http://www.epa.gov/opprd001/inerts/fr54.htm
Last updated on 5/9/2012

Inert Ingredients of Pesticide Products

Inert Ingredients in Pesticide Products; Policy Statement; Revision andModification of Lists

[OPP-36140A; FRL 3667-6]

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA is revising and modifying previously published lists of inert ingredients in pesticide products that are of toxicological concern and require priority testing. EPA is also addressing the period of time allowed to exhaust stocks of old formulations.

EFFECTIVE DATE: The modified lists are effective on November 22, 1989.

ADDRESSES: Three copies of written comments bearing the document control number (OPP-36140A) should be submitted, by mail, to:

Public Docket and Freedom of Information Section,
Field Operation Division (H7504C),
Office of Pesticide Programs,
Environmental Protection Agency,
401 M St. SW.,
Washington, DC 20460.

In person, deliver comments to:
Rm. 246, CM#2,
1921 Jefferson Davis Hwy.,
Arlington, VA.

Information submitted as a comment in response to this Notice may be claimed confidential by marking any part or all of that information as "Confidential Business Information" (CBI). Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. A copy of the comment that does not contain CBI must be submitted for inclusion in the public docket.

Information not marked "confidential" will be included in the public docket without further notice. The public docket is available for public inspection in room 246 at the address given above from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: EPA announced its policy on toxic inert ingredients in pesticide products in the Federal Register of April 22, 1987 (52 FR 13305). Through this policy, EPA encourages the use of the least toxic inert ingredients available and requires the development of data necessary to determine the conditions of safe use of products that contain toxic inert ingredients. In developing this policy EPA categorized inert ingredients of the following four lists according to toxicity:

List 1 Inerts of toxicological concern.
List 2 Potentially toxic inerts, with high priority for testing
List 3 Inerts of unknown toxicity
List 4 Inerts of minimal concern

List 1 and list 2 were published as part of the April 22, 1987 policy statement.

The criteria developed by EPA to categorize List 1 meets were reviewed by the Federal Insecticide. Fungicide, and Rodenticide Act's Scientific Advisory Panel FIFRA SAP. Chemicals were placed on the list of inerts of toxicological concern if they met any one of the following criteria.

(1) Carcinogenicity:

-A rating as a human carcinogen of probable human carcinogen (rating 1. 2A or 2B) by International Agency for Research on Cancer.
-Characterized by the National Toxicology Program as an animal carcinogen in at least one species and one sex.
-Being regulated by some Federal agency as a carcinogen.

(2) Neurotoxicity and other Chronic Effects:

-Identified in the Occupational Diseases, a Guide to their Recognition (1977), as causing neurotoxicological and other chronic effects in the workplace environment.
-Being regulated by some Federal agency as a neurotoxin.
-Peer reviewed study, included in the Toxicology Data Bank of the National Library of Medicine, reporting neurotoxic or other chronic effects.

(3) Adverse Reproductive Effects:

-Being regulated by some Federal agency as causing adverse reproductive effects.
-Peer reviewed study, included in the Toxicology Data Bank of the National Library of Medicine, reporting adverse reproductive effects.

(4) Ecological Effects:

-An LC50 of less than one part per million.

Revision of List of Inert Ingredients

Since the publication of the policy. EPA has received additional data on some of the listed inerts. EPA scientists have reviewed this information according to criteria previously developed and used in the creation of the initial lists. As a result of this recent examination of new data, EPA proposed modifications to the lists. These modifications were submitted to the FIFRA SAP for review. The FIFRA SAP concluded that the proposed changes were justified.

EPA is announcing the following revised List 1 and list 2.

