

SCREENING-LEVEL HAZARD CHARACTERIZATION

Dicamba and Acifluorfen Intermediates Category

SPONSORED CHEMICALS

(See Section 1)

SUPPORTING CHEMICALS

(See Section 1)

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

<p>Chemical Abstract Service Registry Number (CASRN)</p>	<p><u>Sponsored Chemicals</u> 1982-69-0 68938-79-4 68938-80-7 583-78-8 52166-72-0 68938-81-8 1984-58-3 63734-62-3 72252-48-3</p> <p><u>Supporting Chemicals</u> 1918-00-9 50594-66-6 62476-59-9</p>
<p>Chemical Abstract Index Name</p>	<p>See Section 1</p>
<p>Structural Formula</p>	<p>See Section 1</p>
<p style="text-align: center;">Summary</p> <p>The members of the dicamba and acifluorfen intermediates category are divided into three subcategories for human health endpoints. Subcategory I is Dicamba Salts and is composed of three chemicals that are grouped together since all are derivatives of the free acid, CASRN 1918-00-9, which is used as a supporting chemical. Subcategory II, 2,5-Dichlorophenols, is composed of four chemicals that are grouped together since all are 2,5-dichlorophenols used as intermediates in the manufacture of benzoic acid, 3,6-dichloro-2-methoxy. Subcategory III, Benzoic Acids, is composed of four chemicals grouped together because they are benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro- (acifluorfen), its sodium salt, and its two intermediates used in the manufacture of benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-. Subcategories for ecotoxicity are explained below.</p> <p>The substances of subcategory I, II, and III are either solids or liquids with moderate to high water solubility and low to negligible vapor pressure. There are two exceptions, CASRN 583-78-8 and CASRN 1984-58-3, which have high and moderate water solubilities, respectively, and moderate vapor pressures. The members of Subcategory I are expected to possess high mobility in soil. The members of Subcategory II and III are expected to have moderate mobility in soil. Volatilization is considered moderate for CASRN 583-78-8 and CASRN 1984-58-3. Volatilization for all other category members is expected to be low since they are either salts or have low estimated Henry's Law constants. The rate of hydrolysis is considered negligible for all subcategories. The rate of atmospheric photooxidation for nearly all chemicals in subcategories I, II and III is considered slow to negligible. The overall weight of evidence suggests that the members of the dicamba and acifluorfen intermediates category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1). The two exceptions are CASRN 72252-48-3 and CASRN 63734-62-3, which are expected to have moderate persistence (P2) and moderate bioaccumulation potential (B2).</p>	

Human Health Hazard

Subcategory I: Dicamba Salts

Acute oral toxicity for CASRN 1982-69-0 and the supporting chemical, CASRN 1918-00-9, is low in rats. Acute inhalation toxicity in rats for the supporting chemical, CASRN 1918-00-9, and acute dermal toxicity in rabbits for CASRN 1982-69-0 are moderate. In a 13 week repeated-dose study, dietary exposure of rats to the supporting chemical, CASRN 1918-00-9, significantly decreased body weight gain and food consumption and increased mean liver weight in both sexes at 1000 and 1065 mg/kg-bw/day in males and females, respectively. Additional changes in hematology, blood chemistry, and urinalysis occurred at the same doses. The NOAEL for systemic toxicity is ~ 479 mg/kg-bw/day in males and ~ 535 mg/kg-bw/day in females. In another 13 week repeated-dose study, dietary exposure of a different strain of rats to the supporting chemical, CASRN 1918-00-9, did not cause any treatment-related effects. The NOAEL for systemic toxicity is ~ 682 mg/kg-bw/day in males and ~ 751 mg/kg-bw/day in females. In a dietary two-generation reproductive toxicity study in rats, the supporting chemical, CASRN 1918-00-9, showed no adverse systemic effects up to the highest dose tested. The NOAEL for systemic toxicity for F0 males, F0 females, F1 males, and F1 females, is 347, 390, 432, and 458 mg/kg-bw/day, respectively. Based on effects on decreased pregnancy rate and reduced litter size at ~ 135 mg/kg-bw/day (significance not indicated), the NOAEL for reproductive toxicity is ~ 44 mg/kg-bw/day. Based on decreased pup weights and delayed sexual maturation at 432 – 458 (male-female) mg/kg-bw/day, the NOAEL for developmental toxicity is 121-135 (male-female) mg/kg-bw/day. An oral gavage prenatal developmental toxicity study with the supporting chemical CASRN 1918-00-9, in rats, found mortality and decreased weight gain in dams at 400 mg/kg-bw/day and no effects on offspring; the NOAEL for maternal toxicity is 160 mg/kg-bw/day and the NOAEL for developmental toxicity is 400 mg/kg-bw/day. An oral gavage prenatal developmental toxicity study with the supporting chemical CASRN 1918-00-9, in rabbits, found spontaneous abortions at 150 mg/kg-bw/day and above, and no effects on offspring; the NOAEL for maternal toxicity is 30 mg/kg-bw/day and the NOAEL for developmental toxicity is 300 mg/kg-bw/day (highest dose tested). The supporting chemical, CASRN 1918-00-9, was not mutagenic in a bacterial reverse mutation assay and did not induce chromosomal aberrations *in vitro* or *in vivo*. The supporting chemical, CASRN 1918-00-9, induced sister chromatid exchange *in vitro*.

No data gaps were identified under the HPV Challenge Program.

Subcategory II: 2,5-Dichlorophenols

Acute oral, and inhalation toxicity of CASRN 583-78-8 are low in rats and acute dermal toxicity is low in rabbits. A repeated-dose inhalation study in rats found significant effects of CASRN 583-78-8 on body weight gain, hematology, organ weight, and histopathology of lung and liver at 0.3 mg/L; the NOAEL for systemic inhalation toxicity is 0.1 mg/L. A repeated-dose dermal toxicity study of CASRN 583-78-8 in rabbits found skin lesions and associated pathological changes at 1 mg/kg-bw/day, the lowest dose tested; the NOAEL for systemic dermal toxicity was not established. A combined oral gavage repeated-dose/reproductive/developmental toxicity study of CASRN 1984-58-3 in rats showed increased kidney weight with chronic progressive nephropathy in males at 150 mg/kg-bw/day and above. Treatment-related findings in the liver and thyroid gland were also observed. Females showed reduced body weights at 450 mg/kg-

bw/day; the NOAEL for systemic toxicity is 50 and 150 mg/kg-bw/day in males and females, respectively. No adverse effects were observed for reproductive or developmental toxicity endpoints; the NOAEL for reproductive toxicity is 450 mg/kg-bw/day (highest dose tested). The NOAEL for maternal and developmental toxicity is 150 and 450 (highest dose tested) mg/kg-bw/day, respectively. CASRN 583-78-8 was not mutagenic in a bacterial reverse mutation assay and did not induce mouse micronuclei *in vivo*.

No data gaps were identified under the HPV Challenge Program.

Subcategory III: Benzoic Acids

The acute oral toxicity of CASRN 63734-62-3 in rats is low. For the supporting chemical, CASRN 62476-59-9, acute inhalation toxicity in rats is high and acute dermal toxicity in rabbits is moderate. A 90-day oral repeated-dose study in rats, with the supporting chemical CASRN 62476-59-9, showed increased liver and kidney weights in males with corresponding changes in clinical chemistry at 23.7 mg/kg-bw/day; the NOAEL for systemic toxicity is 6.1 mg/kg-bw/day. A three-week dermal repeated-dose study in rabbits with the supporting chemical, CASRN 62476-59-9, showed severe skin irritation and clinical signs of toxicity at 92 mg/kg-bw/day, the lowest dose tested; the NOAELs for local effects and systemic toxicity were not established. A dietary 2-generation reproductive toxicity study in rats with the supporting chemical, CASRN 62476-59-9, showed increased incidence of kidney lesions in both sexes at 30 mg/kg-bw/day and above; the NOAEL for systemic toxicity is 2 mg/kg-bw/day. Decreased gestation duration and pup viability were observed at 30 mg/kg-bw/day and above; the NOAEL for reproductive/developmental toxicity is 2 mg/kg-bw/day. A prenatal gavage developmental toxicity study in rats with the supporting chemical, CASRN 62476-59-9, showed decreased body weight, clinical symptoms and behavioral changes in dams and increased incidence of visceral and skeletal abnormalities in pups at 90 mg/kg-bw/day; the NOAEL for maternal and developmental toxicity is 20 mg/kg-bw/day. In a prenatal developmental toxicity study in rabbits with the supporting chemical, CASRN 62476-59-9, dietary exposure resulted in reduced body weight gain and food consumption in dams at 36 mg/kg-bw-day and no signs of developmental toxicity at 36 mg/kg-bw/day; the NOAEL for maternal toxicity is 12 mg/kg-bw/day and the NOAEL for developmental toxicity is 36 mg/kg-bw/day (highest dose tested). The supporting chemical, CASRN 50594-66-6 was not mutagenic in a bacterial reverse mutation assay *in vitro* and the supporting chemical, CASRN 62476-59-9 did not induce chromosomal aberrations in mice *in vivo*. CASRN 63734-62-3 was irritating to rabbit skin and eyes.

No data gaps were identified under the HPV Challenge Program.

Hazard to the Environment

For the ecotoxicity endpoints, subcategories I and II designated above, are further subdivided based on their chemical functionality, resulting in five overall subcategories for the evaluation of hazard to the environment. Subcategory I (dicamba salts) is now subcategory 1 (contains a methoxy functional group) and subcategory 2 (hydroxyl functional group). Subcategory II (2,5-dichlorophenols) has been divided following the same rationale: subcategory 3, which contains a methoxy functional group; and subcategory 4, which contains a hydroxyl functional group. Subcategory III (benzoic acids) has been designated subcategory 5.

Subcategory 1

The 96-h LC₅₀ for fish exposed to CASRN 1982-69-0 is 558 mg/L. The 48-h EC₅₀ for aquatic invertebrates exposed to CASRN 1982-69-0 is 38.1 mg/L. The 96-h EC₅₀ for aquatic plants from exposure to CASRN 1982-69-0 is 36.4 mg/L for growth rate.

No data gaps were identified under the HPV Challenge Program.

Subcategory 2

There are no data available for the chemicals in this subcategory.

Acute toxicity to fish, aquatic invertebrates and toxicity to aquatic plants were identified as data gaps under the HPV Challenge Program.

Subcategory 3

For CASRN 1984-58-3, the 96-h LC₅₀ for fish is 2.4 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 5.89 mg/L. The 72-h EC₅₀ for aquatic plants is 8.1 mg/L for biomass and 10.1 mg/L for growth rate.

No data gaps were identified under the HPV Challenge Program.

Subcategory 4

For CASRN 52166-72-0, the 96-h LC₅₀ for fish is 3.2 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 15 mg/L. The 72-h EC₅₀ for aquatic plants is 0.34 mg/L for biomass and 0.78 mg/L for growth rate.

No data gaps were identified under the HPV Challenge Program.

Subcategory 5

For CASRN 63734-62-3, the 96-h LC₅₀ for fish is 2.6 mg/L. For the supporting chemical, CASRN 62476-59-9, the 96-h LC₅₀ for fish is 17 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 28.1 mg/L. The 72-h EC₅₀ for aquatic plants is not addressed adequately.

Toxicity to aquatic plants was identified as a data gap under the HPV Challenge Program.

The sponsor, BASF Corporation, submitted a Test Plan and Robust Summaries to EPA for dicamba and acifluorfen intermediates on December 20, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on January 31, 2002 (www.epa.gov/oppt/chemrtk/pubs/summaries/dicambaa/c13451tc.htm). EPA comments on the original submission were posted to the website on December 2, 2002. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on February 27, 2003, December 31, 2007 and May 29, 2008, which were posted to the ChemRTK website on March 14, 2003, March 12, 2008 and July 7, 2008, respectively. The sponsor sold all interest in intermediates of acifluorfen in 2003 and has withdrawn sponsorship of these chemicals under the HPV Challenge Program; however, the EPA has kept these chemicals in the category for the sake of completeness in this Hazard Characterization.

Category Justification

The Dicamba and Acifluorfen Intermediates category covers nine intermediates formed in the production of the herbicides dicamba (CASRN 1918-00-9) and acifluorfen (CASRN 50594-66-6). The sponsor subdivided the category members into three subcategories based on common functional groups, common precursors or breakdown products, and the expectation that the members of each group would have similar environmental and toxicological properties. EPA considers the sponsor's definition of the three subcategories under this category acceptable for human health toxicity. For human health hazard, the use of CASRN 1918-00-9 data (methoxy group supporting chemical) to read across to the sponsored chemicals (hydroxyl group) would represent a reasonable worst-case scenario (given the potentially longer half-life of the methoxy compound). The dissociation data offers further general support for the grouping of these chemicals within Subcategories I and II. For hazard to the environment, subcategories I and II are further divided based on their chemical functionality. The original Subcategory I is divided into two separate subcategories: Subcategory 1, which contains a methoxy functional group; and Subcategory 2, which contains a hydroxyl functional group. The original Subcategory II has been divided following the same rationale: Subcategory 3, which contains a methoxy functional group; and Subcategory 4, which contains a hydroxyl functional group. The third subcategory stays as Subcategory 5. The distribution of subcategories is outlined in Table 1.

