



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

6-27-91 R.F.

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

JUN 27 1991

MEMORANDUM

Subject: Protocols for the Sampling of and for the Analysis of Technical Chlorothalonil for Polychlorinated Dibenzo-p-Dioxins and Dibenzofurans. Chemical 081901. I. D. 50534-7. DP Barcode D160986. MRID None. CBRS No. 7632.

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Background

ISK Biotech Corporation (formerly Fermenta Plant Protection Corp.) previously submitted manufacturing data for technical 97% chlorothalonil (2,4,5,6-tetrachloro-1,3-benzenedicarbonitrile, daconil 2787) in response to a DCI. The purpose of the DCI was to evaluate certain manufacturing processes for the potential to form polyhalogenated dibenzo-p-dioxins and/or dibenzofurans. The data were reviewed and it was concluded that the potential existed for the formation of halogenated dibenzo-p-dioxins and dibenzofurans under the manufacturing conditions described (DEB Memorandum 07/01/88, M. Flood, DEB No. 3762; DEB Memorandum 07/17/90, S. Funk, DEB No. 6576). The registrant was requested to supply the sampling and analysis protocols for the analyses of seven lots of technical chlorothalonil - for polychlorinated dibenzo-p-dioxins and

dibenzofurans. The registrant has responded (01/11/91; received 01/14/91) with a document entitled "Protocol for Obtaining Samples of Technical Chlorothalonil (EPA Reg. No. 50434-7) for Analysis for Polyhalogenated Dibenzo-p-Dioxins/Dibenzofurans and Laboratory Analytical Procedure."

Discussion

QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED
FIFRA REGISTRATION DATA IS NOT INCLUDED

Sampling-

Chlorothalonil

Each sample of about 80 grams is collected in a 2 ounce glass jar. Samples will be collected in duplicate approximately every 15 days by dipping the jar (on a rod) into the #2 converter. Label information includes date, time, and operator initials. A chain of custody form accompanies each sample. In the plant laboratory, new labels are affixed containing the following information: chlorothalonil production unit no.; batch number; date; time; purpose; person preparing shipment; date prepared for shipment. One sample is sent for analysis, and the duplicate is stored (under secure conditions). Copies of the COC form and labels are included with the protocol.

The registrant proposes to utilize new jars to avoid sample contamination. New jars can be contaminated with materials that will interfere with analyses. The registrant is advised to clean the containers per the instructions given in the Guidelines for the Determination of Halogenated Dibenzo-p-Dioxins and Dibenzofurans in Commercial Products (EPA-560/5-87/007), Appendix A, paragraph 8.2. Bottles are to be washed in detergent solution, rinsed sequentially with tap water and distilled water, and heated to 400° C or rinsed with pesticide grade acetone or hexane and air dried. If analyses are invalidated by contamination and a proper sample container cleaning protocol was not followed, resampling and reanalyses will be required.

Analysis-

Chlorothalonil

Page 3 is not included in this copy.

Pages _____ through _____ are not included.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
 - ☐ Identity of product impurities.
 - ☐ Description of the product manufacturing process.
 - ☒ Description of quality control procedures.
 - ☐ Identity of the source of product ingredients.
 - ☐ Sales or other commercial/financial information.
 - ☐ A draft product label.
 - ☐ The product confidential statement of formula.
 - ☐ Information about a pending registration action.
 - ☒ FIFRA registration data.
 - ☐ The document is a duplicate of page(s) _____.
 - ☐ The document is not responsive to the request.
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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

The proposed deliverables consists of:

- (1). For the initial calibration, all chromatograms and all ion areas for all standard analyses; source and concentration of all standards; the ion ratios for native analytes and labeled standards; native response factors, mean response factors, and relative standard deviations; response factors for the internal standards and for the cleanup recovery standard relative to the recovery standard; the $\pm 20\%$ limits for determining acceptability of daily (continuing) calibrations.
- (2). Documentation of isomer specificity for each column used.
- (3). Documentation of mass spectrometer resolution for each instrument and each day of analyses.
- (4). Daily calibration data, including chromatograms, dates and times, ion ratios, relative response factors, and percent relative difference. No mention is made of ion areas.
- (5). Method blank data, including chromatograms, tabular summaries of estimated detection limits, ion ratios, internal standard

recoveries, cleanup standard recoveries, and ion ratios and concentrations for any detected target analytes.

(6). Sample results, laboratory duplicate results, and native spike (matrix spike) results, including sample identification number, sample weight, date sample preparation started, all chromatograms, internal standard and analyte ion ratios, internal standard and cleanup recovery standard recoveries, and analyte concentrations detected. Relative percent differences will be calculated for the laboratory duplicate. Native spike recoveries will be reported for the matrix spike. No mention is made of the laboratory blank native spike, and apparently raw data (ion areas and retention times) will not be reported.

