



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Pesticide Findings in Lanolin

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The Office of Pesticide Programs has received a request from the Food and Drug Administration (FDA) to review the results of analyses of lanolin-based emollients found to contain pesticides and to provide them with an assessment of the significance of these levels on human health from the use(s) of these products. This memo summarizes those determinations based on the residue analyses provided by the FDA (dated 8/15/88). Three additional analyses performed by Dr. Sheldon Wagner (5/27/88) were also included.

FDA identified 16 pesticides in the lanolin-containing samples. Some of the products analyzed were creams containing a small percentage of lanolin and in about 10 cases, anhydrous lanolin was analyzed; not surprisingly, the latter cases contained the highest concentrations of pesticides.

The exposure scenario used was that of a nursing mother using lanolin as an emollient on her breasts to prevent drying and cracking, assuming all of the lanolin applied is consumed by the nursing infant. This provides a considerably higher exposure to the infant than a daily rubdown with lanolin-containing baby oil. It also leads to higher intake than frequent application of lipstick. It, therefore, probably constitutes a "worst-case" scenario.

Dr. Eiermann from the FDA provided EPA with an exposure analysis for this scenario. He estimated a nipple/areola area of 20 cm² (about a 1 inch radius), a thickness of 0.005 cm of lanolin and six applications and nursings per day. He estimated 0.6 gms/day intake based on nursing from one breast. We considered that nursing could include both breasts where the intake of lanolin would be 1.2 g/day. For convenience of calculation, I used a figure of 1 g/day, the same number used by the Australian expert group which considered this issue in February of 1987.

The highest concentrations reported in the FDA analyses were used ("worst-case") and the amount found in one gram was divided by 5 kg to obtain a dose per kg body weight for an infant considerably under one year of age, those most likely to be nursing six times per day. The exposure estimate was then compared to the available toxicity data base for each pesticide. Each evaluation includes a comparison to: (1) the chemical's ADI/RfD (RfD = reference dose, synonymous with the term ADI); (2) the NOAEL (no observed adverse effect level) for the response of concern (e.g. cholinesterase inhibition for organophosphates, OPs); and/or (3) an estimate of the oncogenic potency (Q₁) if the pesticide is an oncogen and if such an estimate has been calculated (e.g. organochlorinated pesticides). A few of the pesticides are not registered in the U.S. In those cases, we utilized evaluations conducted by the World Health Organization (WHO), where available.

For those pesticides where a cancer risk assessment was appropriate, I assumed the dose was consumed daily for two years and prorated this daily dose for a 70-year lifetime. This is quite conservative since most infants do not nurse for two years (certainly not six times per day) and a one year old is generally assumed to weigh 10 kg which would correspond to half the daily dose of the younger infant, all other factors being equal. Since the cancer risks were low, this conservatism is reassuring and no further refinement appears necessary.

Further, some organochlorinated pesticides have been detected in mother's milk from a survey conducted in 1975 and 1978 (National Study of Chlorinated Hydrocarbon Insecticide Residues in Human Milk, U.S.A.). The source of these background levels is undetermined, but the information is provided in order to compare the background level of exposure to the estimated levels from lanolin-based nursing emollients.

Since the source of these pesticide contaminants in lanolin is presumed to be sheep wool, we have attempted to identify U.S. tolerances and/or CODEX MRLs for sheep/sheep products. In addition, tolerances/MRLs for cow's milk are also provided. As you are aware, however, the existence of a U.S. tolerance does not necessitate a U.S. registered use on the same commodity (e.g. toxaphene). Tolerances are occasionally established for imported commodities where there is no existing U.S. use.

Finally, please note that the highest level reported is provided along with the range of values found, as well as the number of positive samples from the total number analyzed. This may assist in assessing the magnitude of concern for each pesticide contaminant.

1. Bromophos ethyl

ADI/RfD

EPA: No estimate. No U.S. uses.

