

US EPA ARCHIVE DOCUMENT

(10-12-94)

**MEMORANDUM**

**SUBJECT:** Chlorpropham. Response to August 22, 1994 Task Force Inquiry re:  
Independent Laboratory Validation of Analytical Methodology in Potatoes.  
DP Barcode: D207719; CBRS No. 14403; No MRID No.; Case No. 0271

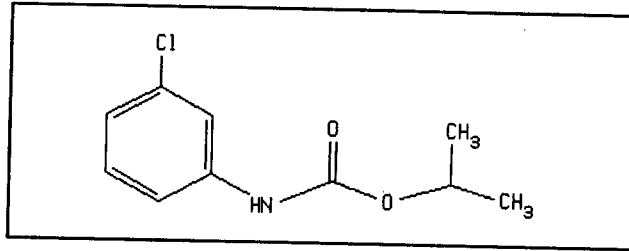
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**THRU:** Francis B. Suhre, Section Head  
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**TO:** Margery Exton, PM Team 71  
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CBRS has been requested to review the Chlorpropham Task Force's 8/22/94 response to a CBRS review of an independent laboratory validation of the analytical method used by the registrant to detect chlorpropham in potatoes. Chlorpropham is a fumigant registered for use on potatoes. Tolerances have been established for residues of chlorpropham in 40 CFR 180.181 in or on potatoes at 50 ppm.

The structure of chlorpropham is presented below.



The registrant previously submitted an independent laboratory validation for the determination of chlorpropham in whole potatoes. No data were provided for the 3-chloroaniline (3-CA) metabolite. This material (MRID 3160101) was reviewed in a previous CBRS memorandum (D. Miller, CBRS No. 13438, 6/8/94) and the registrant, in its current submission is responding to the deficiencies cited in the original review.

#### CONCLUSIONS:

- 1) CBRS previously determined that the submitted method instructed that fortification was to occur following initial extraction with methanol, and required that the method instructions be revised to require that it be the raw agricultural commodity (or a macerate thereof) which is fortified instead. The Task Force has modified the proposed regulatory enforcement method such that spiking occurs following thawing and immediately prior to extraction. CBRS now finds that the method has been appropriately modified with respect to this concern and that Conclusion 1 in the CBRS review dated 6/8/94 (CBRS No. 13438) is satisfied.
- 2) CBRS previously determined that the submitted method instructed that a potato matrix calibration standard be used, and required that the method be rewritten so as not to require the use of a matrix calibration standard. The Task Force has modified the regulatory method such that potato calibration standards are not necessary and calibration standards instead now use *n*-hexane. CBRS finds that the method has been appropriately modified with respect to this concern and that Conclusion 2 in the CBRS review dated 6/8/94 (CBRS No. 13438) is satisfied.
- 3) CBRS previously requested that the registrant supply additional chromatograms for all spiking levels, including the claimed limit of quantitation so that the reported limits of detection and quantitation could be

assessed. With the present submission, additional chromatograms were supplied which provide evidence for detection/quantitation at 4 ng column loadings (equivalent to ca. 0.3 µg chlorpropham/g tissue). The registrant also supplied acceptable chromatograms supporting both the controls and the spike recoveries. CBRS finds that the additional submitted chromatograms satisfy CBRS concerns, and that Conclusion 3 in the CBRS review dated 6/8/94 (CBRS No. 13438) is satisfied.

- 4) CBRS has previously indicated that the performing laboratory was unable to obtain a linear response with the injected standards, with both the hexane and potato matrix calibration curves demonstrating a change in slope at the 40 ng level. The registrant in the current submission maintains that the injected standards did not deviate from linearity, and reported that both the hexane and potato matrix calibration curves had high correlation coefficients. CBRS will permit the submitted method to pass to EPA-Beltsville for Method Try-out.
- 5) The submitted ILV only attempted to determine residue levels in whole potatoes, and not additional processed commodities such as french fries, potato chips, dehydrated granules, and potato peels (although instructions for analysis of these commodities are included in the method)<sup>1</sup>. CBRS will request that Beltsville's Method Try-out include french fries and dehydrated granules.
- 6) The method contains instructions for determination of residues in canola oil. Any instructions referring to determination of chlorpropham/3-CA residues in canola oil should be deleted.
- 7) The submitted studies only attempted to determine chlorpropham levels, although the method is described as determining both chlorpropham and 3-chloroaniline. At this time, CBRS has not determined if 3-chloroaniline metabolite will be regulated. If this latter metabolite is regulated as part of the tolerance expression in the future, CBRS will require additional method validations for 3-CA, and the method will likely require hydrolysis reactions in order to liberate bound residues. The registrant should remove all references from the method which refer to determination of 3-CA residues.

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<sup>1</sup> CBRS does note that the original method trial did examine recoveries from the various processed potato commodities, and the CBRS review at that time (J. Abbotts, CBRS Nos. 11217, 11422, 11428) concluded that "recoveries by the analytical method of parent chlorpropham residues from fortified samples of potato commodities were acceptable".

**RECOMMENDATION:**

CBRS concludes that the analytical method entitled "Analytical Method for Magnitude of Residues in Stored Potatoes from Post-harvest Treatments of Chlorpropham" dated August 11, 1994 has been adequately described and had undergone successful independent validation with respect to determination of chlorpropham *per se* in raw tubers. CBRS will forward the submitted method to EPA Beltsville for a method try-out.

