information claimed as CBI must be submitted for inclusion in the public version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person identified in the **FOR FURTHER INFORMATION CONTACT** section.

II. What Action is EPA Taking?

EPA is making available preliminary risk assessments that have been developed as part of EPA's process for making reregistration eligibility decisions for the organophosphate pesticides and for tolerance reassessments consistent with the FFDCA, as amended by the FQPA. The Agency's preliminary human health effects risk assessments for these organophosphate pesticides are available in the OPP docket.

As additional comments, reviews, and risk assessment modifications become available, these will also be docketed for the two organophosphate pesticides listed in this notice. The Agency cautions that these risk assessments are preliminary assessments only and that further refinements of the risk assessments may be appropriate for the coumaphos and fenitrothion organophosphate pesticides. This document reflects only the work and analysis conducted as of the time it was produced and it is appropriate that, as new information becomes available and/or additional analyses are performed, the conclusions in it may change.

As the preliminary risk assessments for the remaining organophosphate pesticides are completed and registrants are given a 30-day review period to identify possible computational or other clear errors in the risk assessment, these risk assessments and registrant responses will be placed in the individual organophosphate pesticide dockets. A notice of availability for subsequent assessments will appear in the **Federal Register**.

The Agency is providing an opportunity, through this notice, for interested parties to provide written comments and input to the Agency on the preliminary risk assessments for the chemicals specified in this notice. Such comments and input could address, for example, the availability of additional data to further refine the risk assessments, such as percent crop treated information or submission of residue data from food processing studies, or could address the Agency's risk assessment methodologies and assumptions as applied to this specific chemical. Comments should be limited to issues raised within the preliminary risk assessments and associated documents. EPA will provide other opportunities for public comment on other science issues associated with the organophosphate tolerance reassessment program. Failure to comment on any such issues as part of this opportunity will in no way prejudice or limit a commenter's opportunity to participate fully in later notice and comment processes. All comments should be submitted by November 1, 1999 at the address given under **ADDRESSES**. Comments will become part of the Agency record for each individual organophosphate pesticide to which they pertain.

List of Subjects

Environmental protection, Chemicals, Pesticides and pests.

Dated: August 25, 1999.

Lois Rossi,

Director, Special Review and Reregistration Division, Office of Pesticide Programs.

[FR Doc. 99–22746 Filed 9–1–99; 8:45 am]

BILLING CODE 6560–50–F

ENVIRONMENTAL PROTECTION AGENCY

[PF–883; FRL–6094–5]

Notice of Filing Pesticide Petitions to Establish a Tolerance for Certain Pesticide Chemicals in or on Food

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces the initial filing of pesticide petitions proposing the establishment of regulations for residues of certain pesticide chemicals in or on various food commodities.

DATES: Comments, identified by docket control number PF–883, must be received on or before October 4, 1999.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I.C. of the ''SUPPLEMENTARY INFORMATION'' section. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–883 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: The product manager listed in the table below:

Product Manager	Office location/telephone number/e-mail address	Address	Petition number(s)
Dana Pilitt (PM 13) ...	Rm. 202, CM #2, 703–305–7071, e-mail: pilitt.dana@epamail.epa.gov.	1921 Jefferson Davis Hwy, Arlington, VA	PP 9F6022
Shaja Brothers	Rm. 284, CM #2, 703–308–3194, e-mail: brothers.shaja@epamail.epa.gov.	Do.	PP 7E4862, 7E4866, 8E4939, 7E4877, 7E4861, and 4E4302
Mary Waller (PM 21)	Rm. 249, CM #2, 703–308–9354, e-mail: waller.mary@epamail.epa.gov.	Do.	PP 1F4030, 2F4155, and 9F3812
Amelia M. Acierto	Rm. 707B, CM #2, 703–308–8377, e-mail: acierto.amelia@epa.gov.	Do.	PP 9E6010

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

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

Categories	NAICS	Examples of potentially affected entities
Industry	111	Crop production
	112	Animal production
	311	Food manufacturing
	32532	Pesticide manufacturing

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 the table could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether or not this action might apply to certain entities. If you have questions regarding the applicability of this action to a particular entity, consult the person listed in the ''FOR FURTHER INFORMATION CONTACT'' section.

B. How Can I Get Additional Information, Including Copies of this Document and Other Related Documents?

1. *Electronically*. You may obtain electronic copies of this document, and certain other related documents that might be available electronically, from the EPA Internet Home Page at http://www.epa.gov/. To access this document, on the Home Page select ''Laws and Regulations'' and then look up the entry for this document under the ''**Federal Register**--Environmental Documents.'' You can also go directly to the **Federal Register** listings at http://www.epa.gov/fedrgstr/.

2. *In person*. The Agency has established an official record for this action under docket control number PF–883 The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as confidential business information (CBI). This official record includes the documents that are physically located in the docket, as well as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number PF–883 in the subject line on the first page of your response.

1. *By mail*. Submit your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

2. *In person or by courier*. Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. The PIRIB is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305–5805.

3. *Electronically*. You may submit your comments electronically by E-mail to: ''*opp-docket@epa.gov* ,'' or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in Wordperfect 5.1/6.1 or ASCII file format. All comments in electronic form must be identified by docket control number PF–883. Electronic comments may also be filed online at many Federal Depository Libraries.

D. How Should I Handle CBI That I Want to Submit to the Agency?

Do not submit any information electronically that you consider to be CBI. You may claim information that you submit to EPA in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comment that includes any 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 version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person identified in the ''FOR FURTHER INFORMATION CONTACT'' section.

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

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.

2. Describe any assumptions that you used.

3. Provide copies of any technical information and/or data you used that support your views.

4. If you estimate potential burden or costs, explain how you arrived at the estimate that you provide.

5. Provide specific examples to illustrate your concerns.

6. Make sure to submit your comments by the deadline in this notice.

7. To ensure proper receipt by EPA, be sure to identify the docket control number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

II. What Action is the Agency Taking?

EPA has received pesticide petitions as follows proposing the establishment and/or amendment of regulations for residues of certain pesticide chemicals in or on various food commodities under section 408 of the Federal Food, Drug, and Comestic Act (FFDCA), 21 U.S.C. 346a. EPA has determined that these petitions contain data or information regarding the elements set forth in section 408(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

List of Subjects

Environmental protection, Agricultural commodities, Feed additives, Food additives, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: August 25, 1999.

James Jones,

Director, Registration Division, Office of Pesticide Programs.

Summaries of Petitions

Petitioner summaries of the pesticide petitions are printed below as required

by section 408(d)(3) of the FFDCA. The summaries of the petitions were prepared by the petitioners and represent the views of the petitioners. EPA is publishing the petition summaries verbatim without editing them in any way. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

1. Centre Internationale d'Etudes du Lindane (C.I.E.L.) and its Member Company Inquinosa S.A.

PP 9F6022

EPA has received a pesticide petition (9F6022) from Centre Internationale d'Etudes du Lindane (C.I.E.L.) and its member company Inquinosa S.A. , c/o Charles A. O'Conner III, Esq., McKenna & Cuneo, L.L.P., 1900 K St., NW., Washington, DC 20006-1108 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a time-limited tolerance for residues of lindane in or on the raw agricultural commodities (RAC) canola seed at 0.01 parts per million (ppm). EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

1. *Plant metabolism*. The metabolism of lindane in plants is adequately understood. Lindane is rapidly absorbed and eliminated by plants. Lindane translocates rapidly from treated seeds into the growing plant but concentrates primarily in the plant root. Both lindane and its metabolites appear to be readily lost to air and to soil. In almost all studies, the metabolites found in plants were identical to those found in animals although there may be variations in the conjugates detected. The same processes found in animals metabolize lindane in plants, i.e., dehydrogenation, dehydrochlorination, hydroxylation, and conjugation.

2. *Analytical method*. There is a practical analytical method for detecting and measuring levels of lindane in or on food with a limit of quantitation (LOQ) that allows monitoring of food with residues at or above the levels set in the tolerances. The parent is analyzed by gas chromatography/electronic capture detector (GC/ECD).

