Randy S.

Linda S. Adams
Secretary for Environmental Protection

Air Resources Board

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Arnold Schwarzenegger
Governor

TO: Tobi Jones, Ph.D.
Assistant Director
Department of Pesticide Regulation

FROM: Janette Brooks, Chief
Air Quality Measures Branch
Stationary Source Division

DATE: July 6, 2007

SUBJECT: REVIEW OF INTERNAL DRAFT ENDOSULFAN RISK ASSESSMENT

At your request, we reviewed an internal draft of the environmental fate and exposure assessment documents related to the Department of Pesticide Regulation's risk assessment for the insecticide endosulfan. Overall, the documents are well prepared and thorough. We have no significant comments. We had several minor comments, which we discussed with your staff. If you have questions, please contact me at (916) 322-7072 or have your staff contact Mr. Lynn Baker of my staff at (916) 324-6997.

cc: Mr. Lynn Baker
Staff Air Pollution Specialist
Substance Evaluation Section
Air Quality Measures Branch

Air Resources Board

Mary D. Nichols, Chairman
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Linda S. Adams
Secretary for Environmental Protection

Arnold Schwarzenegger
Governor

TO: Pam Wofford
Environmental Monitoring Branch
Department of Pesticide Regulation

FROM: Jim Aguila, Manager
Substance Evaluation Section
Air Quality Measures Branch
Stationary Source Division

DATE: August 21, 2007

SUBJECT: REVIEW OF DRAFT ENDOSULFAN RISK CHARACTERIZATION

We reviewed portions of the draft risk characterization, exposure assessment, and environmental fate documents for the insecticide endosulfan that pertain to air monitoring conducted by the Air Resources Board. Overall, the document is well prepared. We have one minor comment, which is attached.

Previously, we reviewed an internal draft of the exposure assessment and environmental fate documents for endosulfan. We had only minor comments, which we discussed with you in early July 2007. All of our prior comments were addressed except one, which is included in the attached comments.

If you have questions, please contact me at (916) 322-8283 or Mr. Lynn Baker of my staff at (916) 324-6997.

cc: Mr. Lynn Baker
Staff Air Pollution Specialist
Substance Evaluation Section
Air Quality Measures Branch

Attachment

Attachment

Comments on Draft Endosulfan Risk Characterization Document

1. Distances from application to samplers – In the Executive Summary, dated July 2007, and the body of the Risk Characterization Document, dated May 25, 2007, we noted some inconsistencies. In describing the air monitoring conducted by the Air Resources Board (ARB) near an application of endosulfan to an apple orchard in San Joaquin County, the text is inconsistent with regard to the distances from the application to perimeter air samplers. On page v of the Executive Summary, under the question of "who will be exposed to endosulfan," the text states that bystander exposure was based on application site monitoring conducted 6-86 meters from the edge of the orchard. On page 130 of the Risk Characterization Document, the text states that these samplers were 8-16 meters from the edge of the orchard and that two samplers were situated at the north sampling site. Based on ARB's monitoring report, the samplers were situated at distances of 6-16 meters from the edge of the orchard, with two collocated samplers located at the south sampling site.

2. Exposure assessment – On page 73 of the Exposure Assessment, dated June 2007, the text states that air concentrations decrease as the distance from the application site "decreases." This is incorrect and should state that concentrations decrease as the distance "increases."

CALIFORNIA COTTON GINNERS AND GROWERS ASSOCIATIONS

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Fresno, CA 93727
Telephone: 559 / 252-0684
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August 13 2007

Ms. Pam Wofford
Department of Pesticide Regulation
Environmental Monitoring Branch
P.O. Box 4015
Sacramento, CA 95812-4015

Re: Comments on the Preliminary Report – "Endosulfan-Risk Characterization Document"

Dear Ms. Wofford,

ON behalf of the over 1200 cotton growers in the State of California, we wish to provide comments on the California Department of Pesticide Regulation's preliminary report entitled "Endosulfan – Risk Characterization Document." Most of our comments will focus on the significant reduction in the use of endosulfan and the significant reduction in cotton acreage. We will also provide responses to some of the assumptions that have been made in the development of the risk assessment that may not accurately reflect current practice. Since the initial air monitoring and risk characterization began on endosulfan in 1996, many things have changed. Most of which would result in significantly lower exposure and risk from endosulfan.

Endosulfan Risk Characterization Document –

Page 21 – Usage
Decline in cotton acreage –
One of the core issues throughout the document are the comments regarding the usage of endosulfan. It is noted several times, including on page 21, that usage on cotton accounts for the highest usage. We believe that this is no longer the case. For many years, cotton acreage has been declining. From an all-time high of 1.6 million acres in 1979, cotton acreage has declined to 1.3 million acres in 1995 to slightly more than 450,000 acres in 2007. The data presented in the document is not reflective of current cotton acreage, or usage of endosulfan. Cotton acreage has dropped dramatically in the past several years due to several reasons, primarily due to a large increase in permanent crops including almonds and pistachios. This acreage will not come back to cotton. In the RCD, DPR uses an average endosulfan usage based on the years of 1999 to 2003. Cotton acreage during that time vacillated between 700,000 acres and 900,000 acres. As noted previously, cotton acreage has declined to just over 450,000 acres statewide in 2007, and we expect the acreage to decline even further in 2008, with preliminary estimates being as low as 400,000 acres. Therefore, we think that endosulfan usage will continue to decline as well.

Alternative pesticides –
It is also important to note that many new products have come on line. According to U.C. Cooperative Farm Advisors, and confirmed in discussions with our members, usage of endosulfan is being replaced with newer products such as Centric (Thiamethoxam) and Assail (acetamiprid), and now Carbine (Flonicamid). The use of insect growth regulators (IGRs) has really addressed the whitefly issue that popped up in 2001 through 2004, and the introduction of neonicitinoids has dramatically reduced the reliance on endosulfan.

Page 98 – Exposure Assessments
i. Aerial applications
Here DPR states that they will assume "open cockpits" because there is "no requirement" for closed cockpits during applications. In discussions with the California Agricultural Aircraft Association (CAAA) and confirmed through an aerial applicator here in the San Joaquin Valley, there are no longer any open cockpit aircraft making pesticide applications. All applications of endosulfan performed via aerial application are made with closed cockpits. The exposure assessment must be modified to correct the current assumption of open cockpits. Furthermore, the section on exposure assessment also notes the use of "flaggers". It should be noted that with the widespread adoption and usage of GPS, "flaggers" are no longer used on aerial applications. This was also confirmed with CAAA.

Page 110 – 111 – Dietary Exposure
Once again, the usage of endosulfan plays a key role here. We feel strongly that the usage of endosulfan has decreased and will continue to decrease. Accordingly, any risk assessment on dietary exposure should reflect the most current usage data.

Page 129 through 131 – Air – All Populations
According to the RCD, the ambient monitoring that took place in Fresno County occurred in 1996, a time when usage of endosulfan was near its peak. According to DPR pesticide use reports, 223,632 pounds of endosulfan was applied in 1996, and only 83,185 pounds were applied in 2005. That is a 63% decrease in endosulfan usage. Consequently, with such a significant reduction in the usage of endosulfan, we would expect a significant reduction in the ambient concentration of endosulfan, assuming that most of the endosulfan is applied during roughly the same high use period. To further substantiate this, the cotton acreage Fresno County in 1996 was 395,400 acres and was down to 180,800 acres in 2006. This equates to a 54% reduction in acreage.

