(2-8-93)

MEMORANDUM

SUBJECT: DSMA Reregistration: a List B Chemical
(Chemical No.: 013802; Case No. 2395).
Registrants Response to the DSMA Product Chemistry Data Requirements.
(MRID # 423883-01, 423883-02, 423610-01, and 42120701)
CBRS # 9143, 10156, and 10216; DP BARCODE: D172598, D180025, D180715)

FROM: Freshteh Toghrol, Ph.D., Chemist
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Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

THRU: William J. Hazel, Ph.D., Section Head
Reregistration Section II
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To: Lois Rossi, Chief/B. Briscoe, PM 51
Reregistration Branch
Special Review and Reregistration Division (H7508W)

Attached is a review of the 81% DSMA T product chemistry data submitted by Luxembourg-Pamol, APC Holdings, Isk-Biotech, and MAA Research Task Force Three in response to the DSMA Phase 4 Review (dated 3/28/91). These data were reviewed by Dynamac Corporation under the supervision of Chemistry Branch II: Reregistration

Support, Health Effects Division (CBRS, HED).

This Dynamac review has undergone secondary review in CBRS and has been revised to reflect the Branch policies.

Summary of Conclusions:

The 81% DSMA T product chemistry data gaps regarding the physical and chemical characteristic vapor pressure (Guideline # 63-9), and preliminary analysis (62-1) are resolved. Additional data are required for description of starting materials and manufacturing process (Guideline 61-2), Discussion of formation of impurities (Guideline 61-3), and the analytical method (Guideline # 62-3). The chemical structure of DSMA is given below.

Attachment: DSMA: Registrants Response to Product Chemistry Data Requirement.

cc: DSMA S.F., R.F., F. Toghrol, List B File, Dynamac.

RDI: W. Hazel (2/3/93): M. Metzger (2/8/93): E. Zager (2/8/93)

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H7509C:CBRS:F.Toghrol:F.T.:RM:804B:CM#2:(703)305-7887:10/20/92.

DSMA

Shaughnessy No. 013802; Case 2395

(CBRS No. 9143; DP Barcode D172598)

(CBRS No. 10156; DP Barcode D180025)

(CBRS No. 10216; DP Barcode D180715)

Task 4

PHASE V - PRODUCT CHEMISTRY REREGISTRATION REVIEW

BACKGROUND

In response to the Methanearsonic Acid and Salts Phase IV Review by C. L. Olinger (dated 3/28/91) and a CBRS review by S. Funk (CBRS No. 8916, dated 1/13/92), the MAA Task Force Three and two of its members, Luxembourg-Pamol, Inc., and APC Holdings, Inc., have submitted the corresponding product chemistry data for the disodium methanearsonate (DSMA) end-use products (EPs) and formulation intermediates (FI) listed below in Table 1. The MAA Task Force Three members are Luxembourg-Pamol, APC Holdings, and ISK-Biotech Corp. (formerly Fermenta ASC Corp.).

Table 1. The registrants, their products, and corresponding MRID submissions.

Registrant Product	EPA Reg. No.	CBRS No.	MRID(s) submitted
Luxembourg-Pamol:			
81% EP	42519-7	10216	42388301, 42388302
APC Holdings:			
81% EP	63239-4	10156	42361001
37% EP	62329-14	10156	42361001

Registrant Product	EPA Reg. No.	CBRS No.	MRID(s) submitted
ISK-Biotech:			
81% FI	50534-39		
MAA Research Task Force Three:			
Luxembourg, APC Holdings, ISK-Biotech	products listed above	9143	42120701

Neither Luxembourg-Pamol nor APC-Holdings has registered DSMA manufacturing-use products. Data submitted for the TGAIs of the products listed in Table 1 are reviewed in this document.

Note To PM:

We note that the submission for APC Holdings (MRID 42361001) included data for the 21.83% EP (EPA Reg. No. 62329-3) which was canceled 9/30/91.