3. *Magnitude of residues*. Lindane was applied to seeds of canola. The RAC canola seed was harvested at the appropriate growth stage. A portion of harvested seed was processed into meal, which is an animal feed item, and edible canola oil, which is the only canola product that constitutes an appreciable portion of the human diet. Subsequent analyses determined that the residues of lindane will not exceed the proposed tolerance of 0.01 ppm for canola seed. Residues of canola in the processed commodities were < 0.005 ppm for meal and < 0.0005 ppm for edible oil. A cattle feeding study (20 ppm) was conducted to support foliar applications of lindane. Data was derived from extrapolation of this study to the 0.024 ppm maximum theoretical dietary burden in beef and diary cattle. Anticipated residues were 0.008 ppm in milk, 0.013 ppm in beef fat, 0.0011 ppm in beef muscle, 0.00038 ppm in beef kidney, and 0.00011 ppm in beef liver. Similarly, results of a poultry feeding study and the maximum anticipated dietary burden for poultry from lindane use as a seed treatment were used to derive anticipated residues of 0.0011 ppm in eggs, 0.00014 ppm in breast muscle, 0.00086 ppm in thigh muscle, and 0.00055 ppm in liver.

B. Toxicological Profile

1. *Acute toxicity*. Lindane demonstrates moderate oral, dermal and inhalation toxicity. Reported acute oral LD_{50} values in the rat range from 90 to 250 milligrams/kilograms (mg/kg). The acute dermal LD_{50} value was 200 to 300 mg/kg for rabbits and 900 to 1,000 mg/kg in rats. The acute inhalation LC_{50} value in the rat was 1,600 milligrams per liter (mg/L)/4h. Lindane is not irritating to rabbit skin and is slightly irritating to rabbit eyes. It did not cause skin sensitization in guinea pigs.

2. *Genotoxic*. The mutagenicity of lindane has been adequately studied. Lindane has been extensively investigated for its ability to induce gene mutation in both bacteria and mammalian cells, and for its activation in the assay for sex-linked recessive lethal mutation in D. melanogaster. Negative results were obtained consistently. Lindane's ability to induce chromosomal damage and sister chromatid exchange has been investigated in mammalian cells both *in vitro* and *in vivo*, again with negative results. Both assays for DNA damage in bacteria and studies *in vivo* to investigate covalent binding to DNA in the liver of rats and mice following oral administration also gave negative results. The few studies in which positive results were obtained involved invalid study designs or lindane of unknown purity. Overall, lindane appears not to have mutagenic potential.

3. *Reproductive and developmental toxicity*. Lindane is not considered to be a reproductive or a developmental toxin. In a 2-generation reproduction study, the no observed adverse effect level (NOAEL) for reproductive and developmental toxicity was 2 mg/kg/day. In a developmental toxicity study, the rat maternal NOAEL was 5 mg/kg while the developmental NOAEL was 10 mg/kg. The developmental and parental (based on reduced food consumption, reduced weight gain, slight tachypnea and lethargy) NOAEL for the rabbit was greater than 20 mg/kg/day. or a developmental toxin.

4. *Subchronic toxicity*. 90–day feeding studies were conducted in mice and rats with lindane. The NOAEL for the mouse study was greater than 10 ppm highest dose tested (HDT). For the rat study, the NAOEL was 10 ppm (0.75 mg/kg/bwt/day). Renal effects observed were related to α_{2U}-globulin and are not relevant to human safety. Hepatocellular hypertrophy and neurotoxicity were observed at the HDT. A 14–week inhalation study in mice had a NOAEL of 0.3 mg/cubic meter. In a 90–day inhalation study in rats, the NOAEL was 0.6 mg/cubic meter. 90–day dermal toxicity studies have been conducted in rats and rabbits. In both species, the NOAELs were 10 mg/kg/bwt/day.

5. *Chronic toxicity*. A 2–year feeding study was conducted in dogs with lindane. The NOAEL for this study was 50 ppm. A chronic study in rats found a NOAEL of 10 ppm (0.47 mg/kg/bwt/day) based upon liver toxicity at higher dose levels. Lindane is not carcinogenic to rats. A 2–year combined chronic toxicity/oncogenicity study in the rat was negative for carcinogenicity. A total of 8 mouse oncogenicity studies have been conducted in several strains of mice. None of the mouse studies were considered by the Agency, however, to be adequate for a cancer risk assessment. Thus, a ninth study is in progress.

6. *Animal metabolism*. The metabolism of lindane has been thoroughly investigated. Lindane does not appear to bioaccumulate in tissues. Lindane is rapidly absorbed and metabolized. The metabolism of lindane occurs via several different pathways. Major routes of metabolism include stepwise elimination of chlorines and conjuations with sulfates and glucuronides. Another pathway is via the formation of mercapurates.

7. *Metabolite toxicology*. Dietary residues are comprised of lindane and a variety of metabolites. The dietary residues are qualitatively the same as those formed in the rat and have thus been bioassayed in the available toxicity studies. These metabolites are not considered to present a significant toxicological risk.

8. *Endocrine disruption*. An evaluation of the potential effects on the endocrine systems of mammals has not been done. Reproductive effects of lindane are observed only at dose levels higher than those causing other forms of toxicity.

C. Aggregate Exposure

1. *Dietary exposure.—Food*. Estimates dietary exposure from the proposed uses would account for approximately 1% or less of the reference dose (RfD). The available data do not indicate any evidence of significant toxicity from a 1–day or single event exposure by the oral route. The only crop use for lindane at this time is seed treatment which results in extremely low dietary exposure. Thus an acute dietary risk assessment is not necessary.

2. *Drinking water*. Studies have shown that lindane will not move into ground water; therefore water has not been included in the dietary risk assessment.

3. *Non-dietary/non-occupational exposure*. There are very few remaining registered uses of lindane and the potential for non-occupational non-dietary exposure to the general population is negligible. As a seed treatment, lindane is limited to a small number of crops with extremely limited market share. The treated seed is either planted immediately, or stored in areas with limited access to the general public prior to sale and shipment to the user. Exposure is basically limited to occupational scenarios, i.e., application to seed and planting treated seed.

D. Cumulative Effects

EPA is required to consider the potential for cumulative effects of lindane and other substances that have a common mechanism of toxicity. EPA consideration of a common mechanism of toxicity is not appropriate at this time since EPA does not have information to indicate that toxic effects produced by lindane would be cumulative with those of any other chemical compounds; thus only the potential risks of lindane are considered in this exposure assessment.

E. Safety Determination

1. *U.S. population*. Using the conservative exposure assumptions described and based on the completeness and reliability of the toxicity data, the aggregate exposure to lindane will utilize less than 1% of the RfD for the U.S population. EPA generally has no concern for exposures below 100% of the RfD. Therefore, based on the completeness and reliability of the toxicity data and the conservative exposure assessment, there is a reasonable certainty that no harm will result from aggregate exposure to residues of lindane, including all anticipated dietary exposure and all other non-occupational exposures.

2. *Infants and children*. In assessing the potential for additional sensitivity of infants and children to residues of lindane, EPA considers data from developmental toxicity studies in the rat and rabbit and the 2-generation reproduction study in the rat. The developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from pesticide exposure during prenatal development. Reproduction studies provide information relating to effects on the reproductive capacity of males and females exposed to the pesticide. Developmental toxicity was not observed in toxicity studies using rats and rabbits. In these studies, the rat maternal NOAEL was 5 mg/kg/day and developmental NOAEL was 10 mg/kg/day. The parental and developmental NOAELs for the rabbit were greater than 20 mg/kg/day. In a 2-generation reproduction study in rats, the NOAEL for reproductive and developmental toxicity was 2 mg/kg/day. Section 408 of the FFDCA provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base. Based on the current toxicological data requirements, the data base relative to prenatal and postnatal effects for children is complete and an additional uncertainty factor is not warranted. Therefore, at this time, the RfD of 0.0047 mg/kg/bwt/day is appropriate for assessing aggregate risk to infants and children.

F. International Tolerances

Acceptable daily intake for lindane is 0.008 mg/kg/bwt. Codex Maximum Residue Levels (MRLs) have been set for several commodities for which tolerances have previously been proposed. In all cases, these MRLs are equal to or greater than the requested tolerances. The Canadian MRL for lindane in canola products is 0.1 ppm, i.e. negligible.

