



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCESOPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361MEMORANDUM**Date:** June 11, 2002**Subject:** **PP# 1F6312. Sulfuryl Fluoride in/on Cereal Grain Commodities.
Request for Tolerance Method Validation.**DP Barcode: **D282407**PC Code: **078003**

MRID#s: 45603901, 45632901, 45632902.

To: Francis D. Griffith, Jr., Chief
ACL/BEAD (7503C)**From:** Michael Doherty, Chemist
RAB2/HED (7509C)

Thru: Richard Loranger, Branch Senior Scientist
RAB2/HED (7509C)

Introduction

Dow AgroSciences has submitted a petition (PP#1F6312) for the establishment of permanent tolerances for residues of sulfuryl fluoride and fluoride anion in/on cereal grain commodities resulting from the post-harvest fumigation of stored grains and grain mills with sulfuryl fluoride. The proposed tolerances, as listed in Federal Register, are provided in Table 1.

Commodity	Proposed Tolerance, ppm	
	Sulfuryl Fluoride	Fluoride Anion
Barley, grain	0.01	10
Corn, field, grain	0.04	7
Corn, pop, grain	0.04	7

Commodity	Proposed Tolerance, ppm	
	Oat, grain	0.01
Rice, grain	0.04	10
Sorghum, grain	0.05	25
Triticale, grain	0.05	25
Millet, grain	0.05	25
Rice, wild, grain	0.05	10
Wheat, grain	0.05	25
Corn, field, flour	0.01	26
Corn, field, grits	0.01	10
Corn, field, meal	0.01	28
Corn, field, refined oil	9.0	3
Rice, brown	0.01	14
Rice, polished	0.01	18
Rice, bran	0.01	31
Rice, hulls	0.08	35
Wheat, bran	0.01	40
Wheat, flour	0.03	10
Wheat, milled by products	0.01	35
Wheat, germ	0.01	98
Wheat, shorts	0.01	38

Method for Sulfuryl Fluoride

The proposed enforcement method for the analysis of sulfuryl fluoride in/on cereal grain commodities is contained in Appendix A of the following volume, which is appended to this memorandum as Attachment 3:

MRID# 45632902 Davis, B. (2002): "Independent Laboratory Validation of Dow AgroSciences LLC Method 'Determination of Residues of Sulfuryl Fluoride in Corn, Wheat and Rice Commodities by Gas Chromatography with Electron Capture Detection,' as included in Lab Report code: 011057, Appendix B, 'Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride'". Unpublished study conducted by Minnesota Valley Testing Laboratories, Inc. and submitted by Global Environmental Chemistry Laboratory-Indianapolis Lab. 72 pages.

Quantitation of sulfuryl fluoride is performed by headspace gas chromatography with electron capture detection (GC/ECD). HED has reviewed the submitted method; the DER is appended to this memorandum as Attachment 6. HED has some concerns about the appropriateness of the fortification procedure used to validate the method.

Method for Fluoride Anion

The proposed enforcement method for the analysis of fluoride anion in/on cereal grain commodities is contained in Appendix A of the following volumes, which are appended to this memorandum as Attachments 4 and 5:

MRID# 45603901. Davis, B. (02/07/02) Independent Laboratory Validation of Dow AgroSciences LLC Method "Residue Method Validation for the Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour," as included in Lab Report Code 011057, Appendix A, "Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride." Lab Project Number: 010115. Unpublished study prepared by Dow AgroSciences LLC. 63 pages.

MRID# 45632901. Lala, M and Randolph, R (03/12/02) Independent Laboratory Validation for Corn Oil and Raisins using Dow AgroSciences Method GRM 01.17-Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour. Lab Project Number: 1404. Unpublished study prepared by Dow AgroSciences LLC. 65 pages.

Fluoride detection is accomplished using a fluoride-selective ion electrode. Quantification of residues are done using a double known addition technique. HED has reviewed the submitted method; the DER is appended to this memorandum as Attachment 7. HED has some concerns about the appropriateness of the fortification procedure used for corn oil to validate the method.

TMV Trials to be Conducted

Sulfuryl Fluoride. RAB2 requests that BEAD conduct TMV trials of the proposed enforcement methods for the analysis of sulfuryl fluoride in/on cereal grain commodities.