Justification for Supporting Chemicals

Supporting chemicals for human health hazard include CASRN 1918-00-9 for Subcategory I and CASRN 50594-66-6 and CASRN 62476-59-9 for Subcategory III. Production of the supporting chemical CASRN 1918-00-9 produces the intermediates that are sponsored in Subcategory I. There is a high degree of structural and physicochemical similarity and the sponsor's provided information on acid and salt dissociation support the use of CASRN 1918-00-9 as a reasonable supporting chemical for Subcategory I for human health endpoints. In Subcategory III, benzoic acid intermediates are chemicals generated in the production of CASRN 50594-66-6 and CASRN 62476-59-9. CASRN 50594-66-6 and CASRN 62476-59-9 are reasonable supporting chemicals for Subcategory III because of their similar structural and physicochemical properties. CASRN 62476-59-9 is also a supporting chemical for ecotoxicity endpoints.

Table 1. Subcategories in the Dicamba and Acifluorfen Intermediates Category	
HUMAN HEALTH HAZARD	ECOTOXICITY
Subcategory I <ul style="list-style-type: none"> • CASRN 1982-69-0 • CASRN 68938-79-4 • CASRN 68938-80-7 • CASRN 1918-00-9, <i>supporting chemical</i> 	Subcategory 1 <ul style="list-style-type: none"> • CASRN 1982-69-0
	Subcategory 2 <ul style="list-style-type: none"> • CASRN 68938-79-4 • CASRN 68938-80-7
Subcategory II <ul style="list-style-type: none"> • CASRN 1984-58-3 • CASRN 583-78-8 • CASRN 52166-72-0 • CASRN 68938-81-8 	Subcategory 3 <ul style="list-style-type: none"> • CASRN 1984-58-3
	Subcategory 4 <ul style="list-style-type: none"> • CASRN 583-78-8 • CASRN 52166-72-0 • CASRN 68938-81-8
Subcategory III <ul style="list-style-type: none"> • CASRN 63734-62-3 • CASRN 72252-48-3 • CASRN 62476-59-9, <i>supporting chemical</i> • CASRN 50594-66-6, <i>supporting chemical</i> 	Subcategory 5 <ul style="list-style-type: none"> • CASRN 63734-62-3 • CASRN 72252-48-3 • CASRN 62476-59-9, <i>supporting chemical</i>

A Re-registration Eligibility Document (RED) exists for CASRN 1918-00-9 and CASRN 62476-59-9. These documents can be found at http://www.epa.gov/oppsrrd1/REDs/dicamba_red.pdf and http://www.epa.gov/oppsrrd1/REDs/acifluorfen_red.pdf.

1. **Chemical Identity**

1.1 **Identification and Purity**

The substances are all intermediates found in the production of the pesticide active ingredients CASRN 1918-00-9 and 50594-66-6, and include salt and acid forms of the same chemicals. As stated in the 2007 Final Test Plan, the chemicals used to produce the herbicide CASRN 1918-00-9 are all considered closed system intermediates. These chemicals exist in process streams diluted by various aqueous and organic solutions and processing occurs in closed systems with no routine exposure possible except for sampling. The purity of the sponsored and supporting chemicals for which test data was included in the Robust Summaries ranged from 20% (CASRN 1982-69-0) to >98-99% (Subcategory II chemicals). The purity of CASRN 1918-00-9 ranged

from 85.8-90.4% and was of a technical grade. Chemical structures of the sponsored and supporting chemicals in the Dicamba and Acifluorfen Intermediates category are depicted in Table 2.

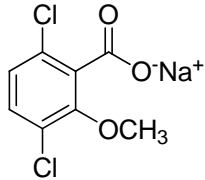
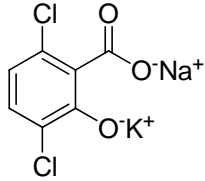
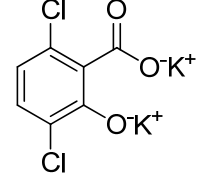
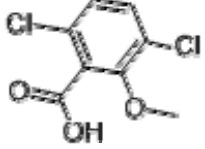
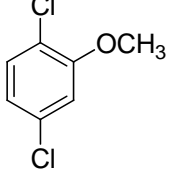
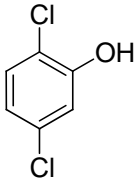
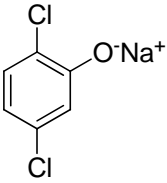
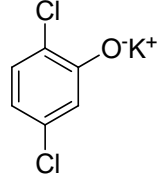
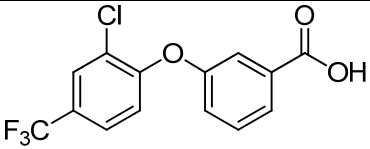
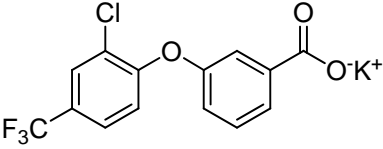
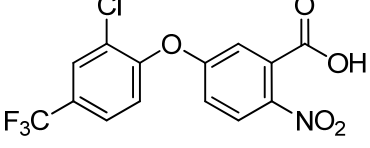
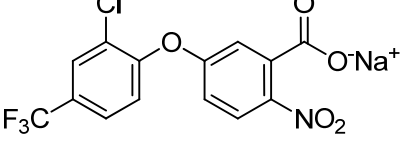
Table 2. Dicamba and Acifluorfen Intermediates Category		
Chemical Abstract Index Name	CASRN	Representative Structure
Subcategory I:		
Benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1)	1982-69-0	
Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (1:1:1)	68938-79-4	
Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium salt (1:2)	68938-80-7	
Supporting Chemical		
2-Methoxy-3,6-dichlorobenzoic acid	1918-00-9	
Subcategory II:		
Benzene, 1,4-dichloro-2-methoxy-	1984-58-3	
Phenol, 2,5-dichloro-	583-78-8	

Table 2. Dicamba and Acifluorfen Intermediates Category		
Chemical Abstract Index Name	CASRN	Representative Structure
Phenol, 2,5-dichloro-, sodium salt (1:1)	52166-72-0	
Phenol, 2,5-dichloro-, potassium salt (1:1)	68938-81-8	
Subcategory III:		
Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-	63734-62-3	
Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-, potassium salt (1:1)	72252-48-3	
Supporting Chemicals		
Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-	50594-66-6	
Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1)	62476-59-9	

1.2 Physical-Chemical Properties

The members of the dicamba and acifluorfen intermediates category contain both solids and liquids with moderate to high water solubility and low to negligible vapor pressures. Two exceptions are phenol, 2,5-dichloro- and benzene, 1,4-dichloro-2-methoxy- have moderate to high water solubilities, and moderate vapor pressures.

The physical-chemical properties of the dicamba and acifluorfen intermediates category are summarized in Tables 3, 4 and 5 while their environmental fate properties are provided in Tables 6, 7 and 8.

Table 3. Physical-Chemical Properties of the Dicamba and Acifluorfen Intermediates Category, Subcategory I: Dicamba Salts¹			
Property	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (1:1:1)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium salt (1:2)
CASRN	1982-69-0	68938-79-4	68938-80-7
Molecular Weight	243.02	267.09	283.19
Physical State	Solid	Solid	Solid
Melting Point	320-325°C (decomposes)	>25°C (solid)	>25°C (solid)
Boiling Point	Decomposes before boiling	Decomposes before boiling	Decomposes before boiling
Vapor Pressure	<1.0×10 ⁻¹⁰ mmHg at 25°C (estimated) ²	<1.0×10 ⁻¹⁰ mmHg at 25°C (estimated) ²	<1.0×10 ⁻¹⁰ mmHg at 25°C (estimated) ²
Water Solubility	360,000 mg/L at 25°C (measured) ³	480,000 mg/L at 25°C (measured) ³	>1.0×10 ⁶ mg/L at 25°C (estimated) ²
Dissociation Constant (pK _a)	Not applicable	Not applicable	Not applicable
Henry's Law Constant	<1.0×10 ⁻¹⁰ atm-m ³ /mole (estimated) ²	<1.0×10 ⁻¹⁰ atm-m ³ /mole (estimated) ²	<1.0×10 ⁻¹⁰ atm-m ³ /mole (estimated) ²
Log K _{ow}	-0.90 (estimated) ²	-4.15 (estimated) ²	-4.15 (estimated) ²

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of May 27, 2010.

³ Tomlin C.D.S. The Pesticide Manual 10th ed Surrey, UK: The British Crop Protection Council (1994).

Table 4. Physical-Chemical Properties of the Dicamba and Acifluorfen Intermediates Category, Subcategory II: 2,5-Dichlorophenols¹				
Property	SPONSORED CHEMICAL Phenol, 2,5-dichloro-	SPONSORED CHEMICAL Phenol, 2,5-dichloro-, sodium salt (1:1)	SPONSORED CHEMICAL Phenol, 2,5-dichloro-, potassium salt (1:1)	SPONSORED CHEMICAL Benzene, 1,4-dichloro-2-methoxy-
CASRN	583-78-8	52166-72-0	68938-81-8	1984-58-3
Molecular Weight	163.00	184.99	201.09	177.03
Physical State	Solid ²	Solid	Solid	Liquid
Melting Point	59°C (measured)	350°C (measured)	>300°C (based on the value measured for the sodium salt)	19.9 (measured)
Boiling Point	211°C (measured)	Decomposes before boiling	Decomposes before boiling	231.3°C (measured)
Vapor Pressure	1.2×10^{-2} mmHg at 25°C (extrapolated) ⁴	$<1.0 \times 10^{-10}$ mmHg at 25°C (estimated) ³	$<1.0 \times 10^{-10}$ mmHg at 25°C (estimated) ³	0.05 mmHg at 25°C (measured)
Water Solubility	2,000 mg/L at 25°C (measured) 6,194 mg/L at 25°C (measured) ⁵	41,000 mg/L at 25°C (estimated) ³	34,410 mg/L at 25°C (estimated) ³	84-90 mg/L at 25°C (measured)
Dissociation Constant (pK _a)	7.51 (measured) ⁶	Not applicable	Not applicable	Not applicable
Henry's Law Constant	6.0×10^{-6} atm-m ³ /mole (estimated) ³	$<1.0 \times 10^{-10}$ atm-m ³ /mole (estimated) ³	$<1.0 \times 10^{-10}$ atm-m ³ /mole (estimated) ³	1.9×10^{-4} atm-m ³ /mole (estimated) ³
Log K _{ow}	3.06 (measured)	0.12 (estimated) ³	0.12 (estimated) ³	3.5 (measured)

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² Lide, D.R. CRC Handbook of Chemistry and Physics 88th Edition 2007-2008. CRC Press, Taylor & Francis, Boca Raton, FL 2007, p. 3-158

³ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuite4l.htm> as of May 27, 2010.

⁴ Dolfing, J., Harrison, B.K. Gibbs Free Energy of Formation of Halogenated Aromatic Compounds and Their Potential Role as Electron Acceptors in Anaerobic Environments. Environ. Sci. Technol. (1992) 26:2213-18.

⁵ Blackman GE, Parke MH, Garton G (1955) The physiological activity of substituted phenols. II. Relationships between physical properties and physiological activity. Arch. Biochem. Biophys. 54 (1) : 55-71.

⁶ Serjeant, E.P., Dempsey B.; Ionisation Constants of Organic Acids in Aqueous Solution. International Union of Pure and Applied Chemistry (IUPAC). IUPAC Chemical Data Series No. 23, 1979. New York, New York: Pergamon Press, Inc.

