



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**MEMORANDUM**

Date: 22 December 2004

Subject: Agency response to comments for the Proposed Section 3 Use of **Chlorfenapyr** on Food Handling Establishment.

Petition No.: 3F6560  
DP Barcode: D309567  
Decision No: 341951  
PC Code: 129093 Chlorfenapyr

Reviewer: John Redden, ARIA Team Leader *JCR*  
Alternative Risk Integration Assessment (ARIA) Team  
Technical Review Branch  
Registration Division (7505C)

Through: Prakashchandra Shah, Ph.D., Acting Senior Scientist  
Registration Action Branch 1 (RAB1)  
HED (7509C)

To: Ann Sibold  
Insecticide Branch/Registration Division (7505C)

*W. Brown*  
*for*

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**ACTION REQUESTED**

Comments were received on the pesticide petition notice of filing (NOF) published on July 16, 2003 (see 68 FR 42022-42026) to establish a tolerance for residues of chlorfenapyr on all food items in food handling establishments where food products are held, processed, and/or prepared.

On March, 3, 2004, the Alternative Risk Integration and Assessment Team (ARIA), RD met with HED scientists and HIARC members to consider the public comments and the registrant response to the chlorfenapyr NOF. A second meeting was held on October 21, 2004 to further consider the comments. On November 30, 2004 ARIA met again with HED to discuss the

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comments.

## **I. Comments Received On Notice of Filing**

Three public comments (OPP-2003-0205-0001, -0002, and -0003) were received in response to the notice of filing for a tolerance petition (PP 3F6560) for chlorfenapyr on all food items in a food handling establishment where food products are held, processed and/or prepared, published on July 16, 2003. Commentors included the Green Party, MI; the Fluoride Action Network Pesticide Project, and the chlorfenapyr registrant, BASF.

### **Source: OPP-2003-0205-0001, Green Party, MI**

Comment Summary: "Tolerances should be established for all synthetic pesticides - although I feel there is no safe level- not when you combine all the chemicals being used in our food. Best to ban."

Agency Response: The Agency acknowledges this comment and notes Section 408(b)(2)(A)(i) of the FFDCA allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is "safe." Section 408(b)(2)(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 in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of the FFDCA requires EPA to give special consideration to exposure to infants and children to the pesticide chemical residue in establishing a tolerance to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue..."

### **Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

#### Comment Summary:

- 1.5 Is chlorfenapyr a chemical that induces prion diseases? If not, could the US EPA please explain why.
- 2.0 More studies on chlorfenapyr need to be done.
- 2.1 Is the spongiform encephalopathy induced by chlorfenapyr transmissible?
- 2.2 Why would chlorfenapyr-induced spongiform encephalopathy not be transmissible to

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mice or other species, or to other generations of mice from parents analyzed with chlorfenapyr-induced spongiform encephalopathy.

Agency Response to Comments Nos. 1.5, 2.0, 2.1, and 2.2

The Agency has required BASF to conduct a Developmental Neurotoxicity Study (DNT). At this time the Agency is not requiring any additional studies other than the DNT.

Current scientific knowledge does not suggest that pesticides such as chlorfenapyr are a causative agent in prion disease. Prion disease is a synonym for Transmissible Spongiform Encephalopathies. Well-known prion diseases include scrapie, bovine spongiform encephalopathy (mad cow disease or BSE) and Creutzfeldt-Jakob disease (CJD). Less well known prion diseases include: transmissible mink encephalopathy, chronic wasting disease, feline spongiform encephalopathy, exotic ungulate encephalopathy, German-Straussler-Scheinker syndrome (GSS) and fatal familial insomnia.

Chlorfenapyr has induced brain effects in animal studies. These effects include spongiform myelopathy in the brain and spinal cord of male rats and spongiform encephalopathy in male and female mice. However, the effects observed in these studies differ significantly from Transmissible Spongiform Encephalopathies (TSEs) and there is no reason to suspect that effects caused by exposure to a chemical are in any way transmissible as are infectious diseases such as TSEs.

