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Part III

Environmental Protection Agency

40 CFR Part 180

Carbofuran; Proposed Tolerance Revocations; Proposed Rule

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2005–0162; FRL–8373–8]

Carbofuran; Proposed Tolerance Revocations

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: EPA is proposing to revoke all tolerances for carbofuran. The Agency has determined that the risk from aggregate exposure from the use of carbofuran does not meet the safety standard of section 408(b)(2) of the Federal Food, Drug, and Cosmetic Act (FFDCA). EPA is specifically soliciting comment on whether there is an interest in retaining any individual tolerance, or group of tolerances, and whether information exists to demonstrate that such tolerance(s) meet(s) the FFDCA section 408(b)(2) safety standard. EPA encourages interested parties to comment on the tolerance revocations proposed in this document and on the proposed time frame for tolerance revocation. Issues not raised during the comment period may not be raised as objections to the final rule, or in any other challenge to the final rule.

DATES: Comments must be received on or before September 29, 2008.

ADDRESSES: Submit your comments, identified by docket identification (ID) number EPA–HQ–OPP–2005–0162, by one of the following methods:

• *Federal eRulemaking Portal*: *http://www.regulations.gov*. Follow the on-line instructions for submitting comments.

• *Mail*: Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.

• *Delivery*: OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S–4400, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA. Deliveries are only accepted during the Docket's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket telephone number is (703) 305–5805.

Instructions: Direct your comments to docket ID number EPA–HQ–OPP–2005–0162. EPA's policy is that all comments received will be included in the docket without change and may be made available on-line at *http://www.regulations.gov*, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through regulations.gov or e-mail. The Federal regulations.gov website is an ''anonymous access'' system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses.

Docket: All documents in the docket are listed in the docket index. Although listed in the index, some information is not publicly available, *e.g.*, CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either in the electronic docket at *http://www.regulations.gov*, or, if only available in hard copy, at the OPP Regulatory Public Docket in Rm. S–4400, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA. The hours of operation of this Docket Facility are from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: Jude Andreasen Special Review and Reregistration Division (7508C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave, NW., Washington, DC 20460-0001; telephone number: (703) 305–0076; e-mail address: *andreasen.jude@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

• Crop production (NAICS code 111).

• Animal production (NAICS code 112).

• Food manufacturing (NAICS code 311).

• Pesticide manufacturing (NAICS code 32532).

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. To determine whether you or your business may be affected by this action, you should carefully examine the applicability provisions in [Unit II.A]. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. What Should I Consider as I Prepare My Comments for EPA?

1. *Submitting CBI*. Do not submit this information to EPA through regulations.gov or e-mail. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD ROM that you mail to EPA, mark the outside of the disk or CD ROM as CBI and then identify electronically within the disk or CD ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments*. When submitting comments, remember to:

i. Identify the document by docket ID number and other identifying information (subject heading, **Federal Register** date and page number).

ii. Follow directions. The Agency may ask you to respond to specific questions or organize comments by referencing a

Code of Federal Regulations (CFR) part or section number.

iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

C. What Can I Do if I Wish the Agency to Maintain a Tolerance that the Agency Proposes to Revoke?

This proposed rule provides a comment period of 60 days for any interested person to submit comments on the Agency's proposal. EPA issues a final rule after considering comments that are submitted in response to this proposed rule. Comments should be limited only to the pesticide and tolerances subject to this proposed notice.

EPA's finding that aggregate exposure from all existing uses of carbofuran is not safe does not necessarily mean that no individual tolerance or group of tolerances could meet the FFDCA 408(b)(2) safety standard and be maintained. For example, in its Interim Reregistration Eligibility Decision (IRED), EPA concluded that the Agency could maintain import tolerances for bananas, coffee, rice, and sugarcane, because dietary risks from the food residues from the import tolerances are below the Agency's level of concern when considered together with the food residues from the phase-out crops, but with no other domestic uses (Ref. 35). However, as discussed in more detail below, EPA can only maintain tolerances that it can determine will be ''safe'' within the meaning of section 408(b)(2)(A)(ii). Accordingly, commenters interested in retaining any tolerance or group of tolerances should consider submitting information to demonstrate that the tolerance(s) meet the statutory standard, rather than merely indicating an interest in retaining the tolerance. Commenters should also be aware that even if EPA determines that any carbofuran tolerance(s) meet the safety standard, those tolerances can only be maintained if EPA can also determine that the cumulative effects from those tolerances, when considered with the exposures from other *N*-methyl carbamate pesticide chemicals, will meet the FFDCA 408(b)(2) safety standard. EPA will not respond to any comments on subjects that do not relate to the evaluation or safety of the pesticide tolerances subject to this proposed notice.

After consideration of comments, EPA will issue a final regulation determining whether revocation of the tolerances is appropriate and making a final finding on whether these tolerances are ''safe'' within the meaning of section 408(b)(2)(A)(ii). Such regulation will be subject to objections pursuant to section 408(g) (21 U.S.C. 346a(g)).

In addition to submitting comments in response to this proposal, you may also submit an objection at the time of the final rule. If you anticipate that you may wish to file objections to the final rule, you must raise those issues in your comments on this proposal. EPA will treat as waived, any issue not originally raised in comments on this proposal. Similarly, if you fail to file an objection to the final rule within the time period specified, you will have waived the right to raise any issues resolved in the final rule. After the specified time, issues resolved in the final rule cannot be raised again in any subsequent proceedings on this rule.

II. Introduction

A. What Action is the Agency Taking?

EPA is proposing to revoke all of the existing tolerances for residues of carbofuran. Currently, tolerances have been established on the following crops: alfalfa, fresh; alfalfa, hay; artichoke, globe; banana; barley, grain; barley, straw, sugar beet; sugar beet, tops; coffee bean; corn, forage; corn, fresh (including sweet corn); corn, grain (including popcorn); corn, stover; cotton, undelinted seed; cranberry; cucumber; grape; grape (raisin); melon; milk; oat, grain; oat, straw; pepper; potato; pumpkin; raisins, waste; rice, grain; rice, straw; sorghum, fodder; sorghum, forage; sorghum, grain; strawberry; soybean; soybean, forage; soybean, hay; squash; sugarcane, cane; sunflower, seed; wheat, grain; wheat, straw. The Agency is proposing to revoke tolerances for these crops because aggregate dietary exposure to residues of carbofuran, including all anticipated dietary exposures and all other exposures for which there is reliable information, is not safe.

EPA has determined that aggregate exposure to carbofuran greater than 0.000075 mg/kg/day (*i.e.*, greater than the acute Population Adjusted Dose (aPAD)) does not meet the safety standard of section 408(b)(2) of the FFDCA. Based on the contribution from food alone, the more sensitive children's subpopulations receive unsafe exposures to carbofuran. At the 99.9th percentile of exposure, aggregate carbofuran dietary exposure from food alone was estimated to range between 0.000121 mg/kg/day for children 6–12 (160% of the aPAD) and 0.000156 mg/kg/day (210% of the aPAD) for children 3–5 years old, the population subgroup with the highest estimated dietary exposure. In addition, EPA's analyses show that those individuals–both adults and children—who receive their drinking water from vulnerable sources are also exposed to levels that exceed EPA's level of concern—in some cases by orders of magnitude. This primarily includes those populations consuming drinking water from groundwater from shallow wells in acidic aquifers overlaid with sandy soils that have had crops treated with carbofuran. Aggregate exposures from food and from drinking water derived from ground water in vulnerable areas (*i.e.*, from shallow wells associated with sandy soils and acidic aquifers, such as are found in the Delmarva Peninsula of Delaware, Maryland, and Virginia) result in even higher estimated exceedances. The aggregate estimates for food and ground water exposure range between 1100% of the aPAD for adults over 50 years, to over 10,000% of the aPAD for infants. Similarly, EPA analyses show substantial exceedances for those populations that obtain their drinking water from reservoirs (*i.e.*, surface water) located in small agricultural watersheds, prone to runoff, and predominated by crops that are treated with carbofuran, even though there is more uncertainty associated with these exposure estimates. For example, estimated aggregate exposures from food and drinking water derived from surface water, based on the corn use in Nebraska, range between 340% of the aPAD for youths 13–19, and 3900% of the aPAD for infants.

Every sensitivity analysis EPA has performed has shown that estimated exposures (both for food alone as well as for food and water) significantly exceed EPA's level of concern for children. Although the magnitude of the exceedance varies depending the level of conservatism in the assessment, the fact that in each case aggregate exposures from carbofuran fail to meet the FFDCA section 408(b)(2) safety standard, including where EPA relied on highly refined estimates of risk,

using all relevant data and methods, strongly corroborates EPA's conclusion that aggregate exposures from carbofuran are not safe.

B. What is the Agency's authority for Taking this Action?

EPA is taking this action, pursuant to the authority in FFDCA sections 408(b)(1)(b), 408(b)(2)(A), and 408(e)(1)(A). 21 U.S.C. 346a(b)(1)(b), (b)(2)(A), (e)(1)(A).

III. Statutory and Regulatory Background

A ''tolerance'' represents the maximum level for residues of pesticide chemicals legally allowed in or on raw agricultural commodities (including animal feed) and processed foods. Section 408 of the FFDCA, 21 U.S.C. 346a, as amended by the Food Quality Protection Act (FQPA) of 1996, Public Law 104–170, authorizes the establishment of tolerances, exemptions from tolerance requirements, modifications in tolerances, and revocation of tolerances for residues of pesticide chemicals in or on raw agricultural commodities and processed foods. Without a tolerance or exemption, food containing pesticide residues is considered to be unsafe and therefore ''adulterated'' under section 402(a) of the FFDCA, 21 U.S.C. 342(a). Such food may not be distributed in interstate commerce (21 U.S.C. 331(a)). For a food-use pesticide to be sold and distributed, the pesticide must not only have appropriate tolerances under the FFDCA, but also must be registered under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et seq.*). Food-use pesticides not registered in the United States must have tolerances in order for commodities treated with those pesticides to be imported into the United States.

Section 408(e) of the FFDCA, 21 U.S.C. 346a(e), authorizes EPA to modify or revoke tolerances on its own initiative. EPA is proposing to revoke these tolerances to implement the Agency's findings made during the reregistration and tolerance reassessment processes. As part of these processes, EPA is required to determine whether each of the existing tolerances meets the safety standard of section 408(b)(2) (21 U.S.C. 346a(b)(2)). Section 408(b)(2)(A)(i) of the FFDCA requires EPA to modify or revoke a tolerance if EPA determines that the tolerance is not ''safe.'' (21 U.S.C. 346a(b)(2)(A)(i)). Section 408(b)(2)(A)(ii) of the FFDCA defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' This includes exposure through drinking water and in residential settings, but does not include occupational exposure.

Risks to infants and children are given special consideration. Specifically, section 408(b)(2)(C) states that EPA:

> shall assess the risk of the pesticide chemical based on— ...
>
> (II) available information concerning the special susceptibility of infants and children to the pesticide chemical residues, including neurological differences between infants and children and adults, and effects of in utero exposure to pesticide chemicals; and
>
> (III) available information concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity. ...

(21 U.S.C. 346a(b)(2)(C)(i)(II) and (III)).

This provision further directs that ''[i]n the case of threshold effects, ... an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.'' (21 U.S.C. 346a(b)(2)(C)). EPA is permitted to ''use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children.'' (Id.). The additional safety margin for infants and children is referred to throughout this proposal as the ''children's safety factor.''

IV. Carbofuran Background and Regulatory History

In July 2006, EPA completed a refined acute probabilistic dietary risk assessment for carbofuran as part of the reassessment program under section 408(q) of the FFDCA. The assessment was conducted using Dietary Exposure Evaluation Model-Food Commodity Intake Database (DEEM-FCID™, Version 200–2.02), which incorporates consumption data from the United States Department of Agriculture's (USDA's) Nationwide Continuing Surveys of Food Intake by Individuals (CSFII), 1994–1996 and 1998, as well as carbofuran monitoring data from USDA's Pesticide Data Program[1] (PDP), estimated percent crop treated information, and processing/cooking factors, where applicable. The assessment was conducted applying an additional 500–fold safety factor that included a 5X children's safety factor, pursuant to section 408(b)(2)(C). That refined assessment showed acute dietary risks from carbofuran residues in food above EPA's level of concern (Ref 15). Since 2006, EPA has evaluated additional data submitted by the registrant, FMC Corporation, and has further refined its original assessment by incorporating more recent 2005/2006 PDP data, and by conducting additional analyses. In January 2008, EPA published a draft Notice of Intent to Cancel (NOIC) all carbofuran registrations, based in part on carbofuran's dietary risks. As mandated by FIFRA, EPA solicited comments from the Scientific Advisory Panel (SAP) on its draft NOIC. Having considered the comments from the SAP, EPA is initiating the process to revoke all carbofuran tolerances. As noted above, aggregate exposures from food and water to the US population at the upper percentiles of exposure substantially exceed the safe daily levels and thus are ''unsafe'' within the meaning of FFDCA section 408(b)(2) (Ref 12). It is particularly significant that under every analysis EPA has conducted, the levels of carbofuran exceed the safe daily dose for children, even when EPA used the most refined data and models available. Based on these findings, EPA has decided to move as expeditiously as possible to address the unacceptable dietary risks to children. EPA still expects to issue the NOIC subsequent to undertaking the activities required to revoke the carbofuran tolerances.

In May 2008, FMC Corporation, the sole U.S. registrant, submitted a conditional request to cancel use of carbofuran on certain crops and to add use restrictions intended to mitigate ground and surface water contamination from use on other crops (Ref. 32). The tolerances that would have been affected by that proposal are: alfalfa, fresh; alfalfa, hay; artichoke, globe; barley, grain; barley, straw; sugar beet, tops; cranberry; cucumber; grape; grape (raisin); oat, grain; oat, straw; pepper; sorghum, fodder; sorghum, forage; sorghum, grain; strawberry; soybean; soybean, forage; soybean, hay; squash; wheat, grain; wheat, straw. FMC, however, conditioned the request on receiving assurance from EPA that the Agency would permit the retention of several uses that do not meet the FFDCA 408(b)(2) safety standard or the FIFRA registration standard (Id.). EPA, therefore, could not accept the request, and FMC has withdrawn it (Id.). The tolerances that FMC would have sought to retain under that proposal were:

[1] USDA's Pesticide Data Program monitors for pesticides in certain foods at the distribution points just before release to supermarkets and grocery stores.

banana, coffee bean; corn, forage; corn, fresh; corn, grain (including popcorn); corn, stover; cotton, undelinted seed; melon; milk; potato; rice, grain; rice, straw; sugarcane, cane; and sunflower, seed. Based on the contribution from these foods alone, dietary exposures to carbofuran would still be unsafe for the more sensitive children's subpopulations. At the 99.9th percentile, carbofuran dietary exposure from food alone was estimated at 0.000082 mg/kg/day (110% of the aPAD) for children 3–5 years old, the population subgroup with the highest estimated dietary exposure (Ref. 12). In addition, as discussed in more detail in Refs 18 and 54, although FMC's proposed groundwater restrictions would have protected against further contamination in the most vulnerable locations, the Agency could not conclude that the restrictions would be protective of all vulnerable groundwater. EPA also has substantial questions about the efficacy of FMC's proposed surface water restrictions to reduce drinking water exposure in vulnerable reservoirs (Refs. 18 and 54). Accordingly, it has not been shown that drinking water residues of carbofuran would no longer contribute significantly to unsafe aggregate exposures, nor that such exposures would meet the FFDCA safety standard.

V. EPA's Approach to Dietary Risk Assessment

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. A short summary is provided below to aid the reader. For further discussion of the regulatory requirements of section 408 of the FFDCA and a complete description of the risk assessment process, see *http://www.epa.gov/fedrgstr/EPA–PEST/1999/January/Day–04/p34736.htm*.

To assess the risk of a pesticide tolerance, EPA combines information on pesticide toxicity with information regarding the route, magnitude, and duration of exposure to the pesticide. The risk assessment process involves four distinct steps: (1) identification of the toxicological hazards posed by a pesticide; (2) determination of the exposure ''level of concern'' for humans; (3) estimation of human exposure; and (4) characterization of human risk based on comparison of human exposure to the level of concern.