Fluoride Anion. RAB2 requests that BEAD conduct a TMV trial of the proposed enforcement method for the analysis of fluoride anion in/on cereal grain commodities.

General Comments

The TMV trials should be conducted per the experimental designs specified in Attachments 1 and 2. All samples should be run in duplicate. The LOQs should be determined and the LODs should be estimated. Please complete and return Attachments 1 and 2 as part of your report. Also, please include in your report all relevant information and supporting documentation concerning the method validations, including length of time necessary to complete a set of samples, and modifications which were made, and indicate the suitability of the analytical methods for enforcement purposes.

Since one of the purposes of conducting in-house TMVs is to determine whether all necessary instructions are included in the submitted proposed enforcement method(s), your laboratory staff scientists should have minimal contact with the petitioner and the ILV performing laboratories during the conduct of these trials. Any problems encountered in the methods as written should be documented and included in your report. The petitioner will be informed of any deficiencies in the method and asked to resolve them.

The Registration Division Product Manager for this chemical is Dennis McNeilly. Please contact him (703-308-6742) if you require guidance concerning the priority for initiation/completion of these TMV trials.

Please address and send your report (both paper and electronic copy) to Michael Doherty, Chemist, RAB2/HED, 7509C. If you need any further information from me, please e:mail or telephone (703-305-1031).

The following DB Barcode (Attachment 8) has been assigned to ACL/BEAD for your report: D282408. [Note: If a separate barcode is needed for each method to be tested, please advise.]

Attachments

1. Reporting form for Agency Tolerance Method Validation for Residues of Sulfuryl Fluoride in/on cereal grains.
2. Reporting form for Agency Tolerance Method Validation for Residues of Fluoride Anion in/on cereal grains.
3. MRID# 45632902. Independent Laboratory Validation of Dow AgroSciences LLC Method "Determination of Residues of Sulfuryl Fluoride in Corn, Wheat and Rice Commodities by Gas Chromatography with Electron Capture Detection," as included in Lab Report code: 011057, Appendix B, "Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride."
4. MRID# 45603901. Independent Laboratory Validation of Dow AgroSciences LLC Method "Residue Method Validation for the Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour," as included in Lab Report Code 011057, Appendix A, "Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride."
5. MRID# 45632901. Lala, M and Randolph, R (03/12/02) Independent Laboratory Validation for Corn Oil and Raisins using Dow AgroSciences Method GRM 01.17-Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour.
6. DER for MRID# 45632902.

7. DER for MRID#s 45603901 and 45632901.
8. Bean sheet D282408 for use by BEAD in reporting the PMV trials results.

Distribution

cc (with Attachments 1 and 2 only): M. Doherty, RAB2 Reading File, M. Clower (Division of Pesticides and Industrial Chemicals, HFS-335, FDA).

Attachment 1

METHOD: MRID# 45632902 (Appendix A). Determination of Residues of Sulfuryl Fluoride in Corn, Wheat and Rice Commodities by Gas Chromatography with Electron Capture Detection.

Please: (i) Run samples in duplicate; (ii) Indicate the limit of detection and quantitation; (iii) Do not use control values for recovery calculations; and (iv) Do not report control values as zero; if less than the limit of detection, report as such.

Commodity	Chemical Added	ppm Added	ppm Found		Percent Recovery	
Wheat Grain	Sulfuryl Fluoride	0.00				
		0.01				
		0.10*				
Rice Grain	Sulfuryl Fluoride	0.00				
		0.01				
		0.05				
		3.0*				
Corn Oil	Sulfuryl Fluoride	0.00				
		0.01				
		1.0				
		9.0*				
Rice Hulls	Sulfuryl Fluoride	0.00				
		0.01				
		0.08*				

* Tolerance level.

Modifications to Method (Major or Minor):

Special Precautions to be Taken:

Source of Analytical Standards:

If Derivatized Standard Used, Give Source:

Instrumentation for Quantitation:

Instrumentation for Confirmation:

If Instrumentation Parameters Differ from Given in Method, List Parameters Used:

Commercial Source for any Special Chemicals or Apparatus:

Comments:

Attachment 2

METHOD: MRID# 45603901 (Appendix A). Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour.