61-1. Product Identity and Disclosure of Ingredients

Data pertaining to this guideline are not required for the TGAI. However, Luxembourg-Pamol (MRID 1992; 42388301) and APC Holdings (MRID 1992; 42361001) have submitted Confidential Statements of Formula (CSFs) for their DSMA EPs listed in Table 1. These data are presented in the Confidential Appendix for informational purposes only.

61-2. Description of Starting Materials and Manufacturing Process

The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 required additional information pertaining to the starting materials and manufacturing process for the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7). Specific information was required pertaining to the relative amounts of the starting materials, and the reaction conditions associated with each step in the process. In addition a CBRS memo by S. Funk (CBRS No. 8916, dated 1/13/92) required additional information pertaining to the starting materials and manufacturing processes for the TGAI of the 81% and 37% EPs (EPA Reg. Nos. 63239-4 and 63239-14, respectively). Specific information was required pertaining to the chemical equations, durations, and the reaction conditions associated with each step of the process. Funk noted that information pertaining to the starting materials was to be submitted under 61-2 instead of on the CSF.

In response, Luxembourg-Pamol and APC Holdings have submitted (1992; MRID 42388301) information concerning the manufacturing process for the TGAI of the 81% EP (EPA Reg. No. 42519-7) and (1992; MRID 42361001) information concerning the manufacturing process for the TGAI of the 81% and 37% EPs. This information is presented in the Confidential Appendix.

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This information does not satisfy the requirements of 40 CFR §158.160 and §158.162 (Guideline Reference No. 61-2) regarding the starting materials and production process of the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7) and APC Holdings 81% and 37% EPs (EPA Reg. Nos. 63239-4 and 63239-14, respectively) because the specifications and material safety data sheets for the starting materials were not included. Additional information is required.

61-3. Discussion of Formation of Impurities

The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 requires additional information pertaining to the discussion of formation of impurities for the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7). In response, Luxembourg-Pamol has submitted (1992; MRID 42388301) a discussion of impurities formed during the production of the TGAI. These data are presented in the Confidential Appendix.

These data do not satisfy the requirements of 40 CFR §158.167 (Guideline Reference No. 61-3) regarding discussion of formation of impurities in the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7) because the registrant did not submit discussions pertaining to the possible formation of impurities resulting from: (i) the composition of each starting material and its impurities; and (ii) the side reactions which may occur. Additional data are required.

62-1. Preliminary Analysis

The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 requires information pertaining to the preliminary analysis of the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7). In response, Luxembourg-Pamol has provided (1992; MRID 42388302) preliminary analysis data for five samples of the 81% EP. These data are presented in the Confidential Appendix.

These data satisfy the requirements of 40 CFR §158.170 (Guideline Reference No. 62-1) regarding preliminary analysis for the TGAI of the Luxembourg-Pamol 81% EP (EPA Reg. No. 42519-7). No additional data are required.

62-2. Certification of Limits

Although data concerning the certified limits of the TGAI of the DSMA products are not required, Luxembourg-Pamol (MRID 1992; 42388301) and APC Holdings (MRID 1992; 42361001) have submitted CSFs for their DSMA EPs listed in Table 1. Data pertaining to this guideline are not required for the TGAI. These data are presented in the Confidential Appendix for informational purposes only.

Note To PM:

We note that, based on the preliminary analysis data submitted by Luxembourg-Pamol, the upper limit submitted for one impurity (on the CSF) appears to reflect a typographical error.

62-3. Enforcement Analytical Methods

This is not a generic data requirement (i.e., using TGAI as test substance). However, a CBRS review by S. Funk (Meeting with Registrants of Cacodylic Acid, MSMA, and DSMA, dated 12/10/91) concludes that theoretical discussion of the submitted analytical methods for DSMA and MSMA are not required because the titration methods used for the determination of DSMA are defined standard procedures. **No Additional data are required. We do, however, recommend that SRRD obtain concurrence by RD/RSB since these methods will be used to enforce limits in registered products.**

PHYSICAL AND CHEMICAL CHARACTERISTICS

The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 requires information pertaining to the physicochemical properties of DSMA products. An Agency Memorandum (S. Funk; Meeting with Registrants of Cacodylic Acid, MSMA, and DSMA, dated 12/10/91) concluded that an isolated active ingredient must be used for the determination of the physical/chemical properties of the TGAI, and that DSMA can be isolated as the hexahydrate.