A. Hazard Identification and Selection of Toxicological Endpoint

Any risk assessment begins with an evaluation of a chemical's inherent properties, and whether those properties have the potential to cause adverse effects (*i.e.*, a hazard identification). EPA then evaluates the hazards to determine the most sensitive and appropriate adverse effect of concern, based on factors such as the effect's relevance to humans and the likely routes of exposure.

Once a pesticide's potential hazards are identified, EPA determines a toxicological level of concern for evaluating the risk posed by human exposure to the pesticide. In this step of the risk assessment process, EPA essentially evaluates the levels of exposure to the pesticide at which effects might occur. An important aspect of this determination is assessing the relationship between exposure (dose) and response (often referred to as the dose-response analysis). In evaluating a chemical's dietary risks EPA uses a reference dose (RfD) approach, which involves a number of considerations including:

- A 'point of departure'(PoD) — the value from a dose-response curve that is at the low end of the observable data and that is the toxic dose that serves as the 'starting point' in extrapolating a risk to the human population;
- An uncertainty factor to address the potential for a difference in toxic response between humans and animals used in toxicity tests (*i.e.*, interspecies extrapolation);
- An uncertainty factor to address the potential for differences in sensitivity in the toxic response across the human population (for intraspecies extrapolation); and
- The need for an additional safety factor to protect infants and children, as specified in FFDCA section 408(b)(2)(C).

EPA uses the chosen PoD to calculate a safe dose or RfD. The RfD is calculated by dividing the chosen PoD by all applicable safety or uncertainty factors. Typically in EPA risk assessments, a combination of safety or uncertainty factors providing at least a hundredfold (100X) margin of safety is used: 10X to account for interspecies extrapolation and 10X to account for intraspecies extrapolation. Further, in evaluating the dietary risks for pesticide chemicals, an additional safety factor of 10X is presumptively applied to protect infants and children, unless reliable data support selection of a different factor. In implementing FFDCA section 408, EPA also calculates a variant of the RfD referred to as a PAD. A PAD is the RfD divided by any portion of the children's safety factor that does not correspond to one of the traditional additional uncertainty/safety factors used in general Agency risk assessment. The reason for calculating PADs is so that other parts of the Agency, which are not governed by FFDCA section 408, can, when evaluating the same or similar substances, easily identify which aspects of a pesticide risk assessment are a function of the particular statutory commands in FFDCA section 408. For acute assessments, the risk is expressed as a percentage of a maximum acceptable dose or the acute PAD (*i.e.*, the acute dose which EPA has concluded will be ''safe''). As discussed below in Unit V.C., dietary exposures greater than 100 percent of the acute PAD are generally cause for concern and would be considered ''unsafe'' within the meaning of FFDCA section 408(b)(2)(B). Throughout this document general references to EPA's calculated safe dose are denoted as an acute PAD, or aPAD, because the relevant point of departure for carbofuran is based on an acute risk endpoint.

B. Estimating Human Dietary Exposure Levels

Pursuant to section 408(b) of the FFDCA, EPA has evaluated carbofuran's dietary risks based on ''aggregate exposure'' to carbofuran. By ''aggregate exposure,'' EPA is referring to exposure to carbofuran alone by multiple pathways of exposure. EPA uses available data, together with assumptions designed to be protective of public health and standard analytical methods, to produce separate estimates of exposure for a highly exposed subgroup of the general population, for each potential pathway and route of exposure. For acute risks, EPA then calculates potential aggregate exposure and risk by using probabilistic[2] techniques to combine distributions of potential exposures in the population for each route or pathway. For dietary analyses, the relevant sources of potential exposure to carbofuran are from the ingestion of residues in food and drinking water. The Agency uses a combination of monitoring data and predictive models to evaluate

[2] Probabilistic analysis is used to predict the frequency with which variations of a given event will occur. By taking into account the actual distribution of possible consumption and pesticide residue values, probabilistic analysis for pesticide exposure assessments ''provides more accurate information on the range and probability of possible exposure and their associated risk values.'' (Ref. 58). In capsule, a probabilistic pesticide exposure analysis constructs a distribution of potential exposures based on data on consumption patterns and residue levels and provides a ranking of the probability that each potential exposure will occur. People consume differing amounts of the same foods, including none at all, and a food will contain differing amounts of a pesticide residue, including none at all.

environmental exposure of humans to carbofuran.

1. *Exposure from food*. Data on the residues of carbofuran in foods are available from a variety of sources. One of the primary sources of the data comes from federally-conducted surveys, including the PDP conducted by the USDA. Further, market basket studies, which are typically performed by registrants, can provide additional residue data. These data generally provide a characterization of pesticide residues in or on foods consumed by the U.S. population that closely approximates real world exposures because they are sampled closer to the point of consumption in the chain of commerce than field trial data, which are generated to establish the maximum level of legal residues that could result from maximum permissible use of the pesticide. In certain circumstances, EPA will rely on field trial data, as it can provide more accurate exposure estimates (see below in Unit VI.E.1).

EPA uses a computer program known as the DEEM-FCID to estimate exposure by combining data on human consumption amounts with residue values in food commodities. DEEM-FCID also compares exposure estimates to appropriate RfD or PAD values to estimate risk. EPA uses DEEM-FCID to estimate exposure for the general U.S. population as well as for 32 subgroups based on age, sex, ethnicity, and region. DEEM-FCID allows EPA to process extensive volumes of data on human consumption amounts and residue levels in making risk estimates. Matching consumption and residue data, as well as managing the thousands of repeated analyses of the consumption database conducted under probabilistic risk assessment techniques, requires the use of a computer.

DEEM-FCID contains consumption and demographic information on the individuals who participated in the USDA's CSFII in 1994–1996 and 1998. The 1998 survey was a special survey required by the FQPA to supplement the number of children survey participants. DEEM-FCID also contains ''recipes'' that convert foods as consumed (*e.g.*, pizza) back into their component raw agricultural commodities (*e.g.*, wheat from flour, or tomatoes from sauce, etc.). This is necessary because residue data are generally gathered on raw agricultural commodities rather than on finished ready-to-eat food. Data on residue values for a particular pesticide and the RfD or PADs for that pesticide are inputs to the DEEM-FCID program to estimate exposure and risk.

For carbofuran's assessment, EPA used DEEM-FCID to calculate risk estimates based on a probabilistic distribution. DEEM-FCID combines the full range of residue values for each food with the full range of data on individual consumption amounts to create a distribution of exposure and risk levels. More specifically, DEEM-FCID creates this distribution by calculating an exposure value for each reported day of consumption per person (''person/day'') in CSFII, assuming that all foods potentially bearing the pesticide residue contain such residue at the chosen value. The exposure amounts for the thousands of person/days in the CSFII are then collected in a frequency distribution. EPA also uses DEEM-FCID to compute a distribution taking into account both the full range of data on consumption levels and the full range of data on potential residue levels in food. Combining consumption and residue levels into a distribution of potential exposures and risk requires use of probabilistic techniques.

The probabilistic technique that DEEM-FCID uses to combine differing levels of consumption and residues involves the following steps:

(1) Identification of any food(s) that could bear the residue in question for each person/day in the CSFII;

(2) Calculation of an exposure level for each of the thousands of person/days in the CSFII database, based on the foods identified in Step #1, by randomly selecting residue values for the foods from the residue database;

(3) Repetition of Step # 2 one thousand times for each person/day; and

(4) Collection of all of the hundreds of thousands of potential exposures estimated in Steps ## 2 and 3 in a frequency distribution.

The resulting probabilistic assessment presents a range of exposure/risk estimates.

2. *Exposure from water*. EPA may use field monitoring data and/or simulation water exposure models to generate pesticide concentration estimates in drinking water. Monitoring and modeling are both important tools for estimating pesticide concentrations in water and can provide different types of information. Monitoring data can provide estimates of pesticide concentrations in water that are representative of the specific agricultural or residential pesticide practices in specific locations, under the environmental conditions associated with a sampling design (*i.e.*, the locations of sampling, the times of the year samples were taken, and the frequency by which samples were collected). Although monitoring data can provide a direct measure of the concentration of a pesticide in water, it does not always provide a reliable basis for estimating spatial and temporal variability in exposures because sampling may not occur in areas with the highest pesticide use, and/or when the pesticides are being used and/or at an appropriate sampling frequency to detect high concentrations of a pesticide that occur over the period of a day to several days.

Because of the limitations in most monitoring studies, EPA's standard approach is to use simulation water exposure models as the primary means to estimate pesticide exposure levels in drinking water. Modeling is a useful tool for characterizing vulnerable sites, and can be used to estimate peak pesticide water concentrations from infrequent, large rain events. EPA's computer models use detailed information on soil properties, crop characteristics, and weather patterns to estimate water concentrations in vulnerable locations where the pesticide could be used according to its label. (69 FR 30042, 30058–30065 (May 26, 2004)). These models calculate estimated water concentrations of pesticides using laboratory data that describe how fast the pesticide breaks down to other chemicals and how it moves in the environment at these vulnerable locations. The modeling provides an estimate of pesticide concentrations in ground and surface water. Depending on the modeling algorithm (*e.g.*, surface water modeling scenarios), daily concentrations can be estimated continuously over long periods of time, and for places that are of most interest for any particular pesticide.

EPA relies on models it has developed for estimating pesticide concentrations in both surface water and ground water. Typically EPA uses a two-tiered approach to modeling pesticide concentrations in surface and ground water. If the first tier model suggests that pesticide levels in water may be unacceptably high, a more refined model is used as a second tier assessment. The second tier model is actually a combination of two models: the Pesticide Root Zone Model (PRZM) and the Exposure Analysis Model System (EXAMS).

A detailed description of the models routinely used for exposure assessment is available from the EPA OPP Water Models web site: *http://www.epa.gov/oppefed1/models/water/index.htm*. These models provide a means for EPA to estimate daily pesticide concentrations in surface water sources of drinking water (a reservoir) using local soil, site, hydrology, and weather

characteristics along with pesticide application and agricultural management practices, and pesticide environmental fate and transport properties. Consistent with the recommendations of the FIFRA SAP, EPA also considers regional percent cropped area factors (PCA) which takes into account the potential extent of cropped areas that could be treated with pesticides in a particular area. The PRZM and EXAMS models used by EPA were developed by EPA's Office of Research and Development (ORD), and are used by many international pesticide regulatory agencies to estimate pesticide exposure in surface water. EPA's use of the percent cropped area factors and the Index Reservoir scenario was reviewed by the FIFRA SAP in 1999 and 1998, respectively (Refs. 25 and 26).

In modeling potential surface water concentrations, EPA attempts to model areas of the country that are highly vulnerable to surface water contamination rather than simply model ''typical'' concentrations occurring across the nation. Consequently, EPA models exposures occurring in small highly agricultural watersheds in different growing areas throughout the country, over a 30 year period. The scenarios are designed to capture residue levels in drinking water from reservoirs with small watersheds with a large percentage of land use in agricultural production. EPA believes these assessments are likely reflective of a small subset of the watersheds across the country that maintain drinking water reservoirs, representing a drinking water source generally considered to be more vulnerable to frequent high concentrations of pesticides than most locations that could be used for crop production.

EPA uses the output of daily concentration values from tier two modeling as an input to DEEM-FCID, which combines water concentrations with drinking water consumption information in the daily diet to generate a distribution of exposures from consumption of drinking water contaminated with pesticides. These results are then used to calculate a probabilistic assessment of the aggregate human exposure and risk from residues in food and drinking water.

C. Selection of Acute Dietary Exposure Level of Concern

Because probabilistic assessments generally present a realistic range of residue values to which the population may be exposed, EPA's starting point for estimating exposure and risk for such aggregate assessments is the 99.9th percentile of the population under evaluation. When using a probabilistic method of estimating acute dietary exposure, EPA typically assumes that, when the 99.9th percentile of acute exposure is equal to or less than the aPAD, the level of concern for acute risk has not been exceeded. By contrast, where the analysis indicates that estimated exposure at the 99.9th percentile exceeds the aPAD, EPA would generally conduct one or more sensitivity analyses to determine the extent to which the estimated exposures at the high-end percentiles may be affected by unusually high food consumption or residue values. To the extent that one or a few values seem to ''drive'' the exposure estimates at the high end of exposure, EPA would consider whether these values are reasonable and should be used as the primary basis for regulatory decision making (Ref 58).

VI. Aggregate Risk Assessment and Conclusions Regarding Safety

Consistent with section 408(b)(2)(D) of FFDCA, EPA has reviewed the available scientific data and other relevant information in support of this action. EPA's assessment of exposures and risks associated with carbofuran use follows:

A. Toxicological Profile

Carbofuran is an *N*-methyl carbamate (NMC) pesticide. Like other pesticides in this class, the primary toxic effect seen following carbofuran exposure is neurotoxicity resulting from inhibition of the enzyme acetylcholinesterase (AChE). AChE breaks down acetylcholine (ACh), a compound that assists in transmitting signals through the nervous system. Carbofuran inhibits the AChE activity in the body. When AChE is inhibited at nerve endings, the inhibition prevents the ACh from being degraded and results in prolonged stimulation of nerves and muscles. Physical signs and symptoms of carbofuran poisoning include headache, nausea, dizziness, blurred vision, excessive perspiration, salivation, lacrimation (tearing), vomiting, diarrhea, aching muscles, and a general feeling of severe malaise. Uncontrollable muscle twitching and bradycardia (abnormally slow heart rate) can occur. Severe poisoning can lead to convulsions, coma, pulmonary edema, muscle paralysis, and death by asphyxiation. Carbofuran poisoning also may cause various psychological, neurological and cognitive effects, including confusion, anxiety, depression, irritability, mood swings, difficulty concentrating, short-term memory loss, persistent fatigue, and blurred vision (Refs. 15 and 16).

The most sensitive and appropriate effect associated with the use of carbofuran is its toxicity following acute exposure. Acute exposure is defined as an exposure of short duration, usually characterized as lasting no longer than a day. EPA classifies carbofuran as Toxicity Category I, the most toxic category, based on its potency by the oral and inhalation exposure routes. The lethal potencies of chemicals are usually described in terms of the ''dose'' given orally or the ''concentration'' in air that is estimated to cause the death of 50 percent of the animals exposed (abbreviated as LD_{50} or LC_{50}). Carbofuran has an oral LD_{50} of 7.8–6.0 mg/kg, and an inhalation LC_{50} of 0.08 mg/l (Refs. 12, 16 and 48). The lethal dose and lethal concentration levels for the oral and inhalation routes fall well below the limits for the Toxicity Category I, < 50 mg/kg and < 0.2 mg/l, respectively (40 CFR 156.62).

Carbofuran has a steep dose-response curve. In other words, a marginal increase in administered doses of carbofuran can result in a significant change in the toxic effect. For example, carbofuran data in juvenile rats (postnatal day 11 and 17) demonstrate that small differences in carbofuran doses (0.1 mg/kg to 0.3 mg/kg) can change the measured effect from significant brain and red blood cell (RBC) AChE inhibition without clinical signs (0.1 mg/kg) to significant AChE inhibition, and resultant tremors, and decreased motor activity (0.3 mg/kg) (Refs. 31 and 46). In other words there is a slight difference in exposure levels that produce no noticeable outward effects and the level that causes adverse effects. This means that small differences in human exposure levels can have significant adverse consequences for large numbers of individuals. For example, as discussed in greater detail in Unit VI.E.1.b below, the difference between the amount of food with carbofuran residues that can be safely consumed without adverse effect, and the amount that provides a dose that exceeds safe levels is minimal. Children who consume typical amounts of watermelon (*i.e.*, 8 grams) containing carbofuran residues of 0.009 ppm–a residue level detected in PDP data—receive a safe daily dose, but those consuming the same amount of watermelon with a PDP residue level of 0.013 receive an exposure of 130% of the safe daily dose.