WHO: 0.003 mg/kg/day

NOAELs

0.78 mg/kg (rat, plasma cholinesterase inhibition)
0.25 mg/kg (dog, plasma cholinesterase inhibition)

Other

No information on oncogenic potential

Tolerances/MRLs

U.S. tolerances: None

Codex MRLs: 3 ppm in sheep fat
0.008 ppm in milk

Level in Lanolin Products

Highest level reported: 13 ppm (0.3-13 ppm; 13 of 25 samples)

Background Levels in Mother's Milk

No information

Daily Dose to Infant

0.0026 mg/kg bw

The daily dose is at the WHO ADI and 100-fold lower than the dog NOAEL. WHO last reviewed bromophos ethyl in 1975.

2. Carbophenothion

ADI/RfD

EPA: 0.00013 mg/kg/day

WHO: 0.0005 mg/kg/day

NOAELs

0.25 mg/kg (rat, cholinesterase inhibition)

>0.01 mg/kg (human, no inhibition of cholinesterase)

LELs [Note dose level is lower than rat and man]

LEL: 0.125 mg/kg (dog, cholinesterase inhibition)

Other

No information on oncogenic potential

Tolerances/MRLs

U.S. Tolerances: 0 ppm in milk
0.1 ppm in sheep fat

CODEX MRLs: 0.004 ppm in milk
1.0 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 1.6 ppm (0.2-1.6 ppm; 3 of 25 samples)

Background Level in Mother's Milk

No information

Daily Dose to Infant

0.00032 mg/kg

The daily dose is 3-fold higher than the EPA ADI/RfD and 400-fold less than the dog LEL for cholinesterase inhibition.

3. Chlorfeninfos

ADI/RfD

EPA: 0.0015 mg/kg/day (Provisional ADI)

WHO: 0.002 mg/kg/day

NOAELs

0.05 mg/kg (rat 90-day study)

0.025 mg/kg (dog 4-month study)

Other

No information on oncogenic potential.

Tolerances/MRLs

U.S. Tolerances: 0.005 ppm in milk fat
0.2 ppm in sheep fat

CODEX MRLs: 0.008 ppm in milk
No use in sheep

Level in Lanolin Products

Highest level reported: 10.2 ppm (0.7-10.2 ppm; 12 of 25 samples)

Daily Dose to Infant

0.002 mg/kg bw

The daily exposure is at the WHO ADI and 10-fold less than the dog NOAEL for cholinesterase inhibition. WHO last reviewed chlorfeninfos in 1971.

4. Chlorpyrifos

ADI/RfD

EPA: 0.003 mg/kg/day
WHO: 0.01 mg/kg/day

NOAELs

0.03 mg/kg (cholinesterase inhibition in human 20-day study)
0.01 mg/kg (dog, cholinesterase inhibition)
0.1 mg/kg (rat, cholinesterase inhibition)

Other

Not oncogenic in rats or mice.

Tolerances/MRLs

U.S. Tolerances: 0.5 ppm in milk fat
0.02 ppm in whole milk
1 ppm in sheep fat

CODEX MRLs: 0.01 ppm in milk
0.2 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 1.6 ppm (0.1-1.6 ppm; 7 of 25 samples)

Daily Dose to Infant

0.00032 mg/kg bw

The daily exposure is 1/10 the EPA ADI/RfD and 100-fold less than the human NOAEL for cholinesterase inhibition.

5. Cypermethrin

ADI/RfD

EPA: 0.025 mg/kg/day

WHO: 0.05 mg/kg/day

NOAELs

7.5 mg/kg (rat chronic study)

1 mg/kg (dog chronic study)

Other

Weak "C" oncogen (no Q₁* estimated)

Tolerances/MRLs

U.S. Tolerances: 0.05 ppm sheep fat
0.05 ppm milk

CODEX MRLs: 0.01 ppm in milk
0.2 in carcass fat of all animals

Level in Lanolin Products

Highest level reported: 13.6 ppm (8.7-13.6 ppm; 3 of 25 samples) /

Daily Dose to Infant

0.003 mg/kg bw

The daily exposure is about 1/10 the EPA ADI/RfD.