In response, the MAA Task Force Three has submitted (1991; MRID 42120701) information pertaining to the vapor pressure of the DSMA purified active ingredient (PAI). Using a gas-saturation method, the vapor pressure of DSMA (99.0% purity) was determined to be less than 1×10^{-7} mm Hg at 25 C.

The submitted data satisfy the requirements of 40 CFR §158.190 (Guideline Reference No. 63-9) concerning the vapor pressure for the Luxembourg-Pamol, APC Holdings, and ISK-Biotech DSMA products listed in Table 1. The outstanding physicochemical data

requirements are identified in the product chemistry data summary tables that follow.

MASTER RECORD IDENTIFICATION NUMBERS

References (used):

42388301 Bellet, E. M. (1992) DSMA 81 P: Product Identity and Composition. Unpublished compilation. 9 p.

42388302 Bellet, E. M. (1992) DSMA 81 P: Product Identity and Composition. Unpublished compilation. 10 p.

42361001 Haefele, Louis R. (1992) Supplement to Product Chemistry. DSMA Products. Unpublished compilation. 13 p.

42120701 Pesselman, Robert L. (1991) Vapor Pressure Determination of DSMA. Unpublished Study prepared by MAA Research Task Force Three. 36 p.

Case No. 2395
Chemical No. 013802

Case Name: DSMA
Registrant: Luxembourg-Pamol, Inc.
Product(s): TGAI of the 81% EP (EPA Reg. No. 42519-7)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N/A[b]	
61-2	Beginning Materials and Manufacturing Process	N[c]	42388301
61-3	Discussion of Formation of Impurities	N[d]	42388301
62-1	Preliminary Analysis	Y	42388302
62-2	Certification of Ingredient Limits	N/A[b]	
62-3	Analytical Methods to Verify the Certified Limits	N/A[e]	
63-2	Color	Y[f]	
63-3	Physical State	Y[f]	
63-4	Odor	Y[f]	
63-5	Melting Point	Y[g]	
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	Y[h]	
63-9	Vapor Pressure	Y	42120701
63-10	Dissociation Constant	Y[g]	
63-11	Octanol/Water Partition Coefficient	Y[g]	
63-12	pH	Y[i]	
63-13	Stability	N[j]	

[a] Y = Yes; N = No; N/A = Not Applicable. Data were submitted in response to The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91. Data requirements followed by MRID citations reflect conclusions determined in this document (CBRS Nos. 9143, 10156, and 10216).

[b] Data concerning this guideline are not required for the TGAI. We note that, based on the preliminary analysis data, the upper limit submitted for one impurity appears to reflect a typographical error.

[c] The registrant must submit the manufacturers, specifications, and material safety data sheets for the starting materials.

[d] The registrant must submit a discussion pertaining to the possible formation of impurities resulting from: (i) the composition of each starting material and its impurities; and (ii) the side reactions which may occur.

[e] Not required for the TGAI because this is a product specific requirement. However, a CBRS review by S. Funk (Meeting with Registrants of Cacodylic Acid, MSMA, and DSMA, dated 12/10/91) concludes that a theoretical discussion of the submitted analytical methods for DSMA and MSMA are not required because the titration methods used for the determination of DSMA are defined standard procedures. Concurrence

by RD/RSB is recommended since these methods will be used to enforce limits in registered products.

[f] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602501 is a candidate for Phase V review in fulfilling data requirements.

[g] CBRS No. 8810, S. Funk, dated 1/13/92.

[h] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602502 is a candidate for Phase V review in fulfilling data requirements.

[i] CBRS No. 8473, F. Toghrol, dated 7/6/92.

[j] CBRS No. 8526, F. Toghrol, dated 7/6/92 required that the registrant submit data for the stability of DSMA to metals and metal ions which were determined analytically rather than visually.