Pg. 158 – Re-entry Exposure Estimates
The RCD speaks to the issue of re-entry exposure and treats employees performing harvesting, roguing and weeding as being exposed the same as scouts. This is a flawed and inaccurate statement for many reasons. Let's start with cotton harvesters. First of all, 100% of the cotton acreage in California is machine harvested, with an enclosed cab cotton harvester. Second, the harvesting occurs long after the application of endosulfan, maybe as long as one or two months after any endosulfan. So, endosulfan concentrations on any plant surface have to be many times

lower than that which occurs during the growing season. This leads to the third point, which is the fact that cotton has to have been defoliated in order for the cotton to be harvested. Without the leaves, it is expected that any contact plants would have minuscule if any exposure to workers.

Weeding in cotton has gone by the wayside. This is primarily due to the high cost of weeding crews, which can be in excess of $40 per acre. However, an ever increasing reason is the introduction of herbicide tolerant cotton varieties, including glyphosate and bromoxynil resistant varieties, have eliminated the need for weeding crews in cotton. Any worker exposure should reflect this.

As for roguing, this is also a practice that has all but been eliminated. Upon surveying some of our members, most have never heard of roguing, or it had been eliminated several years ago. This is true even in the fields where the cottonseed has been saved for planting. Most certainly, it cannot be used as an equivalent exposure to that of scouting.

Appendix E – Estimation of Exposure of Persons in California To Pesticide Products that Contain Endosulfan

Pg. 8 – Pesticide Use and Sales
Please refer to our comments above regarding declining cotton acreage and declining usage of endosulfan overall. Exposure estimate must be revised to reflect this reduction.

Pg. 12 – Exposure Scenarios
Here DPR notes that the use of flaggers is on the decrease due to the increased adoption of newer technologies. According to CAAA, that time is here now and flaggers are no longer used. DPR must recalculate the exposure risk here.

Pg. 28 – Ambient Air
Again, the ambient air monitoring is described. It must be noted that due to the significant reduction in endosulfan usage noted above, ambient air concentrations should be significantly lower. Therefore, the exposure assessment for ambient air exposure must be revised.

Pg. 42 – Aerial Applications
Again, reference is made here to the use of open cockpits. There are no open cockpit aircraft in use today for aerial application of pesticides and this must be noted and reflected in the exposure assessment.

Pg. 71 – Reentry Exposure Assessments
The discussion here revisits the issue of weeding, roguing and harvesting of cotton and the perceived exposure. Please refer to comments presented above with regards to these specific work practices and their diminishing or eliminated use as current practice today.

Volume II - Endosulfan Exposure Assessment –

Pg. 8 – Pesticide Use and Sales
DPR discusses the use of endosulfan on cotton and the increased usage of endosulfan from 2001 to 2004. This was a reflection of a major outbreak of the Silverleaf Whitefly (SLWF). While the threat remains, the SLWF has been held in check since then primarily through the effective use of two insect growth regulators (IGRs): pyriproxyfen (Knack) and buprofezin (Courier).

This section includes a table on usage of endosulfan, which our comments have already addressed. This table needs to be updated to reflect 2005 and 2006 data as it becomes available (2005) data already is and shows cotton usage for 2005 to be at 11,952 pounds, which is an 84% reduction in usage. We believe that 2006 and 2007 usage will be even lower.

Pg. 14 Exposure Scenarios – Reentry
The description of "roguing" is referred to again, and as noted in our comments above, this is a practice that is no longer performed. The exposure assessment must be revised to reflect the elimination of this practice.

Pg. 29 – Environmental Concentrations – Ambient Air
As indicated above in our comments on the RCD, there have been reductions in cotton acreage and significant reductions in the usage of endosulfan. Correspondingly, we expect ambient air concentrations to be lower.

Pg. 72 - Reentry Exposure Estimates
Repeating our comments previously made here, roguing is no longer being conducted, harvesting is being done solely with enclosed cab mechanical harvesters, and weeding is being eliminated through the increased use of herbicide tolerant cotton varieties. Therefore, we believe the proposal to use "scouting" exposure estimates for roguing, harvesting and weeding is in accurate and overstated. This must be changed.

Pg. 91 – Appendix I: Agricultural Reentry Scenarios Table
The table includes the discussion of cotton "scouting" to include hand weeding, roguing, and harvesting. As noted above this is in error and must be changed.

Endosulfan Environmental Fate –

Pg 10 – Use Profile in California
As stated previously, endosulfan usage is on the decrease, especially on cotton. The environmental fate determination must be revised to reflect this.

Pgs. 18 through 28 – References to Studies on Endosulfan Applied to Cotton in Australia

The document continually refers to measurements taken in Australia, where endosulfan is a much more prevalent insecticide. Any measurements taken in Australia will not reflect use patterns nor total use amounts in 2007.

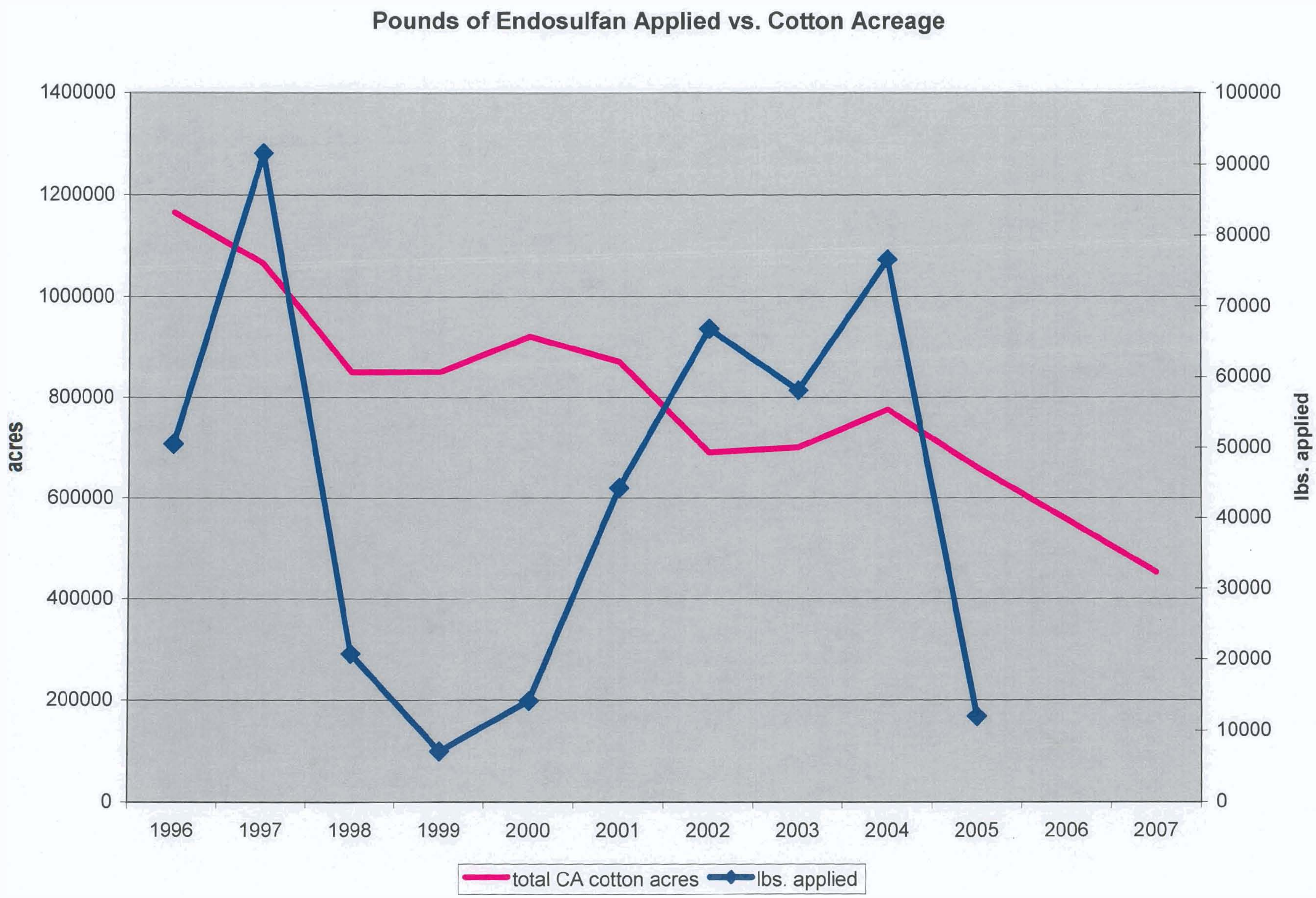
Pg. 30 – Ambient Air Monitoring
The document provides additional insight to the ambient air monitoring performed by ARB in 1996. Here the document indicates that the monitoring sites were only 50 to 100 yards away. Again, this monitoring was conducted during a time period when endosulfan was much more prevalent and just a short distance from a cotton field. This would not be reflective of an average person exposure in the San Joaquin Valley, especially now. The monitoring data is outdated and overstates the true exposure for valley residents.