According to the *National Institute of Neurological Disorders and Stroke National Institutes of Health* (Bethesda, MD 20892):

“Transmissible spongiform encephalopathies (TSEs), also known as prion diseases, are a group of rare degenerative brain disorders characterized by tiny holes that give the brain a "spongy" appearance. These holes can be seen when brain tissue is viewed under a microscope.

“Creutzfeldt-Jakob disease (CJD) is the most well-known of the human TSEs. It is a rare type of dementia that affects about one in every one million people each year. Other human TSEs include kuru, fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker disease (GSS). Kuru was identified in people of an isolated tribe in Papua New Guinea and has now almost disappeared. FFI and GSS are extremely rare hereditary diseases, found in just a few families around the world. A new type of CJD, called variant CJD (vCJD), was first described in 1996 and has been found in Great Britain and several other European countries. The initial symptoms of vCJD are different from those of classic CJD and the disorder typically occurs in younger patients. Research suggests that vCJD may have resulted from human consumption of beef from cattle with a TSE disease called bovine spongiform encephalopathy (BSE), also known as "mad cow disease."

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Other TSEs found in animals include scrapie, which affects sheep and goats; chronic wasting disease, which affects elk and deer; and transmissible mink encephalopathy. In a few rare cases, TSEs have occurred in other mammals such as zoo animals. These cases are probably caused by contaminated feed. CJD and other TSEs also can be transmitted experimentally to mice and other animals in the laboratory.

“Research suggests that TSEs are caused by an abnormal version of a protein called a prion (prion is short for proteinaceous infectious particle). Prion proteins occur in both a normal form, which is a harmless protein found in the body's cells, and in an infectious form, which causes disease. The harmless and infectious forms of the prion protein are nearly identical, but the infectious form takes on a different folded shape from the normal protein.

“Human TSEs can occur three ways: sporadically; as hereditary diseases; or through transmission from infected individuals.

“Sporadic TSEs may develop because some of a person's normal prions spontaneously change into the infectious form of the protein and then alter the prions in other cells in a chain reaction. Inherited cases arise from a change, or mutation, in the prion protein gene that causes the prions to be shaped in an abnormal way. This genetic change may be transmitted to an individual's offspring. Transmission of TSEs from infected individuals is relatively rare. TSEs cannot be transmitted through the air or through touching or most other forms of casual contact. However, they may be transmitted through contact with infected tissue, body fluids, or contaminated medical instruments. Normal sterilization procedures such as boiling or irradiating materials do not prevent transmission of TSEs.”

As the information quoted above explains, prions affect animals by entering brain cells and converting the normal cell protein PrPC to the prion form of the protein, called PrPSC. When normal cell proteins transform into prions, amino acids that are folded tightly into alpha helical structures relax into looser beta sheets. More and more PrPC molecules transform into PrPSC molecules, until eventually prions completely clog the infected brain cells.

Although chlorfenapyr has induced brain effects in animal studies, those effects differ significantly from those caused by TSEs. There is no reason to suspect that effects created by exposure to a chemical are in any way transmissible as are infectious diseases such as TSEs. The spongiform encephalopathy caused by chlorfenapyr is not as the encephalopathy in TSEs. TSEs cause severe and fatal neurological signs and symptoms. TSEs are characterized by bilaterally symmetrical, non-inflammatory vacuolization of neural perikarya and gray matter neurophil. TSE are a slowly progressive, degenerative, inevitably fatal disease, possibly transmitted by prions.

In contrast, sub chronic and chronic dietary administration of chlorfenapyr to rodents induces translucent vacuoles, which probably represents edema accumulation, in the CNS white matter of

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the brain, spinal cord and/or spinal nerve roots. There was no evidence of neuronal (axonal) degeneration in the brain and the vascular myelinopathy observed in these studies has not been associated with any clinical behavioral effects in rats or mice. Further, these vacuolization effects are completely reversible (the chronic RfD is based on vacuolization).