6. p,p' - DDT

ADI/RfD

EPA: 5×10^{-4} mg/kg/day

WHO: 0.02 mg/kg/day

NOAELs

6.25 mg/kg (rat, chronic study)

10 mg/kg (monkey, 7 year study)

0.25 mg/kg (human, 25 year study)

Other

EPA - $Q_1^* = 0.34 \text{ (mg/kg/day)}^{-1}$

WHO - oncogenic in mouse; "no significant risk of DDT producing tumors in man".

Tolerances/MRLs

CODEX Extraneous Residue Limits (ERLs) for DDT + DDE

5 ppm in sheep fat

0.05 ppm in milk

Level in Lanolin Products

Highest level reported: 0.3 ppm (0.2-0.3 ppm; 3 of 25 samples)

Daily Dose to Infant

0.06 ug/kg

Background Levels in Mother's Milk

Median level in breast milk: 40.3 ppb

Daily dose to infant from DDT in breast milk: 5.64 ug/kg/day

Lifetime Cancer Risk from Lanolin on Nipples:

5×10^{-7}

Exposure from lanolin on nipples is 10-fold lower than the EPA ADI/RfD. It is 100-fold lower than the background levels found in human breast milk.

7. DDE

ADI/RfD

EPA: None developed.

WHO: see DDT

NOAELs

EPA: no data developed

WHO: see DDT

Other

EPA: same as DDT; $Q_1^* = 0.34 \text{ (mg/kg/day)}^{-1}$

WHO: same as DDT

Tolerances/MRLs

CODEX Extraneous Residue Limits (ERLs): See DDT

Level in Lanolin Products

Highest level reported: 0.3 ppm (0.04-0.3ppm; 7 of 25 samples)

Daily Dose to Infant

0.06 ug/kg

Background Levels in Mother's Milk

same as DDT

Lifetime Cancer Risk from Lanolin on Nipples

same as DDT

8. Diazinon

ADI/RfD

EPA: 9×10^{-5} mg/kg/day

WHO: 0.002 mg/kg/day

NOAELs

0.02 mg/kg (human cholinesterase inhibition as reported by Hayes)

0.009 mg/kg (rat, 90-day, plasma cholinesterase)

0.02 mg/kg (dog, cholinesterase inhibition)

Other

Not oncogenic in rats or mice.

Tolerances/MRLs

U.S. Tolerances: 0.7 ppm in sheep fat

CODEX MRLs: 0.02 ppm in milk
0.7 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 29.2 ppm (0.2-29.2 ppm; 21 of 25 samples)

Background Levels in Mother's Milk

No information.

Daily Dose to Infant

0.006 mg/kg

The exposure is 60-fold higher than the EPA ADI/RfD and 3-fold lower than the human NOAEL for cholinesterase inhibition.

9. Dichlofenthion

ADI/RfD

EPA: None developed. No U.S. uses.

WHO: None developed

NOAELs

1 mg/kg (90-day rat study - cholinesterase inhibition)
0.75 mg/kg (90-day dog study - cholinesterase inhibition)

Other

No information.

Tolerances/MRLs

U.S. Tolerances: None

CODEX MRLs: None

Level in Lanolin Products

Highest level reported: 24.3 ppm (0.2-24.3 ppm; 13 of 25 samples) /

Background Level in Mother's Milk

No information.

Daily Dose to Infant

0.005 mg/kg

Exposure is 150-fold lower than the NOAEL obtained in the 90-day dog study. Unlike diazinon, dichlofenthion has no U.S. or CODEX uses and yet it has been analyzed in 14 of 27 samples. Considering the meager amount of toxicology data this should be one pesticide of special concern since it is apparently used on sheep with little or no control.