In closing, the cotton industry appreciates the opportunity to comment on the proposed Risk Characterization Document for endosulfan. While it remains an important product for cotton, its usage has fallen dramatically as cotton acreage has declined and alternative pesticides have been developed. We believe that much of the data used in this document is over conservative, and reflects outdated information. We believe that DPR must review and incorporate more current information with regards to cotton acreage and endosulfan usage, and consequently reevaluate the RCD and exposure assessments. Again, thank you for your time and consideration. Should you have any questions regarding our comments, please feel free to contact me at (559)252-0684 or via email at roger@ccgga.org.

Sincerely,

Roger A. Isom
Vice President and Director of Technical Services

c: Maryann Warmerdam, CDPR
Paul Gosselin, CDPR
Dr. Tobi Jones, CDPR
Terry Gage, CAAA
Jim Wells, Environmental Solutions


Pounds of Endosulfan Applied vs. Cotton Acreage
1400000
1200000
1000000
800000
600000
400000
200000
0
acres
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
lbs. applied
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
total CA cotton acres
lbs. applied

MANA'S RESPONSE TO CDPR'S PRELIMINARY LISTING OF ENDOSULFAN AS A TOXIC AIR CONTAMINANT

INTRODUCTION

On July 6, 2007, the California Department of Pesticide Regulation (CDPR) announced the publication of a preliminary report entitled "Endosulfan-Risk Characterization Document" (accessible under *www.CDPR.ca.gov/docs/empm/pubs/tac/draftred.htm*), followed by a public workshop on July 20, 2007. It is our understanding that the subject risk assessment is mandated by the California Food and Agriculture Code (CFAC) Section 12824; the Birth Defect Prevention Act of 1984 (CFAC 13121-13135); and the Toxic Air Contaminant Act (CFAC 14021-14027). The Birth Defect Prevention Act of 1984 is often identified as Senate Bill 950 (SB 950), and the Toxic Air Contaminant Act is often identified as Assembly Bills 1807 and 3219 (AB 1807 and 3219). AB 1807 and 3219 establish a procedure for identification and control of toxic air contaminants (TACs) in California. The statutes define TACs as air pollutants that may cause or contribute to an increase in mortality or in serious illness, or that may pose a present or potential hazard to human health. CDPR's TAC program focuses on the evaluation and control of pesticides in ambient community air.

The subject document focuses mainly on the risk assessment from airborne exposure of endosulfan based on existing EPA-Guideline studies, public literature and CDPR's air monitoring data (Air Resource Board, 1998; Report for the Air Monitoring of Endosulfan in Fresno County (Ambient) and in San Joaquin County (Application)).

MANA is concerned about the use of certain toxicological endpoints in this preliminary risk characterization document, the representation and reliability of the analytical results, and the application of "outdated" endosulfan use information (1996).

I. REBUTTAL TO ASSUMPTIONS FOR AGRICULTURAL SPRAYING IN SAMPLING AREA

Since the Endosulfan RED (EPA 2002) new data were submitted, and additional label mitigation measures have been addressed and are being implemented. These changes include the deletion of crops and use sites, requiring "Restricted Use" classification, reducing maximum application rates (in most cases by 25%, in some up to 50%), extending the REIs and PHIs, requiring "closed mixing/loading system" for aerial applications, requiring water soluble bags for WP formulation; requiring "enclosed cabs" for airblast applications, and requiring a vegetative buffer strip of 30 feet within the 100 feet (ground -) and 300 feet spray drift buffer (air application) to reduce potential runoff into adjacent water bodies.

In view of the report – "Air Monitoring of Endosulfan in Fresno County (Ambient air) and in San Joaquin County (Application site for bystander exposure)", CDPR presented endosulfan air monitoring data (4 sites for Fresno County in 1996) and one site (apple orchard in San Joaquin County in 1997). As stated in CDPR's Executive Summary: "Endosulfan use in California decreased from 238,635 pounds in 1997 to 83,242 pounds of active ingredient in 2005. Both total pounds used and acreages applied in 2005 were almost 1/3 of those in 1997."

CDPR also stated in this document that "the use patterns, frequency distribution for pounds used, acres applied, and application rates of individual endosulfan application, were similar compared 1997 to 2005". This might have been the case for the time period of 1996-1997, but since the RED has been issued in November 2002, new mitigation labeling is being implemented, and the use pattern is going to change further based on the additional restrictions, and as outlined in our comments below.

Data from the *"Endosulfan Exposure Assessment: Ambient Air and Bystander Scenarios"* presentation by Sheryl Beauvais, Staff Toxicologist, Worker Health and Safety Branch, CDPR, show 75,400 lbs ai endosulfan used in Fresno County 1996 (year of study). Additionally, the named study sampled from an airblast ground sprayer applying endosulfan to an apple orchard in nearby San Joaquin County at 1.5 lbs ai/A on a 6 acre block.

The realities for today (using 2005 data) are as follows:

- 2005 data show a total of 43,482 lbs ai used in Fresno County (nearly half of use for 1996). State averages reflect the same with 1996 usage statewide at 223,632 lbs ai compared to 2005 use of 110,704 lbs ai.

- Application site monitoring employed an airblast sprayer delivering 1.5 lbs active/acre (3 lbs 50WP formulation) to apples. Data from 2005 PU Reports show no reported use on apples in Fresno County with only 56 total acres in the State receiving applications. Other permanent crops where an airblast sprayer would be used include stone fruits, pears, pecans, and walnuts. In all of California, 2,703 lbs ai of endosulfan were applied to these crops. That represents 6.2% of total endosulfan ai used in all of CA. None of these crops were treated with endosulfan in Fresno County. Grapes were once the major market for endosulfan. In 2005 a total of 143 lbs ai were used on 230 acres of grapes statewide. That represents 0.3% of total endosulfan use. No endosulfan was used on grapes in Fresno County. The use of airblast spray data for exposure studies is not representative of real world conditions today in Fresno County and the State of California.

- Use data from CA and Fresno County: In California, the majority of endosulfan use is on cotton, alfalfa for seed (use on forage/fodder cancelled), lettuce, melons, tomatoes and peppers. Use on trees and vines is virtually non-existent. Endosulfan was used to control Lygus under a Section 24(c) label on alfalfa grown for seed. That SLN has been cancelled at EPA.

- Use rates for cotton, lettuce, melons, tomatoes are 1.0 lbs ai/application and 3.0 lbs. ai/season with peppers maximum use per acre 0.5 lbs and maximum per season at 1.0 lbs. ai.

- According to EPA's RED, significant changes in number of lbs. ai/application and per season are being implemented. Melons, lettuce, and tomatoes will be reduced from 3.0 lbs ai/season to 2.0 lbs. ai/season with maximum per application rate 1.0 lbs ai.