Please: (i) **Run samples in duplicate**; (ii) Indicate the limit of detection and quantitation; (iii) Do not use control values for recovery calculations; and (iv) Do not report control values as zero; if less than the limit of detection, report as such.

Commodity	Chemical Added	ppm Added	ppm Found		Percent Recovery	
Wheat Grain	Fluoride	0.00				
		2				
		10				
		25*				
Wheat Germ	Fluoride	0.00				
		2				
		50				
		98*				
Whole Wheat Flour	Fluoride	0.00				
		2				
		40				
		85*				
Corn Oil	Fluoride	0.00				
		2				
		3*				

* Tolerance level.

Modifications to Method (Major or Minor):

Special Precautions to be Taken:

Source of Analytical Standards:

If Derivatized Standard Used, Give Source:

Instrumentation for Quantitation:

Instrumentation for Confirmation:

If Instrumentation Parameters Differ from Given in Method, List Parameters Used:

Commercial Source for any Special Chemicals or Apparatus:

Comments:

Attachments 3-7: See separate volumes.

Attachment 8

DP BARCODE: D282408

CASE: 294172 DATA PACKAGE RECORD DATE: 05/13/02
 SUBMISSION: S597868 BEAN SHEET Page 1 of 1

*** CASE/SUBMISSION INFORMATION ***

CASE TYPE: TOLERANCE PET ACTION: 230 F PET RAW AGRI COMMO
 RANKING : 30 POINTS ()
 CHEMICALS: 078003 Sulfuryl fluoride %

ID#: 1F06312
 COMPANY: DOW AGROSCIENCES LLC
 PRODUCT MANAGER: 21 MARY WALLER 703-308-9354 ROOM: CM2 249
 PM TEAM REVIEWER: DENNIS MCNEILLY 703-308-6742 ROOM: CM2 211
 RECEIVED DATE: 05/01/01 DUE OUT DATE: 12/27/01

*** DATA PACKAGE INFORMATION ***

DP BARCODE: 282408 EXPEDITE: N DATE SENT: 04/16/02 DATE RET.: / /
 CHEMICAL: 078003 Sulfuryl fluoride
 DP TYPE: 999

	CSF: N		LABEL: N		
ASSIGNED TO	DATE	IN	DATE	OUT	ADMIN DUE DATE: / /
DIV : BEAD	/	/	/	/	NEGOT DATE: / /
BRAN: ACL	/	/	/	/	PROJ DATE: / /
SECT: IO	/	/	/	/	
REVR :	/	/	/	/	
CONTR:	/	/	/	/	

*** DATA REVIEW INSTRUCTIONS ***

Please conduct a tolerance method validation for sulfuryl fluoride and fluoride anion.

*** DATA PACKAGE EVALUATION ***

No evaluation is written for this data package

*** ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION ***

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
275199	RAB2	05/29/01	05/29/02	Y	Y	Y
282407	RAB2/IO	04/16/02	/ /	Y	N	N
282007	RAB2	04/01/02	09/08/02	Y	N	N

ATTACHMENT 6Sulfuryl Fluoride
Cereal GrainsResidue Analytical Method
OPPTS 860.1340PC Code: 078003
MRID: 45632902

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM**Date:** June 10, 2002**Reviewers:** Michael Doherty, Chemist
Registration Action Branch 2William Drew, Chemist
Registration Action Branch 2Richard Loranger, Branch Senior Scientist
Registration Action Branch 2**Petition No.:** PP#1F06312**Citation:** 45632902. Davis, B. (03/05/02) Independent Laboratory Validation of Dow AgroSciences LLC Method "Determination of Residues of Sulfuryl Fluoride in Corn, Wheat and Rice Commodities by Gas Chromatography with Electron Capture Detection," as included in Lab Report Code: 011057, Appendix B, "Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride": Lab Project Number: 010114. Unpublished study prepared by Dow AgroSciences LLC. 72 pages.**Sponsor:** Dow AgroSciences LLC
9330 Zionsville Rd
Indianapolis, IN 46268**Executive Summary**