10. Dieldrin

ADI/RfD

EPA: 5×10^{-5} mg/kg/day

WHO: 0.0001 mg/kg/day

NOAELs

None.

LELs

0.025 mg/kg (rat, minimal liver changes)

0.025 mg/kg (dog, liver changes)

Other

Q_1^* - None estimated

Tolerances/MRLs

CODEX Extraneous Residue Limits (ERLs), Dieldrin + Aldrin
0.2 ppm for meat fat
0.006 ppm for milk

Level in Lanolin Products

Highest level reported: 0.9 ppm (0.05-0.9 ppm; 12 of 25 samples)

Daily Dose to Infant

0.2 ug/kg bw

Background Levels in Mother's Milk

Median level in breast milk: <2ppb

Daily dose to infant from dieldrin in breast milk: <0.3 g/kg

Exposure from lanolin is four times the EPA ADI/RfD.
It is approximately equal to the background levels found in human breast milk.

11. Heptachlor

ADI/RfD

EPA: 0.0005 mg/kg/day

WHO: 0.0005 mg/kg/day

NOAELs

0.25 mg/kg/day (rat chronic study)

0.06 mg/kg/day (dog short-term study)

Other

Q_1^* : $4.5(\text{mg/kg/day})^{-1}$

Tolerances/MRLs

U.S. Tolerances: 0 in meat and milk

CODEX ERLs: 0.006 ppm in milk
0.2 ppm in carcass fat

Level in Lanolin Products

Highest level reported: 0.01 ppm (0.01 ppm; 1 of 25 samples)

Daily Dose to Infant

0.002 ug/kg bw

Background Levels in Mother's Milk

Median level in breast milk: 1.12 ppb

Daily dose to infant from breast milk: 0.157 ug/kg

Lifetime Cancer Risk from Lanolin on Nipples

2.56×10^{-7}

Exposure to heptachlor from lanolin is 1/250 the EPA ADI/RfD. Exposure to heptachlor from breast milk is 75 times greater than the potential exposure from the use of lanolin on breasts.

12. Lindane

ADI/RfD

EPA: 3×10^{-4} mg/kg/day

WHO: 0.01 mg/kg/day

NOAELs

1.25 mg/kg (rat chronic study)

1.6 mg/kg (dog chronic study)

Other

No Q₁* estimated

Tolerances/MRLs

U.S. Tolerances: 7 ppm in sheep fat

CODEX MRLs: 0.01 ppm in milk
2 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 1.5 ppm (0.7-1.5 ppm; 3 of 25 samples)

Background Levels in Mother's Milk

No levels detected.

Daily Dose to Infants

3×10^{-4} mg/kg bw

The daily dose is at the EPA ADI/RfD. Breast milk was analyzed for lindane, but none was detected.

13. Permethrin

ADI/RfD

EPA: 0.05 mg/kg/day

WHO: 0.05 mg/kg/day

NOAELs

5 mg/kg (rat, chronic study)

6.25 mg/kg (dog, 6 month study)

Other

Q_1^* : 2.2×10^{-2}

Tolerances/MRLs

U.S. Tolerances: 2 ppm in sheep fat
3.75 ppm in milk fat

CODEX MRLs: 0.1 ppm in whole milk
1 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 5.9 ppm (0.16-5.9 ppm; 2 of
25 samples)

Background Levels in Mother's Milk

No information.

Daily Dose to Infant

0.0012 mg/kg bw

Daily exposure is about 1/50 the EPA ADI/RfD.

Lifetime Cancer Risk from Lanolin on Nipples

7×10^{-7}

14. Phosphamidon ethyl

ADI/RfD

EPA: None determined. No U.S. uses.

WHO: None determined.

NOAELS

No information

Other

No information

Tolerances/MRLs

U.S. Tolerances: None

CODEX MRLS: None

Level in Lanolin Products

Highest level reported: 0.8 ppm (0.1-0.8 ppm; 2 of 25 samples)

Daily Dose to Infant

0.0016 mg/kg bw

No toxicology data. No information on background levels in mother's milk.