Table 5. Physical-Chemical Properties of the Dicamba and Acifluorfen Intermediates Category, Subcategory III: Benzoic Acids¹				
Property	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-, potassium salt (1:1)	SUPPORTING CHEMICAL Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-	SUPPORTING CHEMICAL Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1)²
CASRN	63734-62-3	72252-48-3	50594-66-6	62476-59-9
Molecular Weight	316.67	354.76	361.66	383.65
Physical State	Off-white solid ³	No data	Solid, off-white ⁴ ; light tan to brown ⁵	Solid, white powder ⁴ ; light yellow ⁵
Melting Point	125-125°C (measured) ³	No data	151.5-157°C (measured) ⁴	Melting begins at 172-176°C and decomposes at 240°C (measured); 124-125°C (measured) ⁴ ; 274-279°C, with decomposition (measured) ⁷
Boiling Point	>300°C (estimated) ⁵	Decomposes before boiling	>300°C (estimated) ⁵	Decomposes before boiling
Vapor Pressure	9.9×10^{-7} mmHg at 25°C (estimated) ⁵	$<1.0 \times 10^{-10}$ mmHg at 25°C (estimated) ⁵	3.9×10^{-8} mmHg at 25°C (estimated) ⁵	$<1.0 \times 10^{-10}$ mmHg at 25°C (estimated) ^{6,8}
Water Solubility	0.95 mg/L at 25°C (estimated) ⁶	1946 mg/L at 25°C (estimated) ⁶	120 mg/L at 23-25°C (measured) ⁴	405 mg/L (measured); >250,000 mg/L (measured) ² ; 250,000 mg/L (measured) ⁴ ; 620,700 mg/L (measured) ⁷
Dissociation Constant (pK _a)	3.64 (estimated) ⁹	Not applicable	3.86 (measured) ¹⁰	Not applicable
Henry's Law Constant	1.5×10^{-8} atm-m ³ /mole (estimated) ⁶	$<1.0 \times 10^{-10}$ atm-m ³ /mole (estimated) ⁶	$<1.0 \times 10^{-10}$ atm-m ³ /mole (estimated) ⁶	$<1.0 \times 10^{-10}$ atm-m ³ /mole (estimated) ⁶
Log K _{ow}	4.70 (estimated) ⁶	0.56 (estimated) ⁶	3.70 (measured)	< 0.3 (measured); 1.5 (measured) ⁷

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1), CAS 62476-59-9, acifluorfen-sodium salt is generally not isolated in solid form, but commercially sold as aqueous solution with 44% w/w due to favorable stability of the sodium salt in solution. This may account for the variability in physical-chemical property data found in the literature

³ Rohm and Haas. Process for preparing phenoxybenzoic acids. US Patent 4,031,131. June 21, 1977.

⁴ O'Neil, M.J. (ed.). The Merck Index - An Encyclopedia of Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co., Inc., 2006.

⁵ Ahrens, W.H. Herbicide Handbook of the Weed Science Society of America. 7th ed. Champaign, IL: Weed Science Society of America, 1994.

⁶ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuite.html> as of May 27, 2010.

⁷ US EPA Reregistration Eligibility Decision For Sodium Acifluorfen CASRN: 62476-59-9, Available online from http://www.epa.gov/opp00001/reregistration/REDS/acifluorfen_red.pdf as of June 2, 2010.

⁸ Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1), CASRN 62476-59-9 is expected to have negligible vapor pressure since it is a salt. The vapor pressure was however measured by the sponsor but the units listed by are not consistent in the submission. The lower detection limit is stated as $<1.33 \times 10^{-5}$ Pa (9.98×10^{-8} mmHg) which was exceeded by the experiment (OECD 104 - gas saturation method) and consequently is listed in the table as $<1.0 \times 10^{-10}$ mmHg. This is consistent with the value listed in the US EPA Reregistration Eligibility Decision For Sodium Acifluorfen

⁹ SPARC. 2010. Online pK_a and Property Calculator v. 4.2.1405-s4.2.1408. Accessed online from <http://ibmcl2.chem.uga.edu/sparc/> on June 2, 2010.

¹⁰ Tomlin CDS, ed. Acifluorfen-sodium (62476-59-9). In: The e-Pesticide Manual, 13th Edition Version 3.1 (2004-05). Surrey UK, British Crop Protection Council.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The Dicamba and Acifluorfen Intermediates category chemicals had an aggregated production and/or import volume in the United States between 36 million pounds and 210 million pounds in calendar year 2005.

- CASRN 583-78-8: 1 to <10 million pounds;
- CASRN 1982-69-0: 10 to <50 million pounds;
- CASRN 1984-58-3: 1 to <10 million pounds;
- CASRN 52166-72-0: 1 to <10 million pounds;
- CASRN 68938-79-4: 10 to <50 million pounds;
- CASRN 68938-80-7: 10 to <50 million pounds;
- CASRN 68938-81-8: 1 to <10 million pounds;
- CASRN 50594-66-6: 1 to <10 million pounds;
- CASRN 62476-59-9: 1 to <10 million pounds;

CASRN 63734-62-3 and 72252-48-3 were not reported in the 2006 IUR.

CASRN 583-78-8:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include pesticide and other agricultural chemical manufacturing as intermediates. No commercial and consumer uses were reported.

CASRN 1982-69-0:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include pesticide and other agricultural chemical manufacturing. Non-confidential commercial and consumer uses of this chemical include “other.”

CASRN 1984-58-3, 52166-72-0, 68938-79-4, 68938-80-7, 68938-81-8 and 62476-59-9 (supporting chemical):

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include pesticide and other agricultural chemical manufacturing as intermediates. No commercial and consumer uses were reported.

CASRN 50594-66-6 (supporting chemical):

Industrial processing and uses for the chemical were claimed confidential. No commercial and consumer uses were reported.

2.2 Environmental Exposure and Fate

The members of Subcategory I from the dicamba and acifluorfen intermediates category are expected to have high mobility in soil. Members of subcategory II and III are expected to have moderate mobility in soil. Each subcategory has at least one experimental biodegradation study which was applied to the other members of the subcategory due to structural similarities. Benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1) from subcategory I (Dicamba Salts) was found not readily biodegradable only achieving 5% biodegradation in 28 days as measured by a manometric respirometry test, OECD 301F. Benzoic acid, 3,6-dichloro-2-methoxy- (CASRN 1918-00-9) had a half-life of 31 days under aerobic conditions using a Midwestern agricultural soil. Another study found that benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1) had a much shorter half-life of only 6 days in soil. Structural similarities of benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1) with the other members of Subcategory I suggest that both benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (1:1:1) and benzoic acid, 3,6-dichloro-2-hydroxy-, potassium salt (1:2) will also not be readily biodegradable, but should not be persistent under environmental conditions. Phenol, 2,5-dichloro- from subcategory II, (2,5-Dichlorophenols), was not readily biodegradable only achieving 5% of its theoretical biochemical oxygen demand (BOD) using a modified MITI test (OECD TG 301C). Another biodegradation study reported phenol, 2,5-dichloro- underwent 52% ring degradation in 4 days using an activated sludge. In addition, 90% degradation of phenol, 2,5-dichloro- was measured in acidic sandy loam at pH 4.8 over 54 days and 90% degradation in sandy silt loam at pH 7.8 over 51 days. Benzene, 1,4-dichloro-2-methoxy- was not readily biodegradable achieving 0% degradation in 28 days as measured by manometric respirometry test, OECD 301F; however, the nominal concentration of the test substance was 50 mg/L which is below the 100 mg/L specification for OECD 301F. These data suggest that the structurally similar members of subcategory II may not be readily biodegradable; however, substantial degradation may occur under certain environmental conditions. Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1) from subcategory III (Benzoic Acids) was found to have a half life of 108 days in silt-loam, 200 days in clay-loam, and 117 days in water. These data suggest that the structurally similar members of subcategory III will have similar degradation kinetics. The rate of hydrolysis of the substances in the dicamba and acifluorfen intermediates category is expected to be negligible under environmental pH and temperature. Volatilization is considered moderate for phenol, 2,5-dichloro- and benzene, 1,4-dichloro-2-methoxy-. Volatilization for all other category members is expected to be negligible since they are either salts or have low estimated Henry's Law constants. The overall weight of evidence suggests that the members dicamba and

acifluorfen intermediates category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1). The two exceptions are the compounds benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]- and its potassium salt, benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-, potassium salt (1:1), which are expected to have moderate persistence (P2) and moderate bioaccumulation potential (B2).

Property	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-methoxy-, sodium salt (1:1)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (1:1:1)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium salt (1:2)
CASRN	1982-69-0	68938-79-4	68938-80-7
Photodegradation Half-life	50.3 days at 25°C in pH 7 water (measured) ^{1,2} ; 26.4 hours (estimated) ³	31.9 hours (estimated) ³	31.9 hours (estimated) ³
Hydrolysis Half-life	0-7.6% after 30 days at 35°C at pH 5,7,and 9 (measured) ^{1,2}	No data	No data
Biodegradation	5% in 28 days not readily biodegradable) ^{1,2} ; Half-life of 31 days in soil; Half-life of 6 days in soil ⁴	No data	No data
Bioaccumulation Factor	BAF = 17.7 (estimated) ³	BAF = 41.8 (estimated) ³	BAF = 40.3 (estimated) ³
Log K _{oc}	1.5 (estimated) ³	1.8 (estimated) ³	1.8 (estimated) ³
Fugacity (Level III Model) ³	0.55	<0.1	<0.1
Air (%)	28	20.5	20.5
Water (%)	71.4	79.4	79.4
Soil (%)	<0.1	<0.1	<0.1
Sediment (%)			
Persistence ⁵	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation ⁵	B1 (low)	B1 (low)	B1 (low)

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² The test substance used for these experiments is dicamba (CASRN 1918-00-9) rather than the dicamba sodium salt.

³ U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episutedl.htm> as of May 27, 2010.

⁴ US EPA Reregistration Eligibility Decision for Dicamba and Associated Salts. Available online from <http://www.regulations.gov/search/Regs/contentStreamer?objectId=09000064809d6faf&disposition=attachment&contentType=pdf> as of June 3, 2010.

⁵ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Table 7. Environmental Fate Characteristics of the Dicamba and Acifluorfen Intermediates Category, Subcategory II: 2,5-Dichlorophenols¹				
Property	SPONSORED CHEMICAL Phenol, 2,5-dichloro-	SPONSORED CHEMICAL Phenol, 2,5-dichloro-, sodium salt (1:1)	SPONSORED CHEMICAL Phenol, 2,5-dichloro-, potassium salt (1:1)	SPONSORED CHEMICAL Benzene, 1,4-dichloro-2-methoxy-
CASRN	583-78-8	52166-72-0	68938-81-8	1984-58-3
Photodegradation Half-life	18.4 hours (estimated) ²	29.1 hours (estimated) ²	29.1 hours (estimated) ²	24.5 hours (estimated) ²
Hydrolysis Half-life	No data	No data	No data	No data
Biodegradation	5% after 28 days (not readily biodegradable) ³ ; 52% after 4 days (measured in an acclimated sludge) 90% after 54 days, sandy loam, pH of 4.8, half-life of 18 days ⁴ ; 90% in 51 days in sandy silt loam, pH of 7.8, half-life of 17 days ⁴	No data	No data	0 % after 28 days (not readily biodegradable)
Bioaccumulation Factor	BCF = 4-35 (measured in carp) ³ ; BAF = 72.3 (estimated) ²	BAF = 97.0 (estimated) ²	BAF = 95.0 (estimated) ²	BAF = 325.5 (estimated) ²
Log K _{oc}	2.7 (estimated) ²	2.7 (estimated) ²	2.7 (estimated) ²	2.4 (estimated) ²
Fugacity (Level III Model) ²				
Air (%)	1.14	0.5	<0.1	2.99
Water (%)	18.1	14.5	12.6	17
Soil (%)	79.5	84.6	87.1	19.8
Sediment (%)	0.5	0.4	0.34	0.24
Persistence ⁵	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation ⁵	B1 (low)	B1 (low)	B1 (low)	B1 (low)

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category.

Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of May 27, 2010.

³ National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.

⁴ Loehr R.C., Matthews J.E.; J. Soil Contam. 1992, 4: 339-360.

⁵ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194-60204.

Table 8. Environmental Fate Characteristics of the Dicamba and Acifluorfen Intermediates Category, Subcategory III: Benzoic Acids¹				
Property	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-, potassium salt (1:1)	SUPPORTING CHEMICAL Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-	SUPPORTING CHEMICAL Benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-, sodium salt (1:1)
CASRN	63734-62-3	72252-48-3	50594-66-6	62476-59-9
Photodegradation Half-life	70.3 hours (estimated) ²	69.0 hours (estimated) ²	12.3 days (estimated) ² ; 110 hours (UV light, measured in water);	25.8 hours (estimated) ² 2 hours (measured in water) ³
Hydrolysis Half-life	No data	No data	Stable at pH 3-9, 40°C (measured) ³	Stable >2 years at 20-25 °C in aqueous solution(measured) ³
Biodegradation	No data	No data	No data	Half-life of 108 days in silt-loam ⁴ , Half-life of 200 days in clay-loam ^{3,4} , Half-life of 117 days in water ³
Bioaccumulation Factor	BAF = 2,866 (estimated) ²	BAF = 2,403 (estimated) ²	BAF = 336 (estimated) ²	BAF = 4.0
Log K _{oc}	3.4 (estimated) ²	3.4 (estimated) ²	3.6 (estimated) ²	3.6 (estimated) ²
Fugacity (Level III Model) ²				
Air (%)				
Water (%)	<0.1	0.3	<0.1	0.11
Soil (%)	9.0	8.78	4.08	4.5
Sediment (%)	89.3	89.7	94.3	93.6
	1.6	1.51	1.64	1.81
Persistence ⁵	P2 (moderate)	P2 (moderate)	P2 (moderate)	P2 (moderate)
Bioaccumulation ⁵	B2 (moderate)	B2 (moderate)	B1 (low)	B1 (low)

¹ BASF Corporation, December 26, 2007. Revised Robust Summary and Test Plan for the Dicamba and Acifluorfen Intermediates Category. Available online from: <http://www.epa.gov/chemrtk/pubs/summaries/dicambaa/c13451tc.htm> as of May 27, 2010.