B. Deriving Carbofuran's point of departure

EPA uses a weight of evidence approach to determine the toxic effect that will serve as the appropriate PoD for a risk assessment for AChE inhibiting pesticides, such as carbofuran (Ref. 61). The neurotoxicity that carbofuran causes can occur in both the central (brain) and peripheral nervous systems (PNS). In its weight of the evidence analysis, EPA reviews data, such as AChE inhibition data from the brain, peripheral tissues and blood (*e.g.*, RBC or plasma), in addition to data on clinical signs and other functional effects related to AChE inhibition. Based on these data, EPA selects the most appropriate effect on which to regulate; such effects can include clinical signs of AChE inhibition, central or peripheral nervous tissue measurements of AChE inhibition or RBC AChE measures (Id.). Although RBC AChE inhibition is not adverse in itself, it is a surrogate for inhibition in peripheral tissues when peripheral data are not available. As such, RBC AChE inhibition provides an indirect indication of adverse effects on the nervous system (Id.). Due to technical difficulties regarding dissection of peripheral nerves and the rapid nature of carbofuran toxicity, measures of AChE inhibition in the PNS are very rare for NMC pesticides. For these reasons, other state and national agencies such as California, Washington, Canada, the European Union, as well as the World Health Organization (WHO), all use blood measures in human health risk assessment and/or worker safety monitoring programs.

AChE inhibition in brain and the PNS is the initial adverse biological event which results from exposure to carbofuran, and with sufficient levels of inhibition leads to other effects such as tremors, dizziness, as well as gastrointestinal and cardiovascular effects, including bradycardia (Ref. 16). Thus, AChE inhibition provides the most appropriate effect to use in risk extrapolation for derivation of RfDs and PADs. Protecting against AChE inhibition ensures that the other adverse effects mentioned above do not occur.

EPA has relied on a benchmark dose approach for deriving the PoD from the available rat toxicity studies. A benchmark dose, or BMD, is a point estimate along a dose-response curve that corresponds to a specific response level. For example, a BMD_{10} represents a 10% change from the background or typical value for the response of concern. Generically, the direction of change from background can be an increase or a decrease depending on the biological parameter and the chemical of interest. In the case of carbofuran, inhibition of AChE is the toxic effect of concern. Following exposure to carbofuran, the normal biological activity of the AChE enzyme is decreased (*i.e.*, the enzyme is inhibited). Thus, when evaluating BMDs for carbofuran, the Agency is interested in a decrease in AChE activity compared to normal activity levels, which are also termed ''background'' levels. Measurements of ''background'' AChE activity levels are usually obtained from animals in experimental studies that are not treated with the pesticide of interest (*i.e.*, ''negative control'' animals).

In addition to the BMD, a ''confidence limit'' was also calculated. Confidence limits express the uncertainty in a BMD that may be due to sampling and/or experimental error. The lower confidence limit on the dose used as the BMD is termed the BMDL, which the Agency uses as the PoD. Use of the BMDL for deriving the PoD rewards better experimental design and procedures that provide more precise estimates of the BMD, resulting in tighter confidence intervals. Use of the BMDL also helps ensure with high confidence (*e.g.*, 95% confidence) that the selected percentage of AChE inhibition is not exceeded. From the PoD, EPA calculates the RfD and aPAD.

Numerous scientific peer review panels over the last decade have supported the Agency's application of the BMD approach as a scientifically supportable method for deriving PoDs in human health risk assessment, and as an improvement over the historically applied approach of using no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect-levels (LOAELs). The NOAEL/LOAEL approach does not account for the variability and uncertainty in the experimental results, which are due to characteristics of the study design, such as dose selection, dose spacing, and sample size. With the BMD approach, all the dose response data are used to derive a PoD. Moreover, the response level used for setting regulatory limits can vary based on the chemical and/or type of toxic effect (Refs. 27, 28, 29 and 57). Specific to carbofuran and other NMCs, the FIFRA SAP has reviewed and supported the statistical methods used by the Agency to derive BMDs and BMDLs on two occasions, February 2005 and August 2005 (Refs. 28 and 29). Recently, in reviewing EPA's draft NOIC, the SAP again unanimously concluded that the Agency's approach in using a benchmark dose to derive the PoD from carbofuran brain AChE data in juvenile rats is ''state of the art science and the Panel strongly encouraged the Agency to follow this approach for all studies where possible'' (Ref. 30).

There are laboratory data on carbofuran for cholinesterase activity in plasma, RBC, and brain. EPA evaluated the quality of the AChE data in all the available studies. In this review, particular attention was paid to the methods used to assay AChE inhibition in the laboratory conducting the study. Because of the nature of carbofuran inhibition of AChE, care must be taken in the laboratory such that experimental conditions do not promote enzyme reactivation (*i.e.*, recovery) while samples of blood and brain are being processed and analyzed. If this reactivation occurs during the assay, the results of the experiment will underestimate the toxic potential of carbofuran (Refs. 33, 37, 43, 66 and 67). Through its review of available studies, the Agency identified problems and irregularities with the RBC AChE data from both FMC supported studies. These problems are described in detail in the Agency's study review (Refs. 19 and 20). As such, the Agency determined that the RBC AChE inhibition data from both FMC studies were unreliable and not useable in extrapolating human health risk. In addition, RBC data from a study performed at EPA ORD did not provide doses low enough to adequately characterize the full dose-response in postnatal day 11 (PND11) rats. In the recent SAP review of the draft carbofuran NOIC, the Panel unanimously agreed with the Agency's conclusion, remarking that ''[t]he Agency is well-justified in taking the position that the data on AChE inhibition in rat RBC, particularly with regard to the PND11 pups, are not acceptable for the purpose of predicting health risk from carbofuran'' (Ref. 30). By contrast, the brain AChE data from the FMC and EPA-ORD studies are acceptable and have been used in the Agency's BMD analysis.

In EPA's BMD dose analysis to derive PoDs for carbofuran, the Agency used a response level of 10% brain AChE inhibition and thus calculated BMD_{10}s and $BMDL_{10}$s based on the available carbofuran brain data. These values (the central estimate and lower confidence bound, respectively) represent the estimated dose where AChE is inhibited by 10% compared to untreated animals. In the last few years EPA has used this 10% value to regulate AChE inhibiting pesticides, including organophosphate pesticides and NMCs including carbofuran. For a variety of toxicological and statistical reasons, EPA chose 10%

brain AChE inhibition as the response level for use in BMD and BMDL calculations. EPA analyses have demonstrated that 10% is a level that can be reliably measured in the majority of rat toxicity studies; is generally at or near the limit of sensitivity for discerning a statistically significant decrease in AChE activity across the brain compartment; and is a response level close to the background AChE level (Refs. 28 and 29)

The Agency used a meta-analysis to calculate the BMD_{10} and $BMDL_{10}$ for pups and adults; this analysis includes brain data from studies where either adult or juvenile rats or both were exposed to a single oral dose of carbofuran. The Agency used a dose-time-response exponential model where benchmark dose and half-life to recovery can be estimated together. This model and the statistical approach to deriving the BMD_{10}s, $BMDL_{10}$s, and half-life to recovery have been reviewed and supported by the FIFRA SAP (Refs. 28 and 29). The meta-analysis approach offers the advantage over using single studies by combining information across multiple studies and thus provides a robust PoD.

There are three studies available which compare the effects of carbofuran on PND11 rats with those in young adult rats (herein called 'comparative AChE studies') (Refs. 1, 2 and 46). Two of these studies were submitted by FMC, the registrant, and one was performed by EPA-ORD. An additional study conducted by EPA-ORD involved PND17 rats (Ref. 45). Although it is not possible to directly correlate ages of juvenile rats to humans, PND11 rats are believed to be close in development to newborn humans. PND17 rats are believed to be closer developmentally to human toddlers (Ref. 9). Other studies in adult rats used in the Agency's analysis included additional data from EPA-ORD (Refs 44 and 46).

Using quality brain AChE data from the three studies (2 FMC, 1 EPA–ORD) conducted with PND11 rats, in combination, provides data to describe both low and high doses. By combining the three studies in PND11 animals together in a meta-analysis, the entire dose-response range is covered (see Figure 1 in Unit VI.C. below). The Agency believes the BMD analysis for the PND11 brain AChE data is the most robust analysis for purposes of PoD selection.

The studies in juvenile rats show a consistent pattern that juvenile rats are more sensitive than adult rats to the effects of carbofuran. These effects include inhibition in AChE in addition to incidence of clinical signs of neurotoxicity such as tremors. This pattern has also been observed for other NMC pesticides, which exhibit the same mechanism of toxicity as carbofuran (Ref. 63). It is not unusual for juvenile rats, or indeed, for infants or young children, to be more sensitive to chemical exposures as metabolic detoxification processes in the young are still developing. Because juvenile rats, called 'pups' herein, are more sensitive than adult rats, data from pups provide the most relevant information for evaluating risk to infants and young children and are thus used to derive the PoD. In addition, typically (and is the case for carbofuran) young children (ages 0–5) tend to be the most exposed age groups because they tend to eat larger amounts of food per their body weight than do teenagers or adults. As such, the focus of EPA's analysis of carbofuran's dietary risk from residues in food and water is on young children (ages 0–5). Since these age groups experience the highest levels of dietary risk, protecting these groups against the effects of carbofuran will, in turn, also protect other age groups.

Using data from PND11 pup brain AChE levels, the estimated oral dose that will result in 10% brain AChE inhibition (BMD_{10}) is 0.04 mg/kg. The lower 95% confidence limit on the BMD_{10} ($BMDL_{10}$) is 0.03 mg/kg—this $BMDL_{10}$ of 0.03 mg/kg provides the PoD.

As noted, although EPA does not consider RBC AChE inhibition as an adverse effect in its own right, in the absence of data from peripheral tissues, RBC AChE inhibition data are a critical component to determining that a selected PoD will be sufficiently protective of PNS effects. Because of the problems discussed previously with the available RBC AChE inhibition data, there remains uncertainty surrounding the dose-response relationship for RBC AChE inhibition in pups, which the EPA-ORD data clearly show to be a more sensitive endpoint than brain AChE. Consequently, EPA cannot reliably estimate the BMD_{10} and $BMDL_{10}$ for RBC AChE data in pups. Furthermore, given that the EPA-ORD data clearly show RBC AChE to be more sensitive than brain AChE, EPA cannot conclude that reliance on the pup brain data as the PoD would be sufficiently protective of PNS effects in pups. This uncertainty provides the scientific basis, in part, for retention of the children's safety factor as described below.

C. Safety Factor for Infants and Children

1. *In general.* Section 408 of the FFDCA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA assessments either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses acceptable risk to humans.

In applying the children's safety factor provision, EPA has interpreted the statutory language as imposing a presumption in favor of applying an additional 10X safety factor (Ref. 60). Thus, EPA generally refers to the additional 10X factor as a presumptive or default 10X factor. EPA has also made clear, however, that the presumption can be overcome if reliable data demonstrate that a different factor is safe for children (Id.). In determining whether a different factor is safe for children, EPA focuses on the three factors listed in section 408(b)(2)(C) - the completeness of the toxicity database, the completeness of the exposure database, and potential pre- and post-natal toxicity. In examining these factors, EPA strives to make sure that its choice of a safety factor, based on a weight-of-the-evidence evaluation, does not understate the risk to children (Id.).

2. *Prenatal and postnatal sensitivity.* As noted in the previous section, there are several studies in juvenile rats that show they are more sensitive than adult rats to the effects of carbofuran. These effects include inhibition of brain AChE in addition to the incidence of clinical signs of neurotoxicity (such as tremors) at lower doses in the young rats. The SAP concurred with EPA that the data clearly indicate that the juvenile rat is more sensitive than the adult rat with regard to brain AChE (Ref. 30). However, the Agency does not have AChE data for cabofuran in the peripheral tissue of adult or juvenile animals; nor does the Agency have adequate RBC AChE inhibition data at low doses relevant to risk assessment to serve as a surrogate in pups. As previously noted the RBC AChE data from both FMC supported studies are not reliable and thus are not appropriate for use in risk assessment. Although the EPA studies did provide reliable RBC data, they did not include data at the low end of the dose-response curve, which is the area on the dose-response curve most relevant for risk assessment (see Figure 1).

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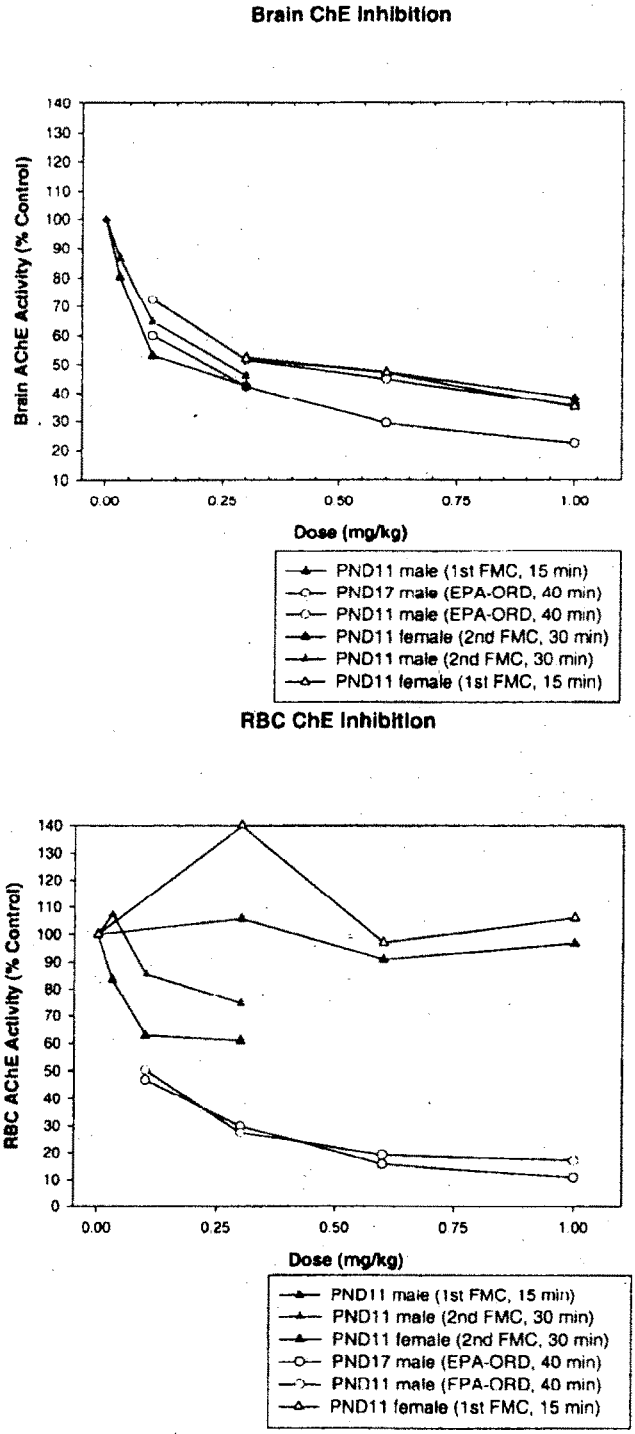
Figure 1. Brain and RBC AChE inhibition in pups following exposure to carbofuran



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There is indication in a toxicity study where pregnant rats were exposed to carbofuran that effects on the PNS are of concern; specifically, chewing motions or mouth smacking was observed in a clear dose-response pattern immediately following dosing each day (Ref. 64). Based on this study, the California Department of Pesticide Regulation calculated a BMD_{05} and $BMDL_{05}$ of 0.02 and 0.01 mg/kg/day, and established the acute PoD (Refs. 11 and 30). These BMD estimates are notable as they are close to the values EPA has calculated for brain AChE inhibition and being used as the PoD for extrapolating risk to children. It is important to note that these clinical signs have been reported for at least one other cholinesterase inhibiting pesticide at doses producing only blood, not brain, AChE inhibition (Ref. 38). Thus, although RBC AChE inhibition is not an adverse effect, per se, blood measures are used as surrogates in the absence of peripheral tissue data. Assessment of potential for neurotoxicity in peripheral tissues is a critical element of hazard characterization for NMCs, like carbofuran. The lack of an appropriate surrogate to assess the potential for RBC AChE inhibition is a key uncertainty in the carbofuran toxicity database. Thus, EPA cannot conclude that reliance on the pup brain data solely as the PoD will be protective of PNS effects in pups.

To account for the lack of RBC data in pups at the low end of the response curve, and for the fact that RBC AChE inhibition appears to be a more sensitive point of departure compared to brain AChE inhibition (and is considered an appropriate surrogate for the peripheral nervous system), EPA is retaining a portion of the children's safety factor. On the other hand, there are data available, albeit incomplete, which characterize the toxicity of carbofuran in juvenile animals, and the Agency believes the weight of the evidence supports reducing the statutory factor of 10X to a value lower than 10X. This results in a children's safety factor that is less than 10 but more than 1.