2. International Specialty Products

PP 9E6010

EPA has received a pesticide petition [PP 9E6010] from International Specialty Products, 1361 Alps Road, Wayne, NJ 07470, proposing pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for N-(n-octyl)-2-pyrrolidone (Agsolex 8) in or on the RACs soybeans, soybean forage, soybean fodder and soybean hay when used as an inert ingredient (solvent) in seed treatment applied at a maximum rate of 3 grams/acre. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data supports granting of the petition. Additional data may be needed before EPA rules on the petition.

A. Residue Chemistry

The Agency does not generally require residue chemistry data or environmental fate data to rule on the exemption from the requirements of a tolerance for an inert ingredient. However, relevant dietary residue modeling has been completed on N-(n-octyl)-2-pyrrolidone and is discussed in the appropriate section below.

B. Toxicological Profile

1. *Acute toxicity*. In a battery of acute studies, N-(n-octyl)-2-pyrrolidone has a low order of mammalian toxicity by oral, dermal and inhalation exposure routes. It is a skin and eye irritant in rabbits and a dermal sensitizer in guinea pigs. However, these acute irritation and sensitization data are not relevant for oral exposures. Therefore, no special susceptibility is anticipated from minor dietary oral exposures to N-(n-octyl)-2-pyrrolidone.

i. *Acute oral toxicity in rats*. N-(n-octyl)-2-pyrrolidone was administered by gavage to groups of five male and female rats (Wistar strain albino) at graded doses of 0.63-5.00 g/kg. Mortality and clinical observations, including signs of toxicity and pharmacological effects were conducted over a 14–day period. The acute oral LD_{50} for N-(n-octyl)-2-pyrrolidone was found to be 2.05 g/kg bodyweight, placing it in Category III for acute oral toxicity.

ii. *Primary ocular irritation in rabbits*. Undiluted N-(n-octyl)-2-pyrrolidone (i.e., as sold) was intra-ocularly applied once to each of nine New Zealand white rabbits at a volume of 0.1 milliliter (mL). An additional nine animals received a

single application of a 2% aqueous suspension of N-(n-octyl)-2-pyrrolidone. In both assays, the eyes of six animals remained unwashed for 24 hours while the eyes of the remaining three animals were washed 30 seconds after instillation of the test materials.

Ocular irritations were evaluated at 24, 48, and 72 hours following instillation of test material. Additional readings were made at 4, 7, 14, and 21 days in the assay with undiluted N-(n-octyl)-2-pyrrolidone. The eyes were scored for corneal opacity, iritis, conjunctivitis and other effects.

The results indicate that N-(n-octyl)-2-pyrrolidone was extremely irritating when tested as sold (i.e., undiluted), with wash procedures reducing the severity of the irritation observed. The 2% aqueous suspension was nonirritating both with and without washout procedures. Undiluted N-(n-octyl)-2-pyrrolidone is considered extremely irritating, placing it in category I or II for eye irritation. However, the 2% aqueous suspension was nonirritating both with or without washout procedures, placing it in Category IV for eye irritation.

iii. *Primary dermal irritation in rabbits*. The backs of six New Zealand white rabbits were closely clipped and the skin on the right side was abraded by making longitudinal epidermal incisions. The skin on the left side was left intact. A single application of 0.5 mL of N-(n-octyl)-2-pyrrolidone, in commercially available form, was made to each test site. In a second assay, an additional six rabbits received single applications of a 2% aqueous suspension of N-(n-octyl)-2-pyrrolidone.

In both assays, the wrapping and compound were removed at 24 hours and the sites scored at 24 and 72 hours for erythema and edema using the Draize scale. The mean scores at 24 and 72 hours were averaged to yield a Primary Irritation Index of 7.45 for N-(n-octyl)-2-pyrrolidone, when tested as sold, and 0.50 when tested as a 2% gravimetric aqueous suspension. N-(n-octyl)-2-pyrrolidone, when tested as commercially available, is therefore, considered to be extremely irritating to rabbit skin, and is minimally irritating as a 2% suspension. N-(n-octyl)-2-pyrrolidone, as sold, will therefore, be placed in Category I or II for skin irritation. However, the 2% aqueous suspension was only minimally irritating, placing it in Category II or III for skin irritation.

iv. *Acute dermal toxicity in rabbits*. Six New Zealand white rabbits each received a single dermal application of undiluted N-(n-octyl)-2-pyrrolidone at a dose level of 2 g/kg bodyweight. The skin of three animals was abraded, while the remaining animals' skin remained intact. Test sites were occluded for 24 hours at which time the occlusive wrap and any remaining test article were removed. Animals were observed for clinical signs and/or pharmacologic activity 1, 3, 6, and 24 hours after treatment and daily thereafter for a total of 14 days. On day 14, gross necropsy was performed on all animals. There was no mortality at the limit dose of 2 g/kg. The skin at the test sites showed crust formation, scaling and scarring. At necropsy, no gross internal changes and no deviations from normal were observed in any of the animals.

The acute dermal LD_{50} for N-(n-octyl)-2-pyrrolidone when tested undiluted (i.e., as sold) is greater than 2 g/kg body weight, placing it in Category III for acute dermal toxicity.

v. *D.O.T. corrosivity*. Six New Zealand white rabbits each received a single dermal application of 0.5 ml of undiluted N-(n-octyl)-2-pyrrolidone on one intact test site. The test site was occluded for 4 hours at which time the occlusive wrap and any remaining material were removed. Animals were observed for erythema, edema and other effects at 4 and 48 hours and 7–days after application. Crust formation was observed in five of the six animals.

Therefore, N-(n-octyl)-2-pyrrolidone when tested as sold, is corrosive to the skin of rabbits under conditions of this test.

vi. *Guinea pig sensitization study*. Twenty female albino guinea pigs received intradermal injections of 0.05% v/v N-(n-octyl)-2-pyrrolidone in both water and in freund's complete adjuvant (FCA) as well as FCA in water alone. One week after the injections the same interscapular area was covered occlusively for 48 hours with a patch saturated with 30%, v/v N-(n-octyl)-2-pyrrolidone in distilled water. During this induction phase, 10 control animals were treated similarly with the exception that the test material was omitted from the injections and topical applications.

Two weeks after the induction period, both the test and control animals were challenged topically using a patch saturated in 0.2 mL N-(n-octyl)-2-pyrrolidone, 10% v/v in distilled water applied to an anterior site on the flank and N-(n-octyl)-2-pyrrolidone, 5% v/v in distilled water applied in a similar manner to a posterior site. The patches were sealed to the flank covered for 24 hours. The challenge sites were evaluated at 24, 48, and 72 hours after patch removal. N-(n-octyl)-2-pyrrolidone produced evidence of delayed contact hypersensitivity in 2 of the 20 test animals.

vii. *Clinical studies*. Clinical exposure studies including phototoxicity, photoallergenicity and comedogenicity were conducted with N-(n-octyl)-2-pyrrolidone. N-(n-octyl)-2-pyrrolidone did not induce contact dermal phototoxic response, contact dermal photoallergy or contact dermal sensitization in human subjects under the exposure conditions of these tests.

viii. *Phototoxicity*. Each of 10 human subjects, all female, received 0.2 mL of a 1% suspension of test material in tap water on both volar forearms. Following a 24–hour exposure period under occlusive wrapping, the patches were removed and the sites scored for erythema and edema. Immediately following scoring one arm was irradiated with UV-A light. Test sites were scored immediately after irradiation and again at 24 and 48 hours. The nonirradiated arm served as a control.

No reactions were exhibited on either the irradiated or nonirradiated sites. N-(n-octyl)-2-pyrrolidone did not induce contact dermal phototoxic response in human subjects under the conditions of this test.

ix. *Photoallergy*. Each of 25 human subjects, 6 male and 19 females, received 0.2 mL of a 1% suspension of test material in tap water on both volar forearms. Following a 24-hour exposure period under occlusive wrapping, the patches were removed and the sites scored for erythema and edema. Immediately after scoring one arm was irradiated with both ultraviolet (UV-A) and UV-B light. The UV-A exposure period was 15 minutes; the UV-B exposure period was adjusted based on each subject's skin type. Sites were scored immediately following irradiation. A series of six induction patches was applied twice a week for 3 weeks.