² U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: <http://www.epa.gov/opptintr/exposure/pubs/episuite4.htm> as of May 27, 2010.

³ Tomlin CDS, ed. Acifluorfen-sodium (62476-59-9). In: The e-Pesticide Manual, 13th Edition Version 3.1 (2004-05). Surrey UK, British Crop Protection Council.

⁴ US EPA Reregistration Eligibility Decision for Sodium Acifluorfen CASRN: 62476-59-9, Available online from http://www.epa.gov/opp00001/reregistration/REDS/acifluorfen_red.pdf as of June 2, 2010.

⁵ Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: The members of the dicamba and acifluorfen intermediates category are divided into three subcategories. Subcategory I is Dicamba Salts and is composed of three chemicals that are grouped together since all are derivatives of the free acid, benzoic acid, 3,6-dichloro-2-methoxy- (dicamba). Subcategory II is 2,5-Dichlorophenols and is composed of four chemicals that are grouped together since all are 2,5-dichlorophenols used as intermediates in the manufacture of benzoic acid, 3,6-dichloro-2-methoxy. Subcategory III, Benzoic Acids is composed of four chemicals grouped together because they are benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro- (acifluorfen), its sodium salt, and its two intermediates used in the manufacture of benzoic acid, 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitro-. The substances of subcategory I, II, and III are either solids or liquids with moderate to high water solubility and low to negligible vapor pressure. There are two exceptions, phenol, 2,5-dichloro- and benzene, 1,4-dichloro-2-methoxy- which have high and moderate water solubilities, respectively, and moderate vapor pressures. The members of Subcategory I are expected to possess high mobility in soil. The members of Subcategory II and III are expected to have moderate mobility in soil. Volatilization is considered moderate for phenol, 2,5-dichloro- and benzene, 1,4-dichloro-2-methoxy-. Volatilization for all other category members is expected to be low since they are either salts or have low estimated Henry's Law constants. The rate of hydrolysis is considered negligible for all subcategories. The rate of atmospheric photooxidation for nearly all chemicals in subcategories I, II and III is considered slow to negligible. The overall weight of evidence suggests that the members of the dicamba and acifluorfen intermediates category are expected to have moderate persistence (P2) and low bioaccumulation potential (B1). The two exceptions are the compounds benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]- and its potassium salt, benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy]-, potassium salt (1:1), which are expected to have moderate persistence (P2) and moderate bioaccumulation potential (B2).

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Tables 9, 10 and 11 for Subcategories I, II and III, respectively. The tables also indicate where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral Toxicity

Subcategory I

Dicamba, sodium salt (CASRN 1982-69-0)

Sprague-Dawley rats (5/sex) were orally administered a single dose of dicamba, sodium salt (20% purity) in water at 5000 mg/kg-bw and observed for 14 days. No mortalities were observed.

LD₅₀ > 1000 mg a.i./kg-bw

Dicamba (CASRN 1918-00-9, supporting chemical)

Spartan rats (5/sex/dose) were orally administered a single dose of dicamba (85.8% purity) at 500, 794, 1250, 1984, 3150 and 5000 mg/kg-bw in corn oil and observed for 14 days. No mortality occurred at 500 mg/kg-bw and mortality increased in a dose-dependent manner at higher doses. All rats died at 3150 and 5000 mg/kg-bw. The LD₅₀ was reported as 1879 mg/kg-bw in male rats and 1581 mg/kg-bw in female rats.

LD₅₀ = 1465 mg a.i./kg-bw

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

Wistar female rats (10/dose) were administered a single dose of 2,5-dichlorophenol in sesame oil by gavage at 1600, 2500 and 4000 mg/kg-bw and observed for 14 days. Within 24 hours, mortality was observed with 1/10, 4/10, and 10/10 deaths occurring at the three doses.

LD₅₀ = 2475 mg/kg-bw

Subcategory III

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] (CASRN 63734-62-3, supporting chemical)

(1) Sprague-Dawley male rats (6/dose) were administered a single dose of benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] in 10% w/v dispersion of 0.5% methylcellulose in water via an unspecified oral route at 50 and 500 mg/kg-bw and observed for 14 days. No mortality was observed. Study details are from TSCATS (OTS0537712).

LD₅₀ > 500 mg/kg-bw

(2) CF Nelson male rats (5/dose) were administered a single dose of benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] in a 20% (W/V) corn oil dispersion via an unspecified oral route at 625, 1250 and 2500 mg/kg-bw and observed for 14 days. Mortality was observed at 1250 and 2500 mg/kg-bw. Study details are from TSCATS (OTS0537709).

LD₅₀ = 1170 mg/kg-bw

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

CF Nelson male rats (10/dose) were orally administered acifluorfen, sodium salt at 625, 1250, 2500 and 5000 mg/kg-bw and observed for 14 days. Mortality was observed at all doses above 625 mg/kg-bw.

LD₅₀ = 122 mg/kg-bw

Acute Inhalation Toxicity

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

Spartan rats (5/sex) were exposed whole-body to dicamba (85.8% purity) as a dust at 9.6 mg/L (8.2 mg/L active ingredient) for 4 hours and observed for 14 days. No other experimental details were provided. Mortalities did not occur.

LC₅₀ > 9.6 mg/L

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

Spartan rats (5/sex/dose) were exposed whole-body to 2,5-dichlorophenol at 50,000 and 185,000 mg/m³ (~ 50 and 185 mg/L, respectively) for 4 hours and observed for 14 days. No other information about exposure was provided. Two females died during exposure at 185,000 mg/m³.

LC₅₀ > 185 mg/L-bw

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

Albino King (Kng:(SD)BR) rats (5/sex/dose) were exposed whole-body to acifluorfen, sodium salt as an aerosol at nominal concentration of 17.9 mg/L for 4 hours and observed for 14 days. The measured concentration was 6.91 mg/L. No mortalities were observed.

LC₅₀ > 1.38 mg/L

Acute Dermal Toxicity

Subcategory I

Dicamba, sodium salt (CASRN 1982-69-0)

New Zealand White rabbits (5/sex) were dermally administered dicamba, sodium salt to abraded skin at 2000 mg/kg-bw (400 mg/kg-bw active ingredient) under occluded conditions for an unspecified duration and observed for 14 days following dosing. No other experimental details were provided. No mortalities were observed.

LD₅₀ > 400 mg/kg-bw

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

New Zealand White rabbits (2/sex/dose) were administered 2,5-dichlorophenol via the dermal route at 1000, 2000, 4000 and 8000 mg/kg-bw under occluded conditions for an unspecified duration and observed for 14 days following dosing. No mortalities were observed.

LD₅₀ > 8000 mg/kg-bw

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

Five Albino male rabbits were administered acifluorfen, sodium salt via the dermal route at 2500, 3540 and 5000 mg/kg-bw under occluded conditions for an unspecified duration and observed for 14 days. Mortality was observed in all doses (1/5, 2/5, 4/5).

LD₅₀ = 1457 mg/kg-bw

Repeated-Dose Toxicity

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

(1) Wistar rats (10/sex/treatment, an additional 10/sex for control and high dose for recovery) were administered dicamba in the diet at 500, 3000, 6000 and 12,000 ppm (~ 40.1, 239, 479 and 1000 mg/kg-bw/day in males and ~ 43.2, 266, 535 and 1065 mg/kg-bw/day in females) daily for 13 weeks. Control diet was administered to animals for 4 weeks during recovery. Observations included mortality, clinical signs, body weight, food consumption, eye examination, clinical chemistry, and histopathology. No mortality occurred. Clinical signs were observed at 12,000 ppm including reduced activity and slowed movement (throughout the treatment period for some animals) and being cold to the touch (during the first four weeks of treatment). Body weight gain was significantly decreased at 12,000 ppm in both sexes (28% in males and 40% in females) and this effect was reversed during recovery. Food consumption was significantly decreased in animals at 12,000 ppm and the animals at this level had a low food conversion ratio. Females at 12,000 ppm had a higher incidence of thin blood vessels in the retina that resolved after recovery. At 12,000 ppm, both sexes had significantly decreased platelet count, plasma protein, and globulins and significantly increased alkaline phosphatase and alanine and aspartate aminotransferase activities. Females at 12,000 ppm had significantly decreased hemoglobin concentration and red blood cell count and increased mean corpuscular hemoglobin, white blood cells, and lymphocytes as well as significantly increased gamma glutamyl transferase activity, triglyceride, cholesterol, creatinine, and phosphorus levels. Males at 12,000 ppm had decreased cholesterol, triglycerides and glucose, and increased urea. Urine had triple phosphate crystals in males or uric acid crystals in females. Significantly reduced adipose tissue and increased mean liver weight relative to body weight was observed in both sexes at 13 weeks, but not after recovery. Liver weight changes were accompanied by histopathological changes (hypertrophy and hyperpigmentation as well as the clinical chemistry findings for certain enzymes detected in serum indicative of liver damage.

LOAEL (male) ~ 1000 mg/kg-bw/day (based on reduced body weight gain and food consumption, hematology, clinical chemistry and increased liver weight with associated histopathology)

NOAEL (male) ~ 479 mg/kg-bw/day

LOAEL (female) ~ 1065 mg/kg-bw/day (based on reduced body weight gain and food consumption, effects on retina, hematology, clinical chemistry and increased liver weight with associated histopathology)

NOAEL (female) ~ 535 mg/kg-bw/day

(2) Sprague-Dawley rats (20/sex/dose) were administered dicamba in diet at 1000, 5000 and 10,000 ppm (~ 69.4, 342 and 682 mg/kg-bw/day in males and 79.5, 392 and 751 mg/kg-bw/day

in females) for 13 weeks. At the end of 13 weeks, there was 84, 96 and 83% of the target concentration remaining, respectively. Observations included mortality, clinical signs, body weight, food consumption, hematology, biochemistry, urinalysis, organ weights, and organ histopathology. One female rat died at each of the control, 5000, and 10,000 ppm doses. At 10,000 ppm, significantly decreased body weight gains occurred in males. Significantly increased alkaline phosphatase activity was observed in females at all doses and in males at 10,000 ppm. No effects on hematology or organ weight occurred. At 10,000 ppm, a reduction in cytoplasmic vacuolization in hepatocytes was observed (affected sex not indicated).

NOAEL (male) ~ 682 mg/kg-bw/day (highest dose tested)

NOAEL (female) ~ 751 mg/kg-bw/day (highest dose tested)

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

(1) Sprague-Dawley rats (10/sex/dose) were administered 2,5-dichlorophenol vapor (no other details provided) by whole-body inhalation at 0.1, 0.3 or 1.0 mg/L for 6 hours/day, 5 days/week for 4 weeks. Clinical observations included mortality, body weight, hematology, chemistry, and urinalysis. Organs were examined macroscopically at all doses and microscopically in the control and 1.0 mg/L dose. No mortality was observed. Nasal and ocular irritation and discharge was observed at all doses. Salivation and dyspnea were observed at 0.3 and 1.0 mg/L. Significantly decreased body weight gain occurred at 0.3 and 1.0 mg/L. Aspartate aminotransferase (ASAT) was significantly increased in males and females at 0.3 and 1.0 mg/L. Hemoglobin was significantly increased at 1.0 mg/L and the number of leukocytes was significantly increased in females at 0.3 and 1.0 mg/L. In males, significantly decreased absolute liver and brain weight occurred at 0.3 and 1.0 mg/L and decreased absolute heart weight occurred at 0.3 mg/L. Relative kidney weight was significantly increased in males at all doses. Females exhibited significantly increased relative lung weights at 1.0 mg/L. Inflammation of the nasal cavity was observed at 1.0 mg/L. Histopathology indicated that at all doses livers exhibited increased inflammation and necrosis; kidneys were hemorrhagic and discolored and there was inflammatory cell/lymphocyte infiltrate, macrophage congregation and septal fibrosis in the lungs of all treated animals.

LOAEL = 0.3 mg/L (based on effects on body weight gain, changes in hematology parameters, changes in organ weight (liver, brain, heart and kidney) and histopathology of the lung and liver)

NOAEL = 0.1 mg/L

(2) New Zealand White rabbits (4/sex/dose) were administered 2,5-dichlorophenol dermally at 1, 10 and 100 mg/kg-bw/day to skin under unoccluded conditions 6 hours/day, 5 days/week for 3 weeks. Animals were fitted with collars to minimize test substance ingestion. Mortality was observed in one male at 10 mg/kg-bw/day (likely not treatment-related since there were no deaths at 100 mg/kg/d in any males) and three females at 100 mg/kg-bw/day. There were no dose-related effects on body weight gain. Dermal effects occurred at the application site including erythema, edema, atonia, coriscesousness, fissuring and desquamation at all doses with increasing incidence and severity. Hematological changes included significant increases in erythrocytes, leukocytes and hemoglobin in males at 10 and 100 mg/kg-bw/day, while a significant increase in leukocytes was observed in females at 10 mg/kg-bw/day. Clinical chemistry changes were noted in the single surviving female at 100 mg/kg-bw/day (significance unknown). Significantly decreased absolute and relative liver and relative spleen weights were

observed in females at 10 and 100 mg/kg-bw/day, but were not related to dose or microscopic changes. At all doses, the skin lesions at the application site displayed thickening, encrustation, sloughing, necrosis, leatherness and foci in the dermis and epidermis. Histopathology analysis of skin lesions at 1 mg/kg-bw/day (sex not specified) detected inflammatory cell infiltrate, acanthosis, hyperkeratosis and necrotic exudates on the epidermal surface. Dermal fibroplasia and ulceration were noted at 10 and 100 mg/kg-bw/day (sex not specified) in addition to skin effects.