Finally, HED has no basis for concluding those effects caused by exposure to a chemical can somehow create an infectious agent that is transmissible to other animals. In fact, there is nothing in the Agency's toxicology database or available in the open literature to support a correlation between TSEs and the chemically induced spongiform encephalopathy observed in the laboratory studies with chlorfenapyr. In this regard, the Agency contacted Mary Dunkle (Vice President of Communications National Organization for Rare Disorders 55 Kenosia Avenue PO Box 1968 Danbury, CT 06813-1968) and received the following response:

“...In response to your question about prion diseases: We are not aware of anything that's been published suggesting that these diseases are related to chemical/pesticide exposure.”

Accordingly there is no evidence, in the scientific literature, to suggest that chlorfenapyr or any other chemical induces prion diseases.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

2.3, 2.4, and 2.5. The formula for chlorfenapyr should be altered by removing the bromine. Then government scientists should repeat the sub chronic oral toxicity study in mice with the reformulated pesticide to determine if spongiform encephalopathy is induced. Further, this same procedure should be followed after reformulating chlorfenapyr without the fluorine. Such an experiment may lead to an understanding of the effects of fluorine and bromine on the brain. It may also resolve the question of what is inducing the observed spongiform encephalopathy.

**Agency Response to Comments Nos. 2.3, 2.4, and 2.5**

Under section 408 of the FFDCA, EPA is required to review and determine the safety of pesticide tolerances that are presented to EPA by petition. If EPA finds that the pesticide tolerance is safe, EPA establishes the pesticide tolerance. Once EPA has concluded that exposure to the pesticide under the tolerance is safe, EPA is under no obligation to evaluate the toxicological mechanism that produced the toxic effects contained in the available data. Although investigating toxicological mechanisms advance scientific knowledge, once EPA has found the exposures permitted by a given tolerance to be safe, further understanding of the mechanism by which the pesticide causes toxic effects – at higher exposures – will not change the underlying safety finding. If EPA concludes that the tolerance is not safe, it denies the petition. EPA's scientific analysis of why exposure to the pesticide is not safe may lead the

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petitioner to reformulate the pesticide and do further testing but that is up to the petitioner and not EPA.

EPA can provide the following information to FAN relevant to the role of fluorine and bromine in the chlorfenapyr toxicological studies. The nature of the residue in plants is adequately understood based on acceptable metabolism studies conducted on cotton, citrus, lettuce, potato and tomato. Metabolism of chlorfenapyr proceeds via: 1) N-dealkylation of the parent compound and 2) oxidation of the dealkylated metabolite. The release of bromine from chlorfenapyr during plant and animal metabolism does occur (minor pathways in plants, major pathways in liver). Fluoride does not dissociate in animals or plants to form free ions.

The Agency, however, believes that bromine compounds would have much less chronic toxicity than the fluoride compounds (10/26/2004 e: mail response: George Kramer, Chemist and PV Shah, Ph.D. Toxicologist).

As noted in the Reregistration Eligibility Document (RED) for Potassium Bromide (April 1991). The human toxicology profile for bromine is well understood and minimal. KBr (potassium bromide) dissolves in water and dissociates into potassium and bromide ions. Bromide ion is present in small amounts, and is not known to concentrate, in man and all other organisms; and has no detectable effect at concentrations that might be associated with pesticide exposure. Moreover, the use of bromide salts as tranquilizers has demonstrated the low and reversible toxicity of the bromide ion.

The central nervous system (CNS) effect of the bromide salts in humans is well characterized, and requires repeated daily administration of doses in the order of 1 to 2 grams per day to produce an effect. However, the effect is slowly reversed when dosing is stopped. The bromide ion acts in the organism by replacing the chloride ion and inhibiting depolarization and transmission in nerve cells.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 3.0 US EPA should provide the public with more information to allow an informed discussion and decision making process in regards to this petition.

Agency Response to Comment No. 3:

EPA is currently reviewing its procedures concerning the material included for dockets created in conjunction with petitions to establish, modify, or revoke tolerances. As to chlorfenapyr,

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however, EPA already has extensive information available on its website. That information was available at the time the notice of filing for the chlorfenapyr petition was published. EPA memoranda on the health and safety are available on the Regulating Pesticides portions of the website: <http://www.epa.gov/opprd001/chlorfenapyr/toc.htm>.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

- 3.1 US EPA should provide data to the public on all pesticides, and chemicals used in pesticidal formulations, known to produce spongiform encephalopathy and spongiform myelopathy.