Following a 2–week rest period, challenge patches were applied to virgin sites on each forearm. After a 24–hour exposure period, both sites were scored and the previously designated arm was irradiated. The sites were scored immediately after irradiation and again at 24 and 48 hours.

During the induction phase, 5 subjects exhibited a faint, minimal reaction on the irradiated contact site and one subject exhibited erythema and/or slight edema on the nonirradiated site. No reactions were exhibited at the challenge phase. N-(n-octyl)-2-pyrrolidone did not induce contact dermal photoallergy nor contact dermal sensitization in human subjects under the conditions of this test.

x. *Comedogenicity in rabbits*. The comedogenicity potential of N-(n-octyl)-2-pyrrolidone was assessed in New Zealand white rabbits. The external ear canal of six animals received dermal applications of 0.5 ml of 2% N-(n-octyl)-2-pyrrolidone in distilled water for 5 days a week, over a 4–week period. This was followed by microscopic examinations of the treated tissues.

Minimal to moderate local irritation was noted in all test animals characterized by redness, eschar, dryness and flaking. A mild to moderate comedogenic response was observed in 4 of the treated rabbits each receiving a comedogenic grade of 1.0 on a scale of 0 to 5. The remaining test animals received a grade of 0 (negative), yielding a mean comedogenic grade of 0.67. Under the conditions of this study, a mean comedogenic grade of > 2.0 in rabbits is considered to indicate a potential for comedogenesis in humans.

Therefore, N-(n-octyl)-2-pyrrolidone is not expected to be comedogenic in humans. There were no neoplastic microscopic findings in this study.

2. *Genotoxicity— Ames Salmonella*/microsome/reverse mutation assay: N-(n-octyl)-2-pyrrolidone and potential metabolite(s) formed as a result of liver S9 fraction activation was tested, as sold, in the Ames Assay with *Salmonella typhimurium* tester strains TA 1,535, TA 1,537, TA 1,538, TA 98 and TA 100. The entire 5-strain assay, with and without rat liver S9 fraction preparation, was performed twice.

In both experiments, with and without metabolic activation, there was no increase in the incidence of histidine protrotrophic mutants, relative to the negative controls. Therefore, N-(n-octyl)-2-pyrrolidone when tested as sold, using the *Ames Salmonella* assay system, is not a mutagen.

i. *Mouse micronucleus test in vivo*. N-(n-octyl)-2-pyrrolidone was tested for clastogenic (chromosome breaks) and aneugenic (numerical aberrations) effects on mouse bone marrow cells *in vivo*. Mice were administered N-(n-octyl)-2-pyrrolidone by intragastric gavage at a dose level of 1,720 mg/kg, based on results of a preliminary toxicity test. Negative controls receiving dosing vehicle alone and positive control (mitomycin C, 12 mg/kg) were also included. Bone marrow smears were obtained at 24, 48, and 72 hours post-dosing and examined for the presence of micronuclei in polychromatic and normochromatic erythrocytes. The ratio of polychromatic to normochromatic erythrocytes (P/N ratio) was also assessed.

Mice treated with N-(n-octyl)-2-pyrrolidone showed no significant increase in frequency of micronucleated polychromatic erythrocytes, and no significant decrease in P/N ratio at any of the sampling times. N-(n-octyl)-2-pyrrolidone is not mutagenic in this *in vivo* cytogenetic test system. There was no evidence of clastogenic or aneugenic effects in this test.

ii. *Mouse lymphoma mutagenesis assay*. In this assay, N-(n-octyl)-2-pyrrolidone was tested for its potential to induce mutations at the thymidine kinase (TK) locus of L5128Y TK+/- mouse lymphoma cells both in the presence and absence of exogenous metabolic activation. Based on the results of a range finding test N-(n-octyl)-2-pyrrolidone was tested at doses ranging 0.005 to 100 ul/ml which produced varying degrees of reduction in cell growth.

The results of this assay indicate that N-(n-octyl)-2-pyrrolidone did not produce mutagenic response in cultures treated in both the absence and presence of exogenous activation with Aroclor-induced rat liver S-9 preparation.

3. *Reproductive and developmental toxicity*. N-(n-octyl)-2-pyrrolidone was administered orally by gavage, once daily, to pregnant female Wistar rats from day 6 through day 15 post coitum, at dosages of 50, 200, or 800 mg/kg/body weight/day in order to assess the effects on embryonic and fetal development.

At 800 mg/kg, one dam died after the 7th and one after the 10th test article administration. The females of this group had marked treatment-related clinical signs, reduced food consumption, slight body weight loss during the first day of dosing, and reduced corrected body weight gain. The mean fetal body weight was reduced at this dosage, combined with a delay in skeletal ossification.

At 50 or 200 mg/kg, no treatment-related effects on maternal or fetal parameters were observed.

Based on these findings, the NOAEL for the maternal and fetal parameters was determined to be 200 mg/kg/bwt/day. N-(n-octyl)-2-pyrrolidone is not teratogenic to Wistar rats even at the maternally toxic dose of 800 mg/kg/bwt/day. Fetal body weight loss and delays in skeletal ossification at 800 mg/kg/day are not considered evidence of developmental toxicity since they occurred in the presence of severe maternal toxicity.

4. *Subchronic toxicity*—i. *Twenty–eight day oral toxicity in rats*. N-(n-octyl)-2-pyrrolidone, formulated as a solution in corn oil, was administered daily to rats (5 male, 5 female per dosage level) by intragastric intubation at dose levels of 5, 55 or 320 mg/kg, for 28 consecutive days. Similarly, control animals received corn oil (5 ml/kg/day).

At the high dose level (320 mg/kg/day), specific changes in general health, bwt gain, hematological and biochemical parameters were recorded. Statistically significant observations noted included:

ii. Lower body weight gains - females (week 3).

iii. Lower packed cell volume (PCV) and red blood cell counts - males.

iv. Higher mean corpuscular hemoglobin concentration (MCHC)-males.

v. Higher glutamic-pyruvic transaminase levels-females.

In all other respects including food consumption, organ weights, macro and microscopic pathology, no treatment-related changes were noted at all the tested dose levels.

In this 28–day study, the NOAEL of N-(n-octyl)-2-pyrrolidone was determined to be 55 mg/kg/day.

5. *90–Day oral toxicity in dogs*. Groups of 4 male and 4 female beagle dogs were given N-(n-octyl)-2-pyrrolidone orally via capsule at dose levels of 30, 90, and 240 mg/kg/day, for 90 days. All animals were observed daily for mortality and clinical signs of toxicity. At euthanatization, all surviving animals were subjected to histological examinations.

Dose related neurological signs and bwt loss were observed at 90 and 240 mg/kg levels. At 90 and 240 mg/kg treatment-related changes in clinical pathological parameters were also observed. In addition, dose-related increases in both absolute and relative liver weights were observed in all dose groups but was statistically significant in only the 90 and 240 mg/kg/day groups. One female death occurred on day 42 in the 240 mg/kg group. No treatment-related toxicity or clinical signs were observed in the 30 mg/kg/day group. Thirty mg/kg/day was a clear NOAEL.

6. *90–Day dietary toxicity in rats*. Groups of 10 male and 10 female rats were given diets containing 0, 60, 600, or 10,000 ppm N-(n-octyl)-2-pyrrolidone for 90 days. The approximate mean daily intakes of N-(n-octyl)-2-pyrrolidone were calculated to be 0, 5.3, 53, or 686 mg/kg/bwt.

All animals were observed daily for clinical signs of toxicity. At euthanatization, all animals were necropsied and subjected to macroscopic and microscopic examinations.

Reduced weight gain, increased absolute and relative liver weights and mild liver hypertrophy were observed at 10,000 ppm (686 mg/kg/bwt). No

treatment-related effects were observed at 60, (5.3 mg/kg bw/day), and 600 (53 mg/kg/bwt/day) ppm.

The liver was identified as a target organ and 600 ppm (53 mg/kg/day) was a clear NOAEL.