LOAEL (local effects) = 1 mg/kg-bw/day (based on skin lesions and histopathology)

NOAEL (local effects) = Not determined

LOAEL (systemic effects) = 10 mg/kg-bw/day (based on changes in hematology parameters, changes in organ weight (liver and spleen))

NOAEL (systemic effects) = 1 mg/kg-bw/day

2,5-Dichloroanisole (CASRN 1984-58-3)

In a combined repeated dose, reproductive and developmental toxicity study, Wistar rats (10/sex/dose) were administered 2,5-dichloroanisole via gavage at 0, 50, 150 and 450 mg/kg-day for 35 days for males and 44 days for females. No mortality occurred. Significantly decreased body weight was observed in females during the first week of gestation and during the first 4 days of lactation at 450 mg/kg-day. Food consumption was significantly decreased in females during the first week of pre-mating and during the first 4 days of lactation at 450 mg/kg-day. No treatment-related findings were observed on motor activity or in the functional observational battery. Hematological analyses detected no dose-related effects. The absolute and relative kidney weight in males was significantly increased at 150 and 450 mg/kg-day. An increase in the incidence and severity of chronic nephropathy was observed at 450 mg/kg-day (sex not indicated). Treatment-related findings in the liver and thyroid gland are mentioned in the Robust Summary, but are not described further.

LOAEL (males) = 150 mg/kg-day (based on increased kidney weight)

NOAEL (males) = 50 mg/kg-day

NOAEL (females) = 450 mg/kg-day

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

(1) Fischer 344 rats (30/sex/dose) were administered a pesticide product formulation (TACKLE 2AS; 20-21.6% acifluorfen, sodium salt) in the diet at 0, 20, 80, 320, 1250, 2500 and 5000 ppm (actual intakes of 1.5, 6.1, 23.7, 92.5, 191.8 and 401 mg/kg-bw/day in males and ~ 1.8, 7.4, 29.7, 116.0, 237.1 and 441.8 mg/kg-bw/day in females) for 90 days. No mortality was observed. Dorsal hair loss was the only clinical sign observed for animals in all exposure groups. Body weight gain was significantly decreased in both sexes at 2500 and 5000 ppm. Food intake was statistically different from control treatments at all doses; however, there was no consistent positive or negative correlation (data not provided in summary). Hematological changes included lowered red blood cells counts, hemoglobin and hematocrit and an increase in reticulocytes in males at doses greater than 1250 ppm. These hematological effects were seen to a lesser extent in females at 2500 and 5000 ppm (statistical significance not indicated). Clinical chemistry changes observed include significantly decreased blood glucose in males at doses greater than 320 ppm. At 5000 ppm, both males and females showed significantly decreased serum protein levels, and other changes (significance not stated): elevated serum cholesterol,

decreased serum calcium and increased phosphorus in males, and elevated alkaline phosphatase and transaminase in both sexes. Indications of reduced renal function were noted including significantly increased blood urea nitrogen (BUN) in both sexes and increased BUN/creatinine ratio at 30 days in males at 2500 and 5000 ppm. At 30 days, urinalysis (statistical significance of urinalysis results not stated) indicated an increased urobilinogen in males at 5000 ppm and frequency of trace amounts of nitrite in males at doses of 320 ppm and greater and decreased protein excretion in both sexes at 5000 ppm. At 90 days, urinalysis indicated an increased urobilinogen in both sexes at 2500 and 5000 ppm and frequency of trace amounts of nitrite in females at 2500 and 5000 ppm and decreased protein excretion with increasing dose in females or males at 5000 ppm. Significantly increased absolute and relative liver and kidney weights was observed in males at 320 ppm and greater and in females at 2500 and 5000 ppm. Liver and kidney discoloration was observed at 5000 ppm at 30 and 90 days. Histopathology observations of 5000 ppm animals at day 30 revealed increased liver cell hypertrophy and liver tissue damage in both sexes and increased mitotic figures in males and females to a lesser extent. Histopathology observations of high-exposure animals at day 90 revealed increased liver cell hypertrophy in males and hypertrophy in part of the female animals, increased proliferation of oval cells and bile duct in majority of males and yellow pigmentation of Kupfer cells in all treated males.

LOAEL = 23.7 mg/kg-bw/day (based on increased liver and kidney weight and changes in blood chemistry indicative of both liver and kidney damage)

NOAEL = 6.1 mg/kg-bw/day

(2) New Zealand White rabbits (10/sex/dose) were administered acicfluorfen, sodium salt in a NaOH solution via the dermal route at 0, 92, 277 and 923 mg/kg-bw/day to skin under occluded conditions 6 hours/day, 5 days/week for 3 weeks. Mortality was observed in all doses including control. Nineteen of 20 animals receiving 923 mg/kg-bw/day did not survive past day 8 of the study (this dose was reduced to 4.62 mg/kg-bw on day 4 of the test). One male died in the 92 and 277 mg/kg dose groups, and one male and one female died in the control group. Nasal discharge, hair loss, soft stool, tremors, diarrhea, bloating, ataxia, decreased activity, respiratory distress and salivation were observed with increasing severity at increasing doses. It was noted that a white crystalline substance was observed at the application site at all doses. Body weight gain and food consumption was significantly decreased at 923 mg/kg-bw/day in females. Histopathology suggests that the microscopic changes were indicative of macroscopic findings. Significantly increased mean relative adrenal weight was observed in females at 277 mg/kg-bw/day. A relationship with the amount of acicfluorfen, sodium salt applied was evident in the severe dermal irritation and eschar formation that was seen from days 2 – 3 to day 21 in all exposure groups. There were no changes in clinical chemistry.

LOAEL (local effects) = 92 mg/kg-bw/day (based on dermal irritation/local effects)

NOAEL (local effects) = Not established

LOAEL (systemic effects) = 92 mg/kg-bw/day (based on severe clinical signs)

NOAEL (systemic effects) = Not established

Reproductive Toxicity

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

In a two-generation reproductive toxicity study, Sprague-Dawley rats (32/sex/treatment in parental generation and 28/sex/treatment in F1 generation) were administered dicamba in diet at 0, 500, 1500 and 5000 ppm (~ 35, 105, and 347 mg/kg-bw/day for F0 males and ~ 41, 125, and 390 mg/kg-bw/day for F0 females; ~ 40, 121, and 432 mg/kg-bw/day for F1 males and ~ 44, 135, and 458 mg/kg-bw/day for F1 females) for 10 weeks (F1) or 12 weeks (F2) prior to mating until weaning (50-week maximum test duration). At 500 and 5000 ppm, one F0 female died at each dose. Mortality occurred in the F1 controls (2 male/1 female), 500 (1 male/1 female), 1500 (1 male, and 5000 (1 male) ppm doses. Differences in body weight gain were observed in F0 females and in F1 males and females at 5000 ppm. Food consumption was decreased in F1 animals at 5000 ppm. Macroscopic examinations revealed an increase of the number of pale foci on the lungs of F0 males. Microscopic examination revealed no treatment-related findings in either generation. Increased liver weight was observed in F0 males and females and decreased epididymides, prostate and relative kidney weights were observed in males at 5000 ppm. Decreased relative pituitary weights were observed at all doses. Increased liver weight and decreased lung and absolute brain weight were noted in the F1 pups at 1500 and 5000 ppm. F1 females showed lower body weight gain during pregnancy and signs of increased bodytone and slow righting reflex during late lactation, but the significance of these results is unknown. No systemic effects were observed in the F2 generation. Mating and fertility parameters were assessed in males and females with dietary administration of dicamba. Females from the F0 generation were able to become pregnant at all doses. In the F1 generation, reproductive effects included decreased pregnancy rate (at 5000 ppm), decreased litter weight, and increased pup mortality resulting in reduced litter size (at 1500 and 5000 ppm). Sperm motility, morphology and number were within normal limits for the F1 generation. In the F0 generation a shift in the duration of pregnancy from 22/23 to 21 days was noted as well as decreased litter and pup weights at 5000 ppm. Decreased epididymides and prostate weight occurred in F0 males at 5000 ppm. Decreased litter and pup weights and delayed sexual maturation in males was observed at 5000 ppm in F1 offspring. In the F2 pups, decreased pup weight and delayed sexual maturation was observed in males and females at 5000 ppm. Statistical significance of any of the reported effects was not indicated in the summary.

NOAEL (parental, F0) ~ 347-390 (male-female) mg/kg-bw/day (highest dose tested)

NOAEL (parental, F1) ~ 432-458 (male-female) mg/kg-bw/day (highest dose tested)

LOAEL (reproductive toxicity) = 135 mg/kg-bw (based on pregnancy effects and reduced litter size in the F1 generation)

NOAEL (reproductive toxicity) = 44 mg/kg-bw

LOAEL (developmental toxicity) ~ 432-458 (male-female) mg/kg-bw/day (based on impaired growth of F1 and F2 offspring and delayed sexual maturation in both sexes)

NOAEL (developmental toxicity) ~ 121-135 (male-female) mg/kg-bw/day

Subcategory II

2,5-Dichloroanisole (CASRN 1984-58-3)

In the combined repeated-dose, reproductive and developmental toxicity study in Wistar rats described previously, animals were mated for 2 weeks. No changes were observed in male mating and female fertility indices. Reproductive organ weight (prostate, testes, uterus and ovaries) and histology (prostate, seminal vesicles, testes, uterus and ovaries) were similar to controls at doses up to 450 mg/kg-day, the highest dose tested. One female in each dose group failed to deliver pups or reveal in utero implantations upon necropsy. One control female had

implantation sites, but did not deliver a litter. This variation is within normal range and is not considered treatment related. Implantation, intrauterine embryo- and fetolethality, the mean number of F1 pups delivered per dam and the number of stillborn pups were not significantly different from controls.

NOAEL (reproductive toxicity) = 450 mg/kg-day (highest dose tested)

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

In a two-generation reproductive toxicity study, Sprague-Dawley rats (35 or 40/sex/group for parent and F1, respectively) were administered acifluorfen, sodium salt (purity not specified) in the diet at concentrations of 0, 25, 500 or 2500 ppm (see Robust Summary for estimates of actual intakes in pre-mating males and females, pregnant and lactating females; for the purposes of this hazard characterization the following values will be used: males: 1.6, 31, and 158 mg/kg-bw/day; females [pre-mating and pregnancy]: 1.7, 30, and 160 mg/kg/day, and females [lactation]: 3, 59 and 269 mg/kg/day) for 12 weeks and were then mated over a 3-week period. The actual exposure in terms of the average mg/kg-bw/day dosage was calculated to be higher in females than in males for each generation and within each sex the second generation received higher dosages than the first generation. Mortality was observed in the parental generation (one low dose female and one high dose male). In the F1 generation, the following deaths were recorded: one female (control), one male (low dose) and one male and five females (high dose). Decreased body weight was observed in all generations at 2500 ppm and increased body weights were observed in only parental generation females and only during lactation. In the parent generation, food consumption was decreased in females at 500 ppm and decreased in males and lactating females at 2500 ppm. In the F1 generation, food consumption was increased at 2500 ppm. Clinical signs observed in the parent and F1 generation at 2500 ppm include chromodacryorrhoea and urine stained abdominal fur in males and emaciation in females. Parental generation and F1 adult animals revealed kidney lesions in both males and females (macroscopically, mid and high dose levels) and microscopic effects characterized by dilation of tubules in the outer medulla in females at the mid and high dose levels. Low incidences of a mottled renal pelvis and a dark red to black areas of the stomach was observed in parent generation animals, which progressed to gross kidney lesions, gastric lesions and dilation of the kidney pelvis in F1 and F2 generation animals. In the parent generation, reproductive effects included decreased numbers of implantation sites (at 2500 ppm) and decreased pup weights between birth and day 21 postpartum (at 2500 ppm). In the F1 generation, reproductive effects included decreased gestation duration (at 2500 ppm) and decreased pup viability on days 1 – 4 postpartum (at 500 and 2500 ppm). Two litters of F2 pups died after day 2 or 5 postpartum at 500 and 2500 ppm, respectively. Microscopic examinations of parent animals revealed kidney lesions characterized by dilation of tubules in the outer medulla in females. An increased incidence of pelvic dilation was seen in F1 generation males in addition to microscopic effects observed in the parent generation.