## DETAILED ANALYSIS

The Chlorpropham Task Force has submitted a revised analytical method for chlorpropham incorporating the changes recommended earlier by CBRS in its 6/8/94 review of the independent laboratory validation data (D. Miller, CBRS No. 13438). The newly submitted method is entitled "Analytical Method for Magnitude of Residues in Stored Potatoes from Postharvest Treatments of Chlorpropham," and has an effective date of August 11, 1994. With this new submission, the Task Force has responded to the following CBRS concerns expressed in the 6/8/94 review:

- 1) For this independent laboratory validation, fortification occurred following initial extraction with methanol. CBRS requires that the method instruction be revised such that the raw agricultural commodity, or a macerate thereof, be fortified rather than the crop extracts.
- 2) The CIPC Task Force method requires potato matrix calibration standards (i.e., requires fortification of blank potato matrix in order to develop a whole potato matrix calibration curve). The method should be rewritten so as not to require the use of a potato matrix calibration standard.
- 3) The registrant provided only two chromatograms in the submitted report. No additional chromatograms were provided for the calibration standards nor were any chromatograms provided for the four potato matrix CIPC spike recovery tests. Chromatograms should be submitted for all spiking levels, including the claimed limit of quantitation. There is a need for more control and method blank chromatograms so that the reported limits of detection and quantitation can be assessed.
- 4) The laboratory was unable to obtain a linear response with the injected standards, with both the hexane and potato matrix calibration curves demonstrating a change in slope at the 40 ng level. Given that the N-P detector is a linear response detector and that the method when originally performed (MRID 42653401) was demonstrated to be linear over the same tested range, the registrant is required to better characterize the reasons for deviation from linearity.

CBRS response to the Task Force to each of the points raised by the Task Force submission is presented below:

CBRS Concern #1: *Fortification occurred following initial extraction with methanol. The laboratory should insure that it is the raw agricultural commodity that is spiked and not an extracted solution.*

Registrants Response: The Task Force has modified the regulatory method such that spiking occurs following thawing and immediately prior to dichloromethane extraction.

CBRS Comments: CBRS finds that the method has been appropriately modified with respect to this concern.

CBRS Concern #2: *The CIPC Task Force method requires potato matrix calibration standards. The method should be rewritten so as not to require the use of a potato matrix calibration standard.*

Registrants Response: The Task Force has modified the regulatory method such that potato calibration standards are not necessary and calibration standards instead now use *n*-hexane calibration standards.

CBRS Comments: CBRS finds that the method has been appropriately modified with respect to this concern.

CBRS Concern #3: *The registrant provided only two chromatograms in the submitted report. There is a need for more control and method blank chromatograms so that the reported limits of detection and quantitation can be assessed.*

Registrants Response: The Task Force has provided an additional 20 chromatograms.

CBRS Comments: The registrant originally supplied only chromatograms for a 10 ng hexane and a 10 ng whole potato matrix calibration standard. With the present submission, additional chromatograms were supplied which provide evidence for detection/quantitation at 4 ng column loadings (equivalent to ca. 0.3 µg chlorpropham/g tissue). The registrant also supplied acceptable chromatograms supporting both the controls and the spike recoveries. CBRS finds that the additional submitted chromatograms satisfy CBRS concerns.

CBRS Concern #4: *The laboratory was unable to obtain a linear response from the injected standards.*

**Registrants Response:** The registrant maintains that the injected standards did not deviate from linearity, and defined a linear response as anything with a correlation coefficient of  $> 0.9$ . They reported that both the hexane and potato matrix calibration curves had correlation coefficients greater than or equal to 0.986. They state that in order to minimize quantitation errors and increase accuracy of the assay, the results were calculated using two curves based on the change in slope at the 40 -ng to 50- ng level, and that there are ample precedents for "curve splitting", even for presumably linear curves, especially when the curve encompasses two orders of magnitude.

**CBRS Comments:** CBRS will permit the submitted method to pass to EPA-Beltsville for Method Try-out. If Beltsville determines that such curve-splitting is acceptable and achieves adequate recoveries (i.e., 70% to 120%), then the method will be judged acceptable. The registrant is reminded, however, that if Beltsville determines that curve-splitting is inappropriate, then it is likely that the tight recovery ranges (91.4% to 107% with an average 98.7% recovery) calculated by the registrant in the ILV will be considerably broadened, and this may impact CBRS judgement on the acceptability of the method.

Additionally, CBRS makes the following comments regarding the submitted method:

- The submitted studies only attempted to determine chlorpropham levels, although the method is described as determining both chlorpropham and 3-chloroaniline. The registrant should remove all references from the method which refer to determination of 3-CA residues.
- The submitted ILV only attempted to determine residue levels in whole potatoes, and not additional processed commodities such as french fries, potato chips, dehydrated granules, and potato peels. CBRS will request that Beltsville's Method Try-out include french fries and dehydrated granules. If Beltsville is unable to perform method try-outs with these commodities, CBRS may require that the registrant perform additional method validations for these commodities.



- The method contains instructions for determination of residues in canola oil. Any instructions referring to determination of chlorpropham/3-CA residues in canola oil should be deleted.

cc: RF, SF, List A File, Circ., DJM.  
RDI: FSuhre:10/7/94; MMetzger:10/10/94; EZager:10/11/94.