The proposed method utilizes headspace analysis to quantitate residues of sulfuryl fluoride in whole cereal grains as well as processed products. Residues of sulfuryl fluoride are extracted from the grain commodities with water in an air-tight blender. The samples are agitated in the blender for five minutes to transfer residues of the highly volatile sulfuryl fluoride from the grain commodity to the headspace above the sample. The headspace is then analyzed for residues of sulfuryl fluoride by injecting an aliquot into a gas chromatograph with electron-capture detection (GC/ECD). The method has been validated using fortification/recovery experiments on wheat, corn, and rice commodities. Fortification levels ranged from 0.008 to 0.08 ppm (0.2 ppm for wheat). Average recoveries and standard deviations were $88 \pm 14\%$ for

Sulfuryl Fluoride
Cereal Grains

Residue Analytical Method
OPPTS 860.1340

PC Code: 078003
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wheat, $94 \pm 16\%$ for corn, and $82 \pm 11\%$ for rice. Standard deviations at the 0.008-ppm fortification level ranged from 0.00099 to 0.00129 ppm, resulting in calculated limits of detection and quantification of approximately 0.003 and 0.010 ppm, respectively. There were no apparent residues of sulfuryl fluoride in the control samples. Due to the gaseous nature of sulfuryl fluoride, fortifications were made to the headspace above the commodities and not to the commodities themselves. The method has not been radiovalidated and it is unclear if the method will successfully extract weathered residues. The method has not been shown to be specific to sulfuryl fluoride. It is likely that the method would extract and detect other volatile halogenated compounds (e.g., methyl bromide).

The method underwent an independent laboratory validation. After a considerable amount of consultation between the confirming laboratory and Dow AgroSciences, the laboratory was able to successfully validate the method for wheat grain (average recovery = $104 \pm 10\%$) and wheat flour ($94 \pm 10\%$). Other cereal grain commodities were not tested.

Prior to final acceptance by the agency, the method will need to be radiovalidated, shown to be specific to sulfuryl fluoride, and undergo a successful Agency validation. HED notes that although control samples of corn oil were analyzed, the method was not validated for corn oil. Due to the physicochemical properties of sulfuryl fluoride, oily commodities are the most likely to bear residues following fumigation.

GLP Compliance

Signed and dated GLP, quality assurance, and data confidentiality information were provided. The only noted deviation was that the GLP status of the sulfuryl fluoride standard is unknown.

1. Materials and Methods

1.1. Test Substances

Table 1.1.1. List of Analytes Tested with the Sulfuryl Fluoride Headspace GC/ECD Method.	
Common Name:	Sulfuryl Fluoride
IUPAC Name:	Sulfuryl Fluoride
CAS Name:	Sulfuryl Fluoride
CAS Number:	002699-79-8
Trade Name:	Vikane, ProFume
Other Synonyms:	–

Table 1.1.2. Matrices Tested with the Sulfuryl Fluoride Headspace GC/ECD Method.			
Matrix	Wheat	Corn	Rice
Matrix Form	Whole grain, flour, germ, bran, red dog, shorts	Whole grain, flour, starch, grits	Polished rice, bran

Sulfuryl Fluoride
Cereal GrainsResidue Analytical Method
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Table 1.1.3. Fortification Levels Tested with the Sulfuryl Fluoride Headspace GC/ECD Method.	
Matrices	Sulfuryl Fluoride Fortification Levels, ppm*
Wheat Commodities	0.008, 0.020 (germ only), 0.080, 0.20 (germ only)
Corn Commodities	0.008, 0.080
Rice Commodities	0.008, 0.080

* Fortifications were made to the headspace above the grain commodity. The fortification level is the equivalent concentration for the grain commodity assuming that all of the sulfuryl fluoride in the headspace came from the grain.

1.2. Methods

Because of the volatile nature of sulfuryl fluoride and the headspace analysis technique of this method, the extraction process is carried out in blender jars whose lids have been modified to provide an air-tight seal to the jar and to provide access to the headspace through a standard GC septum.

To validate the method, 25 grams of grain commodity (10 grams in the case of low-density commodities) are transferred to the blender jar. To the jar is added 200 ml of HPLC-grade water. The jar is then sealed with the modified lid. Sulfuryl fluoride stock standard is then injected into the system to fortify the samples and the sample/water mixture is blended for 5 minutes. The sample is then allowed to equilibrate for 5 minutes prior to analysis. Following the equilibration period, an aliquot of the headspace is removed via the GC septum in the lid and injected directly into a gas chromatograph equipped with an electron-capture detector (GC/ECD). The GC/ECD parameters are:

Injection Method: Splitless
Injection Volume: 100 μ L
Injector Temp.: 150 °C
Column: Varian PLOT - Poraplot Q - 25 m x 0.53 mm (capillary column)
Oven Temp.: 70 °C (isothermal)
Detector: ⁶³Ni Electron Capture
Detector Temp.: 250 °C

2. Results

2.1. Stability of Reference Materials

The stability of the reference materials or their storage conditions was not discussed in either the method writeup or the ILV report.