N-(n-octyl)-2-pyrrolidone is used mostly in household and institutional cleaners, especially as a constituent of hard-surface cleaners. Consistent with this public use, N-(n-octyl)-2-pyrrolidone is readily biodegradable in various microbially active matrices. It is freely soluble in water and has a relatively high polarity. For most compounds, there is a direct correlation between tissue uptake and bioaccumulation, and simple physical organic parameters such as log P, molecular mass and water solubility (Davies and Dobbs, 1984; Veith et al., 1979; Zitko and Hutzinger, 1976). The low bioaccumulation potential of N-(n-octyl)-2-pyrrolidone indicates that it is unlikely to accumulate in endocrine tissues, or disrupt endocrine functions. The safety, low uptake and low bioaccumulation potential of pyrrolidones in biological systems has also been experimentally demonstrated, even in active human sperms (Goldstein et al., 1998). These data strongly demonstrate that N-(n-octyl)-2-pyrrolidone is not an endocrine disrupter, and does not have any physiologically disruptive effects on endocrine processes. Additionally, it does not share any mechanistic or chemical similarity with currently known or suspected chemicals or chemical classes being studied for endocrine effects.

Additionally, pyrrolidones are natural products of ornithine metabolism found in many edible plant tissues, including carrots and tobacco. No physiologically disruptive effects have been reported from dietary exposures to these plants.

C. Aggregate Exposure

1. *Dietary exposure*. Residue data are generally not required for inert ingredient exemptions from a tolerance. Specific residue data for the inert ingredient N-(n-octyl)-2-pyrrolidone when used as a seed treatment are not available. Residue data are available to EPA for a number of pesticide products when applied as a seed treatment to soybeans at rates equal to or greater than 3 grams per acre. These data show that residues are non-detectable (< 0.01ppm) in soybeans, soybean forage, soybean fodder and soybean hay at harvest.

For the purpose of determining the potential dietary exposure from the proposed use of N-(n-octyl)-2-pyrrolidone as an inert ingredient in pesticides applied as a soybean seed treatment, an ultra conservative assumption was made that residues in soybean products would be 0.66 ppm. This assumption is based upon a maximum of 3 grams per acre of N-(n-octyl)-2-pyrrolidone being applied per acre as a seed treatment and resulting crop yields of 35 bushels of soybeans per acre (2,100 pounds of soybeans yield per acre based on an average weight of 60 pounds per bushel). Further, the soybean seed yield per acre is equal to approximately 36% of the total weight of soybean products at harvest per acre (soybeans equal 36%; the remaining 64% is soybean fodder, stems and roots). It is further assumed that the 3 grams of N-(n-octyl)-2-pyrrolidone is not degraded at all during the growth of the soybeans crop but instead at harvest is equally distributed in all plant parts at harvest.

N-(n-octyl)-2-pyrrolidone has been exempted from the requirement of a tolerance when used as an inert ingredient in certain pesticide products applied to defoliate cotton. No specific residue data are available for N-(n-octyl)-2-pyrrolidone in cotton products. For the purpose of this dietary assessment, the ultra conservative assumption was made that residues of N-(n-octyl)-2-pyrrolidone in cotton products would be 2x the highest residue tolerance established by EPA for any pesticide in cotton products. This results in dietary calculations based upon 70 ppm in cotton seed and cotton seed products including cotton seed oil (based on a 35 ppm tolerance for dalapon in cotton seed) and 200 ppm in cotton gin byproducts (based on a 100 ppm tolerance for glyphosate in cotton gin byproducts). Also, for the purposes of this assessment, the ultra conservative assumption was made that eggs, milk, meat, fat and meat byproducts would contain 0.5 ppm residues of N-(n-octyl)-2-pyrrolidone.

2. *Chronic dietary exposure assessment for N-(n-octyl)-2-pyrrolidone*. Chronic dietary exposure was assessed for the U.S. population and population sub-groups utilizing the Dietary Exposure Evaluation Model (DEEM™) from Novigen Sciences, Inc. Food consumption information (soybean food items only) was taken from USDA's 1994-96 Continuing Survey of Food Intake by Individuals (CSFII).

Exposure was compared to a chronic reference dose (RfD) of 0.03 mg/kg/bwt/day which was based on a no observable adverse effect level (NOAEL) of 30 mg/kg/bwt obtained from a 90–day feeding study in dogs and a 1,000-fold safety factor.

Results indicate that exposure for the overall U.S. population was 21.4% the chronic RfD for the soybean proposed plus the current use on cotton. The most sensitive subpopulation (children 1-6 years old) results in a chronic that uses 68% of the chronic RfD. This assessment is extremely conservative since residue reduction probably occurs with exposure of the treated seed to the environment as well as processing (not taken into account in this assessment) and market shares for both crops were assumed to be 100%.

3. *Acute dietary exposure assessment for N-(n-octyl)-2-pyrrolidone*. Using the same exposure estimates discussed above for soybean products results in an ultra conservative acute exposure for the overall U.S. population of 37.74% of the acute RfD for the proposed use on soybeans plus the current uses on cotton. The most sensitive subpopulation (children 1-6 years old) had an exposure of 52.85% of the acute RfD. These calculations were conducted at the 99.9% level.

i. *Food*. See exposure estimate discussed above.

ii. *Drinking water*. Based on its very low application rate, i.e., < 3 grams/acre, as well as the environmental fate studies, N-(n-octyl)-2-pyrrolidone would not be expected to persist in the environment, nor contaminate drinking water supplies.

4. *Non-dietary exposure*. N-(n-octyl)-2-pyrrolidone may also be used in certain cleaners, specifically hard-surface cleaners. Annual volumes market volume for this use is modest and is not expected to significantly contribute to the exposure profile for N-(n-octyl)-2-pyrrolidone.

D. Cumulative Effects

While the Agency has some information in its files that may be helpful in determining whether chemicals share a common mechanism of toxicity with any other substances, EPA does not at this time have the methodology to resolve the scientific issues concerning common mechanism of toxicity in a meaningful way.

E. Safety Determination

1. *U.S. population*. As per the details in the Dietary Residue Exposure System analysis, even the most sensitive population, children, 1- 6 years old, would be exposed to considerably less than 100% of the RfD even using the ultra conservative assumptions discussed above.

2. *Infants and children*. No developmental, embryotoxic, or teratogenic effects have been associated with N-(n-octyl)-2-pyrrolidone.

F. International Tolerances

The Applicant is not aware of any international tolerance or codes of Maximum Residue Limits (MRLs) for N-(n-octyl)-2-pyrrolidone on any crop or livestock commodities.

3. Interregional Research Project Number 4 and The Rohm and Haas Company

PP 7E4862, 7E4866, 8E4939, 7E4877, 7E4861, 4E4302 PP 1F4030, 2F4155, and 9F3812

EPA has received pesticide petitions [PP 7E4862, 7E4866, 8E4939, 7E4877, 7E4861, and 4E4302] from the Interregional Research Project Number 4 (IR-4), New Jersey Agricultural Experiment Station, P. O. Box 231 Rutgers University, New Brunswick, NJ 08903. EPA has also received pesticide petitions [PP 1F4030, 2F4155, and 9F3812] from the Rohm and Haas Company, 100 Independence Mall West, Philadelphia, PA 19106-2399. The petitions propose, pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing tolerances for residues of the fungicide, myclobutanil [alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole)-1-propanenitrile], and it's metabolite, alpha -(3-hydroxybutyl)-alpha-(4-chloro-phenyl)-1H-1,2,4-triazole-1-propanenitrile (free and bound) in or on the RAC commodity at the tolerance level ppm as follows:

1. *PP 7E4862*. Proposes the establishment of a tolerance for asparagus at 0.02 ppm.

2. *PP 7E4866*. Proposes the establishment of a tolerance for caneberry at 1.0 ppm.

3. *PP 8E4939*. Proposes the establishment of tolerances for currant at 3.0 ppm and gooseberry at 2.0 ppm.

4. *PP 7E4877*. Proposes the establishment of a tolerance for mint at 3.0 ppm.

5. *PP 7E4861*. Proposes the establishment of a tolerance for snap bean at 1.0 ppm.