LIST 1. INERTS OF TOXICOLOGICAL CONCERN

CAS No.	Chemical Name
62-53-3	Aniline
1332-21-4	Asbestos fiber
1332-21-9	1,4-Benzenediol
7440-43-0	Cadmium compounds
56-23-5	Carbon tetrachloride
67-66-3	Chloroform
106-46-7	p-Dichlorobenzene
103-23-3	Di-(2-ethlhexyl) adipate
78-87-6	1,2-Dichloropopane
117-87-8	Di-ethylhexylphthalate
68-12-2	Dimethylformanide
123-91-1	Dioxane
106-89-8	Epichlorohydrin
110-80-5	2-Ethoxiyethanol
110-80-5	Ethanol, 2-ethoxy (celulosive)
111-15-9	Ethanol ethoxy acetate
96-45-7	Ethylene thiourea
107-06-2	Ethylene dichloride
109-86-4	Ethylene glycol monomethyl ether; methyl celulosive
140-88-5	Ethyl acrylate
110-54-3	n-Hexane
302-01-2	Hydrazine
78-59-1	Isophorone
7439-92-1	Lead compounds
568-64-2	Malachite Green
591-78-6	Methyl n-butyl ketone
74-87-3	Methyl chloride
75-09-2	Methylene chloride
25154-52-3	Nonylphenol
127-18-4	Perchloroethylene

108-95-2	Phenol
90-43-7	o-Phenylphenol
75-56-9	Propylene oxide
8003-34-5	Pyrethrins and pyrethroids
81-88-9	Rhodamine B
10588-01-9	Sodium dichromate
26471-62-5	Toluene diisocyanate
79-00-5	1,1,2-Trichloroethane
56-35-9	Tributyl tin oxide
79-01-6	Trichloroethylene
1330-78-5	Tri-orthocresylphosphate (TOCP)
78-30-8	Tri-orthocresylphosphate (TOCP)

LIST 2. POTENTIALLY TOXIC INERTS/HIGH PRIORITY FOR TESTING

CAS No.	Chemical Name
85-68-7	Butyl benzyl phthalate
84-74-2	Dibutyl phthalate
84-66-2	Diethyl phthalate
131-11-3	Dimethyl phthalate
117-84-0	Dioctyl phthalate
95-49-6	2-Chlorotoluene
1319-77-3	Cresols
95-48-7	o-Cresol
106-44-5	p-Cresol
108-39-4	m-Cresol
108-94-1	Cyciohexanone
95-50-1	o-Dichlorobenzene
112-34-5	Diethylene glycol monobutyl ether
111-90-0	Diethylene glycol monoethyl ether
111-77-3	Diethylene glycol monomethyl ether
34590-94-8	Dipropylene glycol monomethyl ether
111-76-2	2-Butoxy-l-ethanol
5131-86-8	1-Butoxy-2-propanol
124-16-3	1-Butoxyethoxy-2-propanol
107-98-2	1-Methoxy-2-propanol
29387-86-8	Propylene glycol monobutyl ether
25498-49-1	Tripropylene glycol monomethyl ether
141-79-7	Mesityl oxide
106-10-1	Methyl isobutyl ketone

96-29-7	Methyl ethyl ketoxime
106-90-7	Monochlorobenzene
75-52-5	Nitromethane
108-88-3	Toluene
29395-43-1	Tolyl triazole
95-14-7	1,2,3-Benzotriazole
120-32-1	2-Benzyl-4-chlorophenol
7500-3	Chloroethane
88-04-0	p-Chloro-m-xylenol
97-23-4	Dichlorophene
100-41-4	Ethyl benzene
149-30-4	Mercaptobenzothiazole
74-83-9	Methyl bromide
75-43-4	Cholordifluoromethane
75-43-4	Dichloromonofluoromethane
75-45-6	Chlorodifluoromethane
75-37-6	1,1-Difluoroethane
75-68-3	1-Chloro-1,1-difluoroethane
25168-06-3	Isopropyl phenols Petroleum hydrocarbons
1330-20-7	Xylene
100-02-7	p-Nitrophenol
106-88-7	Butylene oxide
79-24-3	Nitroethane
75-05-8	Acetonitrile
96-48-0	gamma-Butyrolacetone
71-55-6	1,1,1-Trichloroethane
102-71-6	Triethanolamine
111-42-2	Diethanolamine
97-88-1	Butyl methacrylate
80-62-6	Methyl methacrylate. Xylene-range aromatic solvents
95-82-9	2,5-Dichloroaniline
95-76-1	3,4-Dichloroaniline
626-43-7	3,5-Dichloroaniline
554-00-7	2,4-Dichloroaniline
608-27-5	2,3-Dichloroaniline
608-31-1	2,6-Dichloroaniline
101-84-8	Diphenyl ether
76-13-1	Trichlorotrifluoroethane
75-69-4	Trichlorotrifluoroethane
75-71-8	Dichlorotetrafluoromethane