Sulfuryl Fluoride
Cereal Grains

Residue Analytical Method
OPPTS 860.1340

PC Code: 078003
MRID: 45632902

2.2. Method Characteristics

2.2.1. Chromatography

Sample chromatograms provided with the submission show no interferences in control samples. Sulfuryl fluoride has a retention time of approximately 1.13 minutes on the GC system used for method validation. Sulfuryl fluoride peak shape is good from both standard and sample injections.

2.2.2. Linearity

The example standard curve provided with the submission showed good linearity over the range 0.004 to 0.080 ppm. The coefficient of determination (r^2) for the example curve is 0.994 and is based on six injections at each concentration (0.004, 0.008, and 0.080 ppm).

2.2.3. Specificity

There are no peaks at the retention time of interest in control samples; however, an interference study has not been conducted to determine if the method will distinguish the analytes of interest from other agrochemicals that may co-occur in the matrix. Based on the simplicity of the method and lack of any cleanup, it is likely that other volatile, halogenated compounds (e.g., methyl bromide) could interfere with the analysis. It is unknown whether or not the system would provide adequate chromatographic separation between sulfuryl fluoride and any potentially interfering compounds.

2.2.4. Method Limits

The method has a lower limit of method validation of 0.008 ppm. Based on recovery variability at the 0.008-ppm fortification level, the method has calculated limits of detection and quantification of approximately 0.003 and 0.010 ppm, respectively. The calculated limits are based on 3x and 10x the standard deviation of the method's response at 0.008 ppm.

Sulfuryl Fluoride
Cereal Grains

Residue Analytical Method
OPPTS 860.1340

PC Code: 078003
MRID: 45632902

2.2.5. Analyte Recoveries

Table 2.2.5.1. Recovery of Sulfuryl Fluoride from Cereal Grain Commodities using the Sulfuryl Fluoride Headspace GC/ECD Method.			
Matrix	Sulfuryl Fluoride		
	Fortification Level, ppm	Recoveries, %* (n<70 or >120)	Mean ± SD, % (n)
Wheat commodities	0.008	53 - 153 (10)	90 ± 16 (82)
	0.080	75 - 114 (0)	88 ± 8 (56)
	0.020 (germ only)	65 - 126 (3)	86 ± 14 (22)
	0.20 (germ only)	67 - 92 (1)	79 ± 8 (10)
Corn commodities	0.008	81 - 129 (7)	102 ± 13 (42)
	0.080	58 - 118 (7)	87 ± 15 (54)
Rice commodities	0.008	52 - 105 (5)	81 ± 12 (31)
	0.080	67 - 99 (1)	83 ± 9 (32)

* Due to the number of samples, individual recovery values are not listed. Individual values can be found on pages 22-32 of the method study volume.

2.2.6. Independent Laboratory Validation

An independent laboratory validation was conducted for this method using wheat grain and wheat flour. The validation was performed by Minnesota Valley Testing Laboratories, Inc. (1126 N. Front Street; New Ulm, MN 56073). There was considerable communication between the validating laboratory and Dow AgroSciences. The communications were by telephone or electronic mail and dealt with a number of troubleshooting issues, including use of specialized equipment, non-reproducible calibration curves, advice on sample processing and sample integrity, assurance of gas dilution calculations, and a failed wheat grain trial. The validating laboratory suggests that the method be revised to specify side-port needles, since they experienced problems with other needle types becoming clogged with debris. No other revisions were recommended.