This modified safety factor should take into account the greater sensitivity of the RBC AChE. The preferred approach to comparing the relative sensitivity of brain and RBC AChE inhibition would be to compare the BMD_{10} estimates. However, as described above, BMD_{10} estimates from the available RBC AChE inhibition data are not reliable due to lack of data at the low end of the dose response curve (Figure 1). As an alternative approach, EPA has used the ratio of brain to RBC AChE inhibition at the BMD_{50}, since there are quality data at or near the 50% response level such that a reliable estimate can be calculated. There is, however, an assumption associated with using the 50% response level—namely that the magnitude of difference between RBC and brain AChE inhibition is constant across dose. In other words, EPA is assuming the RBC and brain AChE dose response curves are parallel. There are currently no data to test this assumption for carbofuran.

The Agency has recommended the application of a children's safety factor of 4X, based on a weight-of-evidence approach. This safety factor is calculated using the difference in RBC and brain AChE inhibition, using the data on administered dose for the animals from the EPA-ORD studies and the FMC studies combined. In other words, EPA estimated the BMD_{50} for PND11 animals from each quality study and used the ratio from the combined analysis, resulting in a BMD_{50} ratio of 4.1X[3]. EPA also compared the BMD_{50} ratios for PND17 pups (who are slightly less sensitive than 11–day olds; see Figure 2) in the EPA-ORD study, resulting in a BMD_{50} of 3.3 X. Conceptually, the RBC to brain potency ratio could be estimated using two different approaches: 1) EPA's data for RBC (the only reliable RBC data in PND11 animals for carbofuran) and all available data in PND11 animals for brain; or 2) using only EPA's data in PND11 animals for both RBC and brain. The former procedure, the approach used by EPA, yields a ratio of about fourfold, while the latter gives a twofold ratio for carbofuran. EPA has elected to use the 4X factor as the more health protective choice. This selection was made based on: 1) uncertainty regarding lack of an appropriate measure of peripheral toxicity (*i.e.*, lack of RBC AChE inhibition data at the low end of the dose response curve), and 2) the RBC to brain AChE ratio at the BMD_{50} for PND17 animals of 3.3X which suggests that a factor of 2X would not be protective of PND11 pups.

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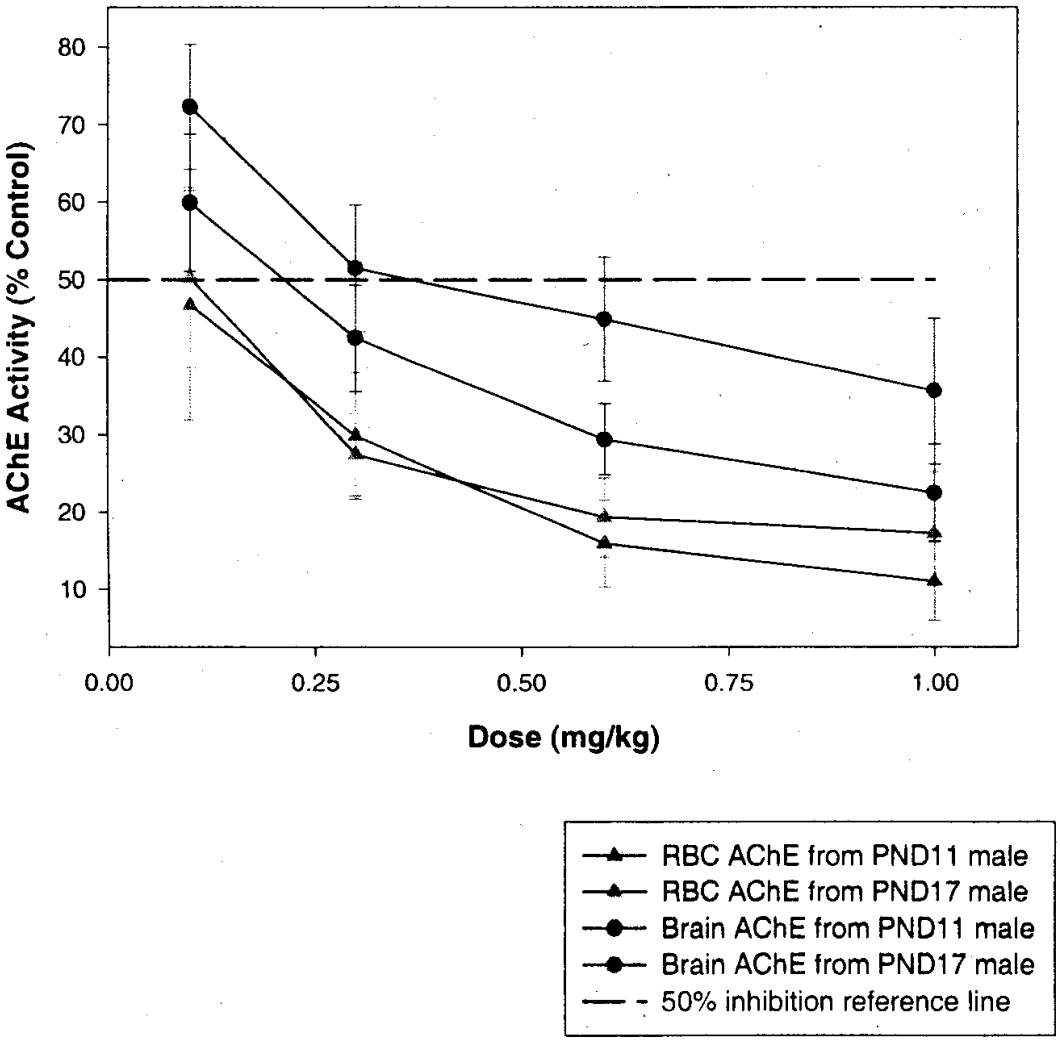
[3] EPA made a mathematical error when it originally calculated the children's safety factor, which resulted in a factor of 5X (Ref. 50). Correcting the mathematical error results in a 4X actor.

Figure 2. Comparison of brain and RBC AChE inhibition in PND11 and PND17 pups.



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EPA recently presented its dietary risk assessment of carbofuran to the FIFRA SAP, and requested comment on the Agency's approach to selecting the point of departure and the children's safety factor. Overall, the Agency believes that the Panel's responses support the Agency's approach with regard to carbofuran's hazard identification and hazard characterization. For example, the Agency notes that the Panel ''unanimously'' agreed with the Agency with regard to the conclusion that the second FMC comparative cholinesterase (ChE) study provides reliable brain, but not RBC, AChE data. The Panel further remarked that, ''EPA is well-justified in taking the position that the data on AChE inhibition in rat RBC, particularly with PND11 pups, are not acceptable for the purpose of predicting health risk from carbofuran'' (Ref. 30). The Panel went on to concur with the Agency that the brain AChE inhibition data from the FMC and EPA-ORD studies show ''good concordance.'' With regard to the use of a benchmark dose approach to derive a PoD from brain AChE data in pups, the Panel stated that the Agency's approach is ''state-of-the-art science and the Panel strongly encouraged the Agency to follow this approach for all studies where possible'' (Id.).

The Panel provided five 'scenarios' or options for applying the children's safety factor and/or PoD. Four of the five scenarios included the application of a children's safety factor. Because the Panel report stated that the Panel was ''not in agreement regarding the magnitude of a [children's] safety factor,'' it is reasonable to conclude that a majority did not support any one of the five scenarios, including the one advocating removal of the children's safety factor (Ref. 30). It follows that a majority of the Panel agreed with the Agency that at least a portion of the safety factor should be retained; however, recommendations for the appropriate factor ranged between a 2X and 10X. Two of the scenarios were consistent with the Agency's approach in which the magnitude of the safety factor is derived based on the differences in RBC and brain AChE responses, quantified by the administered dose. The remaining two scenarios were based on retention of the 10X safety factor. Those Panel members supporting retention of the 10X safety factor did so on the basis that the statutory requirement that EPA may use a different factor '''*only if, on the basis of reliable data, such margin will be safe for infants and children*.' Given the uncertainty in the data and in its interpretation for risk assessment by the entire Panel, these Panel members believes that this standard for change had not been met'' (Id.). EPA believes that, on balance, the application of a 4X children's safety factor is consistent with the SAP's advice. Additional detail on the SAP's advice and EPA's responses can be found at Ref. 23.

In sum, EPA has concluded that there is reliable data to support the application of a 4X safety factor and has therefore applied this safety factor in its dietary risk estimates. However, in light of the disagreement among the SAP panelists on the appropriate factor to apply, the Agency solicits comment on this issue.

D. Hazard Characterization and Point of Departure Conclusions

The doses and toxicological endpoints selected and Margins of Exposures for various exposure scenarios are summarized in Table 1 below.

TABLE 1—TOXICOLOGY ENDPOINT SELECTION

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA factor and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary Infants and Children	$BMDL_{10}$ = 0.03 mg/kg/day UF = 100 Acute RfD = 0.0003 mg/kg/day	Children's SF = 4X aPAD = 0.000075 mg/kg/day	Comparative AChE Studies in PND11 rats (FMC and EPA-ORD) BMD_{10} = 0.04 mg/kg/day $BMDL_{10}$ = 0.03 mg/kg/day, based on brain AChE inhibition of postnatal day 11 (PND11) pups
Acute Dietary Youth (13 and older) and Adults	$BMDL_{10}$ = 0.02 mg/kg/day UF = 100 Acute RfD = 0.00024 mg/kg/day	Children's SF = 1X aRfD = 0.0002 mg/kg/day	Comparative AChE Study (EPA-ORD), Padilla et al (2007), McDaniel et al (2007) BMD_{10} = 0.06 mg/kg/day $BMDL_{10}$ = 0.02 mg/kg/day, based on RBC AChE inhibition in adult rat

E. Dietary Exposure and Risk Assessment

1. *Dietary exposure to carbofuran (food)*—a. *EPA methodology and background*. EPA conducted a refined (Tier 3) acute probabilistic dietary risk assessment for carbofuran residues in food. Carbofuran is registered for use on the following crops: alfalfa, artichokes, banana, barley, corn, cranberry, cucumber, grapes, melons, milk, oats, peppers, potatoes, pumpkin, rice, sorghum, soybean, spinach, squash, strawberry, sugar beets, sugar cane, sunflower seed, and wheat. To conduct the assessment, EPA relied on DEEM-FCID, Version 2.00–2.02, which uses food consumption data from the USDA's CSFII from 1994–1996 and 1998.

Using data on the percent of the crop actually treated with carbofuran and data on the level of residues that may be present on the treated crop, EPA developed estimates of combined anticipated residues of carbofuran and 3-hydroxycarbofuran on food. 3-Hydroxycarbofuran is a degradate of carbofuran and is assumed to have toxic potency equivalent to carbofuran (Refs. 12, 16 and 48). Anticipated residues of carbofuran for most foods were derived using USDA PDP monitoring data from recent years (through 2006 for all available commodities). In some cases, where PDP data were not available for a particular crop, EPA translated PDP monitoring data from surrogate crops based on the characteristics of the crops and the use patterns. For example, PDP data for cantaloupes were used to derive anticipated residues for casaba and honeydew.

USDA PDP provides the most comprehensive sampling design, and the most extensive and intensive sampling procedures for pesticide residues of the various data sources available to EPA. Additionally, the intent of PDP's sampling design is to provide statistically representative samples of food commodities eaten by the U.S. population specifically for the purpose of performing dietary risk assessments for pesticides. The program focuses on high-consumption foods for

children and reflects foods typically available throughout the year. A complete description of the PDP program (including all data through 2006) is available online.

The PDP analyzed for parent carbofuran and its metabolite of concern, 3-hydroxycarbofuran. Most of the samples analyzed by the PDP were measured using a high Level of Detection (LOD) and contained no detectable residues of carbofuran or 3-hydroxycarbofuran. Consequently, the acute assessment for food assumed a concentration equal to ½ of the LOD for PDP monitoring samples with no detectable residues, and 0.00 ppm carbofuran to account for the percent of the crop not treated with carbofuran.

An additional source of data on carbofuran residues was provided by a market basket survey of NMC pesticides in single-serving samples of fresh fruits and vegetables collected in 1999–2000 (Ref. 14), which was sponsored by the Carbamate Market Basket Survey Task Force. EPA relied on these data to construct the residue distribution files for 2 crops (bananas and grapes) because the use of these data resulted in more refined exposure estimates. The combined Limits of Quantitation (LOQs) for carbofuran and its metabolite in the Market Basket Survey (MBS) were between tenfold and twentyfold lower than the combined LODs in the PDP monitoring data.

For certain crops where PDP data were not available (sugar beets, sugarcane, and sunflower seed), anticipated residues were based on field trial data. EPA also relied on field trial data for particular food commodities that are blended during marketing (barley, field corn, popcorn, oats, rice, soybeans and wheat), as use of PDP data can result in significant overestimates of exposure when evaluating blended foods. Field trial data are typically considered to overestimate the residues that are likely to occur in food as actually consumed because they reflect the maximum application rate and shortest preharvest interval allowed by the label. However, for crops that are blended during marketing, such as corn or wheat, use of field trial data can provide a more refined estimate than PDP data, by allowing EPA to better account for the percent of the crop actually treated with carbofuran.

EPA used average and maximum percent crop treated (PCT) estimates for most crops, following the guidance provided in HED SOP 99.6 (*Classification of Food Forms with Respect to level of Blending; 8/20/99*), and available processing and/or cooking factors. The maximum PCT estimates were used to refine the acute dietary exposure estimates. Maximum PCT ranged from <1 to 35%. The estimated percent of the crop imported was applied to crops with tolerances currently maintained solely for import purposes (cranberry, rice, strawberry).

b. *Acute dietary exposure (food alone) results and conclusions*. The estimated acute dietary exposure from carbofuran residues in food alone (*i.e.*, assuming no additional carbofuran exposure from drinking water), exceeds EPA's level of concern for all but one of the children's population subgroups at the 99.9th percentile of exposure. Carbofuran dietary exposure at the 99.9th percentile was estimated at 0.000156 mg/kg/day (210% of the aPAD) for children 3–5 years old, the population subgroup with the highest estimated dietary exposure. Estimated dietary exposure to carbofuran also exceeds EPA's level of concern for children 1–2 years old and 6–12 years at the 99.9th percentile of exposure. (See results Table 2 below).

TABLE 2—RESULTS OF ACUTE DIETARY EXPOSURE ANALYSIS FOR FOOD ALONE

Population Subgroup	aPAD (mg/kg/day)	99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.000025	33	0.000070	93
Children 1–2 years old	0.000075	0.000045	60	0.000152	200
Children 3–5 years old	0.000075	0.000036	48	0.000156	210
Children 6–12 years old	0.000075	0.000024	32	0.000121	160

Exposure estimates for all of the major food contributors were based on PDP monitoring data adjusted to account for the percent of the crop treated with carbofuran and, therefore, may be considered highly refined.

As noted previously, because most of the PDP samples contained no detectable residues of carbofuran or its 3-hydroxy metabolite, the acute assessment for food assumed a concentration equal to ½ of the LOD for PDP monitoring samples with no detectable residues, with 0.00 ppm carbofuran incorporated to account for the percent of the crop not treated with carbofuran. In accordance with OPP policy for analyzing commodities with non-detectable residues, EPA performed additional analyses to determine the impact of using ½ the LOD to estimate exposure (Ref. 56).

In the first analysis (Sensitivity Analysis #1), those commodities that had no detectable residues at all in either the monitoring data or field trials were eliminated from the assessment. The commodities that were eliminated included barley, coffee, corn, cranberry, oats, potato, raisin, rice, soybean, spinach, strawberry, sugar beet, sunflower, winter squash, and wheat. For the remaining commodities, on which carbofuran was detected, EPA continued to substitute the ½ LOD values for the percent of the crop treated with carbofuran, with 0.00 ppm carbofuran incorporated to account for the remaining untreated percent of the crop. This analysis resulted in estimated exposures that were still above EPA's level of concern for children 1–2 at the 99.9th percentile (115% of the aPAD; see Table 3 below).