- Cotton: Use rate per application is reduced from 2.0 lbs. ai to 1.5 lbs ai by ground and 0.75 lbs ai by air. The maximum season rate is reduced from 3 lbs ai/season to 2 lbs ai/season by ground, and 1.5 lbs. ai by air.

- Much of the cotton use has been as part of a University of California IPM (Integrated Pest Management) system where endosulfan was used only late season for whitefly and aphid control (sticky cotton issue). This use was allowed under a Section 24 (c) for application after boll opening. This SLN is now cancelled and the use on cotton will drop dramatically.

II. REBUTTAL TO USING 1996 / 1997 SAMPLING DATA AS A BASIS FOR DETERMINING RISK TO PERSONS EXPOSED TO AMBIENT AIR AND TO BYSTANDERS

The presented monitoring data (4 ambient air plus one bystander site in Fresno) are very limited (4-week interval, from July 29 to August 29, 1996) and can not be considered to be representative (near cotton and grape areas), especially considering the present use level and pattern. As also stated by the authors of the report (Endosulfan- Risk Characterization Document - Volume ii - Exposure Assessmenths-1647- final draft): "The reported concentrations were based on very limited monitoring data and must be considered as having some degree of uncertainty. The representativeness of the monitoring sites is unknown". Besides the lack of sufficient sites and sampling periods, the Quality Assurance Results of the ARB report (1998) (p.9 – 12) indicate that the integrity and reproducibility of some of the analytical work is questionable.

Under EPA's Guidelines (Residue Analytical Method: OPPTS 860.135) and standard laboratory practices, analytical results would be unacceptable if supported by field, trip and laboratory spike recoveries outside of the range of 70% to 120% (Jiang 2005, US EPA 1998).

Based on these findings the data used for CDPR's evaluation of endosulfan for possible listing as a Toxic Air Contaminant (ARB 1998) would be rejected by the US EPA as well as CDPR, based on the high number of low recovery rates (<70%) for the different spike samples, requiring "adjustments" to the data that result in values of low confidence. These analytical reports, if submitted in support of a registration, would have been rejected by the regulatory agencies. For example, recoveries noted in the ARB report include the following:

Table 10 (p.29). Endosulfan I and II Ambient Laboratory Spike Results

Sample	Date	Endosulfan I Mass (ng)	Expected Mass (ng)	Percent Recovery
QA-EL1	8.30.97	48.0	118	41%
2	8.30.97	35.0	118	38%
3	8.30.97	<LOD	0	NA
4	8.30.97	<LOD	8.40	0%
5	8.30.97	<LOD	8.40	0%
6	8.30.97	16.0	42.0	38%
7	8.30.97	16.0	42.0	38%

Sample	Endosulfan II Mass (ng)	Expected Mass (ng)	Percent Recovery
1	30	27	111%
2	29	27	107%
3	<LOD	0	NA
4	<LOD	0	NA
5	<LOD	0	NA
6	26	27	96%
7	28	27	104%

Table 11 (p.29), Ambient Trip Spike Results, 10/4/96

Endosulfan I	12.0 ng 10% (AccuStandard)	
	12.0	10%
	27.0	23% (Axact)
	27.0	23%
Endosulfan II	27.0	0% (AccuStandard)
	27.0	0%
	27.0	74% (Axact)
	27.0	70%

Table 12(p.29), Ambient Field Spike Results, 10/9/96

Endosulfan I	4.5	54%
	3.9	46%
	45	38%
	45	38%
Endosulfan II	27	85%
	27	81%

Table 13 (p.30), Application Laboratory Spike Results, 4/21/97

Endosulfan I	44.9	90%
	39.9	80%
	39.8	80%
	40.7	81%
Endosulfan II	33.2	66%
	26.6	58%
	30.1	60%
	31.2	62%

Table 14 (p.30), Application Trip Spike Results 4/21/97

Endosulfan I	41.5	83%
	40.2	80%
	43.3	87%
	39.2	78%
Endosulfan II	30.0	60%
	28.6	57%
	33.1	66%
	29.5	59%

Table 15 (p.30), Application Field Spike Results 4/21/97

Endosulfan I	42.1	84%
	44.8	90%
	41.9	84%
	40/7	81%
Endosulfan II	30.0	60%
	28.6	57%
	33.1	66%
	29.5	59%

While some recovery data do meet minimum standards (recovery of 70% - 120%), many do not. This is a critical flaw in the analysis that was conducted.

III. REBUTTAL TO USING A 1000-FOLD MARGIN OF EXPOSURE FOR THE BASIS OF LISTING COMPOUNDS AS TOXIC AIR CONTAMINANTS

CDPR notes that the applicable legislation mandating TAC review states that the threshold for listing compounds is ten-fold below the level that the Director judges is safe; that is, ten-fold below a level that is 100-fold below the no adverse effect level (NOAEL) in an appropriate toxicological study (Silva 2007). This "safety factor upon safety factor" results in a threshold that is 1000 times below the no effect level for each compound considered.

CDPR acknowledges that 100-fold (Dourson et al. 2002) is normally adequate but children require 1000-fold safety (Silva et al. 2006).

There is insufficient toxicological basis for the additional 10-fold safety factor. Legislative mandate is, in effect, a political judgment where judgments should be left to science.

IV. REBUTTAL TO THE PROPOSED LISTING OF ENDOSULFAN AS A TOXIC AIR CONTAMINANT.

Pursuant to our objections using a 1000-fold MOE as the threshold for listing chemicals under the TAC legislation, the risk assessment for endosulfan demonstrates acceptable MOEs, both for those exposed to ambient air and bystanders (assuming for the moment that the ARB analyses were valid).

The MOEs using the 0.194 mg/kg bw/day NOAEL from the 21-day inhalation study are noted below.

MOEs based on a NOAEL of 0.194 mg/kg bw/day and the residue data developed by the California Air Resources Board (ARB 1998).

	Dose	NOAEL	MOE
Adult	mg/kg bw/day	mg/kg bw/day	
Ambient STADD	NA	0.194	NA
Ambient Seasonal ADD	0.00022	0.194	888
Ambient Annual ADD	0.000005	0.194	37117
Bystander STADD	0.00059	0.194	330
Bystander Seasonal ADD	0.00022	0.194	888
Bystander Annual ADD	0.000018	0.194	10659
Infant			
Ambient STADD	NA		NA
Ambient Seasonal ADD	0.000019	0.194	10275
Ambient Annual ADD	0.000011	0.194	17615
Bystander STADD	0.00124	0.194	157
Bystander Seasonal ADD	0.00046	0.194	422
Bystander Annual ADD	0.000038	0.194	5059

CDPR notes that there are three operable NOAELs for risk assessments: acute effects = 0.7 mg/kg bw/day; subchronic effects = 0.194 mg/kg bw/day; and chronic effects = 0.57 mg/kg bw/day. While CDPR choose to use the subchronic NOAEL for calculation of endosulfan MOEs, use of the acute or chronic NOAELS would increase the resultant MOEs in an arithmetic manner.

V. CONCLUSION

Based on the questionable monitoring data (unreliable, questionable analytical standards, not representative, unrealistic usage data), and in view of the additional 10-fold safety factor (total of 1000-fold), which stands in opposition to the mandates of the California TAC legislation, there should be no risk or harm to the public by airborne endosulfan exposure. Therefore, endosulfan should not be listed as a toxic air contaminant.