79-14-2	Dichlorotetrafluoromethane

The changes made and the reasons for the changes are explained below.

Additions to List -1

Di-(2-ethylhexyl)adipate and methyl-formamide (DMF) were moved to List 1 from Lists 3 and 2 respectively. Based on a National Toxicology Program bioassay, positive results for oncogenicity were indicated for di-(2-ethyl-hexyl)adipate: This chemical caused increased incidences of hepatocellular carcinomas in female mice, and thus meets one of the criteria for categorization as a List 1 inert.

For dimethylformamide (DMF), hepatotoxicity has been reported at very low doses in animal studies and it is commonly observed in case reports of industrial exposure. Developmental toxicity has also been reported to occur in animal studies in the literature. In addition, recent reports of clusters of testicular cancer associated with human exposure to DMF have added to the weight of evidence which supports upgrading this compound from List 2 to List 1.

Additions to List 2

Based on data available at the time of the April 27, 1987, FR Notice, monochlorobenzene was determined to be an oncogen as well as an ecotoxin. For these reasons, it was placed on List 1. The EPA Science Advisory Board has reviewed the oncogenicity data on monochlorobenzene and concluded that it is a class D oncogen, i.e., not classifiable. EPA scientists have reevaluated the ecotoxicity data and concluded that monochlorobenzene does not meet List 1 ecotoxicity triggers. Because of these determinations, monochlorobenzene is being moved from List 1 to List 2 and is now considered as a high priority for testing.

Methyl ethyl ketoxime has been moved from List 3 to List 2 because of its close structural relationship to acetoxime, which has been reported as being carcinogenic in preliminary tests and is also positive in a mouse lymphoma test. Methyl ethyl ketoxime has been proposed for testing under section 4 of the Toxic Substances Control Act.

Additions to Lists 3 and 4

To accommodate revision of the lists, EPA has decided to subdivide List 4 into two parts. The previous list 4, representing inerts generally recorded as safe, has become List 4A, and a new List 4B has been created. List 4B is composed of inerts for which EPA has sufficient information to reasonably conclude that the current use pattens in pesticide products will not adversely affect public health and the environment. List 4B inerts in formulations proposed for new use pattems which cause signifcant increases in exposure will receive further scrutiny.

Two inerts, gammabutyrolactone and dioctyl sodium sulfosuccinate (DSS), are being removed from List 2 because EPA now has a complete human health effects data base indicating that they do not meet the criteria for List 1 and that their current use in pesticides should not adversely affect human health.

The placement of gammabutyrolactone on List 2 was based on structural analogy to the known oncogen, betabutyrolactone. Further review indicates this analogy is inappropriate. In addition, a review of toxicity data for gammabutyrolactone, including acute and subchronic data, developmental toxicy, mutagenicity, and oncogenicity indicates a low order of toxicity. Thus EPA has decided to remove gammabutyrolactone from List 2 and add it to List 4B because current use pattems pose minimal risk for human health. Because gammabutyrolactone has not been adequately tested for ecotoxicity, however, it is being placed on List 3 for these effects. EPA decided to list the inert on two lists to reflect the different degree of knowledge the Agency has about the inert's various effects. EPA considered it appropriate to place the inert on List 4B because it has sufficient information about human health effects, and to also place it on List 3 to reflect inadequate information

concerning the ecotoxicity of this inert.