To further understand the extent to which the ½ LODs from the PDP monitoring data were affecting the risk assessment, EPA conducted an additional sensitivity analysis, (Sensitivity Analysis #2) that excluded the crops for which PDP and MBS data were not available and assigned 0.00 ppm carbofuran for all non-detected residues in commodities sampled in the PDP or MBS. In other words, an analysis using only detectable residues from residue monitoring programs was conducted. In this analysis, estimated dietary exposures at the 99.9th percentile of exposure remained above EPA's level of concern for children 1–2 yrs. old (114% of the aPAD). The

results of these sensitivity analyses at the 99.9th percentile of exposure are compared to the results using ½ LOD for non-detectable residues in Table 3 below.

TABLE 3—IMPACT OF USING ½ LOD FOR NON-DETECTABLE RESIDUES ON ESTIMATED EXPOSURE FROM FOOD[1]

Population Subgroup	aPAD (mg/kg/day)	Analysis Assuming ½ LOD for Non-Detectable Residues		Sensitivity Analysis #1[2]		Sensitivity Analysis #2[3]	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.000070	93	0.000044	58	0.000043	57
Children 1–2 years old	0.000075	0.000152	200	0.000086	115	0.000086	114
Children 3–5 years old	0.000075	0.000156	210	0.000066	88	0.000065	87
Children 6–12 years old	0.000075	0.000121	160	0.000039	52	0.000038	51

[1] At the 99.9th Percentile of Exposure.
[2] Non-detectable PDP residues assumed to be zero only for commodities having no detectable residues at all in the PDP monitoring data and field trials (*i.e.*, these commodities were eliminated from the analysis). Crops without PDP data and detectable residues in field trials were included, based on the distribution of residues from field trial studies.
[3] Non-detectable residues assumed to be zero for all commodities. Commodities without PDP or Market Basket data were excluded from the analysis.

The major contributors in Sensitivity Analysis #2, to the estimated dietary exposure of children are listed in Table 4 below.

TABLE 4—MAJOR CONTRIBUTORS TO CARBOFURAN ACUTE EXPOSURE AT THE 99.9TH PERCENTILE IN SENSITIVITY ANALYSIS #2 (EXPRESSED AS AN APPROXIMATE PERCENT OF TOTAL EXPOSURE)

Food	Infants, <1 year old	Children, 1–2 Years Old	Children, 3–5 Years Old
Cantaloupe	9	18	20
Squash	10	2	1
Grape	15	10	5
Cucumbers	2	20	29
Milk	32	<1	1
Watermelon	29	39	41

EPA's evaluation of these two sensitivity analyses and other information on carbofuran residue levels yields three conclusions. First, the results of the sensitivity analyses indicate that the dietary risk assessment for carbofuran is sensitive to the assumed concentrations (*i.e.*, ½ LOD) for non-detectable residues in the PDP monitoring data. This sensitivity appears to be more of a factor for commodities with no detections because the main difference between the Sensitivity Analyses #1 and #2 was substituting 0.00 ppm for ½ LODs for commodities with detects in the second analysis yet that analysis yielded similar results to the first sensitivity analysis. On the other hand, both sensitivity analyses were approximately 2X lower than the analysis that used ½ LOD for all treated commodities. The finding that the use of a ½ LOD assumption had a noticeable impact on the risk estimate is contrary to EPA's experience in conducting pesticide risk assessments. Generally, risk estimates do not show noticeable differences whether non-detects are treated as true zeros or ½ LODs. In all likelihood, this is a factor of the relatively insensitive level of the carbofuran method's LOD.

Second, given that there are data showing that carbofuran is found at levels below the LOD when a more sensitive method was used, EPA finds that use of either of the approaches in the sensitivity analyses will understate carbofuran risk. The available information demonstrates that carbofuran residues are present; when a lower level of detection was utilized, both in the most recent PDP milk analyses and in the Carbamate MBS data; residues of carbofuran and 3-hydroxycarbofuran were detected in commodities that previously had no detections. Moreover, detected residues ranged between levels below and above ½ LOD. Thus, unlike the circumstance where a relatively sensitive method of detection is used and there is some uncertainty as to whether a non-detect may mask an actual exposure, with cabofuran there is no question – treating all non-detects as zero clearly would mask actual exposures to carbofuran. Thus, these sensitivity analyses do not provide a basis for concluding that EPA has overestimated risk.

Third, and most important, EPA would call attention to the fact that these sensitivity analyses, although clearly underestimating actual carbofuran exposure and risk, still indicate that one group of children will have exposures exceeding the safe level.

Because it appears that carbofuran's dietary risks to children are driven by

relatively low residues in a small percentage of commodities, and to try to gain further insight into the potential impact of using ½ LOD in this case, EPA conducted a third sensitivity analysis to evaluate whether its estimates that food only and aggregate carbofuran exposure results in risks of concern were overstated. EPA combined actual residue values measured in the food supply (from PDP and MBS data) with the typical (50th percentile) and high-end (90th percentile) amounts of a single commodity that a child would be expected to consume, and compared that to the aPAD, without considering the likelihood that a child would be exposed to that residue value. The results one of these analyses are summarized in Table 5 below.

TABLE 5—RISK TO CHILDREN CONSUMING TYPICAL OR HIGH-END AMOUNTS OF FRESH (UNCOOKED) CUCUMBERS CONTAINING CARBOFURAN RESIDUES

Food	Population Subgroup	Typical: 50th Percentile of Consumption				High-End: 90th Percentile of Consumption			
		Consumption (g/kg bw)	PDP Residue[1] (ppm)	Exposure (mg/kg bw)	% aPAD	Consumption (g/kg bw)	PDP Residue[1] (ppm)	Exposure (mg/kg bw)	% aPAD
Cucumbers (Uncooked) DEEM food form 110	Children 1–2	1.0	0.005	0.000005	7	4.3	0.005	0.000022	29
			0.029	0.000029	39		0.029	0.000125	170
			0.063	0.000063	84		0.063	0.000271	360
			0.117	0.000117	160		0.117	0.000503	670
			0.137	0.000137	180		0.137	0.000589	790
			0.147	0.000147	200		0.147	0.000632	840
			0.437	0.000437	580		0.437	0.001879	2,500
			0.537	0.000537	720		0.537	0.002309	3,100
	Children 3–5	0.8	0.005	0.000004	5	5.1	0.005	0.000026	34
			0.029	0.000023	31		0.029	0.000148	200
			0.063	0.000050	67		0.063	0.000321	430
			0.117	0.000094	120		0.117	0.000597	800
			0.137	0.000110	150		0.137	0.000699	930
			0.147	0.000118	160		0.147	0.000750	1,000
			0.437	0.000350	470		0.437	0.002229	3,000
			0.537	0.000430	570		0.537	0.002739	3,700

[1] The PDP detected residues of carbofuran in 11 of 1479 cucumber samples at levels ranging from 0.005 ppm to 0.537 ppm.

Detectable residues of carbofuran and/or 3-hydroxycarbofuran were found in only a few samples of cucumber in monitoring data (11 out of 1479 or less than one percent). However, if young children aged 1 to 5 consume moderate amounts of cucumber (*i.e.*, the median or 50th percentile of consumption, corresponding to approximately 1 gram per kg of body weight of cucumber) that contain actual levels of carbofuran measured in the food supply, the percent of the aPAD that would be utilized ranges from about 7% of the safe daily dose for the lower observed residue values to 720% of the safe daily dose for the higher observed values. For children who consume larger amounts of cucumber (*i.e.*, the 90th percentile of consumption, corresponding to 5 grams per kg of body weight of cucumber or roughly ½ cup), exposure increases approximately tenfold (29% to over 3700% of the aPAD). Many of these values significantly exceed the Agency's level of concern based on the consumption of a single daily serving of one commodity.

Additional analyses are summarized in Table 6 below, and analyses on additional foods can be found in Ref. 12. EPA focused on children in making these calculations, because children have the highest estimated dietary exposure to carbofuran; however, it is reasonable to assume that adult exposures from a single treated food item could also exceed EPA's level of concern, particularly at the high end of consumption.

TABLE 6—RISK TO CHILDREN CONSUMING TYPICAL OR HIGH-END AMOUNTS OF CANTALOUPE OR WATERMELON CONTAINING CARBOFURAN RESIDUES

Population Subgroup	Typical: 50th Percentile of Consumption				High-End: 90th Percentile of Consumption			
	Consumption (g/kg bw)	PDP Residue (ppm)	Exposure (mg/kg bw)	% aPAD	Consumption (g/kg bw)	PDP Residue (ppm)	Exposure (mg/kg bw)	% aPAD
Cantaloupe								
Children 1–2	Approx. 6g	0.009	0.0000531	71	Approx. 12 g	0.009	0.0001035	140
		0.01	0.000059	79		0.01	0.000115	150
		0.02	0.000118	160		0.02	0.00023	310
		0.06	0.000354	470		0.06	0.00069	920
		0.085	0.0005015	670		0.085	0.0009775	1,300
		0.357	0.0021063	2,800		0.357	0.0041055	5,500
Children 3–5	approx. 5g	0.009	0.0000441	59	approx. 15g or ½ cup	0.009	0.0001368	180
		0.01	0.000049	65		0.01	0.000152	200
		0.02	0.000098	130		0.02	0.000304	400
		0.06	0.000294	390		0.06	0.000912	1,200
		0.085	0.0004165	560		0.085	0.001292	1,700
		0.357	0.0017493	2,300		0.357	0.0054264	7,200
Watermelon								
Children 1–2	approx. 8g	0.0057	0.00004332	58	less than 30g	0.0057	0.00014706	200
		0.009	0.0000684	91		0.009	0.0002322	310
		0.0132	0.00010032	130		0.0132	0.00034056	450
		0.014	0.0001064	140		0.014	0.0003612	480
		0.062	0.0004712	630		0.062	0.0015996	2,100
		0.081	0.0006156	820		0.081	0.0020898	2,800
		0.205	0.001558	2,100		0.205	0.005289	7,100
Children 3–5	approx. 12g	0.0057	0.00007125	95	approx. 35g	0.0057	0.00019893	270
		0.009	0.0001125	150		0.009	0.0003141	420
		0.0132	0.000165	220		0.0132	0.00046068	610
		0.014	0.000175	230		0.014	0.0004886	650
		0.062	0.000775	1,000		0.062	0.0021638	2,900
		0.081	0.0010125	1,400		0.081	0.0028269	3,800
		0.205	0.0025625	3,400		0.205	0.0071545	9,500

The analyses in Tables 5 and 6 demonstrate three significant points. First, the fact that individual children, consuming typical amounts of a single food item receive unsafe levels of carbofuran, based on actual residue levels measured in the food supply, strongly supports EPA's findings that aggregate exposures to carbofuran are unsafe. It is true that the results described in Tables 5 and 6, as well as the additional analyses in Ref. 12, do not describe the probability that an individual child will receive those residues on the foods they consume. By contrast, EPA's analyses in Tables 2 and 3 account for the probability that a particular level of residues will be present on a food item, as well as the likelihood that an individual will consume a particular food. It is EPA's typical approach, as was done with carbofuran, to conduct its estimates of exposure across the entire population, generally assuming that as long as the 99.9th percentile of the estimated daily exposure is equal to or less than the aPAD, there is a reasonable certainty of no harm to the general population, including all significant subpopulations (Ref. 58). In practice, this can mean that if only a small portion of the population reported eating the commodity, or if the residues are infrequently detected, individual high-end risks may fall above EPA's usual benchmark of the 99.9th percentile, or in other words, fall in the ''tail end'' of the distribution curve. Admittedly, some of the results described in Tables 5 and 6 would be expected to fall within this tail end, given the relatively infrequent detections of carbofuran in sampled commodities. However, taking into account the analysis of the risk drivers in Table 4 above, it is clear that some of these values do fall within the 99.9th percentile.

In any event, given all of the facts, it is just as appropriate for EPA to evaluate whether the eating occasions that drive a conclusion that risks at the 99.9th percentile yield unacceptable risks are realistic, as it is for EPA to examine whether eating occasions in the tail of a distribution curve are examples of consumption events the Agency should be concerned about. In this regard, it is notable that even the high-end consumption values described in Tables 5 and 6 are extremely likely to be valid reported consumption events—or in other words, consumption of the amounts at the 90th percentile are quite realistic. For example, a child between 3–5 years, who consumes a ½ cup of cantaloupe would receive a dose ranging between 180% and 7,200% of the aPAD. Accordingly, this analysis by itself supports a conclusion that the carbofuran tolerances are not safe and certainly buttresses EPA's conclusions that exposures from carbofuran in food or water alone or from carbofuran residues in food and water aggregated when assessed at the 99.9th percentile are not safe.

Additionally, because of the uncertainty surrounding carbofuran's exposure potential, investigation of individual children's risks, even if in the ''tail end,'' is particularly relevant. There are a number of reasons that significant uncertainty remains with respect to carbofuran's exposure potential. One primary consideration stems from the high LOD for carbofuran and consequent large numbers of non-detects in the PDP data. The LOD for most commodities is tenfold to twentyfold higher than the more precise methods used for the CMS and some of the more recent PDP data. Generally, EPA would consider use of ½ LOD as a conservative way of addressing non-detects but that may not be the case where the LOD is relatively insensitive and the risk of concern is an acute exposure. For acute risks, the higher values in a probabilistic risk assessment are often driven by relatively high values in a few commodities rather than relatively lower values in a greater number of commodities. This is due to the fact that an acute assessment looks at a narrow window of exposure where there are unlikely to be a great variety of foods consumed. Thus, to the extent that there is a high exposure it will be more likely due to a high residue value in a single commodity. However, assuming ½ LOD for non-detects does not reflect that the non-detects actually will bear a range of values from close to or near zero to close to or near the LOD. Importantly, those commodities bearing residues only slightly below the LOD may result in an exceedance of the aPAD where assuming ½ LOD would not. In this way, the ½ LOD analysis may actually understate risk. In these circumstances, reliance on ½ LOD can skew the distribution of residues, which in turn masks the true ''tail end'' of exposures. In other words, to the extent that the ½ LOD underestimates exposures for some individual commodities, it effectively decreases the probability of receiving higher residues, thereby shifting those values with greater risks to the tail end of the distribution curve, above the 99.9th percentile.

The second important point from these tables is that the exceedances from both the 50th and 90th percentile consumer are quite large—sometimes orders of magnitude above safe doses. The size of these exceedances gives rise to concerns that the exceedances are more likely to result in actual harm to exposed individuals, particularly if they are also consuming carbofuran-contaminated drinking water. Additionally worrisome in this regard is that carbofuran is a highly potent (*i.e.*, has a very steep dose-response curve), acute toxicant, and therefore any aPAD exceedances are more likely to have greater significance in terms of the potential likelihood of actual harm.

Finally, that Tables 5 and 6 show large exceedances across several crops for which relatively more residue data are available suggests these results are not unique to the specific crops for which precise residues have been detected in PDP and MBS. In other words, crops for which such residue data are not available may be posing similar risks.

In sum, these results strongly support EPA's conclusion that its dietary exposure assessment for carbofuran has not overstated exposure and risk. Further, serious questions remain as to the extent to which similar exceedances exist for all crops, but which remain undetected, because, as result of the high LOD, EPA lacks precise residue levels for the majority of crops.