LOAEL (parental toxicity) ~ 30 mg/kg-bw/day (based on increased incidence of kidney lesions in females)

NOAEL (parental toxicity) ~ 2 mg/kg-bw/day

LOAEL (reproductive toxicity) ~ 30 mg/kg-bw/day (based on decreased pup survival in F1 generation)

NOAEL (reproductive toxicity) ~ 2 mg/kg-bw/day

Developmental Toxicity

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

(1) Pregnant Sprague-Dawley female rats (25/dose) were administered dicamba in corn oil once on days 6 – 19 of gestation via oral gavage at 0, 64, 160 and 400 mg/kg/day. Dams were examined for mortality, clinical signs, body weight gain, food consumption, implantations, and resorptions. Fetuses were examined for weight, external, visceral, and skeletal abnormalities. At 400 mg/kg-bw/day, three females died, food consumption was decreased, and body weight was decreased in remaining females. Clinical signs at 400 mg/kg/day included increased incidence of crusty nose/muzzle, wheezing, ataxia, stiffening of the body when held, urine soaked fur, salivation, and decreased motor activity. A decreased percentage of females at 400 mg/kg/day became pregnant (77% vs 92% in controls) and there was an increase in resorptions (8.7% vs 6.4%) and a slight decrease in implantations (13.1 vs. 14.2). Post implantation loss and number of corpora lutea were not measured. Fetal body weight and sex ratio did not differ from controls. One litter at 400 mg/kg/day had increased incidence of renal pelvic cavitation and incomplete frontal and/or parietal ossification was present, but these observations were not considered related to treatment with dicamba. Statistical significance of any of the reported effects was not indicated in the summary.

LOAEL (maternal toxicity) = 400 mg/kg/day (based on mortality decreased body weight, and clinical signs)

NOAEL (maternal toxicity) = 160 mg/kg/day

NOAEL (developmental toxicity) = 400 mg/kg/day (highest dose tested)

(2) Pregnant New Zealand White female rabbits (19-20/dose) were administered dicamba daily on days 6 – 18 of gestation via opaque white gelatin capsules at 30, 150 and 300 mg/kg-bw/day. Observations included mortality, clinical signs, body weight gain, food consumption, uterine content, and fetal sex, weight, external, visceral, and skeletal variations. At 150 mg/kg-bw/day, females showed ataxia and decreased motor activity, reduced body weight gain and feed consumption. At 300 mg/kg-bw/day females exhibited body weight loss, reduced overall food consumption and clinical signs including ataxia, decreased motor activity, labored breathing, perinasal substance, dried or no feces and an impaired righting reflex. Spontaneous abortion occurred in one female at 150 mg/kg-bw/day and four females at 300 mg/kg-bw/day. No significant differences were reported for number of corpora lutea, implantations, litter size, percent resorptions, sex ratio, or fetal body weight. Incidental observations of gross, visceral, and skeletal abnormalities were reported, but were not considered related to dicamba treatment.

LOAEL (maternal toxicity) = 150 mg/kg-bw/day (based on spontaneous abortions, clinical signs, reduced body weight, and reduced feed consumption)

NOAEL (maternal toxicity) = 30 mg/kg-bw/day

NOAEL (developmental toxicity) = 300 mg/kg-bw/day (highest dose tested)

Subcategory II

2,5-Dichloroanisole (CASRN 1984-58-3)

In the combined reproductive and developmental toxicity study in Wistar rats described previously, offspring of females were sexed, weighed on the day of birth and postnatal day 4, examined for clinical signs, and examined for external and visceral changes on postnatal day 4.

All measures of viability, sex ratio, neonatal body weight and postnatal survival in treated animals were not significantly different from controls at any dose tested. Necropsy noted isolated cases of autolysis, empty stomach and absent unilateral testis (data not reported) that were described as not related to treatment.

LOAEL (maternal toxicity) = 450 mg/kg-bw/day (based on reduced body weights during gestation and lactation and reduced feed consumption)

NOAEL (maternal toxicity) = 150 mg/kg-bw/day

NOAEL (developmental toxicity) = 450 mg/kg-day (highest dose tested)

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

(1) Pregnant Crj:COBS-CD(SD)BR female rats (25/group) were administered acifluorfen, sodium salt (91.2% purity) via gavage at of 0, 20, 90 and 180 mg/kg-bw/day on days 6 – 19 of gestation. Three high-exposure females died on gestation days 10 or 17. At 180 mg/kg-bw/day, maternal body weight decreased during treatment (gestation days 9 – 19) and on gestation days 6 – 19 and 0 – 20. Fetal body weights appeared to be decreased in a dose-dependent manner. Clinical signs observed in females include excessive salivation (both mid- and high-dose groups), vocalization, hyperactivity, impaired/lost righting reflex, decreased motor activity, chromodacryorrhoea, rales, urine stained fur and chromorrhinorrhoea all in the high dose groups only. The number of abortions, implantations and corpora lutea were similar across all groups. Number of resorptions (early/late) were 7.3%, 6.6%, 10.4%, and 16.2% for the control, low, mid and high dose groups respectively (reported as percent of implantation sites). No gross pathological changes were observed in the reproductive organs of surviving females. The following fetal effects were observed in the mid and high dose groups: visceral abnormalities (slight dilation of lateral ventricles of the brain) and skeletal abnormalities (delayed ossification of metacarpals, forepaw and hindpaw phalanges). Fetuses in the high dose group also had a higher incidence of delayed ossification of the caudal vertebrae, sternbrae and metatarsals. Statistical significance of any findings were not provided in the robust summary.

LOAEL (maternal toxicity) = 90 mg/kg-bw/day (based on increased clinical signs)

NOAEL (maternal toxicity) = 20 mg/kg-bw/day

LOAEL (developmental toxicity) = 90 mg/kg-bw/day (based on higher incidence of visceral and skeletal abnormalities)

NOAEL (developmental toxicity) = 20 mg/kg-bw/day

(2) Pregnant New Zealand White female rabbits (16/dose) were administered acifluorfen, sodium salt (81.2% purity) via gavage at doses of 0, 3, 12 and 36 mg/kg-bw/day on days 6 – 29 of gestation. No treatment-related clinical signs were observed. Mortalities were observed at all dose levels, but appeared to be incidental in nature. Observations of the maternal toxicity found at 36 mg/kg-bw/day included decreased body weight gain and a marked inhibition of food consumption during gestation days 23 – 24 that was reversed during gestation days 29 – 30. The number of corpora lutea, implantations, litter sizes, early and late resorptions, fetal sex ratio, number of resorbed conceptuses and number of does with resorptions were similar across all groups. The robust summary states that there was an increased number of involuted corpora lutea and congested mucosa; however, these data are not provided. It further states that these are believed to be attributed to interference of acifluorfen, sodium salt with implantation after

fertilization. No treatment-related effects on gross external, visceral or skeletal examinations were observed.

LOAEL (maternal toxicity) = 36 mg/kg-bw/day (based on decreased body weight gain and food consumption)

NOAEL (maternal toxicity) = 12 mg/kg-bw/day

NOAEL (developmental toxicity) = 36 mg/kg-bw/day (highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA102 were exposed to dicamba in DMSO vehicle at concentrations of 8 – 5000 µg/plate with and without metabolic activation. Positive and negative controls were tested concurrently, but control responses were not provided. Cytotoxicity occurred at 1500 µg/plate with and without metabolic activation.

CASRN 1918-00-9 was not mutagenic in this assay.

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

Chinese hamster ovary (CHO) K1-BH4 cells were exposed to 2,5-dichlorophenol without metabolic activation at 100, 125, 150, 200 and 250 µg/mL and with metabolic activation at 62.5, 75, 100, 125, 150, 200 and 250 µg/mL. Positive and negative controls were tested concurrently and responded appropriately. The number of mutants at 62.5 µg/mL with metabolic activation was significantly increased, but no concentration-effect relationship was observed. Cytotoxicity was observed at 250 µg/mL both with and without metabolic activation.

CASRN 583-78-8 was not mutagenic in this assay.

Subcategory III

Acifluorfen (CASRN 50594-66-6, supporting chemical)

Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 were exposed to acifluorfen at concentrations of 0, 20, 100, 500, 2500 and 5000 µg/plate with and without metabolic activation. Positive and negative controls were tested concurrently and appeared to respond appropriately. Slight toxicity was observed to strains TA1535 and TA100 at 5000 µg/plate.

CASRN 50594-66-6 was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

Chinese hamster ovary (CHO) cells (CHO-K1) were exposed to dicamba in DMSO with and without metabolic activation at 300, 590, 1170 and 2330 µg/mL. Positive and negative controls were tested concurrently and responded appropriately.

CASRN 1918-00-9 did not induce chromosomal aberrations in this assay.

In vivo

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

Sprague-Dawley rats (4/sex/dose) were administered dicamba in a water solution with 20% gum Arabic via gavage at 208, 416 and 832 mg/kg-bw. Positive (chemical not identified) and negative controls were tested concurrently; negative control responded appropriately but there was no indication of the results from the positive control group. There were no significant differences in gaps, chromatid breaks, isochromatid breaks, fragments or chromosomal rearrangements measured.

CASRN 1918-00-9 did not induce chromosomal aberrations in this assay.

Subcategory II

2,5-Dichlorophenol (CASRN 583-78-8)

In a micronucleus assay, NMRI mice (10/dose; male/female) were administered a single dose of 2,5-dichlorophenol in corn oil via gavage at 1500 mg/kg-bw. Bone marrow was sampled at 24, 48, and 72 hours after dosing. Positive and negative controls were tested concurrently and responded appropriately. The percentage of polychromatic erythrocytes (PCEs) was significantly decreased at the 72-hour sampling time, indicating cytotoxicity. The mean number of micronucleated PCEs was not significantly different from controls.

CASRN 583-78-8 did not induce micronuclei in this assay.

Subcategory III

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

Male and female CD-1 mice were administered acifluorfen, sodium salt (purity of 42.8%) in distilled water via gavage at 0, 100, 500 and 1000 mg/kg-bw (42.8, 214, 428 mg/kg a.i.). Positive and negative controls were tested concurrently and responded appropriately. There were no significant differences in the number of cells with aberrations.

CASRN 62476-59-9 did not induce chromosomal aberrations in this assay.

Genetic Toxicity – Other

In vitro

Subcategory I

Dicamba (CASRN 1918-00-9, supporting chemical)

(1) Human whole blood lymphocytes from three donors were exposed to dicamba in DMSO without metabolic activation at 10, 20, 50, 100, 200, and 500 µg/mL. Positive and negative controls were tested concurrently. A significant increase in sister chromatid exchange was observed at 200 µg/mL. The fold increase over controls was not reported. Cytotoxicity was observed at 500 µg/mL.

Dicamba induced sister chromatid exchange in this assay.

(2) Human peripheral blood lymphocytes from donors (number not specified) were exposed to dicamba in DMSO with and without metabolic activation at 0, 100, 200, 400, and 800 µg/mL. No data regarding positive controls were provided. A significant increase in the number of sister chromatid exchanges were observed in three trials either with or without metabolic activation, but the frequency did not exceed a 2-fold increase, so there was no clear positive response. No information on cytotoxicity was provided.

Dicamba yielded equivocal results in this assay.

Additional Information

Skin Irritation

Subcategory III

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] (CASRN 63734-62-3)

(1) In four different studies, New Zealand Albino rabbits (six males/dose) were exposed to 0.5 g of benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] as paste, 1:1 with saline on shaved intact or abraded skin under occluded conditions for 4 hours and observed for 7 days. Dessication was noted. Summarized from TSCATS (OTS0537704, OTS0537705, OTS0537706 and OTS0537707).

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] was practically non-irritating to intact rabbit skin and slightly irritating to abraded rabbit skin in this study.

(2) Four New Zealand Albino rabbits were exposed to 0.5 g of benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] as an aqueous paste on shaved intact skin under occluded conditions for 24 hours and were observed for 72 hours. Erythema and edema were noted. Summarized from TSCATS (OTS0537708).

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] was slightly irritating to rabbit skin in this study.

Eye Irritation

Subcategory III

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] (CASRN 63734-62-3)

(1) In studies designed to assess acute ocular irritation in six rabbits, a single instillation of 0.1 g benzoic acid, 3-2-chloro-4-(trifluoromethyl)phenoxy] resulted in effects that included severe corneal injury and conjunctival irritation. Summarized from TSCATS (OTS0537709).

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] was severely irritating to rabbit eyes in this study.

(2) In studies designed to assess acute ocular irritation in six rabbits, a single instillation of 0.1 g benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] resulted in effects that included moderate corneal injury and conjunctival irritation. Summarized from TSCATS (OTS0537712).

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] was moderately irritating to rabbit eyes in this study.