Case No. 2395
Chemical No. 013802

Case Name: DSMA
Registrant: APC Holdings, Inc
Product(s): TGAI of the 81% and 37% EPs (EPA Reg. Nos. 63239-4 and 63239-14, respectively)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Requirement Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N/A[b]	
61-2	Beginning Materials and Manufacturing Process	N[c]	42361001
61-3	Discussion of Formation of Impurities	Y[d]	
62-1	Preliminary Analysis	Y[e]	
62-2	Certification of Ingredient Limits	N/A[b]	
62-3	Analytical Methods to Verify the Certified Limits	N/A[f]	
63-2	Color	Y [g]	
63-3	Physical State	Y[g]	
63-4	Odor	Y[g]	
63-5	Melting Point	N	
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	Y[h]	
63-9	Vapor Pressure	Y	42120701
63-10	Dissociation Constant	N	
63-11	Octanol/Water Partition Coefficient	N	
63-12	pH	N	
63-13	Stability	N	

[a] Y = Yes; N = No; N/A = Not Applicable. Data were submitted in response to The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 and an Agency Memorandum (S. Funk; CBRS No. 8916, dated 1/13/92). Data requirements followed by MRID citations reflect conclusions determined in this document (CBRS Nos. 9143, 10156, and 10216).

[b] Data concerning this guideline are not required for the TGAI.

[c] The registrant must submit the specifications and material safety data sheets for the starting materials.

[d] CBRS No. 8916, S. Funk, dated 3/11/92.

[e] CBRS No. 8916, S. Funk, dated 1/13/92.

[f] Not required for the TGAI because this is a product specific requirement. However, a CBRS review by S. Funk (Meeting with Registrants of Cacodylic Acid, MSMA, and DSMA, dated 12/10/91) concludes that a theoretical discussion of the submitted analytical methods for DSMA and MSMA are not required because the titration methods used for the determination of DSMA are defined standard procedures. Concurrence

by RD/RSB is recommended since these methods will be used to enforce limits in registered products.

[g] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602501 is a candidate for Phase V review in fulfilling data requirements.

[h] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602502 is a candidate for Phase V review in fulfilling data requirements.

Case No. 2395
Chemical No. 013802

Case Name: DSMA
Registrant: ISK-Biotech Corporation
Product(s): TGAI of the 81% FI (EPA Reg. No. 63239-14)

PRODUCT CHEMISTRY DATA SUMMARY

Guideline Number	Requirement	Requirement Fulfilled? [a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N/A[b]	
61-2	Beginning Materials and Manufacturing Process	N[c]	
61-3	Discussion of Formation of Impurities	N[c]	
62-1	Preliminary Analysis	N[c]	
62-2	Certification of Ingredient Limits	N/A[b]	
62-3	Analytical Methods to Verify the Certified Limits	N/A[d]	
63-2	Color	Y[e]	
63-3	Physical State	Y[e]	
63-4	Odor	Y[e]	
63-5	Melting Point	N	
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	N	
63-8	Solubility	Y[f]	
63-9	Vapor Pressure	Y	42120701
63-10	Dissociation Constant	N[c]	
63-11	Octanol/Water Partition Coefficient	N[c]	
63-12	pH	N[c]	
63-13	Stability	N[c]	

[a] Y = Yes; N = No; N/A = Not Applicable. Data were submitted in response to The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91. Data requirements followed by MRID citations reflect conclusions determined in this document (CBRS Nos. 9143, 10156, and 10216).

[b] Data concerning this guideline are not required for the TGAI.

[c] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 indicates that the registrant has committed to conduct the study.

[d] Not required for the TGAI because this is a product specific requirement. However, a CBRS review by S. Funk (Meeting with Registrants of Cacodylic Acid, MSMA, and DSMA, dated 12/10/91) concludes that a theoretical discussion of the submitted analytical methods for DSMA and MSMA are not required because the titration methods used for the determination of DSMA are defined standard procedures. Concurrence by RD/RSB is recommended since these methods will be used to enforce limits in registered products.

[e] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602501 is a candidate for Phase V review in fulfilling data requirements.

[f] The Methanearsonic Acid and Salts Phase IV Review dated 3/28/91 determined that MRID 41602502 is a candidate for Phase V review in fulfilling data requirements.