6. *PP 4E4302*. Proposes the establishment of a tolerance for strawberry at 0.5 ppm.

7. *PP 1F4030*. Proposes the establishment of tolerances for tomato at 0.3 ppm and processed fractions for the following commodities: tomato pomace, wet at 3.0 ppm; tomato pomace, dry at 5.0 ppm; tomato juice at 0.3 ppm; tomato puree at 0.6 ppm; tomato paste at 1.2 ppm; tomato paste juice at 0.6 ppm; and tomato catsup at 0.6 ppm.

8. *PP 2F4155*. Proposes the establishment of tolerances for cucurbits at 0.5 ppm and inadvertent residues at 0.03 ppm for the following rotational crop group: root and tuber vegetables, leaves of root and tuber vegetables, leafy vegetables (except brassica vegetables), brassica (cole) leafy vegetables, legume vegetables (except snapbeans), foliage of legume vegetable group, fruiting vegetables (except cucurbits), cereal grains-commodities; cereal grains-forage, fodder, and straw; and nongrass animal feeds (forage, fodder, straw, and hay).

9. *PP 9F3812*. Proposes the establishment of a tolerance for pome fruit at 0.5 ppm.

EPA has determined that the petitions contain data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petitions. Additional data may be needed before EPA rules on the petitions.

A. Residue Chemistry

1. *Metabolism in plants and animals*—i. *Plants*. Based on the three metabolism studies in wheat, apples, and grapes, which indicate a similar metabolic route for crops in three different crop groups, Rohm and Haas Company (the registrant) concludes that the nature of the residue is adequately understood for the purpose of these tolerances.

ii. *Animals*. The nature of the residue in animals is adequately understood. The residues of concern in animal commodities, except milk, are myclobutanil (RH-3866) and its metabolite RH-9090 (free). The residues of concern in milk are myclobutanil, and its metabolites RH-9090 (free and bound) and alpha-(4-chlorophenyl)-alpha-(3,4-dihydroxybutyl)-1H-1,2,4-triazole-1-propanenitrile; RH-80,294).

2. *Analytical method*. An adequate enforcement method is available to enforce the established and proposed tolerances. Quantitation is by gas-liquid chromatography (GLC) using a nitrogen/phosphorous (NP) detector for RH-3866 and an electron capture (^{63}Ni) for residues measured as the alcohol metabolite (RH-9090). Myclobutanil residues in animal commodities are measured in essentially the same manner with the additional diol metabolite in milk.

3. *Magnitude of residues*. Field residue trials were conducted with wettable powder formulations of myclobutanil in geographically representative regions of the United States. The registrant concludes that the results from these studies support the proposed tolerances, and clearly indicate that the RH-9090 metabolite is a minor contributor to the total residue.

B. Toxicological Profile

1. *Acute toxicity*. According to the Rohm and Haas Company, myclobutanil wettable powder formulations are essentially non-toxic after administration by the oral, dermal and respiratory routes moderately irritating to the eyes, and non-skin sensitizers. Of these test results, ocular irritation at Toxicity Category III (Caution) was shown to be the worst case acute toxicity.

2. *Genotoxicity*. Myclobutanil was negative (non-mutagenic) in an Ames assay with and without hepatic enzyme activation. Myclobutanil was negative in a hypoxanthine guanine phosphoribosyl transferase (HGPRT) gene mutation assay using Chinese hamster ovary (CHO) cells in culture when tested with and without hepatic enzyme activation. In isolated rat hepatocytes, myclobutanil did not induce unscheduled DNA synthesis (UDS) or repair. Myclobutanil did not produce chromosome effects *in vivo* using mouse bone marrow cells or *in vitro* using CHO cells. On the basis of the results from this battery of tests, it is concluded that myclobutanil is not mutagenic or genotoxic.

3. *Reproductive and developmental toxicity*. In the developmental study in rats, the maternal (systemic) no observed adverse effect level (NOAEL) was 93.8 mg/kg/day based on rough hair coat, and salivation at the lowest observed adverse effect level (LOAEL) of 312.6 mg/kg/day. The developmental (fetal) NOAEL was 93.8 mg/kg/day based on incidences of 14th rudimentary and 7th cervical ribs at the LOAEL of 312.6 mg/kg/day.

In the developmental study in rabbits, the maternal (systemic) NOAEL was 60 mg/kg/day based on reduced weight gain, clinical signs of toxicity, and abortions at the LOAEL of 200 mg/kg/day. The developmental (fetal) NOAEL was 60 mg/kg/day based on increases in number of resorptions, decreases in litter size, and a decrease in the viability index at the LOAEL of 200 mg/kg/day.

In the 2-generation reproduction toxicity study in rats, the maternal (systemic) NOAEL was 2.5 mg/kg/day based on increased liver weights and liver cell hypertrophy at the LOAEL of 10 mg/kg/day. The developmental (pup) NOAEL was 10 mg/kg/day based on decreased pup body weight during lactation at the LOAEL of 50 mg/kg/day. The reproductive (parental) NOAEL was 10 mg/kg/day, based on an increased incidence of stillborns, and atrophy of

the testes, epididymides, and prostate at the LOAEL of 50 mg/kg/day.

4. *Subchronic toxicity*—i. Subchronic feeding study in rats was conducted for 13 weeks. The NOAEL was determined to be 1,000 ppm (52 and 66 mg/kg/day in males and females, respectively), and the LOAEL was 3,000 ppm based on increased liver and kidney weights, hypertrophy and necrosis in the liver, pigmentation in convoluted kidney tubules, and vacuolated adrenal cortex.

ii. A subchronic feeding study in mice was conducted for 13 weeks. The NOAEL was determined to be 300 ppm (43 and 66 mg/kg/day in males and females, respectively), and the LOAEL was 1,000 ppm based on increases in liver weight and clinical chemistry parameters, hypertrophy or necrosis and inflammation in the liver, and cytoplasmic eosinophilia and/or hypertrophy of the zona fasciculata cells of the adrenal gland.

iii. A subchronic feeding study in dogs conducted for 13 weeks resulted in a NOAEL of 10 ppm (0.34 mg/kg/day) in males and 200 ppm (8 mg/kg/day) in females. At the LOAEL of 200 ppm and above, hepatocellular centrilobular or midzonal hypertrophy was observed in males. At 800 ppm and above, the same effect was observed in females. In addition, increases in alkaline phosphatase, absolute liver weights in both sexes, and relative liver weights in males were observed. At 1,600 ppm, all the previous effects plus increases in relative liver weights in females, a suggestion of mild red cell destruction or mild anemia, and decreases in body weight and food consumption (possibly related to palatability) were observed.

iv. A 24.99% active ingredient (ai) emulsifiable concentrate (2EC) formulation was dermally applied to rats at 1, 10, or 100 mg/ai/kg/day and a 40% ai wettable powder (40 WP) formulation was dermally applied to rats at 100 mg/ ai/kg/day. Both formulations were applied once per day for a total of 19-20 treatments over a 4–week period. Application of the 2EC formulation resulted in a NOAEL for systemic effects of > 100 mg/ai/kg/day, and a NOAEL and LOAEL for skin irritation of 10 and 100 mg ai/kg/day, respectively. The 40 WP formulation at 100 mg/ai/kg/day the highest dose tested (HDT) did not produce any systemic effects and only produced minor skin irritation.