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LATINO ISSUES FORUM A PUBLIC POLICY & ADVOCACY INSTITUTE

Advancing California's Social, Economic and Environmental Future

August 24, 2007

Pam Wofford
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Department of Pesticide Regulation
Environmental Monitoring Branch
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VIA FACSIMILE: (916) 324-4088

RE: Comments in response to Risk Characterization Document for Endosulfan

Dear Ms. Wofford,

On behalf of Latino Issues Forum I am writing to urge the Department of Pesticide Regulation (DPR) to list Endosulfan as a Toxic Air Contaminant. Latino Issues Forum is a non-profit public policy and advocacy institute dedicated to advancing new and innovative policy solutions for a better more equitable and prosperous society. In an effort to advance this mission we have been working on pesticide issues for many years throughout the state. Through our work in the Central Valley we have witnessed first-hand the huge health impacts pesticide exposure has on farmworkers, their families and agricultural communities. DPR's Risk Characterization Document (RCD) cited that four of the six counties in California with the highest rates of Endosulfan use are in the Central Valley: Fresno, Kings, Kern, and Tulare. These counties also have populations with a large percentage of Latinos residents, who for a variety of social and economic reasons are already exposed to numerous sources of air contamination and experience some of the worst air quality in the nation. The community members we work with in these counties, are farmworkers and/or individuals who live in agricultural communities where tomatoes and cotton are the primary crops. As you are probably aware these are also the crops with very high Endosulfan applications.

The RCD noted that Endosulfan's "overall moderately volatile property enables it to be transported as vapor and spray drift to multiple media, while its moderate adsorptive and persistency properties enable it to stay in the environment for an extended period and can be transported via runoff to surface water bodies or via dust dispersion to atmosphere and redeposit to different areas."[1] This combined with the gruesome results of the animal

[1] http://www.cdpr.ca.gov/docs/empm/pubs/tac/tacpdfs/endosulfan/endosulfan_sum.pdf

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studies conducted on Endosulfan indicate that this is a chemical that is not only hazardous to those handling it but is harmful to the countless residents living adjacent to farms where it is being used.

A recent study in *Environmental Health Perspectives* entitled "Maternal Residence Near Agricultural Pesticide Applications and Autism Spectrum Disorders Among Children in the California Central Valley" by Eric Roberts *et al.* indicated that mothers who were exposed to Endosulfan during pregnancy have higher rates of children who are born with Autism Spectrum Disorder (ASD).[2] The researchers found the highest rates of ASD among children born to mothers living near applications of organochlorine pesticides, specifically endosulfan and dicofol, This study was extremely alarming to us because it reiterates the community testimony we have heard over the last several years. Community members living agricultural San Joaquin Valley communities like Huron, where endosulfan is heavily used, have stated specifically, on numerous occasions, that they have seen higher rates of Autism in children in recent years, and that they believe it is related to the toxic pesticides drifting off the fields. Many of our constituents live in communities completely surrounded by fields where Endosulfan and reside in homes literally across the street from fields where Endosulfan is regularly sprayed.

Research, including DPR's own, clearly documents that people are exposed to dangerous levels of Endosulfan and experience negative health effects because of this exposure. We strongly urge DPR to take strong measures to protect public health and list Endosulfan as a Toxic Air Contaminant and immediately mandate a phase-out of the use of this pesticide. If you have any questions please contact Chione Flegal, Senior Program Manager, at (415) 547-9123 or via email at chionef@lif.org.

Sincerely,

Nora E. Vargas
Executive Director

Chione Flegal
Senior Program Manager

CC: Mary-Ann Warmerdam

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[2] Roberts EM, English PB, Grether JK, Windham GC, Somberg L, and Wolff C, Maternal Residence Near Agricultural Pesticide Applications and Autism Spectrum Disorders Among Children in the California Central Valley, *Environ. Health Perspect.*, in press, published online July 30th, 2007, doi:10.1289/ehp.10168.

August 24, 2007

Ms. Pam Wofford
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Dear Ms. Wofford,

We, the undersigned, are writing to provide comments on the Risk Characterization Document developed for the evaluation of endosulfan as a potential Toxic Air Contaminant. In the attached document, we provide more detail on the following topics:

- We support DPR's use of inhalation toxicology studies to estimate inhalation NOAELs.
- PAN air monitoring data taken near endosulfan application sites demonstrates inhalation exposure to be significant and exceeding levels of concern.
- Results from a recent paper in *Environmental Health Perspectives* show a strong link between maternal exposure to endosulfan/dicofol and incidence of Autism Spectrum Disorder (ASD) in children of the exposed mothers. Incidence increased with proximity to endosulfan applications.
- Some chemical structures of endosulfan displayed in the RCD are not correct.

DPR's and other data indicate that people are exposed to concentrations of endosulfan in air above levels of concern in areas where the pesticide is used. **We therefore recommend that DPR list endosulfan as a TAC. We believe that the most appropriate mitigation would be to phase out all endosulfan use in California.** A phaseout might begin by prohibiting endosulfan applications within a mile of sensitive sites like homes, schools, parks, and other occupied areas.

Thank you for the opportunity to comment on this risk characterization document.

Sincerely yours,

Susan E. Kegley, Senior Scientist
Karl A. Tupper, Staff Scientist
Pesticide Action Network

Amy Leach
Neighbors at Risk

Caroline Farrell, Directing Attorney
Center on Race, Poverty, and the Environment

Joan Poss
Fresno Coalition Against the Misuse of Pesticides

Carolina Simunovic
Environmental Health Director
Fresno Metro Ministry

Teresa DeAnda, Director
El Comite para el Bienestar de Earlimart

Chione Flegal, Senior Program Manager
Latino Issues Forum

We support DPR's use of inhalation toxicology studies to estimate inhalation NOAELs.

We note the fact that inhalation exposure to endosulfan is substantially more toxic to test animals than oral exposure. We agree with OEHHA that use of dietary studies is inappropriate for determining NOAELs when an inhalation study is available. We therefore support DPR's use of the sub-chronic inhalation study to estimate NOELs for acute and chronic exposures.

PAN air monitoring data taken near endosulfan application sites demonstrates inhalation exposure to be above levels of concern

Pesticide Action Network has been conducting air monitoring near homes and schools to quantify the scope and magnitude of off-site, airborne transport of pesticides. At one site near an elementary school in Hastings, Florida,[1] endosulfan was found in air above the dose equivalent to a dose US EPA would characterize as a "level of concern."[*]

Monitoring was conducted near the school for eight days, from December 6–14, 2006, and three pesticides were identified in most of the samples; the insecticides endosulfan and diazinon, and the herbicide trifluralin. The fact that pesticides were detected on most days indicates that volatilization of the pesticides is the primary source of the drift, although application-related drift may have contributed on the day(s) applications took place. Results for concentrations of pesticides in air are provided in Table 1, and a plot of the daily endosulfan concentrations for each pesticide is presented in Figure 1.

Of the eight samples collected (spikes and blanks excluded) between December 6th and 14th, 100% were found to be above the limit of quantitation (LOQ) of 26 nanograms (ng) of α–endosulfan per sample (equivalent to an air concentration of 8.9 ng/m^3 for a 24-hour sample at a 2.00 L/min flow rate and using a 2.00 mL solvent extraction volume). Eighty-eight percent were found to be above the LOQ of 40 ng of β–endosulfan per sample (equivalent to an air concentration of 14 ng/m^3 for a 24-hour sample at a 2.00 L/min flow rate and using a 2.00 mL solvent extraction volume). Thirty eight percent of the samples were above the 24-hour acute and sub-chronic 1-year-old child Reference Exposure Level (REL) of 340 ng/m^3, calculated from the US Environmental Protection Agency's inhalation No Observed Adverse Effect Level (NOAEL). Twenty-five percent of the samples were above the 7-year-old REL of 500 ng/m^3. The highest concentration of total endosulfan observed for a 24-hour period was 626 ng/m^3 (1.8 times the 24-hour acute 1-year-old REL and 1.2 times the 7-year-old REL) on December 6, 2006, and the average concentration for the sampling period was 278 ng/m^3. Endosulfan sulfate was not detected in any of the samples.