Agency Response to Comment No. 3.1: The Agency reviewed an internal database and a literature search and found that only chlorfenapyr contained any reference to spongiform encephalopathy or spongiform myelopathy. Further, the Agency provides pesticide risk assessments to the public by FR Notices, Reregistration Eligibility Decisions (REDs: <http://www.epa.gov/pesticides> ) and by the Freedom of Information Act (FOIA).

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

- 3.2 Due to the growing number of people diagnosed with neurodegenerative diseases, US EPA should provide the public with its rationale for allowing the manufacture and use of pesticides that have the potential to induce spongiform encephalopathy and spongiform myelopathy.

**Agency Response to Comment No. 3.2:**

The Agency conducted a risk assessment for the proposed chlorfenapyr tolerance in/on food handling establishments. The results of this analysis indicate that the proposed uses will not result in exposures and associated risk that are of concern to the Agency.

The Agency has concluded that since a 1000-fold uncertainty factor (10X to account for interspecies extrapolation and 10X for intraspecies variability; 10X for database uncertainty factor ( $UF_{DB}$ ) for lack of a DNT study) is applied to the dose that did not cause any adverse effects (i.e, NOAEL), there is high confidence that exposure to chlorfenapyr will not cause unreasonable adverse effects to humans.

In the submitted food-handling study (for the Food Handling Establishment Use) residues of

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chlorfenapyr were less than the limit of quantitation (LOQ) 0.01 ppm).

In the acute dietary assessments it was concluded that the acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95<sup>th</sup> exposure percentile for females 13-49 years old (< 15% aPAD), and the general U.S. population (< 6% of the aPAD) and all other population subgroups. The most highly exposed population subgroup (other than females 13-49 years old) is children 1-2 years old, at < 9% of the aPAD.

In the chronic assessments it was concluded that the chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (< 23% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at < 45% of the cPAD.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 3.3 US EPA should perform a health risk assessment of the workers involved in the production of chlorfenapyr.

Agency Response to Comment No. 3.3

In examining aggregate exposure to a pesticide in establishing a tolerance, section 408 of the FFDCFA directs EPA not to consider occupational exposures to the pesticide.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 3.4 US EPA should provide a risk assessment and worst-case scenarios for an accidental release into the communities where chlorfenapyr is produced.

Agency Response to Comment No.3.4:

Exposure to a hypothetical accidental release of chlorfenapyr from a production facility is not an aspect of aggregate exposure considered under section 408 of the FFDCFA. In estimating exposure under FFDCFA section 408, EPA has focused on types of exposures that are actually occurring or are reasonably likely to occur and not on exposures that could possibly occur as a result of a rare, catastrophic event.

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**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 3.5 US EPA should provide an explanation as to why male mice were more sensitive to chlorfenapyr-induced spongiform myelopathy.

Agency Response to Comment No.3.5:

As previously indicated, EPA's function in ruling on a pesticide petition under section 408 of the FFDCA is to determine whether aggregate exposure to the pesticide is safe and not to explicate fully mechanisms by which the pesticide causes toxic effects. Safety determinations can often be made without a full understanding of the toxic mechanism through which a pesticide affects organisms or the reason that a pesticide affects different animal species or different sexes of the same animal species differently. Where differing effects are seen, EPA evaluates the safety of a pesticide based upon the most sensitive species and gender.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 4.0 Has the developmental neurotoxicity study for chlorfenapyr, recommended in 1998, been performed?

Agency Response to Comment No.4:

BASF has agreed to conduct a DNT to support the establishment of a permanent tolerance for chlorfenapyr on fruiting vegetables. The protocol review was completed in November 2004 by the HED, and the recommendations of this review have been sent to BASF.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 4.1 Would US EPA explain the modifications to the protocol of the neurotoxicity study requested by the registrant.
- 4.2 If the study recommended by the RfD Committee was performed, it should have been included in the "documents" in the Docket for this petition. Why were no documents available to the public via the Docket?