5. *Chronic toxicity*—i. A 1–year feeding study in dogs resulted in hepatocellular hypertrophy, increases in liver weights, ''ballooned'' hepatocytes, and increases in alkaline phosphatase, serum glutamic pyruvic transaminase (SGPT) and GGT, and possible slight hematological effects. The NOAEL and LOAEL were 100 ppm (3.1 and 3.8 mg/kg/day for males and females, respectively) and 400 ppm (14.3 and 15.7 mg/kg/day for males and females, respectively).

ii. A 24–month chronic/carcinogenicity study in male and female mice was conducted at 0, 20, 100, and 500 ppm myclobutanil, and a second 24–month chronic/carcinogenicity study was conducted in female mice at 0 and 2,000 ppm (394 mg/kg/day). No carcinogenic effects were observed in either study. The NOAEL was 100 ppm (13.7 and 16.5 mg/kg/day for males and females, respectively), and the LOAEL was 500 ppm (70 and 85 mg/kg/day for males and females, respectively) based on increased hepatic mixed-function oxidase (MFO) activity, increased SGPT (males only), increased absolute and relative liver weights, increased incidences and severity of centrilobular hepatocytic hypertrophy, Kupffer cell pigmentation, periportal punctate vacuolation, individual hepatocellular necrosis (males only), and increased incidences of focal hepatocellular alterations and multifocal hepatocellular vacuolation. At 2,000 ppm, these effects, and decreased body weight and body weight gain, and cytoplasmic eosinophilia and hypertrophy of the cells of the zona fasciculata area of the adrenal cortex were observed.

iii. A 24–month chronic/carcinogenicity study in male and female rats was conducted at 0, 25/35/50 (2 weeks/2 weeks/to termination), 100/140/200, and 400/560/800 ppm myclobutanil, and a second 24–month chronic/carcinogenicity was conducted in male and female rats at 0 and 2,500 ppm (125 mg/kg/day). No carcinogenic effects were observed in either study. The NOAEL and LOAEL were 50 ppm (2.5 mg/kg/day) and 200 ppm (10 mg/kg/day), respectively, based on a decrease in testicular weight and increase in testicular atrophy. At 2,500 ppm, these effects, and increases in the incidences of centrilobular to midzonal hepatocellular enlargement and vacuolization in the liver of both sexes, increases in bilateral aspermatogenesis in the testes, increases in the incidence of hypospermia and cellular debris in the epididymides, and increased incidence of arteritis/periarteritis in the testes were observed. The chronic population adjusted dose (cPAD) of 0.025 mg/kg/day was established based on the chronic feeding study in rats with a NOAEL of 2.5 mg/kg/day and an uncertainty factor of 100.

6. *Animal metabolism*. The absorption, distribution, excretion, and metabolism of myclobutanil in rats was investigated. Following oral administration, myclobutanil was completely and rapidly absorbed, extensively metabolized to at least seven major metabolites, and rapidly excreted evenly distributed between urine and feces. Myclobutanil did not accumulate in tissues.

7. *Metabolite toxicology*. Common metabolic pathways for myclobutanil have been identified in both plants (grapes, apples, wheat) and animals (rat, goat, hen). The metabolic pathway common to both plants and animals involves oxidation of the n-butyl alkyl side-chain in the 3- and 4- positions, oxidation of the cyano- group, and subsequent conjugation. Extensive degradation and elimination of polar metabolites occurs in animals such that residues are unlikely to accumulate in humans or animals exposed to these residues through the diet.

8. *Endocrine disruption*. The mammalian endocrine system includes estrogen and androgens as well as other hormonal systems. Myclobutanil is not known to interfere with reproductive hormones; thus, the registrant believes that myclobutanil should not be considered to be estrogenic or androgenic. The Rohm and Haas Company is not aware of any instances of proven or alleged adverse reproductive or developmental effects to people, domestic animals, or wildlife as a result of exposure to myclobutanil or its residues.

C. Aggregate Exposure

1. *Dietary (food) exposure*. Permanent tolerances have been established (40 CFR 180.443) for the residues of myclobutanil in or on a variety of RAC including almond nutmeat at 0.1 ppm, almond hulls at 2.0 ppm, apples at 0.5 ppm, apple pomace, wet/dry at 5.0 ppm, banana whole (Post-H) at 4.0 ppm, stone fruits except cherry at 2.0 ppm, cherries, sweet/sour at 5.0 ppm, plums, dried (prunes) at 8.0 ppm, cotton seed at 0.02 ppm, grapes at 1.0 ppm, grape pomace, wet/dry at 10.0 ppm, raisins at 10.0 ppm, and raisin waste at 25.0 ppm. In addition, permanent tolerances have been established for meat and meat byproducts including cattle, fat at 0.05 ppm, cattle, liver at 1.0 ppm, cattle, meat at 0.1 ppm, cattle, meat byproducts at 0.2 ppm, poultry, fat at 0.02 ppm, poultry, meat at 0.02 ppm, poultry, meat byproducts at 0.02 ppm, eggs at 0.02 ppm, and milk at 0.2 ppm.

Risk assessments were conducted by Rohm and Haas Company to assess

dietary exposures and risks from myclobutanil as follows:

i. *Acute exposure and risk*. No acute endpoint was identified for myclobutanil, and no acute risk assessment is required.

ii. *Chronic exposure and risk*. Risk associated with chronic dietary exposure from myclobutanil was assessed on two levels using two dietary exposure models. In the first assessment, tolerance level residues were assumed (except bananas in which 0.8 ppm was used in the dietary risk assessment rather than the tolerance of 4.0 ppm on whole fruit, since residues in the pulp will not exceed 0.8 ppm), and, in the second assessment average field trial residues were used. Both assessments utilized percent of crop treated refinements. The Anticipated Residue Contribution (ARC) from all proposed and existing food uses of myclobutanil was assessed. Additional proposed food uses of myclobutanil not previously mentioned in this document include peppers, hops, and artichokes (IR-4 petitions for these crops will likely be submitted in 1999). The percent of crop values used in these assessments were 79% for grapes, 60% for apples, 47% for cherries, 40% for bananas, 22% for peaches, 8% for pears, 3% for plums, 1% for apricots, 1% for almonds, and 1% for cottonseed. Percent crop treated data were used for the above commodities in the chronic exposure assessment, but were not considered when calculating the dietary burden from which secondary residue tolerances in meat, milk and poultry were derived or for the proposed uses on tomatoes and tomato processed fractions, cucurbit vegetables, and all of the subject minor crops of this petition. For rotational crops, the assessments conservatively assumed the extreme worse-case that 100% of all plantable United States acreage contained crops with residues at the 0.03 ppm proposed tolerance level.

The cPAD used for the chronic dietary analysis is 0.025 mg/kg/day. Potential chronic exposure was estimated using NOVIGEN'S Dietary Exposure Evaluation Model (DEEM Version 5.31), which uses United States Department of Agricultural (USDA) food consumption data from the 1989-1992 survey. The existing and proposed myclobutanil tolerances, and average myclobutanil residues result in ARCs that are equivalent to the following percentages of the cPAD (assumes residues are present at tolerance levels and includes percent crop treated refinements): For the U.S. Population (48 contiguous states) subgroup, the percent cPAD utilized is 19.1%. For the most highly exposed population subgroup, children (1 to 6 years old), the percent cPAD utilized is 57.7%.

iii. *Drinking water*. There is no established Maximum Concentration Level (MCL) for residues of myclobutanil in drinking water. No drinking water health advisory levels have been established for myclobutanil. There is no entry for myclobutanil in the ''Pesticides in Groundwater Database.'' Submitted environmental fate studies suggest that myclobutanil has low to moderate mobility potential in soil. Myclobutanil is stable to hydrolysis and soil photolysis, but does degrade photolytically in natural waters and soil. Field-trial soil dissipation studies had half-lives in the range of 50 to 400 days and indicated no significant downward movement of residues. Field trials showed myclobutanil degrades much more rapidly outdoors on foliage; the foliar decline on turf has a half-life of approximately 7 days.

The registrant believes that myclobutanil will not contaminate ground water or drinking water because of its adsorptive properties on soil, solubility in water, and degradation rate. Data from laboratory studies and field dissipation studies have been used in the PRZM/EXAMS computer model to predict the movement of myclobutanil. The model predicts that myclobutanil will not leach into ground water, even if heavy rainfall is simulated. The modeling predictions are consistent with the data from environmental studies in the laboratory and the results of actual field dissipation studies. Review of terrestrial field dissipation data indicates that myclobutanil did not leach into ground water in either sandy loam or coastal soil. Based on conducted studies to assess environmental risk, the registrant believes that significant exposure to residues of myclobutanil in drinking water is not anticipated.

2. *Non-dietary exposure*. Myclobutanil has no veterinary applications and is not approved for use in swimming pools. It is labeled for application to golf courses or other recreational areas, for use on ornamentals, and myclobutanil may be applied to residential lawns. However, this latter application represents less than 5% of myclobutanil's total non-dietary applications and is almost exclusively done by professional lawn care service companies. There are no indoor residential uses of myclobutanil; therefore, there is no indoor exposure to myclobutanil. Based on reasonable assumptions of exposure, the registrant does not anticipate significant exposure to residues of myclobutanil via non-dietary routes.