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[*] In order to compare observed concentrations of endosulfan in air with concentrations likely to be associated with adverse effects, the US EPA inhalation NOAEL for acute and sub-chronic exposures to endosulfan of 0.2 mg/kg-day (US EPA 2002 RED for Endosulfan) were used to calculate Reference Exposure Levels (RELs) for a sensitive receptor, a one-year-old infant weighing 7.6 kg, breathing on average 4.5 m^3 of air per day. This calculation takes into account the 10-fold intraspecies, 10-fold interspecies and 10-fold FQPA uncertainty factors used by US EPA for endosulfan.

$$\text{REL (1-year-old)} = \frac{\text{NOEL } (mg/kg \bullet day)}{10_{\text{intra-UF}} \times 10_{\text{inter-UF}} \times 10_{\text{FQPA}}} \times \frac{10^6 \ \ ng/mg \times 7.6 \ \ kg}{4.5 \ \ m^3/day}$$

Table 1: Pesticide Concentrations in Hastings, FL, December 6–14, 2006

Sample Name	Start Date	Start Time (p.m.)	Total Time (min)	Total Volume (m^3)	Total Endosulfan[c] (ng/m^3)	Diazinon (ng/m^3)	Trifluralin (ng/m^3)	Comment
Red[a]	12/6/06	4:24	N/A	N/A	0	0	0	α- & β-Endosulfan, Diazinon & Trifluralin < MDL
Sky	12/6/06	4:36	1355	2.98	626	162	376	Minimum values.[b]
Bird	12/7/06	3:20	1428	3.08	45	116	21	β–Endosulfan & trifluralin < LOQ
Banana	12/8/06	3:18	1759	3.69	92	129	18	Trifluralin < LOQ
Bread	12/9/06	8:44	1237	2.69	204	0	0	Trifluralin & Diazinon < MDL
House	12/10/06	5:28	1511	3.32	244	233	54	
---	12/11/06	ND	ND	ND	ND	ND	ND	No sample taken on this day
Salt	12/12/06	5:24	1547	3.40	511	897	79	
Apple	12/13/06	3:19	1470	3.23	340	684	89	Minimum values.[b]
Mom	12/14/06	3:58	1303	1.82	160	271	35	Trifluralin < LOQ. Minimum values.[b]
Average					**278**	**311**	**84**	

ND = no data

MDLs: α-endosulfan, 1.8 ng/m^3; β-endosulfan, 2.8 ng/m^3; diazinon, 3.5 ng/m^3; trifluralin, 9.0 ng/m^3.

LOQs: α-endosulfan, 8.9 ng/m^3; β-endosulfan, 14 ng/m^3; diazinon, 18 ng/m^3; trifluralin, 45 ng/m^3.

[a] Red was a trip blank sample. The tube was cracked on the day and time indicated at the site, transported along with the samples, and analyzed as though it were a sample. It was never attached to the air sampling device.

[b] Flow rate changed by >10% during sampling, so the maximum flow rate was used to calculate sample air volume. This will give a conservative estimate of concentration.

[c] Total endosulfan includes the sum of the α and β isomers of endosulfan.

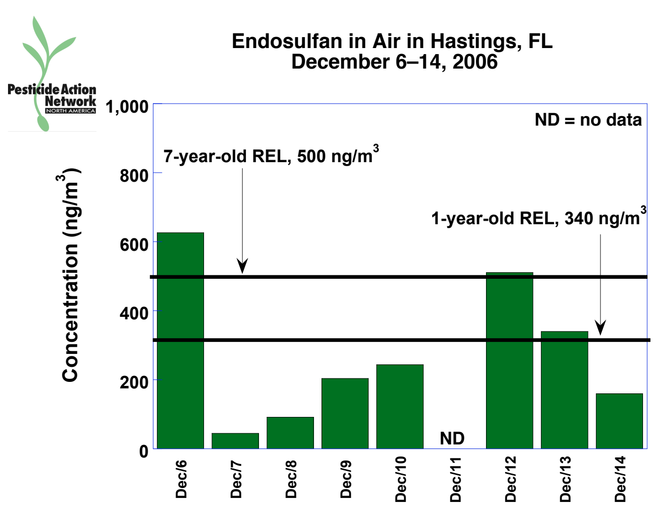


Figure 1: Endosulfan concentrations in Hastings, FL December 6–14, 2006. REL = 24-hour Reference Exposure Level calculated from US EPA's "acceptable" daily dose for acute and sub-chronic exposures.

Endosulfan exposure has been linked to Autism Spectrum Disorders

We would like to bring to DPR's attention new research that suggests a link between prenatal endosulfan exposure and autism spectrum disorder (ASD). On July 30th, 2007, an article describing this research entitled "Maternal Residence Near Agricultural Pesticide Applications and Autism Spectrum Disorders Among Children in the California Central Valley" by Eric Roberts *et al.* was published on the *EHP-in-Press* section of the *Environmental Health Perspectives* website.[2]

To determine whether there may be links between *in utero* pesticide exposure and incidence of ASD, Roberts *et al*. used records from the California Department of Developmental Services to pinpoint where the mothers of children diagnosed with ASD were living when pregnant. They combined DPR pesticide application records and land use data from the Department of Water Resources to determine exactly where and when pesticide applications took place. By combining then these two data sets, the authors where able to look for associations between the incidence of ASD and proximity to pesticide applications during pregnancy. The years examined were 1996-1998.

The researchers found the highest rates of ASD among children born to mothers living near applications of organochlorine pesticides, specifically endosulfan and dicofol, which together accounted for 98% of organochlorine active ingredient poundage applied. (There was not enough data for the researchers to examine either pesticide alone). There are several noteworthy finding in the study, including:

- The highest incidence of ASD was for children born to mothers living closest to applications of these pesticides, suggesting that inhalation of pesticide drift was the most significant route of exposure for this effect. (See *Table 2* in the paper.)
- The relationship between the risk of developing ASD and the timing of pesticide applications is striking—the period of maximum risk coincides with the development of key brain structures during pregnancy. Out of the three developmental periods identified for *a priori* analysis, (neural tube closure, central nervous system embryogenesis, and the entire gestation period), the period of central nervous system (CNS) embryogenesis (7 days prior to 49 after fertilization) appeared to be the most sensitive. The adjusted odds ratio comparing ASD incidence in the 4th non-zero quartile of organochlorine application within a 500 m radius of maternal residence to ASD incidence in the reference group (no organochlorine application within 500 m) is 4.2 (95% CI: 1.7-10.9). *A posteriori* analysis of the data suggested that the 8-week period of highest susceptibility is 26 to 81 after fertilization (adjusted OR = 6.1 (2.4-15.3)).
- A dose-response curve was observed. For exposure during CNS embryogenesis, the odds ratios comparing ASD incidence in the first through forth non-zero quartiles of exposure to the unexposed group are: 0.6 (95% CI: 0.1-4.3), 1.6 (0.4-7.1), 2.4 (0.7-8.2), and 4.2 (1.7-10.9), respectively. (See *Table 3* in the Roberts *et al*. paper.)

The study controlled for known autism risk factors including low birth weight and premature birth as well as date of conception, gender, race, mother's education, and the facility making the ASD diagnosis.

While this is the first study to suggest a link between ASD and endosulfan exposure, we urge DPR to incorporate this emerging work into the RCD, especially in light of the biological plausibility of such a link: endosulfan is known to inhibit GABA-gated chloride channel activity, and there is mounting evidence that GABA is involved with the etiology of ASD.[3]

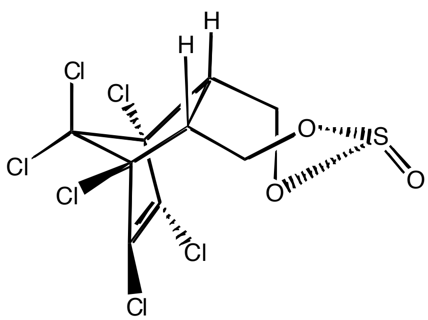
This study provides strong evidence that the developing fetus is very sensitive to exposure to organochlorines endosulfan and dicofol. Therefore, we urge DPR to include uncertainty factors that will protect the developing fetus, regardless of the decision US EPA makes with regard to the FQPA factor.