DSS was placed on List 2 because of developmental and reproductive toxicity concerns as well as ecotoxicity concern for surfactants. Data have now been reviewed for these effects, and indicate a low order of toxicity. Thus, DSS is added to List 4B for nonadverse effects on human health. Because of limited ecotoxicity testing, however, DSS remains on List 3 (unknown toxicity) for these effects.

Deletions From All Lists

Further investigation of ethylene thiourea, carbon disulfide, and 1,1-dimethylhydrazine (UDMH, the impurity in Alar, which is in Special Review), has revealed that these are only impurities, not intentionally added inerts. Furthermore, betabutyrolactone, benzene, dichlorvos, 1, 2-dimethylhydrazine, pentachlorophenol and sodium pentachlorophenate, dinitro-o-cresol, dinitrophenol, ethyl methyl phenylglycidate, formaldehyde and paraformaldehyde, hexachlorophene, mercury oleate, 2-nitropropane, 1,2-dichloropropane, and thiourea are not now used as inerts in any pesticide products. Therefore, these chemicals have been removed from all lists of inert ingredients and are not currently cleared for use as inerts in any pesticide product. Thus, in the event a registrant or applicant purposes to include one of these chemicals as an inert ingredient in a pesticide product, EPA will consider the chemical a new inert.

Impurities in registered products are contaminants from the manufacturing process for the active ingredient, rather than intentionally added inert ingredients. The presence and toxicity of impurities is routinely evaluated during the normal Agency review processes. Impurities are identified in the product chemistry review, and would probably have been presented as part of the test material, during testing considered for support of the registration. Thus, it is not appropriate to subject impurities to the Inerts Strategy.

As discuss in the April 22, 1987 Notice, registrants with products containing List 1 inert ingredients must amend their product registrations by adding the following statement to the label:

This product contains the toxic inert ingredient (name of inert).

The wording should be placed in close proximity to the ingredients statement in a type size comparable to other front panel text. Since dimethylformamide and di-(2-ethylhexyl) adipate have been added to List 1, registrants of products containing these inerts are required to submit applications to amend their product labels not later than May 22. 1990. Products containing one or more of these inert ingredients released for shipment after May 22, 1991 must have the amended label in place.

Registrants of products containing dimethylformamide have already received a Data Call-In. All registrants have either voluntarily cancelled or committed to reformulate the product. Most reformulations have been received: a few time extensions were granted to allow for necessary testing of the reformulated product.

A Data Call-In for di-(2-ethylhexyl) adipate will be issued at the same time as for diethylhexylpthalate since the uses are similar and we expect to find them in the same types of products. Data Call-ins for other original List 1 inerts were mailed in March 1989.

Stocks of Old Formulations

Registrants are encouraged to substitute or remove any List 1 or List 2 inert ingredient from their products by submiting a new Confidential Statement of Formula as a proposed amendment to the registration. The April 22, 1987 Policy statement did not address provisions governing the sale of stock of old formulations. If a registrant reformulates its product to replace a List 1 or List 2 inert ingredient with a less toxic inert, EPA has determined that some limit on continued sale of stock of the old formulation is appropriate.

Once a registrant submits the revised formulation, registrants may manufacture only the old formulation,

properly labeled as containing a toxic inert as described above, until EPA accepts the new formulation. Stocks of the old formulation, bearing the required labeling, may be released for shipment by the registrant for a period not to exceed twelve months from the date EPA accepts the new formulation. Products already in channels of trade (retailers, distributors, dealers) are not subject to this limitation.

Dated: October 10, 1989.
Douglas D. Campt,
Director, Office of Pesticide Programs.
(FR Doc. 89-27213 Filed 11-21- 89: 8:45am)
BILLING CODE 6560-60-M