulfilled.

The updated acute toxicity regulatory status for the subject products is summarized in the table on the next page. The table is followed by clarifying comments in the form of footnotes.

For each data requirement for each product, the table lists the means of support, followed by the study MRID if applicable, followed by the acute Toxicity Category indicated by the study results if applicable, followed by the acceptability rating for the data requirement. Footnote reference numbers are shown in square brackets.

Table: Acute Toxicity Regulatory Profile for the Proposed Registrations

(Footnotes appear in square brackets [])

Product	Means of Support, MRID, Acute Tox Category, Acceptability					
	Acute Oral Toxicity	Acute Dermal Tox.	Acute Inhalation Tox.	Eye Irritation	Skin Irritation	Skin Sensitization
T427 72992-G	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Submitted study MRID 453269-02 Category IV Acceptable[5]	Submitted study MRID 453269-03 Category IV Acceptable	Submitted study MRID 453269-04 Sensitizer Acceptable
T344 72992-E	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Attrition test submitted Category IV assigned Waiver Acceptable[4]	Submitted study MRID 453255-02 Category IV Acceptable[5]	Submitted study MRID 453255-03 Category IV Acceptable	Submitted study MRID 453255-04 Non-sensitizer Acceptable[8]
T426 72992-O	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Cited T427 study MRID 453269-02 (Study: Category IV) Cat. III assigned[6] Citation Acceptable	Cited T427 study MRID 453269-03 Category IV Citation Acceptable[7]	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable
T345 72992-L	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Cited T344 study MRID 453255-02 (Study: Category IV) Cat. III assigned[6] Citation Acceptable	Cited T344 study MRID 453255-03 (Study: Category IV) Cat. III assigned[6] Citation Acceptable	Cited T344 study MRID 453255-04 Non-sensitizer Citation Acceptable
T428 72992-T	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Cited T427 study MRID 453269-02 Category IV Citation Acceptable	Cited T427 study MRID 453269-03 Category IV Citation Acceptable	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable
T333 72992-I	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Cited T344 study MRID 453255-02 Category IV Citation Acceptable	Cited T344 study MRID 453255-03 Category IV Citation Acceptable	Cited T344 study MRID 453255-04 Non-sensitizer Citation Acceptable
T430 72992-A	Cited T535 study[1] MRID 453257-03 Category III[2] Citation Acceptable[3]	Cited T535 study[1] MRID 453257-02 Category III[2] Citation Acceptable[3]	Waiver request Category III assigned Waiver Acceptable[4]	Cited T427 study MRID 453269-02 (Study: Category IV) Cat. III assigned[6] Citation Acceptable	Cited T427 study MRID 453269-03 Category IV Citation Acceptable	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable

Table Footnotes

[1] T535 is the EPA File Symbol 72992-U product.

[2] Based on the limit test.

[3] With the possible exception of T345, the products would not be expected to be more hazardous by acute oral or acute dermal toxicity than would the cited test material (T535, EPA File Symbol 72992-U). If there are any components of a product that are not present in the cited test material, they do not appear to be of significant concern with respect to acute oral or acute dermal toxicity.

As for T345 (EPA File Symbol 72992-L), concentrations of most components are moderately higher than they are in the cited test material. However, the T345 components are not of significant concern in and of themselves at the concentrations present, and the pH of T345 suggests that corrosiveness would not be a factor. Moreover, the quantitative and qualitative data in the acute oral and acute dermal toxicity studies on the T535 test material (to which T345 is being compared) suggest that T535 is probably nearly harmless.

[4] PSB has received the test report for the attrition testing on T344. The results are arguably adequate to support a waiver for T344, given the product's low acute toxicity.

For the seven subject products, acute inhalation toxicity data is waived based on (1) the submitted attrition test for T344, (2) generally low levels of concern regarding product components at the concentrations present, and (3) low acute toxicity and irritation, in particular the acute oral toxicity and eye irritation.

Acute inhalation Tox Category IV is assigned to T344 (the subject of the attrition test). Category III is assigned to the other products in order to indicate the possibility of a mild to moderate hazard. Although some of the other six products are granular (T345, T333 are in powder form, the rest are granular), all six products' limited similarity to T344 does not necessarily imply that particle attrition test results would be as favorable for them as for T344. Therefore, they are not being assigned Category IV. Category III is assigned as worst case.

[5] Based on the newly submitted addendum to the MRID 453269-02 study (for T427) and the MRID 453255-02 study (for T344), the classification for these two studies is being changed to Acceptable. The agency contractor's reviews for both studies reflect this classification.

PSB has edited the agency contractor's review of the MRID 453269-02 study to indicate Tox Category IV, since no 'positive' irritation was noted in the study report.

[6] It appears that T426, T345, or T430 could be of moderately higher eye irritation potential than the test material of the cited study (453269-02 or 453255-02). Based on the non-irritating result of the study (453269-02 or 453255-02), however, the skin irritation hazard of T426, T345, or T430 is not expected to be much worse than that of the test material. Each study places its test material in eye irritation Tox Category IV. It is suitable to assign Category III as worst case, to T426, T345, and T430. Product label statements that reflect eye irritation Category III will caution the user as to the possibility of a mild or moderate hazard.

A similar argument can be made for skin irritation concerning the T345 product, for which MRID 453255-03 was cited, which was accepted on behalf of T344 in support of Tox Category IV. T345 appears moderately but not highly different from T344; accordingly, skin irritation Tox Category III is being assigned to T345 as worst case.

- [7] The skin irritation data citation is acceptable for T426 based on its comparability to two supported products: T427 (on which MRID 453269-03 was conducted) and T344 (on which MRID 453255-03 was conducted). Comparing T426 to the one product results in a concern regarding a pH difference; comparing T426 to the other product results in a concern regarding concentration differences. However, comparing T426 to both products together helps to allay these concerns (since the problems of the one comparison are different than those of the other).
- [8] Based on the newly submitted MRID 454849-02, an addendum to MRID 453255-04, the latter is being upgraded to a rating of Acceptable. The agency contractor's review of MRID 453255-04 reflects this rating.

Product Labeling

Human-hazard precautionary statements:

Based on the products' acute Tox Category profiles in the above table, the following human-hazard precautionary statements should appear on the product labels:

- T427 (EPA File Symbol 72992-G) and T428 (EPA File Symbol 72992-T):

"Harmful if swallowed, absorbed through skin, or inhaled. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals."
- T426 (EPA File Symbol 72992-O) and T430 (EPA File Symbol 72992-A):

"Harmful if swallowed, absorbed through skin, or inhaled. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals."
- T344 (EPA File Symbol 72992-E)

"Harmful if swallowed or absorbed through skin. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling."
- T333 (EPA File Symbol 72992-I):

"Harmful if swallowed, absorbed through skin, or inhaled. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse."

- T345 (EPA File Symbol 72992-L):

"Harmful if swallowed, absorbed through skin, or inhaled. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse."

First-aid statements:

Regarding first-aid label statements, it appears that the proposed labels all include *If Swallowed, If On Skin Or Clothing, and If Inhaled* first-aid statements. Those statements as proposed on the labels are acceptable. However, the following statements should be added (as per Pesticide Registration [PR] Notice 2001-1):

- For T426 (72992-O), T345 (72992-L), and T430 (72992-A):

"If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.
- Call a poison control center or doctor for treatment advice."

- For all seven products: the following general statement is required to be included with the First Aid statements (at the beginning or the end):

"Have the product container or label with you when calling a poison control center or doctor, or going for treatment."