D. Cumulative Effects

The potential for cumulative effects of myclobutanil with other substances that have a common mechanism of toxicity was considered. The primary toxicological target organs for myclobutanil exposures are the rodent testes and liver. Myclobutanil can also produce phytotoxicity at high application rates. Myclobutanil belongs to the class of fungicide chemicals known as triazoles having demethylase inhibition capability. There are data available which suggest that there is a biochemical target site in fungal cell wall synthesis for myclobutanil and other fungicides in this class. However, there are no data which demonstrate that fungicides of this class have a common mode of action for exaggerated-dose phytotoxicity in plants, nor is there evidence that the toxicological effects produced by fungicides of this class in animals have a common mode of action.

EPA does not have, at this time, available data to determine whether myclobutanil has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment

E. Safety Determination

1. *U.S. population*. Using the conservative exposure assumptions described above and taking into account the completeness and reliability of the toxicity data, the percentage of the cPAD that will be utilized by dietary (food only) exposure to residues of myclobutanil from existing, pending, and proposed tolerances is 19.1% and 3.2% for the U.S. population assuming residues are present at their tolerance levels and average levels, respectively. The registrant believes that aggregate exposure (food, water, residential) is not expected to exceed 100% of the cPAD. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. The Rohm and Haas Company concludes that there is a reasonable certainty that no harm will result from aggregate exposure to myclobutanil residues to the U.S. population.

2. *Infants and children—In general*. In assessing the potential for additional sensitivity of infants and children to residues of myclobutanil, data from developmental toxicity studies in the rat and rabbit, and 2-generation reproduction studies in the rat are considered. The developmental toxicity

studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproduction studies provide information relating to effects from exposure to the pesticide on the reproductive capability of mating animals and data on systemic toxicity.

3. *Developmental toxicity studies*—i. *Rat*. In the developmental study in rats, the maternal (systemic) NOAEL was 93.8 mg/kg/day based on rough hair coat, and salivation at the LOAEL of 312.6 mg/kg/day. The developmental (fetal) NOAEL was 93.8 mg/kg/day based on incidences of 14th rudimentary and 7th cervical ribs at the LOAEL of 312.6 mg/kg/day.

ii. *Rabbit*. In the developmental toxicity study in rabbits, the maternal (systemic) NOAEL was 60 mg/kg/day, based on reduced weight gain, clinical signs of toxicity and abortions at the LOAEL of 200 mg/kg/day. The developmental (fetal) NOAEL was 60 mg/kg/day, based on increases in number of resorptions, decreases in litter size, and a decrease in the viability index at the LOAEL of 200 mg/kg/day.

iii. *Reproductive toxicity study*. In the 2-generation reproductive toxicity study in rats, the parental (systemic) NOAEL was 2.5 mg/kg/day, based on increased liver weights and liver cell hypertrophy at the LOAEL of 10 mg/kg/day. The developmental (pup) NOAEL was 10 mg/kg/day, based on decreased pup body weight during lactation at the LOAEL of 50 mg/kg/day. The reproductive NOAEL was 10 mg/kg/day, based on the increased incidences of stillborns, and atrophy of the testes, epididymides, and prostate at the LOAEL of 50 mg/kg/day.

iv. *Prenatal and postnatal sensitivity*. The prenatal and postnatal toxicology data base for myclobutanil is complete with respect to current toxicological data requirements. There is approximately a 25-fold difference between the developmental NOAEL of 60 mg/kg/day from the rabbit developmental toxicity study and the NOAEL of 2.5 mg/kg/day from the chronic rat feeding study which was the basis of the cPAD. It is further noted that in both the rabbit and rat developmental toxicity studies, the developmental NOAEL and maternal NOAEL are comparable (60 mg/kg/day for the rabbit and 93.8 mg/kg/day for the rat). In the rat reproduction study, the maternal NOAEL (2.5 mg/kg/day) was four times lower than the developmental (pup) and reproductive NOAELs (10 mg/kg/day). According to the registrant, these studies indicate that there is no additional sensitivity for infants and children in the absence of maternal toxicity for myclobutanil.

v. *Acute risk*. No acute dietary risk has been identified for myclobutanil.

vi. *Chronic risk*. Using the exposure assumptions described above, the exposure to myclobutanil from food will utilize 14.4% (nursing infants < 1–year old), and 40.9% (non-nursing infants < 1–year old) of the cPAD assuming residues are present at tolerance levels, and will utilize 3.0% (nursing infants < 1–year old), and 7.3% (non-nursing infants < 1–year old) of the cPAD assuming residues are present at their average field residue levels. The percent of the cPAD that will be used by the food exposure for children 1 to 6 years old is 57.7% and 8.0% assuming residues are present at tolerance levels and average field residue levels, respectively. The percent of the cPAD that will be used by the food exposure for children 7 to 12 years old is 28.5% and 4.5% assuming residues are present at tolerance levels and average field residue levels, respectively. EPA generally has no concern for exposures below 100% of the cPAD because the cPAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health.

2. *Non-dietary exposure*. Given the limited potential for exposure to myclobutanil from residential exposure, it is not expected that the aggregate exposure will exceed 100% of the cPAD. The registrant believes that there is a reasonable certainty that no harm will result from aggregate exposure to myclobutanil residues.

3. *Conclusion*. The Rohm and Haas Company concludes that reliable and complete data support the use of the 100-fold uncertainty factor, and that an additional 10-fold factor is not needed to ensure the safety of infants and children from dietary exposure.

F. International Tolerances

There are Codex Maximum Residue Limits (MRLs) for myclobutanil. The myclobutanil data base was evaluated by the World Health Organization (WHO) and the Food and Agricultural Organization (FAO) Expert Panels at the Joint Meeting on Pesticide Residues (JMPR) in September 1992, and an additional evaluation by the FAO Expert Panels was conducted in September 1997 and September 1998. An Acceptable Daily Intake (ADI; cPAD) of 0.025 mg/kg/day was established by the WHO panel and a total of 13 Codex MRLs are approved, including 0.01 ppm for both meat and milk. An additional nine Codex MRLs were proposed in the 1997 data submission including tomatoes (0.3 ppm), tomato paste (2.0 ppm), pome fruit (0.5 ppm), and strawberries (0.5 ppm).

The EPA has established the residue definition as the total of parent plus RH-9090, but the Codex has decided residues of parent alone are sufficient.

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ENVIRONMENTAL PROTECTION AGENCY

[FRL–6432–9]

Proposed CERCLA Administrative Cost Recovery Settlement; In Re: Landmark Farm and Garden, Inc. Superfund Site, North Haven, Connecticut

AGENCY: Environmental Protection Agency.

ACTION: Notice; request for public comment.

SUMMARY: In accordance with section 122(i) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended (''CERCLA''), 42 U.S.C. 9622(i), notice is hereby given of a proposed administrative settlement for recovery of past response costs concerning the Landmark Farm and Garden, Inc. Superfund site in North Haven, Connecticut with the following settling parties: Kerr-McGee Chemical, LLC; IMC Global, Inc.; Agrico Chemical Company; and Phosphate Resources Partners Limited Partnership. The settlement requires the settling parties to pay $775,000 to the Hazardous Substance Superfund. The settlement includes a covenant not to sue the settling parties pursuant to section 107(a) of CERCLA, 42 U.S.C. 9607(a). For thirty (30) days following the date of publication of this notice, the Agency will receive written comments relating to the settlement. The Agency will consider all comments received and may modify or withdraw its consent to the settlement if comments received disclose facts or considerations which indicate that the settlement is inappropriate, improper, or inadequate. The Agency's response to any comments received will be available for public inspection with the Regional Docket Clerk, U.S. Environmental Protection Agency, Region I, One Congress Street, Suite 1100, Mailcode RCG, Boston, Massachusetts (U.S. EPA Docket No. CERCLA I–98–1037).

DATES: Comments must be submitted on or before October 4, 1999.