Chemical structures of endosulfan isomers are incorrect

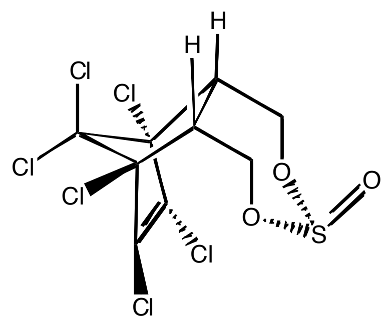
In some parts of the RCD, the chemical structures of the two isomers of endosulfan are drawn incorrectly. The correct structures were only recently determined by X-ray crystallography and NMR spectroscopy and are shown below.[4] We recommend that DPR correct these structures in all documents in which they appear. The correct chemical structures shown below can be downloaded in .gif format from PANNA's PesticideInfo web site, if DPR wishes to use them:

α-Endosulfan: http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC37172#ChemID

β-Endosulfan: http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC35878#ChemID

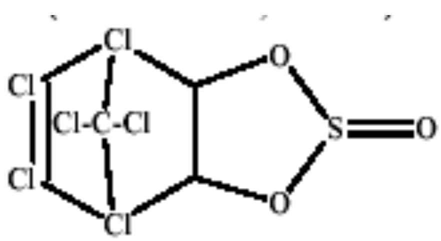


α-Endosulfan

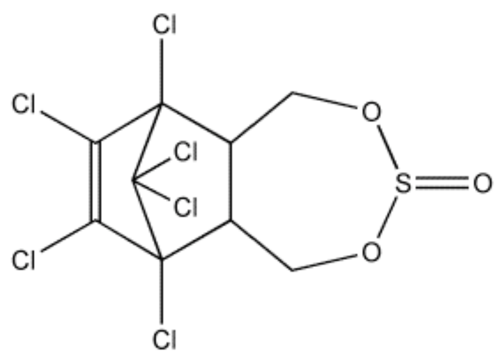


β-Endosulfan

In addition, on pp. 23 and 38 of the RCD, the line drawings of endosulfan are in error. The dioxothiepin ring of endosulfan is depicted as a 5-membered ring, when in fact it should be a 7-membered ring, and several carbon atoms have been replaced by chlorine atoms. The correct structure shown below can be downloaded at http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC35085#ChemID.



Endosulfan as depicted in DPR RCD.



Corrected line drawing of endosulfan.

References

[1] *Drift Catching at South Woods Elementary School, Hastings, FL,* Pesticide Action Network, http://www.panna.org/campaigns/DCHastingsFL06.dv.html.

[2] Roberts EM, English PB, Grether JK, Windham GC, Somberg L, and Wolff C, Maternal Residence Near Agricultural Pesticide Applications and Autism Spectrum Disorders Among Children in the California Central Valley, *Environ. Health Perspect.,* in press, published online July 30th, 2007, doi:10.1289/ehp.10168.

[3] International review of neurobiology vol. 71: GABA in autism and related disorders, Dirk M. Dhossche (ed.), Elsevier Academic Press, London:2005.

[4] (a) Schmidt WF, Hapeman CJ, Fettinger JC, Rice CP, and Bilboulian S, Structure and Asymmetry in the Isomeric Conversion of α– to β–Endosulfan, *J. Ag. Food Chem.,* 1997, 45(4): 1023–1026.

(b) Schmidt WF, Bilboulian S, Rice CP, Fettinger JC, McConnell LL, and Hapeman CJ, Thermodynamic, Spectroscopic, and Computational Evidence for the Irreversible Conversion of β– to α–Endosulfan, *J. Ag. Food Chem.,* 2001, 49(11): 5372–5376.

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RE: COMMENTS ON CDPR'S "ENDOSULFAN—RISK CHARACTERIZATION DOCUMENT"

Dear Ms. Wofford:

Thank you for the opportunity to provide comments on California Department of Pesticide Regulation's (CDPR) "*Endosulfan—Risk Characterization Document*" as well as the upcoming decision on whether or not to list endosulfan as a Toxic Air Contaminant. First of all, we would like to add our support to the comments provided to CDPR by Makhteshim Agan of North America, Inc. In addition to those comments, we would like to add the following.

<u>General</u>

- **The assembled database of toxicology studies appears to represent a "complete toxicology data set" as specified in the Food Quality Protection Act (FQPA) of 1996 for conducting a "high quality" hazard characterization**. Table 1 lists the types of studies that would comprise a "complete toxicology data set" per FIFRA[1], and indicates whether the endosulfan database includes corresponding studies that are "acceptable per FIFRA guidelines." As shown, the endosulfan database more than sufficiently meets these guidelines.

- **DPR's selection of studies for developing the RfDs/ RfCs appears generally appropriate**. For example, in setting the chronic RfD, they selected the NOEL from a 1-year study in dogs of 0.57 mg/kg-day. Per DPR, this study met FIFRA guidelines, and its NOEL is consistent with the NOEL from a 2-year chronic study in rats (0.6 mg/kg-day), which is the study U.S. EPA used in their 2002 risk characterization.

[1] U.S. EPA. 1999. Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process. DRAFT. U.S. Environmental Protection Agency, Office of Pesticide Programs. May.

Table 1: Summary of Studies Required for Evaluation of Pesticides and Whether Studies were Completed for Endosulfan [a,b]

Tier	Group	Study Type	FIFRA Acceptable Study Conducted for Endosulfan?
1	A (oral)	Acute oral toxicity Subchronic (90-day) feeding studies in rodent and nonrodent Chronic feeding studies in rodent and nonrodent Carcinogenicity studies in two rodent species Prenatal developmental toxicity studies in rodents and nonrodents Two-generation reproduction study in rodents General metabolism study in rodents Mutagenicity studies (in vivo and in vitro assay of gene mutation, structural chromosomal aberration, and other genomic effects)	Yes (rat) Yes (rat) Yes (rat, dog) Yes (rat, mouse) Yes (rat, rabbit) Yes (rat) Yes (rat) Yes
1	B (other intake routes)	Acute dermal Acute inhalation Primary eye irritation Primary dermal irritation Dermal sensitization	Yes (guinea pig, rat, rabbit) Yes (rat) Yes (rabbit) Yes (rabbit) Yes (guinea pig)
2	C	Dermal penetration 21-day dermal study (rat) Subchronic (90-day) inhalation or dermal study Acute or subchronic (90-day) delayed neurotoxicity in hens Subchronic neurotoxicity studies in mammals	Yes (rat) Yes (rat) Yes (rat inhalation) Yes
2	D	Acute neurotoxicity study in mammals Immunotoxicity studies: a. Enhancement of observations in subchronic or chronic studies b. Primary antibody response to sheep red blood cells Developmental neurotoxicity in rodents Chronic neurotoxicity in mammals Scheduled controlled operant behavior Peripheral nerve function Sensory evoked potential	Yes (not FIFRA acceptable) Yes (not FIFRA acceptable) Yes (rat)
2	E	Studies designed to investigate specific concerns, for example: Pharmacokinetics in fetuses and/or young animals Direct dosing of the offspring prior to weaning Enhanced developmental neurotoxicity including specialized testing of sensory and/or cognitive function Developmental immunotoxicity Developmental carcinogenesis Enhanced evaluation of potential to induce effects related to endocrine disruption	Yes (not FIFRA acceptable)

[a] Tier 1 studies are required for all food-use chemicals; Tier 2 studies are triggered by potential use and exposure patterns, chemical attributes, toxicological findings, or potential concerns identified in Tier 1 studies.
[b] Cited in 40 CFR Part 158.340 Toxicology Data Requirements as described in this table.