Conclusion:

Subcategory I: Dicamba Salts

Acute oral toxicity for CASRN 1982-69-0 and the supporting chemical, CASRN 1918-00-9, is low in rats. Acute inhalation toxicity in rats for the supporting chemical, CASRN 1918-00-9, and acute dermal toxicity in rabbits for CASRN 1982-69-0 are moderate. In a 13 week repeated-dose study, dietary exposure of rats to the supporting chemical, CASRN 1918-00-9, significantly decreased body weight gain and food consumption and increased mean liver weight in both sexes at 1000 and 1065 mg/kg-bw/day in males and females, respectively. Additional changes in hematology, blood chemistry, and urinalysis occurred at the same doses. The NOAEL for systemic toxicity is ~ 479 mg/kg-bw/day in males and ~ 535 mg/kg-bw/day in females. In another 13 week repeated-dose study, dietary exposure of a different strain of rats to the supporting chemical, CASRN 1918-00-9, did not cause any treatment-related effects. The NOAEL for systemic toxicity is ~ 682 mg/kg-bw/day in males and ~ 751 mg/kg-bw/day in females. In a dietary two-generation reproductive toxicity study in rats, the supporting chemical, CASRN 1918-00-9, showed no adverse systemic effects up to the highest dose tested. The NOAEL for systemic toxicity for F0 males, F0 females, F1 males, and F1 females, is 347, 390, 432, and 458 mg/kg-bw/day, respectively. Based on effects on decreased pregnancy rate and reduced litter size at ~ 135 mg/kg-bw/day (significance not indicated), the NOAEL for reproductive toxicity is ~ 44 mg/kg-bw/day. Based on decreased pup weights and delayed sexual maturation at 432 – 458 (male-female) mg/kg-bw/day, the NOAEL for developmental toxicity is 121-135 (male-female) mg/kg-bw/day. An oral gavage prenatal developmental toxicity study with the supporting chemical CASRN 1918-00-9, in rats, found mortality and decreased weight gain in dams at 400 mg/kg-bw/day and no effects on offspring; the NOAEL for maternal toxicity is 160 mg/kg-bw/day and the NOAEL for developmental toxicity is 400 mg/kg-bw/day. An oral gavage prenatal developmental toxicity study with the supporting chemical CASRN 1918-00-9, in rabbits, found spontaneous abortions at 150 mg/kg-bw/day and above, and no effects on offspring; the NOAEL for maternal toxicity is 30 mg/kg-bw/day and the NOAEL for developmental toxicity is 300 mg/kg-bw/day (highest dose tested). The supporting chemical, CASRN 1918-00-9, was not mutagenic in a bacterial reverse mutation assay and did not induce chromosomal aberrations *in vitro* or *in vivo*. The supporting chemical, CASRN 1918-00-9, induced sister chromatid exchange *in vitro*.

Subcategory II: 2,5-Dichlorophenols

Acute oral, and inhalation toxicity of CASRN 583-78-8 are low in rats and acute dermal toxicity is low in rabbits. A repeated-dose inhalation study in rats found significant effects of CASRN 583-78-8 on body weight gain, hematology, organ weight, and histopathology of lung and liver at 0.3 mg/L; the NOAEL for systemic inhalation toxicity is 0.1 mg/L. A repeated-dose dermal toxicity study of CASRN 583-78-8 in rabbits found skin lesions and associated pathological changes at 1 mg/kg-bw/day, the lowest dose tested; the NOAEL for systemic dermal toxicity was not established. A combined oral gavage repeated-dose/reproductive/developmental toxicity study of CASRN 1984-58-3 in rats showed increased kidney weight with chronic progressive nephropathy in males at 150 mg/kg-bw/day and above. Treatment-related findings in the liver and thyroid gland were also observed. Females showed reduced body weights at 450 mg/kg-bw/day; the NOAEL for systemic toxicity is 50 and 150 mg/kg-bw/day in males and females,

respectively. No adverse effects were observed for reproductive or developmental toxicity endpoints; the NOAEL for reproductive toxicity is 450 mg/kg-bw/day (highest dose tested). The NOAEL for maternal and developmental toxicity is 150 and 450 (highest dose tested) mg/kg-bw/day, respectively. CASRN 583-78-8 was not mutagenic in a bacterial reverse mutation assay and did not induce mouse micronuclei *in vivo*.

Subcategory III: Benzoic Acids

The acute oral toxicity of CASRN 63734-62-3 in rats is low. For the supporting chemical, CASRN 62476-59-9, acute inhalation toxicity in rats is high and acute dermal toxicity in rabbits is moderate. A 90-day oral repeated-dose study in rats, with the supporting chemical CASRN 62476-59-9, showed increased liver and kidney weights in males with corresponding changes in clinical chemistry at 23.7 mg/kg-bw/day; the NOAEL for systemic toxicity is 6.1 mg/kg-bw/day. A three-week dermal repeated-dose study in rabbits with the supporting chemical, CASRN 62476-59-9, showed severe skin irritation and clinical signs of toxicity at 92 mg/kg-bw/day, the lowest dose tested; the NOAELs for local effects and systemic toxicity were not established. A dietary 2-generation reproductive toxicity study in rats with the supporting chemical, CASRN 62476-59-9, showed increased incidence of kidney lesions in both sexes at 30 mg/kg-bw/day and above; the NOAEL for systemic toxicity is 2 mg/kg-bw/day. Decreased gestation duration and pup viability were observed at 30 mg/kg-bw/day and above; the NOAEL for reproductive/developmental toxicity is 2 mg/kg-bw/day. A prenatal gavage developmental toxicity study in rats with the supporting chemical, CASRN 62476-59-9, showed decreased body weight, clinical symptoms and behavioral changes in dams and increased incidence of visceral and skeletal abnormalities in pups at 90 mg/kg-bw/day; the NOAEL for maternal and developmental toxicity is 20 mg/kg-bw/day. In a prenatal developmental toxicity study in rabbits with the supporting chemical, CASRN 62476-59-9, dietary exposure resulted in reduced body weight gain and food consumption in dams at 36 mg/kg-bw-day and no signs of developmental toxicity at 36 mg/kg-bw/day; the NOAEL for maternal toxicity is 12 mg/kg-bw/day and the NOAEL for developmental toxicity is 36 mg/kg-bw/day (highest dose tested). The supporting chemical, CASRN 50594-66-6 was not mutagenic in a bacterial reverse mutation assay *in vitro* and the supporting chemical, CASRN 62476-59-9 did not induce chromosomal aberrations in mice *in vivo*. CASRN 63734-62-3 was irritating to rabbit skin and eyes.

Table 9. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data

Subcategory I				
Endpoints	SPONSORED CHEMICAL Dicamba, sodium salt (1982-69-0)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (68938-79-4)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, dipotassium salt (68938-80-7)	SUPPORTING CHEMICAL Dicamba (1918-00-9)
Acute Oral Toxicity LD₅₀ (mg/kg-bw)	> 1000 a.i.	No Data 1465 (RA)	No Data 1465 (RA)	1465 a.i.
Acute Inhalation Toxicity LC₅₀ (mg/L)	No Data > 8.2 (RA)	No Data > 8.2 (RA)	No Data > 8.2 (RA)	> 8.2 a.i.
Acute Dermal Toxicity LD₅₀ (mg/kg-bw)	> 400 a.i.	No Data 400 (RA)	No Data 400 (RA)	No Data 400 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No Data NOAEL = 500 LOAEL = 1000 (RA)	No Data NOAEL = 500 LOAEL = 1000 (RA)	No Data NOAEL = 500 LOAEL = 1000 (RA)	NOAEL = 500 LOAEL = 1000
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No Data NOAEL = 44 LOAEL = 135 (RA)	No Data NOAEL = 44 LOAEL = 135 (RA)	No Data NOAEL = 44 LOAEL = 135 (RA)	NOAEL = 44 LOAEL = 135
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) Maternal Developmental	No Data LOAEL =150 NOAEL = 30 NOAEL = 300 (RA)	No Data LOAEL =150 NOAEL = 30 NOAEL = 300 (RA)	No Data LOAEL =150 NOAEL = 30 NOAEL = 300 (RA)	(Rabbit) LOAEL =150 NOAEL = 30 NOAEL = 300

Table 9. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data

Subcategory I				
Endpoints	SPONSORED CHEMICAL Dicamba, sodium salt (1982-69-0)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, potassium sodium salt (68938-79-4)	SPONSORED CHEMICAL Benzoic acid, 3,6-dichloro-2-hydroxy-, dipotassium salt (68938-80-7)	SUPPORTING CHEMICAL Dicamba (1918-00-9)
Genetic Toxicity – Gene Mutation <i>In vitro</i>	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	No Data Positive (RA)	No Data Positive (RA)	No Data Positive (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	Negative
Genetic Toxicity – Other <i>In vitro</i>	No Data Positive (RA)	No Data Positive (RA)	No Data Positive (RA)	Positive (SCEs)

Measured data indicated in **bold text**; (RA) = Read Across; (-) = Endpoint not addressed

Table 10. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data

Subcategory II				
Endpoints	SPONSORED CHEMICAL 2,5-Dichloroanisole (1984-58-3)	SPONSORED CHEMICAL Phenol , 2,5-dichloro- (583-78-8)	SPONSORED CHEMICAL Phenol , 2,5-dichloro-, sodium salt (52166-72-0)	SPONSORED CHEMICAL Phenol , 2,5-dichloro-, potassium salt (68938-81-8)
Acute Oral Toxicity LD₅₀ (mg/kg)	No Data 2475 (RA)	2475	No Data 2475 (RA)	No Data 2475 (RA)
Acute Inhalation Toxicity LC₅₀ (mg/L)	No Data > 185 (RA)	> 185	No Data > 185 (RA)	No Data > 185 (RA)
Acute Dermal Toxicity LD₅₀ (mg/kg)	No Data > 2000 (RA)	> 2000	No Data > 2000 (RA)	No Data > 2000 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	NOAEL = 50 LOAEL = 14	No Data NOAEL = 50 LOAEL = 14 (RA)	No Data NOAEL = 50 LOAEL = 14 (RA)	No Data NOAEL = 50 LOAEL = 14 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Inhalation (mg/L/day)	No Data NOAEL = 0.1 LOAEL = 0.3 (RA)	NOAEL = 0.1 LOAEL = 0.3	No Data NOAEL = 0.1 LOAEL = 0.3 (RA)	No Data NOAEL = 0.1 LOAEL = 0.3 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg- bw/day)	No Data NOAEL (syst) = 1 LOAEL (syst) = 10 LOAEL (local)= 1 (RA)	NOAEL (syst) = 1 LOAEL (syst) = 10 LOAEL (local)= 1 (Lowest dose tested)	No Data NOAEL (syst) = 1 LOAEL (syst) = 10 LOAEL (local)= 1 (RA)	No Data NOAEL (syst) = 1 LOAEL (syst) = 10 LOAEL (local)= 1 (RA)
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	NOAEL = 450 (highest dose tested)	No Data NOAEL = 450 (RA)	No Data NOAEL = 450 (RA)	No Data NOAEL = 450 (RA)

Table 10. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data				
Subcategory II				
Endpoints	SPONSORED CHEMICAL 2,5-Dichloroanisole (1984-58-3)	SPONSORED CHEMICAL Phenol , 2,5-dichloro- (583-78-8)	SPONSORED CHEMICAL Phenol , 2,5-dichloro-, sodium salt (52166-72-0)	SPONSORED CHEMICAL Phenol , 2,5-dichloro-, potassium salt (68938-81-8)
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) Maternal	NOAEL = 150 LOAEL = 450	No Data NOAEL = 150 LOAEL = 450 (RA)	No Data NOAEL = 150 LOAEL = 450 (RA)	No Data NOAEL = 150 LOAEL = 450 (RA)
Developmental	NOAEL = 450 (highest dose tested)	NOAEL = 450 (RA)	NOAEL = 450 (RA)	NOAEL = 450 (RA)
Genetic Toxicity – Gene Mutation <i>In vitro</i>	No Data Negative (RA)	Negative	No Data Negative (RA)	No Data Negative (RA)
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	No Data Negative (RA)	Negative	No Data Negative (RA)	No Data Negative (RA)

Measured data indicated in **bold text**; (RA) = Read Across; (-) = Endpoint not addressed

Table 11. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data				
Subcategory III				
Endpoints	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)-phenoxy] (63734-62-3)	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)-phenoxy], potassium salt (72252-48-3)	SUPPORTING CHEMICAL Acifluorfen (50594-66-6)	SUPPORTING CHEMICAL Acifluorfen, sodium salt (62476-59-9)
Acute Oral Toxicity LD₅₀ (mg/kg)	> 50 a.i.	No Data 122 (RA)	-	122 a.i.
Acute Inhalation Toxicity LC₅₀ (mg/L)	No Data > 1.38 (RA)	No Data > 1.38 (RA)	-	> 1.38
Acute Dermal Toxicity LD₅₀ (mg/kg)	No Data 1457 (RA)	No Data 1457 (RA)	-	1457 a.i.
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No Data NOAEL = 6.1 LOAEL = 23.7 (RA)	No Data NOAEL = 6.1 LOAEL = 23.7 (RA)	-	<u>Rat</u> NOAEL = 6.1 LOAEL = 23.7
Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)	No Data LOAEL (local) = 92 NOAEL (syst) = 277 LOAEL (syst) = 923 (RA)	No Data LOAEL (local) = 92 NOAEL (syst) = 277 LOAEL (syst) = 923 (RA)	-	<u>Rabbit</u> NOAEL (local) = Not established LOAEL (local) = 92 NOAEL (systemic) = Not established LOAEL (systemic) = 92
Reproductive Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)	No Data NOAEL ~ 2 LOAEL ~ 30 (RA)	No Data NOAEL ~ 2 LOAEL ~ 30 (RA)	-	NOAEL ~ 2 LOAEL ~ 30

Table 11. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Human Health Data				
Subcategory III				
Endpoints	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)-phenoxy] (63734-62-3)	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)-phenoxy], potassium salt (72252-48-3)	SUPPORTING CHEMICAL Acifluorfen (50594-66-6)	SUPPORTING CHEMICAL Acifluorfen, sodium salt (62476-59-9)
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg/day) Maternal	No Data NOAEL = 12 LOAEL = 36 (RA)	No Data NOAEL = 12 LOAEL = 36 (RA)	–	<u>Rabbit</u> NOAEL = 12 LOAEL = 36
Developmental	No Data NOAEL = 36 (RA)	No Data NOAEL = 36 (RA)		NOAEL = 36 (highest dose tested)
Genetic Toxicity – Gene Mutation <i>In vitro</i>	No Data Negative (RA)	No Data Negative (RA)	Negative	–
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	No Data Negative (RA)	No Data Negative (RA)	–	Negative
Additional Information Skin Irritation Eye Irritation	Slightly irritating Severely irritating	– –	– –	– –

Measured data indicated in **bold text**; (RA) = Read Across; – indicates endpoint not addressed for this chemical

4. Hazard to the Environment

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 12. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. Some additional studies are located in EPA's ECOTOX database (<http://cfpub.epa.gov/ecotox/>).