Agency Response to Comment No. 4.1 and 4.2:

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The registrant submitted protocol has been recently reviewed by the Agency. In general, the review of the DNT protocol focused on: 1) the adequacy of post natal dosing, 2) sample collection and processing, 3) assignment of pups to testing, 4) behavioral evaluations, 5) positive control data and 6) dose levels. The detailed comments on the DNT protocol have been included in the docket for this action.

**Source: OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

5.0 MRID 43492837 seems to contradict the statement that there is no information to suggest that chlorfenapyr is associated with any endocrine effects.

**Agency Response to Comment No. 5:**

There are no biological signals in the toxicology database including the reproductive, developmental and carcinogenicity studies to indicate that Chlorfenapyr is an endocrine disruptor, including MRID 43492837 which is a chronic carcinogenicity study.

The Agency is aware of potential endocrine effects of fluoride being noted in the open literature. From a preliminary review of this literature (Baetcke, et al., 2003), there does not appear to be a sufficient science foundation to permit confident conclusions regarding the ability of fluoride to produce endocrine effects.

**Source: Comment OPP-2003-0205-0003, Fluoride Action Network Pesticide Project**

**Comment Summary:**

6.1 Is EPA aware of any other pesticides where the active ingredient, or the inerts used in a pesticidal formulation, contain both fluorine and bromine?

**Agency Response:**

The Agency is not aware of any active ingredient, other than chlorfenapyr, or inerts used in pesticidal formulations that contain both fluorine and bromine.

***Fluoride:***

The Agency believes that fluoride residues are unlikely to result from the use of fluorinated pesticides due to the nature of the covalent carbon-fluorine bond that occurs in most fluorinated pesticide molecules. A review of the metabolism studies that have been submitted for the

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fluorinated pesticides in question would be required to definitively determine whether or not residues of fluoride *per se* might result from the use of fluorinated pesticides. Further data review would be required to then determine if any fluoride residues occur at biologically significant levels. As a screen to estimate the exposure to fluoride that may occur from fluorinated pesticides, HED has searched the OPP toxicology databases for fluorides. The only compounds for which fluorides is noted are sulfuryl fluoride and cryolite. Since toxicology studies typically include exposure levels that are far in excess of that which would be experienced by humans, HED is confident that the lack of findings of fluorosis provides strong evidence that any fluoride residues occurring from the use of pesticides are insignificant in terms of exposure to humans. Thickening of the bones and teeth is indicative of fluorosis. JMPR acknowledge the concern for fluorosis with this pesticide because the fluoride level in bones and teeth was increased in male mice was seen at 300 ppm. At 7500 ppm, both sexes had white discoloration of the teeth and bone alterations (diffuse hyperostosis of the rib bones, hardened cranial bones, focal hyperostosis of the skull caps). These effects were presumably due to an increased fluorine intake from the active ingredient. But nonetheless, these doses are way above those for the current MCLs for dental and skeletal fluorosis. The fungicide tolylfluanid provides an example of this. Studies with tolylfluanid show that fluoride may be released during the metabolism of the parent compound and toxicology studies show that fluoride levels do, in fact, increase in the teeth and bones of test organisms. However, the increase is well below levels that are known to cause fluorosis. Fluorosis was looked for in these studies and was not observed (Joint FAO/WHO Meeting on Pesticide Residues, 2002 – Tolyfluanid).

*Bromide:*

The release of bromine from chlorfenapyr does occur (minor pathways in plants, major pathways in liver). The Agency, however, believes that bromine compounds exhibit minimal chronic toxicity (10/26/2004 e:mail response: George Kramer, Chemist and PV Shah, Ph.D. Toxicologist). See Agency response to comments 2.3, 2.4 and 2.5.