- Of particular note, a developmental neurotoxicity (DNT) study was conducted in rats and published in 2006[2]. As described by DPR, **the developmental neurotoxicity NOEL was 29.8 mg/kg/day (the highest dose tested), "based upon the lack of neurological effects in the offspring**." For developmental landmarks, body weight was decreased in pups at all doses, and preputial separation was marginally delayed (4-5%) in male pups at all doses. However, **in the maternal dams, body weight and food consumption was also reduced at all doses, indicating no special sensitivity of the pups, and also making it difficult to ascertain whether reduced pup weight and other effects was due to maternal effects or direct toxicity**.

<u>Acute and Chronic Oral RfDs</u>

- In calculating their Acute and Chronic Oral RfDs, DPR applied the default 10X FQPA safety factor. DPR states that application of the 10X safety factor is justified because U.S. EPA applied it in their previous (U.S. EPA, 2002) assessment of endosulfan. U.S. EPA justified applying the safety factor since "there were no reliable data to address the following concerns and uncertainties: 1) evidence for an increased susceptibility to neuro- and reprotoxicity in prepubescent and neonatal rats. 2) many studies indicating endocrine disruption. 3) uncertainty of the neuroendocrine effects in young rats. 4) the request by USEPA for a DNT study"[3]. However, a "FIFRA acceptable" DNT study for endosulfan was published[4] since publication of that U.S. EPA report, and the DNT study found "no increase in neurotoxicity in rats receiving endosulfan treatment in diet during pre- and post-natal development" and "There were no indications of endocrine disruption or neuroendocrine effects in young rats"[5]. **Nonetheless, because U.S. EPA had "not yet commented on the recent DNT study," DPR retained the safety factor in its risk assessment. This is unjustified**.

- According to guidance[6], the 10X FQPA factor is to be applied to account for uncertainties in the toxicity database if there are "Residual concerns for susceptibility given the available evidence on pre- and postnatal toxicity." The RfD developed by DPR already includes a separate 10 fold uncertainty factor for "intraspecies variation in sensitivity." Per U.S. EPA[7], application of the additional 10X FQPA safety factor to account for this endpoint is only justified if "greater concerns regarding pre- and postnatal toxicity cannot be addressed in the derivation of an RfD" (i.e., through the use of traditional uncertainty factors). **The results of the DNT study demonstrate there are no "greater concerns" for pre- or post-natal toxicity or special sensitivity of the fetus or young. Therefore, application of this safety factor is not justified and should be removed**. The resulting acute and

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[2] Gilmore, R.G., Sheets, L.P. and Hoss, H.E., 2006. A Developmental Neurotoxicity Study with Technical Grade Endosulfan in Wistar Rats. Bayer CropScience LP, Toxicology, Stilwell, KS; Report No. 201563; 9/26/06. DPR Volume/record #: 182-0122/228573.
[3] CalEPA. 2007. Endosulfan Risk Characterization Document. Medical Toxicology and Worker Health and Safety Branches, Department Of Pesticide Regulation, California Environmental Protection Agency. May 25. Available at: http://www.cdpr.ca.gov/docs/empm/pubs/tac/draftrcd.htm.
[4] Gilmore et al., 2006.
[5] CalEPA, 2007.
[6] U.S. EPA. 2002. Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment. U.S. Environmental Protection Agency, Office of Pesticide Programs. February 28. Available at: http://www.epa.gov/pesticides/trac/science/determ.pdf.
[7] U.S. EPA, 2002.

chronic RfDs would be 0.007 mg/kg-day and 0.0057 mg/kg-day, respectively, instead of 0.0007 mg/kg-day and 0.00057 mg/kg-day.

Acute and Chronic Inhalation RfC

- DPR based their inhalation RfCs on a "subchronic NOEL" from a rat inhalation study of 0.194 mg/kg-day, in which rats were administered endosulfan in air (aerosol, nose only) 21 times over 29 days[8]. The NOEL was based on decreases in food consumption, clinical signs, and changes in clinical chemistry seen at the next higher dose. To derive the acute RfC, DPR divided this NOEL by a 100-fold uncertainty factor (10 for interspecies and 10 for intraspecies variations in sensitivity) and a default child respiratory rate of 0.59 m^3/kg-day, to yield a resultant acute RfC of 0.0033 mg/m^3. To derive the chronic RfC, DPR divided the acute RfC by an additional UF of 10 (for a combined total uncertainty factor of 1,000), to yield a chronic RfC of 0.00033 mg/m^3.

  This NOEL is far below the NOEL for developmental toxicity noted in the rat DNT study. **Therefore, use of this NOEL in deriving RfCs and other values to apply to the inhalation pathway should be sufficiently protective of the fetus, infants, and children**.

Designation as Toxic Air Contaminant

- Per DPR, a pesticide can be identified as a "toxic air contaminant" if concentrations in ambient air are greater than a level that is ten-fold below "the air concentration which has been determined by the director to be adequately protective of human health"[9].

- In assessing whether endosulfan should be considered a toxic air contaminant, CDPR[10] states (p. 161) "Generally an MOE of at least 100 is considered sufficiently protective of human health when the NOEL for an adverse systemic effect is derived from an animal study. This MOE allows for the possibility of humans being 10 times more sensitive than animals and for a 10-fold variation in sensitivity between the lower range of the normal distribution in the overall population and the sensitive subgroup (Dourson et al., 2002). However, when considering endosulfan exposure for the general public, specifically infants exposed in ambient air or as bystanders, the above MOE of 100 is insufficient. For infants and children exposed in ambient air or as bystanders, MOEs need to be at least 1000-fold or greater. MOEs of less than 1000 for these scenarios result in the consideration of listing endosulfan as a toxic air contaminant (TAC, 2001) based on acute, subchronic and chronic neurotoxicity."

  CDPR further states, "Exposure scenarios for the public involve both dietary and non-dietary components to infants (ambient air, bystanders) and children (swimmers in surface water). Under the FQPA, an additional 10x SF would be added to the calculations for aggregate MOEs for infants and children (USEPA, 2002a; FQPA, 1996). The resulting aggregate (combined dietary + non-dietary) MOE should therefore be 1000 (or greater) at this time."

[8] Hollander, H. and Weigand, W. (Hoechst AG), 1984. Endosulfan B Active ingredient technical: Testing for subchronic inhalation toxicity (21 exposures in 29 days) in SPF Wistar Rats. Hoechst, AG, Germany; 8/15/84, Study #: 84.0103. DPR Vol. 182- 084 #126577.
[9] California Code of Regulations, Title 3, Division 6, Chapter 4, Subchapter 2, Article 1.
[10] CalEPA, 2007.

In other words, DPR divided the NOEL that was used to derive the inhalation RfC (0.194 mg/kg-day) by a combined factor of 1,000, a factor that includes the FQPA 10X safety factor. **However, just as application of this 10X safety factor is inappropriate in derivation of the oral RfD, it is inappropriate here**. The rat DNT study showed that at exposure levels much higher than the NOEL from the rat inhalation study, no developmental toxicity or special sensitivity of the fetus or young was seen. Therefore, **application of an additional 10-fold factor (in addition to the 10x intraspecies and 10x interspecies uncertainty factors already applied) is entirely unwarranted and should be removed.**

Thank you again for the opportunity to comment on the endosulfan risk characterization document and the upcoming decision by CDPR. In summary, we believe that the additional 10-fold uncertainty factor is not appropriate in the endosulfan risk characterization, and that the chronic RfC should be recalculated as 0.0033 mg/m^3. Please do not hesitate to contact me if there is any need to clarify or elaborate on these comments.

Sincerely,

Hank Giclas
Vice President, Science and Technology, Strategic Planning