Additional information should be included in the deliverables. Summary tables of retention times and corresponding ion areas must be provided for each standard, control, and sample analyzed. Sufficient data must be provided to permit independent verification of reported results. An example calculation should also be included to demonstrate each step of the process.

Conclusions

The sampling protocol is acceptable. The protocol does not specify the number of samples to be collected and analyzed. Seven samples must be collected randomly from each production line and analyzed, or a total of fourteen sample analyses.

The final purification would not increase dioxin/dibenzofuran levels. The registrant is advised to consider sample container cleaning to avoid possible resampling/reanalysis.

The analytical protocol fulfills some of the requirements and recommendations of the 06/87 DCI and the Guidelines. The following deficiencies exist:

(1). The proposal provides only for the determination of 2,3,7,8-TCDD and 2,3,7,8-TCDF. The following 2,3,7,8-CDD and 2,3,7,8-CDF isomers must be determined at (or below) the indicated levels of quantitation (LOQ):

QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED
FIFRA REGISTRATION DATA NOT INCLUDED

Analyte	LOQ (ng/g)
2,3,7,8-TCDD	0.1
1,2,3,7,8-PCDD	0.5
1,2,3,4,7,8-HxCDD	2.5
1,2,3,6,7,8-HxCDD	2.5
1,2,3,7,8,9-HxCDD	2.5
1,2,3,4,6,7,8-HpCDD	100.
2,3,7,8-TCDF	1.
1,2,3,7,8-PCDF	5.
2,3,4,7,8-PCDF	5.
1,2,3,4,7,8-HxCDF	25.
1,2,3,6,7,8-HxCDF	25.
1,2,3,7,8,9-HxCDF	25.
2,3,4,6,7,8-HxCDF	25.
1,2,3,4,6,7,8-HpCDF	1000.
1,2,3,4,7,8,9-HpCDF	1000.

(2). One labeled internal standard must be used for each level of chlorinated dioxin and each level of chlorinated dibenzofuran. Thus, a minimum of 8 internal standards are required. Each should be present at or below the LOQ of the respective target analyte. Note that this requires lowering the ¹³C₁₂-2,3,7,8-TCDD concentration level from 1 ng/g to 0.1 ng/g.

(3). Several terms in the sample preparation process must be defined, namely, "IFB" and "Option D2."

(4). A procedure must be adopted to separate the dioxins and/or dibenzofurans from the chlorothalonil.

(5). The internal standard and cleanup recovery standard recoveries must be $\geq 50\%$, not 40%. The registrant may use the proposed 110% upper limit or adopt the less stringent $\leq 150\%$.

(6). The recoveries of the internal standards and the analytes in a sample and its duplicate must have RPD's $\leq 20\%$, not the proposed 50%.

(7). For qualitative identification (limit of detection), the signal-to-noise ratio must be $\geq 3:1$, not the proposed 2.5 : 1.

(8). For calibration standards, the signal-to-noise ratio for each monitored ion of each analyte at or above the EPA LOQ concentration must be $\geq 10 : 1$, not the proposed 5 : 1. The same ratio applies to all internal standards in all calibrations, quality controls, and samples.

(9). Retention time (or relative retention time) criteria must be

developed for those target analytes not having a labeled analog. For example, $\pm 1\%$ of the retention time of the analyte in the continuing standard might be proposed.

(10). For deliverables, summary tables of retention times and ion areas must be provided for each sample, standard, and control. All raw data needed to verify results should be included.

The registrant is advised to validate the complete final analytical method before the analysis of actual sample lots of chlorothalonil. Four or more samples of the technical product should be spiked with the target analytes (at or below the EPA LOQ) and analyzed. Precision and accuracy should be established. The registrant may want to consider the use of control charts for monitoring internal standard recoveries.

A detailed analytical methodology is required with the final report.

Recommendation

ISK Biotech Corporation is advised to collect and to analyze seven samples from each production line (14 samples total) for polychlorinated dibenzo-p-dioxins and dibenzofurans after incorporating the methodology changes noted above (Conclusions, nos. 1 - 10). The registrant need not submit revised protocols before proceeding with sample collections and analyses. The revised protocols may be submitted with the final report. The registrant is advised that failure to follow the requirements of the 06/87 dioxin DCI and the Guidelines for the Analysis of Polyhalogenated Dibenzo-p-Dioxins and Dibenzofurans in Commercial Products may result in a requirement to resample and to reanalyze. The registrant should submit revised protocols or contact CBRS if there are unresolved questions or concerns.

cc: RF, Dioxin SF, Chlorothalonil Reg. Standard File, Circ., S. Funk, C. Furlow (PIB, FOD).

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