2. *Drinking water exposures.* EPA's drinking water assessment uses both monitoring data for carbofuran and modeling methods, and takes into account contributions from both surface water and groundwater sources (Refs. 3, 4, 13, 36 and 47). Concentrations of carbofuran in drinking water, as with any pesticide, are in large part determined by the amount, method, timing and location of pesticide application, the chemical properties of the pesticide, the physical characteristics of the watersheds and/or aquifers in which the community water supplies or private wells are located, and other environmental factors, such as rainfall, which can cause the pesticide to move from the location where it was applied. While there is a considerable body of monitoring data that has measured carbofuran residues in surface and groundwater sources, the locations of sampling and the sampling frequencies generally are not sufficient to capture peak concentrations of the pesticide in a watershed or aquifer where carbofuran is used. Capturing these peak concentrations is particularly important for assessing risks from carbofuran because the toxicity end-point of concern results from single-day exposure (acute effects). Because pesticide loads in surface water tend to move in relatively quick pulses in

flowing water, frequent targeted sampling is necessary to reliably capture peak concentrations for surface water sources of drinking water. Pesticide concentrations in ground water, however, are generally the result of longer-term processes and less frequent sampling can better characterize peak ground water concentrations. However, such data must be targeted at vulnerable aquifers in locations where carbofuran applications are documented in order to capture peak concentrations. As a consequence, monitoring data for both surface and groundwater tends to underestimate exposure for acute endpoints. Simulation modeling complements monitoring by making estimations at vulnerable sites and can be used to represent daily concentration profiles, based on a distribution of weather conditions. Thus, modeling can account for the cases when a pesticide is used in drinking water watersheds at any rate and is applied to a substantial proportion of the crop. It can also account for stochastic processes, such as rainfall represented by 30 years of existing weather data maintained by the National Oceanic and Atmospheric Administration.

a. *Exposure to carbofuran from drinking water derived from ground water sources*. Drinking water taken from shallow wells is particularly vulnerable to contamination in areas where carbofuran is used around sandy, highly acidic soil. Some areas with these characteristics include Long Island, parts of Florida, and the Atlantic coastal plain, in addition to other areas of the country. Exposure estimates for this assessment are drawn primarily from (1) the results of a prospective groundwater (PGW) study developed by the registrant in the early 1980s; and (2) additional groundwater modeling conducted as part of the NMC cumulative assessment in 2007. The results of the PGW study are consistent with a number of other targeted groundwater studies conducted in the 1980s showing that high concentrations of carbofuran can occur in vulnerable areas; the results of these studies as well as the PGW study are summarized in (Refs. 13 and 47). For example, a study in Manitoba, Canada assessed the movement of carbofuran into tile drains and groundwater from the application of liquid carbofuran to potato and corn fields. The application rates ranged between 0.44–0.58 pounds a.i./acre, and the soils at the site included fine sand, loamy fine sand, and silt loam, with pH ranging between 6.5–8.3. Concentrations of carbofuran in groundwater samples ranged between 0 (non-detect) and 158 ppb, with a mean of 40 ppb (Refs. 13 and 47).

While there have been additional groundwater monitoring studies that included carbofuran as an analyte since that time, there has been no additional monitoring targeted to carbofuran use in areas where aquifers are vulnerable. Accordingly, EPA believes the PGW study continues to be the most relevant monitoring data for assessing drinking water exposures from private wells at vulnerable sites. Because this study was conducted over only one growing season, however, and was conducted at use rates that now exceed current label maximum rates for the use being studied (3 lb ai/acre vs. the current 2 lb ai/acre for corn), EPA has scaled the results to represent impacts from carbofuran use over a long-term period (25 years) at current label rates. Temporal scaling was necessary because the PGW study represents water quality impacts from a single application rather than repeated years of use. Based on EPA's assessment, the maximum 90–day average carbofuran concentrations in vulnerable groundwater for various application rates were estimated to range from a low of 11 parts per billion (ppb) based on a 1 pound per acre application rate, to a high of 34 ppb, based on a 3 pound per acre application rate. The peak concentration measured in the PGW study was 65 ppb. Because the degradate 3-hydroxycarbofuran, which is assumed to be of equal potency with the parent compound, was not measured in this study, exposure was not estimated. Although the failure to include the degradate is expected to underestimate exposure to some degree, the extent to which it would contribute to exposure is unclear.

EPA conducted additional groundwater modeling for the NMC cumulative risk assessment, and developed a time series of exposures at locations selected based on potential for exposure to a combination of carbamate insecticides relevant for cumulative exposure assessment for use in probabilistic dietary assessments using DEEM. EPA estimated carbofuran groundwater concentrations associated with two possible use scenarios: potatoes in northeastern Florida and cucurbits on the Delmarva Peninsula in the Mid-Atlantic region. While the modeled potato use scenario in Florida did not show concentrations of carbofuran of concern, estimated carbofuran concentrations associated with the cucurbit use in the Delmarva Peninsula – a region with shallow, acidic groundwater and acidic, sandy soils – are consistent with EPA's assessment of the PGW study discussed above. Specifically, the assessment indicated that at an application rate of 1.25 pounds a.i. per acre, on cucurbits, maximum concentrations were 38.5 ppb (Ref. 63). EPA does not believe the results of this assessment are particularly conservative, since the application rate used in this assessment was less than the maximum rate of 1.94 lb/acre that growers can use. Also, concentrations of the degradate, 3-hydroxycarbofuran were not included in modeling simulations, which would tend to underestimate exposure to some degree.

Based on these estimates, EPA compiled a distribution of estimated carbofuran concentrations in water that could be used to generate probabilistic assessments of the potential exposures from drinking water derived from vulnerable ground water sources. The results of EPA's probabilistic assessments are represented below in Table 7. As discussed in the previous section, it is important to remember that the aPAD for carbofuran is quite low, hence, relatively low concentrations of carbofuran monitored or estimated in vulnerable groundwater can have a significant impact on the aPAD utilized.

TABLE 7—RESULTS OF ACUTE DIETARY (GROUND WATER ONLY) EXPOSURE ANALYSIS USING DEEM FCID AND INCORPORATING THE DELMARVA GROUND WATER SCENARIO (REPRESENTING PRIVATE WELLS)

Population Subgroup	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.003800	5,100	0.006006	8,000	0.010030	>10,000
Children 1–2 years old	0.000075	0.001612	2,100	0.002732	3,600	0.004628	6,200

TABLE 7—RESULTS OF ACUTE DIETARY (GROUND WATER ONLY) EXPOSURE ANALYSIS USING DEEM FCID AND INCORPORATING THE DELMARVA GROUND WATER SCENARIO (REPRESENTING PRIVATE WELLS)—Continued

Population Subgroup	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Children 3–5 years old	0.000075	0.001459	1,900	0.002405	3,200	0.004613	5,600
Children 6–12 years old	0.000075	0.001018	1,360	0.001710	2,300	0.002792	3,700
Youth 13–19 years old	0.0002	0.000809	400	0.001441	720	0.002919	1,500
Adults 20–49 years old	0.0002	0.000955	480	0.001632	820	0.003073	1,500
Adults 50+ years old	0.0002	0.000884	440	0.001345	670	0.002271	1,100

While the registrant has attempted to address drinking water exposure from ground water sources by including on current carbofuran product labeling an advisory statement warning growers against application in vulnerable areas, this language does not prohibit use in such areas. In addition, EPA does not believe that the available information demonstrates that even the additional restrictions that FMC included on its labels submitted in May, 2008 would adequately mitigate the risk of contaminating all vulnerable ground water (Refs. 18 and 54). For example, those restrictions were based on the use of a particular methodology to evaluate the characteristics in the site used in the PGW study in the Delmarva Penninsula. Using that as a surrogate to identify sites with vulnerability to ground water contamination, FMC identified counties that had higher vulnerability scores than the site used for the PGW study in the Delmarva Penninsula, and proposed label restrictions to preclude use in such areas. While EPA agrees in principle that precluding use in sites vulnerable to leaching can mitigate the risks, and even presuming that the methodology used by FMC adequately identifies those sites, sites less vulnerable than the PGW site would still be vulnerable to contamination, and the proposed restrictions in no way addressed the less sensitive, but still vulnerable, sites (Refs. 18 and 54). Accordingly, EPA continues to believe that its assessment of drinking water from groundwater sources based on current labels is a realistic assessment of potential exposures to those portions of the population consuming drinking water from shallow wells in highly vulnerable areas.

b. *Exposure from drinking water derived from surface water sources.* EPA's evaluation of environmental drinking water concentrations of carbofuran from surface water, as with its evaluation of groundwater, takes into account the results of both surface water monitoring and modeling.

Data compiled in 2002 by EPA's Office of Water show that carbofuran was detected in treated drinking water at a few locations. Based on samples collected from 12, 531 ground water and 1,394 surface water source drinking water supplies in 16 states, carbofuran was found at no public drinking water supply systems at concentrations exceeding 40 ppb (the MCL). Carbofuran was found at one public ground water system at a concentration of greater than 7 ppb and in two ground water systems and one surface water public water system at concentrations greater than 4 ppb (measurements below this limit were not reported). Sampling is costly and is conducted typically four times a year or less at any single drinking water facility. The overall likelihood of collecting samples that capture peak exposure events is, therefore, low. For chemicals with acute risks of concern, such as carbofuran, higher concentrations and resulting risk is primarily associated with these peak events, which are not likely to be captured in monitoring unless the sampling rate is very high.

Unlike drinking water derived from private groundwater wells, public water supplies (surface water or ground water source) will generally be treated before it is distributed to consumers. An evaluation of laboratory and field monitoring data indicate that carbofuran may be effectively removed (60 – 100%) from drinking water by lime softening and activated carbon; other treatment process are less effective in removing carbofuran (Ref. 63). The detections between 4 and 7 ppb, reported above, represent concentrations in samples collected post-treatment. As such, these levels are of particular concern to the Agency. An infant who consumes a single 8 ounce serving of water with a concentration of 4 ppb, as detected in the monitoring, would receive 121% of the aPAD. An infant who consumes a single 8 ounce serving of water with the higher detected concentration of 7 ppb, as detected in the monitoring, would receive 210% of the aPAD.

To further characterize carbofuran concentrations in surface water (*e.g.*, streams or rivers) that may drain into drinking water reservoirs, EPA analyzed the extensive source of national water monitoring data for pesticides, the United States Geological Survey National Water Quality Assessment (USGS NAWQA) program. The NAWQA program focuses on ambient water rather than on drinking water sources, is not specifically targeted to the high use area of any specific pesticide, and is sampled at a frequency (generally weekly or bi-weekly during the use season) insufficient to provide reliable estimates of peak pesticide concentrations in surface water. For example, significant fractions of the data may not be relevant to assessing exposure from carbofuran use, as there may be no use in the basin above the monitoring site. Unless ancillary usage data are available to determine the amount and timing of the pesticide applied, it is difficult to determine whether non-detections of carbofuran were due to a low tendency to move to water or from a lack of use in the basin. The program, rather, provides a good understanding on a national level of the occurrence of pesticides in flowing water bodies that can be useful for screening assessments of potential drinking water sources. A detailed description of the pesticide monitoring component of the NAWQA program is available on the NAWQA Pesticide National Synthesis Project (PNSP) web site (http://ca.water.usgs.gov/pnsp/).

A summary of the first cycle of NAWQA monitoring from 1991 to 2001 indicates that carbofuran was the most frequently detected carbamate pesticide in streams and ground water in agricultural areas. Overall, where

carbofuran was detected, these non-targeted monitoring results generally found carbofuran at levels below 0.5 ppb. In the NMC assessment, EPA summarized NAWQA monitoring for carbofuran between 1991 and 2004. Maximum surface-water concentrations exceeded 1 ppb in approximately nine agricultural watershed-based study units, with detections in the sub-ppb range reported in additional watersheds (Ref. 63). The highest concentrations of carbofuran are reported from at a sampling station on Zollner Creek, in Oregon. Zollner Creek, located in the Molalla-Pudding sub-basin of the Willamette River, is not directly used as a drinking water source. This creek is a low-order stream and its watershed is small (approximately 40 km2) and intensively farmed, with a diversity of crops grown, including plant nurseries. USGS monitoring at that location from 1993 to 2006 detected carbofuran annually in 40–100 % of samples. Although the majority of concentrations detected there are also in the sub-part per billion range, concentrations have exceeded 1 ppb in 8 of the 14 years of sampling. The maximum measured concentration was 32.2 ppb, observed in the spring of 2002. The frequency of detections generally over a 14–year period suggests that standard use practices rather than aberrational misuse incidents in the region are responsible for high concentration levels at this location.

While available monitoring from other portions of the country suggests that the circumstances giving rise to high concentrations of carbofuran may be rare, overall, the national monitoring data indicate that EPA cannot dismiss the possibility of detectable carbofuran concentrations in some surface waters under specific use and environmental conditions. Even given the limited utility of the available monitoring data, there have been relatively recent measured concentrations of carbofuran in surface water systems at levels above 4 ppb (concentrations of 4–7 ppb would result in exposures of 121–210% of the aPAD for an infant consuming 8 oz of water) and levels of approximately 1 to 30 ppb measured in streams representative of those in watersheds that support drinking water systems (Ref. 63). Based on this analysis, and since monitoring programs have not been sampling at a frequency sufficient to detect daily-peak concentrations that are needed to assess carbofuran's acute risk, the available monitoring data, in and of themselves, are not sufficient to establish the risks posed by carbofuran in surface drinking water are below thresholds of concern. Nor can this data be reasonably used to establish a lower bound of potential carbofuran risk through this route of exposure.

To further characterize carbofuran risk through drinking water derived from surface water sources, EPA modeled estimated daily drinking water concentrations of carbofuran using PRZM to simulate field runoff processes and EXAMS to simulate receiving water body processes. These models were summarized in Unit V.B.2.

There are sources of uncertainty associated with estimating exposure of carbofuran in surface water source drinking water. Several of the most significant of these are the effect of treatment in removing carbofuran from finished drinking water before it is delivered to the consumer supply system, the impact of percent crop treated assumptions, and the variation in pH across the landscape. The effect of the percent crop treated assumption in the case of carbofuran is discussed in detail in EPA's assessment of additional data submitted by the registrant (Refs. 18 and 54) and summarized below. Available data on the degree to which carbofuran may be removed from treatment systems was summarized previously and is discussed in more detail in Appendix E-3 of the Revised NMC Cumulative Assessment (Ref. 63). Although EPA is aware of the mitigating effects of specific treatment processes, the processes employed at public water supply utilities across the country vary significantly both from location to location and throughout the year, and therefore are difficult to incorporate quantitatively in drinking water exposure estimates. Therefore, EPA assumes that there is no reduction in carbofuran concentrations in surface water source drinking water due to treatment, which is a source of conservatism in surface water exposure estimates used for human health risk assessment. While it is well established that carbofuran will degrade at higher rates when the pH is above 7, and lower rates when below pH 7, due to the high variation of pH across the country a neutral pH (pH 7) default value was used to estimate water concentrations. Finally, available environmental fate studies do not show formation of 3-hydroxycarbofuran through most environmental processes except soil photolysis, where in one study it was detected in very low amounts. Although 3-hydroxycarbofuran was not explicitly considered as a separate entity in the drinking water exposure assessment, it is unclear whether it would significantly add to exposure estimates.

EPA compiled a distribution of estimated carbofuran concentrations in surface water in order to conduct probabilistic assessments of the potential exposures from drinking water. For the IRED, EPA modeled crops representing 80 percent of total carbofuran use at locations that would be considered among the more vulnerable where the crops are grown. Modeling was conducted at a range of application rates and included adjustments to reflect different regional levels for agricultural intensity, resulting in estimated 1-in-10-year (peak) concentrations of 0.11–75 ppb (Refs. 5 and 36). For corn, carbofuran concentration estimates assuming different rates and regional percent cropped area (PCA) factors reflective of corn intensity nationally resulted in a range of peak concentrations of 4 – 26 ppb. For the dietary risk assessment, EPA generated distributions for 13 different scenarios representing all labeled uses of carbofuran treated at maximum label rates and adjusted with PCA factors (Refs. 3, 13 and 47). Peak concentrations for these distributions ranged from 3.2 to 168 ppb (excluding use on bananas), with the corn use at 26 ppb (Refs. 3 and 47).

EPA has subsequently conducted several rounds of modeling to refine estimates for specific uses and agricultural practices. One set of refinements addressed use of carbofuran on corn at typical rather than maximum label rates and application practices that assume the only use of carbofuran in a watershed is on corn. Simulations included those specific to control European corn borer, a rescue treatment for corn rootworm, and an in-furrow application at plant. The assessment also included estimates resulting from treatment at the maximum label rate, for comparative purposes. The peak concentrations estimated ranged from 3.9 to 16.6 ppb for the refined analyses, compared to 32.9 ppb at the maximum application rate (Ref. 4). The range of 3.9 to 16.6 ppb is approximately 1 to 4 times the values of the 4 ppb detected in finished water from a surface water drinking plant, as summarized previously, and approximately twofold to tenfold lower than the maximum peak concentration of 32.2 ppb reported in the USGS-NAWQA data set.