- 7.0 US EPA should provide the public an explanation of the interaction of chlorfenapyr with other pesticides known to impact the brain. For example, does the potential exist for more severe brain effects if a consumer is exposed simultaneously to both, such as exposure to the following *organofluorine pesticides*?
- 7.1 There are several organofluorine pesticides that in animal studies have been found to adversely effect the brain. Due to time constraints, the following is a limited list: sulfuryl fluoride, fluazinam, flufenacet, sodium fluoride, tefluthrin, acifluoren. Diisopropyl fluorphosphate (DFP).
- 8.0 Has EPA considered the cumulative effects of exposure to various brain-toxic pesticides on fetal brain development?

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Agency Response to Comments Nos. 7.0, 7.1, and 8.0:

After considering the available information, the Agency is not aware of any data showing that chlorfenapyr interacts through a common mechanism of toxicity with the pesticides listed above (sulfuryl fluoride, fluazinam, flufenacet, sodium fluoride, tefluthrin, acifluoren, Diisopropyl fluorophosphate (DFP)) or other pesticides. Accordingly, EPA does not expect exposure to chlorfenapyr and other pesticides to have a cumulative effect.

Although the pesticides listed in comment 7.1 (sulfuryl fluoride, fluazinam, flufenacet, sodium fluoride, tefluthrin, acifluoren, DFP) may, in some cases and at some doses, cause brain effects, none of these pesticides cause the specific and unique effects – spongiform myelopathy or spongiform encephalopathy – seen with chlorfenapyr. In fact, these unique effects have not been seen in studies with any other pesticide. Further, HED did a database search for structural analogs of chlorfenapyr. Three fungicides were identified: fludioxnil, fenpiclonil and fluoroimide. Of these three only fludioxnil is registered in the U.S. There is no evidence of brain or neurotoxicity for fludioxnil in the toxicological database.

Finally, it is important to note that dietary exposure to chlorfenapyr as a result of these uses involved in this action (i.e. crack and crevice spray in food-handling establishments) is likely to be extremely low to non-existent. In the submitted food-handling study (for the Food Handling Establishment Use) residues of chlorfenapyr were less than the limit of quantitation (LOQ) 0.01 ppm in/on covered and uncovered composite meals following application of a 25% wettable powder formulation on two consecutive days at the maximum proposed use rate of 0.5% in 1 gallon of spray suspension/1000 ft<sup>2</sup>. Applications included crack and crevice and spot treatment to all areas of the kitchen and storage room of a restaurant to simulate commercial applications for cockroach control. Application areas included but were not limited to: underneath cabinets and overhead storage bins, around conduits and pipes, behind loose baseboards and molding strips, on the under sides of tables and around sinks, and in the open spaces above the drop ceiling.

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

- 9.0 Has US EPA considered the effects of chlorfenapyr on other susceptible subsets of the population with neurodegenerative diseases such as
- Parkinson's
  - Multiple Sclerosis
  - HIV-1 Associated Vascular Myelopathy

Agency Response to Comment No. 9.0:

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The Agency is confident that the 10X intraspecies Uncertainty Factor is adequate to protect the susceptible subsets identified by FAN because this uncertainty factor assumes 1) the variability in response from one human to another and 2) that subpopulations of humans may be more sensitive to the toxicity of the chemical than the general population. In addition, the risk assessment for chlorfenapyr includes 10X UF for the interspecies extrapolation and 10X database uncertainty factor, thus using a total of 1000-fold safety factor. This factor (i.e., 1000X) is applied to a dose (NOAEL) that did not cause any adverse effects of concern. Therefore, the Agency has high confidence that exposure to chlorfenapyr will not cause unreasonable adverse effects in any human population.

Exposure is likely to be extremely low to non-existent as demonstrated in the submitted food-handling study (for the Food Handling Establishment Use). Residues of chlorfenapyr were less than the limit of quantitation (LOQ) 0.01 ppm in/on covered and uncovered composite meals following application of a 25% wettable powder formulation on two consecutive days at the maximum proposed use rate of 0.5% in 1 gallon of spray suspension/1000 ft<sup>2</sup>. Applications included crack and crevice and spot treatment to all areas of the kitchen and storage room of a restaurant to simulate commercial applications for cockroach control. Application areas included but were not limited to: underneath cabinets and overhead storage bins, around conduits and pipes, behind loose baseboards and molding strips, on the under sides of tables and around sinks, and in the open spaces above the drop ceiling.