15. Toxaphene

ADI/RfD

EPA: 2.5×10^{-4} mg/kg/day

WHO: Not cleared toxicologically by JMPR

NOAELs

25 mg/kg/day

Other

Q₁*: None available

Tolerances/MRLs

U.S. Tolerances: 7 ppm in sheep fat (No U.S. uses)

CODEX Guideline Levels (as Camphechlor): 0.02 ppm in milk
5 ppm in sheep fat

Level in Lanolin Products

Highest level reported: 2.9 ppm (1.8-2.9 ppm; 4 of 25
samples)

Daily Dose to Infants

0.0006 mg/kg bw

The daily dose is about 2 1/2 higher than the EPA ADI/RfD.
No information on background levels in mother's milk.

16. BHCs (see Lindane)

Highest level reported in lanolin products is 8.8 ppm
(0.6-8.8 ppm; 3 of 25 samples)

RECOMMENDATIONS/CONCLUSIONS:

On the basis of these very simple analyses, it is obvious that few, if any, pesticide contaminants present an immediate concern to nursing infants. The estimated levels consumed, under worst-case exposure scenario utilized, are generally well below the doses producing effects of concern. In the case of organochlorinated pesticides, there are generally higher background levels in human breast milk from undetermined sources than from the potential contribution from lanolin, rendering the exposure via lanolin insignificant.

EPA recommends close scrutiny of lanolin products which contain some of the "old" organophosphates (OPs), such as bromophos ethyl, chlorfenvinphos and carbophenothion, since the data base is not current and has not undergone a recent evaluation by either EPA or WHO. These OPs were identified frequently in the 25 samples analyzed by FDA. Similarly, the OPs dichlofenthion and pirimiphos ethyl were detected in 14 of 25 and 2 of 25 samples, respectively. They have little or no toxicology data, no U.S. uses, and no evaluation by WHO/FAO. Therefore, there is no valid estimate of the safety/hazard of the levels of these 2 pesticides in lanolin products. EPA recommends a re-examination of these analyses or analytical methodology since there are no indications that they are important pesticides in international commerce (i.e. CODEX) but yet they have been detected in lanolin products.

Diazinon (a fat soluble OP) presents the greatest concern because of the frequent occurrence (21 of 25 samples) and the high levels identified (up to 29.2 ppm) in the U.S. samples analyzed. The Australian Work Group on lanolin (chaired by Dr. A. Black) found residues of diazinon up to 100 ppm in lanolin products marketed in Australia. Our examination of the toxicology data base for diazinon indicates that at the 29 ppm level detected the ADI/RfD may be exceeded. However, this existing ADI/RfD is based on a rat study with a low NOEL. In comparison, studies in dogs, monkeys and humans demonstrated higher NOELs for the same response (plasma cholinesterase inhibition). Furthermore, levels greater than 18 ppm were detected in only 3 of the 25 samples; the remainder of the positive detects were substantially lower. Therefore, diazinon, while it doesn't present an immediate health hazard at the levels found does illustrate an unnecessary potential exposure to a pesticide which should be reduced or eliminated.

The adequacy of the toxicology data bases for the 16 identified pesticide contaminants in lanolin products vary in their completeness: most are reasonably complete, some are partially complete, and a few are totally inadequate (i.e. pirimiphos ethyl and dichlofenthion). Some of these pesticides are no longer used on foods in the U.S. (organo-chlorinated pesticides), while a few have never been registered in the U.S. In general, however, where sufficient data permit comparisons to worse case exposure scenarios, there is no immediate concern to nursing infants or their mothers. Nonetheless, we believe the action taken recently by FDA (i.e. Notice of Adverse Finding) is a step in the right direction to ensure the manufacture of pharmaceutical products which are free of pesticide contaminants.