Additional refined modeling assessments were based on a proposed label submitted by FMC in May 2008. The refinements focused on two uses currently allowed on the existing label that would have remained under the withdrawn label: a corn rootworm rescue treatment, evaluated at 7 representative sites, and an at-plant

treatment for melons evaluated at 4 additional sites. EPA developed 5 additional corn scenarios representing use in states with extensive carbofuran usage at locations more vulnerable than most in each state in areas corn is grown. Using measured rainfall values, and assuming typical rather than maximum use rates, these assessments focused on the corn rescue treatment (Ref. 4). Peak concentrations for the corn rescue treatments simulated for Illinois, Iowa, Indiana, Kansas, Minnesota, Nebraska, and Texas ranged from 16.6 – 36.7 ppb. For refinement of estimates for the other use, melons, EPA developed 3 additional melon scenarios representing states with extensive carbofuran usage at locations more vulnerable than most in each state in areas melons are grown. EPA used measured rainfall values and a wide row spacing to simulate an application rate less than half of what is allowed as the maximum rate for melons (0.65 versus 1.94 lb/A). Peak concentrations resulting from a single ground application of carbofuran at plant in Florida, Michigan, Missouri, and New Jersey resulted in peak concentrations from 4.2 – 24.4 ppb (Id.). Additional details on these assessments can be found at Ref. 4. Consistent with the analysis summarized above these predicted carbofuran water concentrations are similar to or lower than the peak concentrations reported in the USGS-NAWQA monitoring data and similar to or not more than tenfold higher than the 4 ppb reported in finished water from a surface water drinking plant.

There are few surface water field-scale studies targeted to carbofuran use that could be compared with modeling results. Most of these studies were conducted in fields that contain tile drains, which is a common practice throughout midwestern states to increase drainage in agricultural fields (Ref. 13). Drains are common in the upper Mississippi river basin (Illinois, Iowa, and the southern part of Minnesota), and the northern part of the Ohio River Basin (Indiana, Ohio, and Michigan) (Ref. 42). Although it is not possible to directly correlate the concentrations found in most of the studies with drinking water concentrations, these studies confirm that carbofuran use under such circumstances can contaminate surface water, as tile drains have been identified as a pathway for contamination of surface water. For example, one study conducted in the United Kingdom in 1991 and 1992 looked at concentrations in tile drains and surface water treated at a rate of 2.7 lbs a.i. per acre (granular formulation). Resulting concentrations in surface water downstream of the field ranged from 49.4 ppb almost two months after treatment to 0.02 ppb 6 months later, and were slightly lower than concentrations measured in the tile drains, which were a transport pathway. Even with the factors that limit the study's relevance to the majority of current carbofuran use—the high use rate and granular formulation—the study clearly confirms that tile drains can serve as a source of significant surface water contamination. Although EPA's models do not account for tile drain pathways, and acknowledging the uncertainties in comparing carbofuran monitoring data to the concentrations predicted from the exposure models, as noted previously, estimated (model-derived) peak concentrations of carbofuran are similar to peak concentrations reported in stream monitoring studies and are no more than tenfold higher than a value reported from a drinking water plant where it is unlikely the sample design would have ensured that water was sampled on the day of the peak concentration.

EPA conducted dietary exposure analyses based on the modeling scenarios for the current label as well as scenarios comparable to the uses on FMC's proposed label of May 2008. Exposures from all modeled scenarios substantially exceeded EPA's level of concern (Ref. 12). For example, an Illinois corn scenario, assuming 2 foliar applications at a typical 1–lb a.i. per acre use rate, estimated a 1-in-10-year peak carbofuran water concentration of 26 ppb. Exposures at the 99.9th percentile based on this modeled distribution ranged from 860% of the aPAD for youths 13–19 to greater than 10,000% of the aPAD for infants. This scenario is intended to be representative of highly vulnerable sites on which corn could be grown on a national basis, and is used as a screen for corn on a national basis. Similarly, exposures based on an Idaho potato scenario, and using a 3 lb a.i. acre rate, ranged from 230% of the aPAD for children 6–12 to 890% of the aPAD for infants, with a1-in-10-year peak carbofuran concentration of 10 ppb. Although other crop scenarios resulted in higher exposures, estimates for these two crops are presented here, as they are major crops on which a large percentage of carbofuran use occurs. More details on these assessments, as well as the assessments EPA conducted for other crop scenarios, can be found in Refs. 4, 12 and 47.

Table 8 below presents the results of one of EPA's refined exposure analyses that addresses a use comparable to one in FMC's proposed May 2008 label. This example is based on a Nebraska corn rootworm ''rescue treatment'' scenario, and assumes a single aerial application at a typical rate of 1 pound a.i. per acre. To simulate an application made post-plant, at or near rootworm hatch, EPA modeled an application of carbofuran 30 days after crop emergence. EPA used a crop specific PCA of 0.46 which is the maximum proportion of corn acreage in a Hydrologic Unit Code 8-sized basin in the United States. (The U.S. Geological Survey has classified all watersheds in the US into basins of various sizes, according to hydrologic unit codes, in which the number of digits indicates the size of the basin). The full distribution of daily concentrations over a 30–year period was used in the probabilistic dietary risk assessment. The 1-in-10-year peak concentration of the distribution of values for the Nebraska corn rescue treatment was 22.3 ppb. More details on these assessments, as well as the assessments EPA conducted for other crop scenarios, can be found in Refs. 4, 12 and 47.

TABLE 8—RESULTS OF ACUTE DIETARY (SURFACE WATER ONLY) EXPOSURE ANALYSIS INCORPORATING THE NEBRASKA CORN ROOTWORM RESCUE SCENARIO

Population Subgroup	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.000444	590	0.001236	1,650	0.002912	3,900
Children 1–2 years old	0.000075	0.000190	250	0.000517	690	0.001267	1,700
Children 3–5 years old	0.000075	0.000177	240	0.000473	630	0.001144	1,500

TABLE 8—RESULTS OF ACUTE DIETARY (SURFACE WATER ONLY) EXPOSURE ANALYSIS INCORPORATING THE NEBRASKA CORN ROOTWORM RESCUE SCENARIO—Continued

Population Subgroup	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Children 6–12 years old	0.000075	0.000122	160	0.000329	440	0.000801	1,100
Youth 13–19 years old	0.0002	0.000091	45	0.000255	130	0.000671	340
Adults 20–49 years old	0.0002	0.000118	60	0.000313	160	0.000766	380
Adults 50+ years old	0.0002	0.000125	60	0.000307	150	0.000671	340

The populations described in the ''Nebraska corn'' assessments are those people who consume water from a reservoir located in a small watershed predominated by corn production (with the assumption that treatment does not reduce carbofuran concentrations). The only crop treated by carbofuran in the watershed is corn, and all of that crop is assumed treated with carbofuran at the rate of 1 lb per acre. To the extent a drinking water plant drawing water from the reservoir normally treats the raw intake water with lime softening or activated carbon processes the finished water concentrations could be reduced from 60 to 100% with the resultant aPADs ranging from approximately 460 to 102% of the aPAD to 0% of the aPAD, respectively, at the 99.9th percentile of exposure.

As discussed in the previous sections, it is important to remember that carbofuran's aPAD is quite low, hence relatively low concentrations of carbofuran monitored or estimated in surface water can have a significant impact on the percent of the aPAD utilized. Thus, while the refined carbofuran water concentrations for the corn ''rescue'' treatment in the range of approximately 16.6 to 36.7 ppb are comparable to maximum peak concentrations reported in the monitoring studies, these concentrations can result in very significant exceedences of the aPAD for various age groups, primarily because carbofuran is inherently very toxic.

FMC has criticized EPA's assessment for failing to account more fully for the percent of the crop treated (PCT) in its modeling. Uncertainty associated with PCT assumptions can be a major factor in EPA's drinking water exposure assessment for surface-water sources. Estimates of the percent of major crops (for example, corn) that are treated with pesticides are available at the state level, but are generally not available on a smaller scale suitable for estimating drinking water exposure in a watershed. In addition, the PCT should be assessed at a watershed-scale, aggregating all crops treated with the pesticide in a watershed. If state-scale estimates are used to account for PCT it will underestimate the risk for some of the drinking water facilities in the state as the state-wide estimate represents an average: values for individual facilities will be both lower and higher than the state-wide estimate. In some cases, the underestimate can be substantial if the application pattern tends to form cluster or pockets of high usage. Insecticides like carbofuran are particularly prone to this use pattern, as insect outbreaks often tend to be locally intense, rather than widespread. In addition, marginal use practice changes in a given watershed can substantially affect the percentage of the crop treated, and such changes are effectively impossible to track. Without data collected at a finer spatial scale, it is not possible to know whether pesticide usage is evenly dispersed through the state or is locally clustered. This results in large uncertainty in the drinking water exposure assessments when percent crop treated is moderate or low. Consequently, EPA does not typically include such information in its surface-water exposure assessments.

However, in response to FMC's concerns, EPA performed a sensitivity analysis of an exposure assessment using a PCT in the watershed to determine the extent to which some consideration of this factor could meaningfully affect the outcome of the risk assessment. The registrant has at different times, suggested the application of a 5 or 10% crop treated based on county sales data. While substantial questions remain as to the support for these percentages for a given basin where carbofuran may be used, EPA used the upper figure for the purpose of conducting a sensitivity analysis. The results suggest that, even at levels below 10% crop treated, exposures from drinking water derived from surface waters can contribute significantly to the aggregate dietary risks, particularly for infants and children. For example, applying a 10% crop treated figure to the Nebraska corn scenario described above, in addition to the corn-PCA of 0.46 incorporated into that scenario, results in estimated exposures from water alone, ranging from 110% of the aPAD for children 6–12 to 390% of the aPAD for infants, assuming water treatment processes do not affect concentrations in drinking water consumed. Details on the assessments EPA conducted for other crop scenarios, which showed higher contributions from drinking water, can be found in Refs. 12, 13 and 47. Accordingly, these assessments suggest that EPA's use of PCA alone, rather than in conjunction with PCT, will not meaningfully affect the carbofuran risk assessment, as aggregate exposures would still exceed 100% of the aPAD.

In conclusion, the large difference between concentrations seen in the monitoring data on the low side, and the simulation modeling on the high side, is an indication of the uncertainty in the assessment for surface-water source drinking water exposure. The majority of drinking water concentrations resulting from use of carbofuran are likely to be occurring at higher concentrations than those measured in most monitoring studies, but below those estimated with simulation modeling; however the exact values are highly uncertain. However, the monitoring data show a consistent pattern of low concentrations, with the occasional, infrequent spike of high concentrations. Those infrequent high concentrations are consistent with EPA's modeling, which is intended to capture the exposure peaks. For a chemical with an acute risk, like carbofuran, the spikes or peaks in exposures, even though infrequent, are the most relevant for assessing the risks. And, as previously noted, the available monitoring has its own limitations for estimating exposure for risk assessment.

Further, the results of the modeling analyses provide critical insights

regarding locations in the country where the potential for carbofuran contamination to surface water and associated drinking water sources are more likely. These locations include areas with soils prone to runoff (such as those high in clay or containing restrictive layers), in regions with intensive agriculture with crops on which carbofuran is used (*e.g.* corn), which have high rainfall amounts and/or are subject to intense storm events in the spring around the times applications are being made. Drinking water facilities with small basins tend to be more vulnerable, as it is more likely that a large proportion of the crop acreage will be treated in small basins.

Apparently FMC also has determined that some drinking water facilities associated with surface source waters are vulnerable to carbofuran exposure. In the now withdrawn labels FMC proposed to require buffer zones around surface waters in certain locations of the country, presumably to protect surface water. The proposed buffers were for fields where soils were considered to be highly erodible. Buffers were to be 66 feet wide and were to be vegetated with ''crop, seeded with grass, or other suitable crop''. In 2000, EPA participated in the development of a guidance document on how to reduce pesticide runoff using conservation buffers (Ref. 55). Results of this effort found that properly designed buffers can reduce runoff of weakly absorbed pesticides like carbofuran by increasing filtration so that the pesticide can be trapped and degraded in the buffer. However, it is of critical importance that sheet flow be maintained across the buffer in order for this to occur. To ensure sheet flow, buffers need to be specifically designed for that purpose and they must be well-maintained, as over time sediment trapped in the buffer causes flow to become more channelized and the buffer then becomes ineffective. The guidance concludes that un-maintained, un-vegetated buffers around water bodies, often referred to a 'setback,' are ineffective in reducing pesticide movement to surface water.

3. *Aggregate dietary exposures (food and drinking water).* EPA conducted a number of probabilistic analyses to combine the national food exposures with the exposures from the individual region and crop-specific drinking water scenarios. Although food is distributed nationally, and residue values are therefore not expected to vary substantially throughout the country, drinking water is locally derived and concentrations of pesticides in source water fluctuate over time and location for a variety of reasons. Pesticide residues in water fluctuate daily, seasonally, and yearly as a result of the timing of the pesticide application, the vulnerability of the water supply to pesticide loading through runoff, spray drift and/or leaching, and changes in the weather. Concentrations are also affected by the method of application, the location and characteristics of the sites where a pesticide is used, the climate, and the type and degree of pest pressure. Consequently, EPA conducted several estimates of aggregate dietary risks by combining exposures from food and drinking water. All of these estimates showed that aggregate exposures to carbofuran residues are unsafe. More details on the individual aggregate assessments presented below, as well as the assessments EPA conducted for other regional and crop scenarios, can be found in Refs. 12 and 13.

Table 9 below reflects the results of aggregate exposures from food and from drinking water derived from ground water in vulnerable areas (*i.e.*, from shallow wells associated with sandy soils and acidic aquifers, such as are found in the Delmarva Peninsula). The estimates range between 1,100% of the aPAD for adults, to over 10,000% of the aPAD for infants.

TABLE 9—RESULTS OF ACUTE DIETARY (FOOD AND WATER) EXPOSURE ANALYSIS INCORPORATING THE DELMARVA GROUND WATER SCENARIO

Population Subgroup	APAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.003799	5,100	0.006026	8,000	0.010011	>10,000
Children 1–2 years old	0.000075	0.001622	2,200	0.002740	3,700	0.004644	6,200
Children 3–5 years old	0.000075	0.001465	2,000	0.002414	3,200	0.004273	5,700
Children 6–12 years old	0.000075	0.001026	1,400	0.001715	2,300	0.002825	3,800
Youth 13–19 years old	0.0002	0.000813	410	0.001442	720	0.002921	1,500
Adults 20–49 years old	0.0002	0.000958	480	0.001638	820	0.003091	1,500
Adults 50+ years old	0.0002	0.000888	440	0.001351	680	0.002278	1,100

The peak concentration estimates in the Delmarva groundwater scenario time series are consistent with monitoring data from wells in vulnerable areas where carbofuran was used. For example, the maximum water concentration from the time series is 38.5 ppb while maximum values from a targeted ground water monitoring study at the same site was 65 ppb, with studies at other sites having similar or higher peak concentrations (Refs. 13 and 47). For studies with multiple measurements at each well, central tendency estimates were also in the same range as the time series. For example, the mean carbofuran concentration from wells under no-till agriculture in Queenstown, MD was 7 ppb, while the median for the modeling was 15.5 ppb. The 90–day average concentration, based on the registrant's PGW study conducted on corn in the Delmarva (adjusted for current maximum application rates) is 22 ppb.

Table 10 below presents the results of aggregate exposure from food and derived from surface water using the Nebraska corn surface water scenario. This table reflects the risks only for those people in drinking watersheds with characteristics similar to that used in the scenario, and assuming that water treatment does not remove carbofuran.

As discussed previously, the estimated water concentrations are comparable to the maximum peak concentrations reported in monitoring studies that were not designed to detect peak, daily concentrations of carbofuran in vulnerable locations.