The Agency has no information indicating that the cited diseases are aggravated by pesticide exposure.

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

- 9.1 Has US EPA considered the subsets of the population who are exposed to chlorfenapyr through imported food? For example, Japan has maximum residue limits for chlorfenapyr on several agricultural commodities including a very high residue limit of 50 ppm for tea.

**Agency Response to Comment No. 9.1:**

Under the FFDCA, foods bearing pesticide residues are considered adulterated and subject to seizure unless there is a U.S. tolerance in place and the residue level is within the tolerance.

This applies to imported as well as domestic food. Commodities such as tea, which may have foreign maximum residue limits for chlorfenapyr, may not be lawfully imported to the United States if they contain chlorfenapyr unless there is a U.S. tolerance in place. In fact, there is no U.S. tolerance for chlorfenapyr in tea and thus EPA assumed that there would be no exposure in

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the United States to chlorfenapyr from drinking tea. In assessing aggregate exposure to a pesticide, EPA does not consider exposure to a pesticide from commodities on which the pesticide may not be legally present.

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

10.0 Can Chlorfenapyr be safely disposed? Can US EPA explain how.

Agency Response to Comment No. 10:

Issues regarding pesticide disposal are considered under FIFRA and not the FFDCFA. Instructions for safe disposal are on the FIFRA label and Material Safety Data Sheet (MSDS).

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

Comment Summary:

10.1 As the petition requests a tolerance for residues "on all food items in food handling establishments where food products are held, processed, and/or prepared at 0.01 parts per million (ppm)", can these food products be safely

- composted
- fed to farm animals or pets
- fed to birds

Agency Response to Comment No. 10.1

Food products containing 0.01 ppm chlorfenapyr can be safely composted and/or fed to farm animals. This conclusion is based on the acute and chronic dietary analysis for the proposed tolerance for chlorfenapyr in/on food handling establishments.

Separate, unrefined, Tier 1 acute dietary exposure assessments using tolerance-level residues and assuming 100% crop treated (CT) for all registered and proposed commodities were conducted for females 13-49 years old and the general U.S. population and various population subgroups. These assessments conclude that the acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95<sup>th</sup> exposure percentile for females 13-49 years old (< 15% aPAD), and the general U.S. population (< 6% of the aPAD) and all other population subgroups. The most highly exposed population subgroup (other than females 13-49 years old) is children 1-2 years old, at < 9% of the aPAD.

An unrefined, Tier 1 chronic dietary exposure assessment using tolerance-level residues and

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assuming 100% CT for all registered and proposed commodities was conducted for the general U.S. population and various population subgroups. These assessments conclude that the chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (< 23% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at < 45% of the cPAD.

It should be noted that a Tier 1 analysis is an unrefined assessment that uses conservative assumptions. If the result of such an analysis does not suggest a risk concern, as in the case of chlorfenapyr, it gives the Agency high confidence that the pesticide can be used safely.

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

10.2 What are the transformation products when chlorfenapyr is incinerated?

**Agency Response to Comment No. 10.2:**

This comment is not relevant under FFDCA.

**Source: Comment OPP-2003-0205-0002, Fluoride Action Network Pesticide Project**

**Comment Summary:**

11. What are the "inerts" used in Chlorfenapyr pesticide products? If US EPA doesn't provide this information, how can they expect the public to contribute anything substantive when information on the majority of the chlorfenapyr formulation is withheld?

**Agency Response to Comment No. 11:**

The action being commented on establishes a tolerance for the active ingredient, chlorfenapyr, on food. It does not legalize the presence of any inert ingredients that may be used in a chlorfenapyr product in food. To the extent inert ingredients are used in chlorfenapyr products, those inert ingredients must have a tolerance or an exemption from tolerance or their presence in food would render the food adulterated. Inert ingredients are subject to the same safety standard as active ingredients.

Information on the inerts is generally regarded as confidential business information and not disclosable under FIFRA. Therefore, consistent with the existing regulatory framework, information on inert ingredients in pesticide products is not available to the public.