Table 2.2.6.1. Recovery of Sulfuryl Fluoride from Wheat Grain and Wheat Flour using the Sulfuryl Fluoride Headspace GC/ECD Method during the Independent Laboratory Validation.			
Matrix	Fortification Level (ppm)	Recoveries (%)	Mean ± SD
Wheat Grain	0.0083	112, 108, 113, 114, 113	112 ± 3
	0.0789	85, 93, 102, 98, 97	95 ± 6
Wheat Flour	0.0083	94, 95, 86, 95, 97	93 ± 4
	0.0789	98, 74, 105, 90, 108	95 ± 13

Sulfuryl Fluoride
Cereal Grains

Residue Analytical Method
OPPTS 860.1340

PC Code: 078003
MRID: 45632902

3. Discussion

3.1. Recovery and Repeatability

Average recovery of sulfuryl fluoride is acceptable at all fortification levels and for all tested matrices. The standard deviations for the recoveries are within acceptable limits. There does not appear to be any significant affect of matrix or fortification level upon recovery. The recovery of sulfuryl fluoride described in the independent laboratory validation is similar to that found during method validation.

3.2. Method Efficiency

Based on the submitted data, it is not possible to ascertain the efficiency of the method. Neither radiovalidation data nor metabolism studies and their associated methods have been submitted to the Agency. For both the method validation and independent laboratory validation studies, sample headspace was fortified and then sampled. While the Agency realizes that this experimental design was used due to the nature of sufluryl fluoride, we don't believe that the recovery results from those studies reflect the ability of the method to extract weathered residues.

4. Deficiencies

Prior to final acceptance by the agency, the method will need to be radiovalidated, shown to be specific to sulfuryl fluoride, and undergo a successful Agency validation. HED notes that although control samples of corn oil were analyzed, the method was not validated for corn oil. Due to the physicochemical properties of sulfuryl fluoride, oily commodities are the most likely to bear residues following fumigation and we recommend that the method be validated using corn oil.

5. References

None.

ATTACHMENT 7Fluoride Anion (from Sulfuryl Fluoride)
Cereal GrainsResidue Analytical Method
OPPTS 860.1340PC Code: 078003
MRID: 45603901, 45632901

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM**Date:** June 10, 2002**Reviewers:** Michael Doherty, Chemist
Registration Action Branch 2William Drew, Chemist
Registration Action Branch 2Richard Loranger, Branch Senior Scientist
Registration Action Branch 2**Petition No.:** PP#1F06312**Citation:** 45603901. Davis, B. (02/07/02) Independent Laboratory Validation of Dow AgroSciences LLC Method "Residue Method Validation for the Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour," as included in Lab Report Code: 011057, Appendix A, "Magnitude of the Terminal Fluoride Ion Level in Cereal Grain Commodities Fumigated with Sulfuryl Fluoride." Lab Project Number: 010115. Unpublished study prepared by Dow AgroSciences LLC. 63 pages.

45632901. Lala, M. and Randolph, R. (03/12/02) Independent Laboratory Validation for Corn Oil and Raisins using Dow AgroSciences Method GRM 01.17-"Determination of Fluoride Anion in Corn, Wheat, Corn Oil and Flour." Lab Project Number: 1404. Unpublished study prepared by Dow AgroSciences LLC. 65 pages.

Sponsor: Dow AgroSciences LLC
9330 Zionsville Road
Indianapolis, IN 46268**Executive Summary**

The petitioner, Dow AgroSciences, has proposed an analytical method for the enforcement of fluoride tolerances in cereal grain commodities. The method consists of homogenizing and shaking the sample in the presence of water and total ionic strength adjusting buffer, centrifuging the sample, and analyzing an aliquot of the supernatant with a fluoride-

Fluoride Anion (from Sulfuryl Fluoride) Cereal Grains	Residue Analytical Method OPPTS 860.1340	PC Code: 078003 MRID: 45603901, 45632901
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selective electrode. Quantitation of fluoride residues is achieved using a double known addition technique.

The method was validated by the petitioner using whole grain wheat, whole grain corn, wheat flour, and corn oil. Two independent laboratory validations were performed using whole grain wheat and wheat flour, and corn oil and raisins. Recovery of fluoride was comparable across all tested commodities and between the petitioner validations and the independent laboratory validations. Generally, recovery of fluoride fell within the acceptable range of 70-120% after values were corrected for background levels of fluoride in control samples. Initial laboratory validation experiments showed limits of detection (LOD) and quantification (LOQ) of approximately 0.2 and 0.5 ppm, respectively. During the independent laboratory validation, the LOQ was increased to 2.0 ppm.