TABLE 10—RESULTS OF ACUTE DIETARY (FOOD AND WATER) EXPOSURE ANALYSIS USING THE NEBRASKA CORN SURFACE WATER SCENARIO

Population Subgroup	aPAD (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
All Infants (< 1 year old)	0.000075	0.000448	600	0.001240	1,700	0.002899	3,900
Children 1–2 years old	0.000075	0.000200	270	0.000533	710	0.001326	1,800
Children 3–5 years old	0.000075	0.000187	250	0.000486	650	0.001190	1,600
Children 6–12 years old	0.000075	0.000128	170	0.000336	450	0.000824	1,100
Youth 13–19 years old	0.0002	0.000095	48	0.000264	130	0.000685	340
Adults 20–49 years old	0.0002	0.000122	61	0.000318	160	0.000785	390
Adults 50+ years old	0.0002	0.000129	65	0.000312	160	0.000689	340

Typically, EPA's food and water exposure assessments sum exposures over a 24–hour period, and EPA used this 24–hour total in developing its acute dietary risk assessment for carbofuran. Because of the rapid nature of carbofuran toxicity and recovery, EPA considered that it might be appropriate to consider durations of exposure less than 24 hours. EPA has developed an analysis using information about external exposure, timing of exposure within a day, and half-life of AChE inhibition from rats to estimate risk to carbofuran at durations less than 24 hours. Specifically, EPA has evaluated individual eating and drinking occasions and used the AChE half-life information to estimate the residual effects from carbofuran from previous exposures within the day. The carbofuran analyses are described in the July 2008 aggregate (dietary) memo (Ref. 12).

EPA has used two approaches for considering the impact of rapid reversibility on exposure estimates in the food and drinking water risk assessments. EPA previously used these approaches in the cumulative risk assessment of the NMC pesticides and/or risk assessments for other NMC pesticides (*e.g.*, methomyl and aldicarb) (Ref. 63).

Incorporating eating occasion analysis and either the 150 minute or 300 minute recovery half life for carbofuran into the food only analysis does not significantly change the risk estimates when compared to baseline levels (for which a total daily consumption basis – and not eating occasion - was used). From this, it is apparent that modifying the analysis such that information on eating (*i.e.* food) occasions and carbofuran half life is incorporated results in only minor reductions in estimated risk.

The food analysis showed that over 70% of exposures at the top 0.2 percentile for children ages 1–2 and 3–5 are from a single eating event of carbofuran indicating that carbofuran's food risk is not substantively overstated. Moreover, when incorporating half-life to recovery information, risks from summing exposures over 24 hours are similar to those when incorporating half-life to recovery of 150 or 300 minutes. Regarding drinking water exposure, accounting for drinking water consumption throughout the day and using the half-life to recovery information, risk is reduced by approximately 2–3X.

Consequently, risk estimates for which food and drinking water are jointly considered and incorporated (i.e, Food + Drinking Water) are reduced considerably—by a factor of two or more in some cases—compared to baseline. This is not unexpected, as infants receive much of their exposures from indirect drinking water in the form of water used to prepare infant formula. But even though the risk estimates from aggregate exposure are reduced, they nonetheless still substantially exceed EPA's level of concern for infants and children. Using drinking water derived from the surface water from the New Jersey melon scenario, which estimated one of the lower exposure distributions, aggregate exposures ranged from a low of 280% of the aPAD for infants, based on a 150–minute half-life, to a high of 370% of the aPAD for infants, based on a 300–minute half-life.

The two approaches discussed above are used to evaluate the extent to which the Agency's 24–hour approach to dietary risk assessment overestimates risk from carbofuran exposure. The results of both approaches indicate that the risk to carbofuran is indeed not substantively overestimated using the current exposure models and the 24–hour approach. This is due to the fact that exposure to carbofuran occurs predominantly through single eating events and not from multiple events that occur throughout the day. Based on these analyses, the Agency concludes that the current exposure assessment methods used in the carbofuran dietary assessment provide realistic and high confidence estimates of risk to carbofuran exposure through food.

The result of all of these analyses clearly demonstrate that aggregate exposure from all uses of carbofuran fail to meet the FFDCA section 408 safety standard, and revocation of the associated tolerances is warranted. Based on the contribution from food alone, dietary exposures to carbofuran exceed EPA's level of concern for all of the more sensitive subpopulations of infants and children. In addition, EPA's analyses show that those individuals–both adults as well as children—who receive their drinking water from vulnerable sources are also exposed to levels that exceed EPA's level of concern—in some cases by orders of magnitude. This primarily includes those populations consuming drinking water from groundwater from shallow wells in acidic aquifers overlaid with sandy soils that have had crops treated with carbofuran. It could also include those populations that obtain their

drinking water from reservoirs located in small agricultural watersheds, prone to runoff, and predominated by crops that are treated with carbofuran, although there is substantially more uncertainty associated with these exposure estimates. Every sensitivity analysis EPA has performed has shown that estimated exposures significantly exceed EPA's level of concern for children. Although the magnitude of the exceedance varies depending the level of conservatism in the assessment, the fact that in each case, aggregate exposures from dietary exposures of carbofuran fail to meet the FFDCA section 408 safety standard strongly corroborates EPA's conclusion that aggregate exposures from all uses of carbofuran are not safe.

VII. When Do These Actions Become Effective?

The Agency is proposing that the revocations of the tolerances for all commodities except artichoke and sunflower seed become effective 60 days after a final rule is published. EPA is also proposing to establish an extended effective date for artichokes and sunflower seed, to allow growers of these crops additional time to transition to alternative compounds. The revocation for these two tolerances will become effective two years after a final rule or order is published. The Agency believes that these revocation dates will allow users to exhaust stocks of carbofuran currently in their possession. However, if EPA is presented with information during the comment period on this proposal that end-users may need additional time to utilize carbofuran stocks currently in their possession, and that information is verified, the Agency will consider extending the expiration date of the tolerance. If you have comments regarding the effective date, or if you have comments on how long it would take you to utilize the carbofuran stocks currently in your possession, please submit comments as described under **SUPPLEMENTARY INFORMATION.**

Any commodities listed in this proposal treated with the pesticide subject to this proposal, and in the channels of trade following the tolerance revocations, shall be subject to FFDCA section 408(1)(5), as established by FQPA. Under this section, any residues of these pesticides in or on such food shall not render the food adulterated so long as it is shown to the satisfaction of the Food and Drug Administration that:

1. The residue is present as the result of an application or use of the pesticide at a time and in a manner that was lawful under FIFRA, and

2. The residue does not exceed the level that was authorized at the time of the application or use to be present on the food under a tolerance or exemption from tolerance. Evidence to show that food was lawfully treated may include records that verify the dates when the pesticide was applied to such food.

VIII. Are the Proposed Actions Consistent with International Obligations?

The tolerance revocations in this proposal are not discriminatory and are designed to ensure that both domestically-produced and imported foods meet the food safety standard established by the FFDCA. The same food safety standards apply to domestically produced and imported foods.

EPA is working to ensure that the U.S. tolerance reassessment program under FQPA does not disrupt international trade. EPA considers Codex Maximum Residue Limits (MRLs) in setting U.S. tolerances and in reassessing them. MRLs are established by the Codex Committee on Pesticide Residues, a committee within the Codex Alimentarius Commission, an international organization formed to promote the coordination of international food standards. It is EPA's policy to harmonize U.S. tolerances with Codex MRLs to the extent possible, provided that the MRLs achieve the level of protection required under FFDCA. EPA's effort to harmonize with Codex MRLs is summarized in the tolerance reassessment section of individual Reregistration Eligibility Decision documents. EPA has developed guidance concerning submissions for import tolerance support (65 FR 35069, June 1, 2000) (FRL–6559–3). This guidance will be made available to interested persons. Electronic copies are available on the internet at *http://www.epa.gov/*. On the Home Page select ''Laws, Regulations, and Dockets,'' then select Regulations and Proposed Rules and then look up the entry for this document under ''**Federal Register**—Environmental Documents.'' You can also go directly to the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/*.

IX. Statutory and Executive Order Reviews

In this proposed rule, EPA is proposing to revoke specific tolerances established under FFDCA section 408. The Office of Management and Budget (OMB) has exempted this type of action (*e.g.*, tolerance revocation for which extraordinary circumstances do not exist) from review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993). Because this proposed rule has been exempted from review under Executive Order 12866 due to its lack of significance, this proposed rule is not subject to Executive Order 13211, *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001). This proposed rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, or impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104–4). Nor does it require any special considerations as required by Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994); or OMB review or any other Agency action under Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note). In addition, the Agency has determined that this action will not have a substantial direct effect on States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government, as specified in Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999). Executive Order 13132 requires EPA to develop an accountable process to ensure ''meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications.'' ''Policies that have federalism implications'' is defined in the Executive order to include regulations that have ''substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.'' This proposed rule directly regulates growers, food processors, food handlers and food retailers, not States. This

action does not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of the FFDCA. For these same reasons, the Agency has determined that this proposed rule does not have any ''tribal implications'' as described in Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 6, 2000). Executive Order 13175, requires EPA to develop an accountable process to ensure ''meaningful and timely input by tribal officials in the development of regulatory policies that have tribal implications.'' ''Policies that have tribal implications'' is defined in the Executive order to include regulations that have ''substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and the Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.'' This proposed rule will not have substantial direct effects on tribal governments, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes, as specified in Executive Order 13175. Thus, Executive Order 13175 does not apply to this proposed rule.

The Regulatory Flexibility Act (RFA) of 1980, as amended by the Small Business Regulatory Enforcement Fairness Act of 1996 (SBREFA), 5 USC 601 et.seq, generally requires an agency to prepare a regulatory flexibility analysis of any rule subject to notice and comment rulemaking requirements under the Administrative Procedures Act or any other statute. This is required unless the agency certifies that the rule will not have a significant economic impact on a substantial number of small entities. Small entities include small businesses, small organizations, and small governmental jurisdictions. The Agency has determined that no small organizations or small governmental jurisdictions are impacted by today's rulemaking.

For purposes of assessing the impacts of today's determination on businesses, a small business is defined either by the number of employees or by the annual dollar amount of sales/revenues. The level at which an entity is considered small is determined for each North American Industry Classification System (NAICS) code by the Small Business Administration (SBA). Farms are classified under NAICS code 111, Crop Production, and the SBA defines small entities as farms with total annual sales of $750,000 or less.

The Agency has examined the potential effects today's proposed rule may have on potentially impacted small businesses. Based on this analysis, EPA concludes that the Agency can certify that revoking the food tolerances for carbofuran will not have a significant economic impact on a substantial number of small entities (No SISNOSE) for alfalfa, artichoke, banana, chili pepper, coffee, cotton, cucurbits (cucumber, melons, pumpkin, and squash), grape, grains (barley, flax, oats, and wheat), field corn, potato, soybean, sorghum, sugarbeet, sugarcane, sunflower, and sweet corn. Even in a worst-case scenario, in which a grower obtains income only from a single crop and his/her entire acreage is affected, the impact generally amounts to less than 2% of gross income and would be felt by fewer than 3% of affected small producers. Estimates of impacts to corn growers were refined to account for the sporadic nature of need for carbofuran while still maintaining some assumptions that would bias the estimates upward. Refined estimates were also made for artichoke and sunflower, which consider the diversity in growers' revenue. The largest impact may be felt by artichoke growers, with impacts as high as 5% of gross revenue, but fewer than five growers are likely to be affected. EPA could not quantify the impacts to banana, sugarcane, and sweet corn producers, but the number of impacted farms is less than 2% of the farms subject to the action. Additional detail on the analyses EPA conducted in support of this certification can be found in Ref. 49.

X. References

EPA has established an official record for this rulemaking. The official record includes all information considered by EPA in developing this proposed rule including documents specifically referenced in this action and listed below, any public comments received during an applicable comment period, and any other information related to this action, including any information claimed as CBI. This official record includes all information physically CAlocated in docket ID number EPA–HQ–OPP–2005–0162, as well as any documents that are referenced in the documents listed below or in the docket. The public version of the official record does not include any information claimed as CBI.

1. Acute oral (gavage) dose range-finding study of cholinesterase depression from carbofuran technical in juvenile (day 11) rats. Hoberman, 2007. MRID 47143703 (unpublished FMC study) EPA–HQ–OPP–2007–1088–0062.

2. Acute oral (gavage) time course study of cholinesterase depression from carbofuran technical in adult and juvenile (day 11 postpartum) rats. Hoberman, 2007. MRID 47143704 (unpublished FMC study) EPA–HQ–OPP–2007–1088–0063.

3. Additional chemographs for potatoes and cucurbits for drinking water exposure assessment in support of the reregistration of carbofuran (PC Code 090601) (R. David Jones, 10/23/07 D345729). EPA–HQ–OPP–2005–0162–0486.

4. Additional refinements of the drinking water exposure assessment for the use of carbofuran on corn and melons (PC code 090601)(R. David Jones, 06/2008 D353714).

5. An In-Depth Investigation to Estimate Surface Water Concentrations of Carbofuran within Indiana Community Water Supplies. Performed by Waterborne Environmental, Inc., Leesburg, VA, Engel Consulting, and Fawcett Consulting. Submitted by FMC. Corporation, Philadelphia, PA. WEI No 528.01, FMC Report No. PC–0378. MRID 47221603. EPA–HQ–OPP–2007–1088–0023.

6. An Investigation into the Potential for Carbofuran Leaching to Ground Water Based on Historical and Current Use Practices. Submitted by FMC. Corporation, Philadelphia, PA. Report No. PC–0363. MRID 47221602. EPA–HQ–OPP–2007–1088–0022.

7. An Investigation into the Potential for Carbofuran Leaching to Ground Water Based on Historical and Current Use Practices: Supplemental Report on Twenty-one Additional States. Submitted by FMC Corporation, Philadelphia, PA. Report No. PC–0383. MRID 47244901. EPA–HQ–OPP–2007–1088-0025.

8. Benchmark dose analysis of cholinesterase inhibition data in neonatal and adult rats (MRID no. 46688914) following exposure to carbofuran (A.Lowit, 1/19/06, D325342, TXR no. 0054034). EPA–HQ–OPP–2007–1088–0045.

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11. California Department of Pesticide Regulation. Risk Characterization Document for Carbofuran. January 23, 2006. 219 pgs.

12. Carbofuran Acute Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the Reregistration Eligibility Decision (T. Morton, 7/22/08, D351371).

13. Carbofuran Environmental Risk Assessment and Human Drinking Water Exposure Assessment for IRED. March 2006. EPA–HQ–OPP–2005–0162–0080.

14. Carringer, 2000. Carbamate Market Basket Survey. Reviewed by S. Piper, D267539, 8/8/02. (MRID 45164701 S. Carringer, 5/12/00).

15. Carbofuran. HED Revised Risk Assessment for the Reregistration Eligibility Decision (RED) Document (Phase 6). (PC 090601) D 330541, July 26, 2006. EPA–HQ–OPP–2005–0162–0307.

16. Carbofuran. HED Revised Risk Assessment for the Notice of Intent to Cancel. (PC 090601) D 347038, January 2007. EPA–HQ–OPP–2007–1088–0034.

17. Cholinesterase depression in juvenile (day 11) and adult rats following acute oral (gavage) dose of carbofuran technical. Hoberman, 2007. MRID 47143705 (unpublished FMC study). EPA–HQ–OPP–2007–1088–0066.

18. Context Document for Carbofuran Risk Assessment Issues not Specifically Addressed in the FIFRA SAP Charge Questions (M. Panger, C. Salice, R. David Jones, E. Odenkirchen, I. Sunzenauer, 1/08 D348292). EPA–HQ–OPP–2007–1088–0071.

19. Data Evaluation Record for Acute dose-response study of carbofuran technical administered by gavage to adult and postnatal day 11 male and female CD®(Sprague-Dawley) rats. MRID 46688914. EPA–HQ–OPP–2007–1088–0045.

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21. Dose-time response modeling of rat brain AChE activity: carbofuran gavage dosing 10/5/07 (Carbofuran-RatBrainDR.pdf) EPA–HQ–OPP–2007–1088–0053.

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List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: July 23, 2008.

Debra Edwards,

Director, Office of Pesticide Programs.

Therefore, it is proposed that 40 CFR chapter I be amended as follows:

PART 180—[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. Section 180.254 is amended by revising the table in paragraph (a) and the table in paragraph (c), and by removing paragraph (d) to read as follows.

§ 180.254 Carbofuran; tolerances for residues.

(a) * * *

Commodity	Parts per million	Expiration/ Revocation Date
Sunflower, seed (of which no more than 0.2 ppm is carbamate)	1.0	10/31/10

* * * * *

(c) * * *

Commodity	Parts per million	Expiration/ Revocation Date
Artichoke, globe (of which no more than 0.2 ppm is carbamate)	0.4	10/31/10

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