Acute Toxicity to Fish

Subcategory 1

Dicamba, sodium salt (CASRN 1982-69-0)

(1) Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance at unspecified concentrations under static conditions for 96 hours. Study details are from a brief study summary in the OPP Pesticide Ecotoxicity Database.

96-h LC₅₀ = 558 mg/L

(2) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance at unspecified concentrations under static conditions for 96 hours. This study has been retrieved from the ECOTOX database (Office of Pesticide Programs, 2000).

96-h LC₅₀ = 706 mg/L

Subcategory 2

No data are available.

Subcategory 3

2,5-Dichloroanisolole (CASRN 1984-58-3)

Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance at nominal concentrations of 0, 1.0, 2.2, 5.0, 10.0 and 22.0 mg/L under semistatic conditions for 96 hours. All measured concentrations were within 80 – 120% of nominal during the exposure period.

96-h LC₅₀ = 2.4 mg/L

Subcategory 4

2,5-Dichlorophenol (CASRN 583-78-8)

Medaka (*Oryzias latipes*) were exposed to the test substance at unspecified concentrations under static conditions for 96 hours. The study details were retrieved from a published Japanese article from the Pharmaceutical Society of Japan (Shigeoka, *et al.*, 1988).

96-h LC₅₀ = 3.3 mg/L

2,5-Dichlorophenol, sodium salt (CASRN 52166-72-0)

Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance (CASRN 52166-72-0) at nominal concentrations 0.63, 1.3, 2.5, 5.0 and 10.0 mg/L under flow-through conditions for 96 hours. Measured concentrations were 0.66, 1.3, 2.6, 5.0 and 10.0 mg/L. All fish from two high exposure groups died. Signs of toxicity were evident among surviving fish exposed to 2.6 mg/L. No effects were observed at two low exposures.

96-h LC₅₀ = 3.2 mg/L

Subcategory 5

Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] (CASRN 63734-62-3)

(1) In two separate studies, Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance (CASRN 63734-62-3) at nominal concentrations of 0, 100, 180, 320, 560 and 1000 mg/L under static conditions for 96 hours. No mortalities were observed. Additional study details are from TSCATS (OTS0537713, OTS0537714 and OTS0537715).

96-h LC₅₀ > 1000 mg/L

(2) Fathead minnows (*Pimephales promelas*) were exposed to the test substance (CASRN 63734-62-3) at nominal concentrations of 1.4, 1.8, 2.4, 3.2, 4.2, 6.5, 10 and 18 mg/L under static conditions for 96 hours. Mortality was observed in all groups except 1.4 mg/L. Additional study details are from TSCATS (OTS0537710).

96-h LC₅₀ = 2.6 mg/L

Acifluorfen, sodium salt (CASRN 62476-59-9, supporting chemical)

(1) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance (CASRN 62476-59-9) with 25 % purity at nominal concentrations of 0, 22, 36, 60, 100 and 170 mg/L under static conditions for 96 hours. Mortality was observed in all groups except 22 mg/L. At the two highest concentrations, the test solution had a cloudy appearance, which could indicate undissolved substance.

96-h LC₅₀ = 62 mg/L

(2) Rainbow trout (*Salmo gairdneri*; now known as *Oncorhynchus mykiss*) were exposed to the test substance (CASRN 62476-59-9) with 25 % purity at nominal concentrations of 0, 4.6, 7.8, 13, 22 and 36 mg/L under static conditions for 96 hours. Mortalities were observed in the two highest concentration groups.

96-h LC₅₀ = 17 mg/L

(3) Bluegill sunfish (*Lepomis macrochirus*) were exposed to the test substance (CASRN 62476-59-9) with 39.8 % purity at unspecified concentrations under static conditions for 96 hours. This study has been retrieved from the ECOTOX database (Office of Pesticide Programs, 2000).

96-h LC₅₀ = 31 mg/L

(4) Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance (CASRN 62476-59-9) with 39.8 % purity at unspecified concentrations under static conditions for 96 hours. This study has been retrieved from the ECOTOX database (Office of Pesticide Programs, 2000).

96-h LC₅₀ = 54 mg/L

Acute Toxicity to Aquatic Invertebrates

Subcategory 1

Dicamba, sodium salt (CASRN 1982-69-0)

Daphnia magna were exposed to the test substance (CASRN 1982-69-0) at unspecified concentrations under static conditions for 48 hours. Immobilization was observed. This study has been retrieved from the ECOTOX database (Office of Pesticide Programs, 2000).

48-h EC₅₀ = 38.1 mg/L

Subcategory 2

No data are available.

Subcategory 3

2,5-Dichloroanisol (CASRN 1984-58-3)

Daphnia magna were exposed to the test substance (CASRN 1984-58-3) at nominal concentrations of 1.56, 3.13, 6.25, 12.5, 25 and 50 mg/L under semistatic conditions for 48 hours. Mean measured concentrations were 0.925, 1.93, 3.90, 7.78, 16.0 and 33.4 mg/L. Mortality was not noted. Immobilization was observed at 12.5 mg/L and two high-exposure groups.

48-h EC₅₀ = 5.89 mg/L

Subcategory 4

2,5-Dichlorophenol, sodium salt (CASRN 52166-72-0)

Daphnia magna were exposed to the test substance (CASRN 52166-72-0) at nominal concentrations of 0.78, 1.6, 3.1, 6.3 and 13 mg/L under static conditions for 48 hours. Mean measured concentrations were 0.70, 1.4, 2.9, 5.8, 12 and 24 mg/L. Complete mortality was observed only at 24 mg/L. No mortalities or immobile organisms were observed for the negative control or four lowest test concentrations. There were no observed adverse effects at 5.8 mg/L.

48-h EC₅₀ = 15 mg/L

Subcategory 5

Acifluorfen, sodium salt (CASRN 62476-59-9, *supporting chemical*)

(1) *Daphnia magna* were exposed to the test substance (CASRN 62476-59-9) with 25% purity at nominal concentrations of 0, 13, 22, 36, 60 and 100 mg/L under static conditions for 48 hours. Measured concentrations were not provided. Mortality was not noted. Immobility and lethargy were observed at 36 – 100 mg/L.

48-h EC₅₀ = 77 mg/L

(2) *Daphnia magna* were exposed to the test substance (CASRN 62476-59-9) with 39.8 % purity at unspecified concentrations under static conditions for 48 hours. This study has been retrieved from the ECOTOX database (Office of Pesticide Programs, 2000).

48-h EC₅₀ = 28.1 mg/L

Toxicity to Aquatic Plants

Subcategory 1

Dicamba, sodium salt (CASRN 1982-69-0)

Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance (CASRN 1982-69-0) at unspecified concentrations under static conditions for 96 hours to measure the

effect on population changes. This study has been retrieved from the ECOTOX database (Fairchild, J. *et al.*, 1997).

96-h EC₅₀ = 36.4 mg/L (growth rate)

Subcategory 2

No data are available.

Subcategory 3

2,5-Dichloroanisole (CASRN 1984-58-3)

Green algae (*Scenedesmus subspicatus*) were exposed to the test substance (CASRN 1984-58-3) at nominal concentrations of 0, 3.13, 6.25, 12.5, 25.0 and 50.0 mg/L under unspecified conditions for 96 hours. Measured concentrations decreased dramatically during the experiment and no test substance was detected in the two lowest exposure groups. The authors hypothesize that this may be due to the sensitivity of 2,5-dichloroanisole to the light used in the experiment. Cell counts were performed at 0, 24, 48 and 72 hours to measure the effect on cell density and growth rate.

72-h EC₅₀ = 8.1 mg/L (biomass)

72-h EC₅₀ = 10.1 mg/L (growth rate)

Subcategory 4

2,5-Dichlorophenol, sodium salt (CASRN 52166-72-0)

Green algae (*Pseudokirchneriella subcapitata*) were exposed to the test substance (CASRN 52166-72-0) at nominal concentrations of 0.031, 0.063, 0.13, 0.25, 0.5 and 1.0 mg/L under static conditions for 72/96 hours. Measured concentrations were in an acceptable range of nominal concentrations at test initiation, but decreased to less than the limit of quantitation (30%) at 96 hours. Cell counts were performed at 0 and 96 hours to measure the effect on cell density and growth rate.

96-h EC₅₀ = 0.34 mg/L (biomass)

96-h EC₅₀ = 0.78 mg/L (growth rate)

Subcategory 5

No adequate data available.

Conclusion:

Subcategory 1

The 96-h LC₅₀ for fish exposed to CASRN 1982-69-0 is 558 mg/L. The 48-h EC₅₀ for aquatic invertebrates exposed to CASRN 1982-69-0 is 38.1 mg/L. The 96-h EC₅₀ for aquatic plants from exposure to CASRN 1982-69-0 is 36.4 mg/L for growth rate.

Subcategory 2

There are no data available for the chemicals in this subcategory.

Subcategory 3

For CASRN 1984-58-3, the 96-h LC₅₀ for fish is 2.4 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 5.89 mg/L. The 72-h EC₅₀ for aquatic plants is 8.1 mg/L for biomass and 10.1 mg/L for growth rate.

Subcategory 4

For CASRN 52166-72-0, the 96-h LC₅₀ for fish is 3.2 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 15 mg/L. The 72-h EC₅₀ for aquatic plants is 0.34 mg/L for biomass and 0.78 mg/L for growth rate.

Subcategory 5

For CASRN 63734-62-3, the 96-h LC₅₀ for fish is 2.6 mg/L. For the supporting chemical, CASRN 62476-59-9, the 96-h LC₅₀ for fish is 17 mg/L and the 48-h EC₅₀ for aquatic invertebrates is 28.1 mg/L. The 72-h EC₅₀ for aquatic plants is not addressed adequately.

5. References

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Table 12. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Aquatic Toxicity Data

	Sub-category 1	Subcategory 2		Sub-category 3	Subcategory 4			Subcategory 5		
Endpoint	SPONSORED CHEMICAL Dicamba, sodium salt (1982-69-0)	SPONSORED CHEMICAL 3,6-Dichloro-2-hydroxybenzoic acid, potassium sodium salt (68938-79-4)	SPONSORED CHEMICAL 3,6-Dichloro-2-hydroxybenzoic acid, dipotassium salt (68938-80-7)	SPONSORED CHEMICAL 2,5-Dichloroanisole (1984-58-3)	SPONSORED CHEMICAL 2,5-Dichlorophenol (583-78-8)	SPONSORED CHEMICAL 2,5-Dichlorophenol, sodium salt (52166-72-0)	SPONSORED CHEMICAL 2,5-Dichlorophenol, potassium salt (68938-81-8)	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy] (63734-62-3)	SPONSORED CHEMICAL Benzoic acid, 3-[2-chloro-4-(trifluoromethyl)phenoxy], potassium salt (72252-48-3)	SUPPORTING CHEMICAL Acifluorfen, sodium salt (62476-59-9)
Fish 96-h LC₅₀ (mg/L)	558	No data	No data	2.4	3.3	3.2	No data 3.2 (RA)	2.6	No data 2.6 (RA)	17
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	38.1	No data	No data	5.89	No data 15 (RA)	15	No data 15 (RA)	No data 28.1 (RA)	No data 28.1 (RA)	28.1
Aquatic Plants 72/96-h EC₅₀ (mg/L) (Biomass) (Growth rate)	36.4	No data	No data	8.1 10.1	No data 0.34 0.78 (RA)	0.34 0.78	No data 0.34 0.78 (RA)	No data	No data	–

bold = measured data (i.e., derived from testing); (RA) = Read Across; – indicates that endpoint was not evaluated for this substance