The ability of the method to extract weathered residues has not been demonstrated and HED questions the corn oil validations due to the fortification procedures. HED requests that the petitioner characterize the method with respect to weathered residues and validate the method using a fortification technique that will assure transfer of fluoride to corn oil.

GLP Compliance

Signed and dated GLP, quality assurance, and data confidentiality information were provided for both volumes. The only noted deviation was that the GLP status of the sodium fluoride standard is unknown.

1. Materials and Methods

1.1. Test Substances

Table 1.1.1. List of Analytes Tested.	
Common Name:	Fluoride anion
IUPAC Name:	Fluoride anion
CAS Name:	Fluoride anion
CAS Number:	16984-48-8
Trade Name:	—
Other Synonyms:	—

Table 1.1.2. Matrices Tested.		
Matrix	Wheat	Corn
Matrix Form	Whole grain, Flour	Whole grain, Oil

Fluoride Anion (from Sulfuryl Fluoride) Cereal Grains	Residue Analytical Method OPPTS 860.1340	PC Code: 078003 MRID: 45603901, 45632901
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Table 1.1.3. Fortification Levels Tested.	
Matrices	Fluoride Anion, ppm
Whole grain wheat, wheat flour, whole grain corn, corn oil	0.5, 2.0, 5.0, 50, 20 (corn oil only)
Raisins	2.0, 20

1.2. Methods

Samples of commodity are homogenized and shaken in the presence of water and total ionic strength adjusting buffer (TISAB). Following centrifugation, the extract is analyzed for fluoride ion using a fluoride-selective electrode. Residues are quantified using the double known addition (DKA) technique. To validate the method, control samples of whole grain wheat, whole grain corn, wheat flour, and corn oil were fortified with fluoride (as sodium fluoride dissolved in water) to concentrations of 0.5, 2, 5, 20, or 50 ppm. Details regarding equilibration times or conditions were not provided in the submission.

2. Results

2.1. Stability of Reference Materials

Although details regarding the stability of standards were not provided, HED has no reason to believe that standards of sodium fluoride, which are prepared in ultra-pure water, would be unstable. The petitioner did provide data showing that fluoride is stable in fortified grain commodities for up to 7 days under ambient conditions.

2.2. Method Characteristics

2.2.1. Chromatography

This method uses a fluoride-ion-selective electrode. Chromatography is not an issue for this method.

2.2.2. Linearity

The DKA technique, in essence, produces a standard curve within each sample. The addition of two known amounts of analyte to the sample are used to calibrate the ion-selective electrode meter each time a sample is run. Linearity is not an issue for this method.

2.2.3. Specificity

Interference study data have not been submitted to the Agency. The ion-selective electrode used in the method is selective for fluoride.

Fluoride Anion (from Sulfuryl Fluoride)
Cereal Grains

Residue Analytical Method
OPPTS 860.1340

PC Code: 078003
MRID: 45603901, 45632901

2.2.4. Method Limits

Initial laboratory validation experiments conducted by the laboratory that developed the methodology showed limits of detection (LOD) and quantification (LOQ) of approximately 0.2 and 0.5 ppm, respectively. Those values are based on recovery data from the 0.5-ppm fortification level, with the LOD being 3x the standard deviation of recovery and the LOQ being 10x the standard deviation. During the independent laboratory validation, the independent laboratory was not able to achieve an LOQ of 0.5 ppm and the LOQ was increased to 2.0 ppm. The revised LOQ is based on the lowest limit of method validation.

2.2.5. Analyte Recoveries

Recovery of fluoride anion from fortified samples is shown in Table 2.2.5.1. Note that the recoveries are corrected for the amount of fluoride found in the control samples.

Matrix (Background F ⁻ concentration)	Fluoride Anion		
	Fortification Level (ppm)	Recoveries (%)*	Mean ± SD
Whole Grain Wheat (0.260 ppm)	0.5	80, 68, 66, 90, 68, 88, 93	79 ± 11
	2	98, 99, 93	97 ± 3
	5	94, 85, 91	90 ± 4
	50	74, 85, 70	76 ± 8
Whole Grain Corn (0.182 ppm)	0.5	102, 95, 97, 101, 104, 121, 94	102 ± 9
	2	101, 99, 105	102 ± 3
	5	103, 98, 106	102 ± 4
	50	93, 101, 101	98 ± 4
Wheat Flour (0.116 ppm)	0.5	93, 97, 101, 102, 106, 91, 106	99 ± 6
	2	100, 96, 106	101 ± 5
	5	99, 97, 102	99 ± 2
	50	90, 103, 96	96 ± 7
Corn Oil (0.105; 0.0392 for samples marked †)	0.5	100, 85, 104, 118, 107, 101, 116	104 ± 11
	2	123, 120, 120, 102 [†] , 103 [†] , 103 [†]	112 ± 12
	5	110, 119, 100 [†] , 95 [†] , 99 [†]	105 ± 10
	50	116, 114, 127	119 ± 7

*Recovery values are corrected for background levels of fluoride anion.

Fluoride Anion (from Sulfuryl Fluoride) Residue Analytical Method PC Code: 078003
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2.2.6. Independent Laboratory Validation

Two independent laboratory validations were performed, one with wheat grain and wheat flour (MRID 45603901), and a second with corn oil and raisins (MRID 45632901).

Table 2.2.6.1. Recovery of Fluoride Anion from Wheat Grain, Wheat Flour, Corn Oil, and Raisins during the Independent Laboratory Validation.			
Matrix (Background F ⁻ Concentration)	Fluoride Anion		
	Fortification Level (ppm)	Recoveries (%)*	Mean ± SD
Wheat Grain (2.08)	2	108, 113, 92, 97, 107	104 ± 9
	10	84, 100, 105	97 ± 11
	20	102, 107, 106, 107, 95	103 ± 5
Wheat Flour (0.460)	2	105, 94, 87, 98, 91	95 ± 7
	10	97, 96, 92	95 ± 3
	20	99, 108, 95, 92, 99	98 ± 6
Corn Oil (0.048)	2	101, 104, 101, 90, 97	99 ± 6
	20	101, 106, 99, 99, 98	101 ± 3
Raisins (0.640)	2	92, 81, 90, 87, 102	91 ± 8
	20	85, 83, 90, 87, 90	87 ± 3

*Recovery values are corrected for background levels of fluoride anion.

3. Discussion

3.1. Recovery and Repeatability

The reported recoveries and variability obtained during method development validation and independent laboratory validation are comparable and generally acceptable. A few recovery values fell outside the 70 - 120% range recommended in the guidelines.

3.2. Method Efficiency

Neither radiovalidation of this method nor metabolism data for sulfuryl fluoride have been submitted to the Agency. Therefore, HED cannot ascertain the efficiency of the method for extracting weathered residues of fluoride ion from the cereal grain commodities. HED does not believe that the recovery experiments involving corn oil are valid. Corn oil was fortified with fluoride dissolved in water. Because of the immiscibility of water and oil, HED does not believe that fluoride residues were transferred to the oil prior to extraction. It is likely that the fortification solution remained separated from the oil and then combined with the aqueous extraction solvent during the extraction process.

Fluoride Anion (from Sulfuryl Fluoride)	Residue Analytical Method	PC Code: 078003
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HED was initially concerned with the possibility of interference from other ions in the extraction solution. In the manual for the fluoride electrode used in the validation studies, the manufacturer (Thermo Orion) states, "Most cations and anions do not interfere with the response of the fluoride electrode to fluoride. Anions commonly associated with fluoride, such as Cl⁻, Br⁻, I⁻, SO₄²⁻, HCO₃⁻, PO₄³⁻, and acetate, do not interfere with electrode operation. The OH⁻ ion is an electrode interference." Part of the function of the TISAB is to buffer the pH, so variations in OH⁻ concentration should not interfere with accurate sample analysis. The method cannot distinguish whether or not measured fluoride residues are a result of fumigations with sulfuryl fluoride.

4. Deficiencies

The proposed method has not been radiovalidated. The petitioner should demonstrate that the method is capable of extracting weathered residues of fluoride from cereal grain commodities. Comparison of background levels of fluoride in commodities as analyzed by a total fluoride analysis with levels obtained by the proposed method would suffice to demonstrate the capability of the proposed method. In addition, the method should be validated for corn oil using a fortification technique that assures transfer of fluoride residues to the corn oil.

5. References

None.



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