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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: LANOLIN; In-Process Revision to the USP Standard
for Lanolin (Jan-Feb, 1991)

FROM: R. Bruce Jaeger *RBJ 3/5/91*
Designated Federal Official
FIFRA Scientific Advisory Panel
Health Effects Division (H7509C)

THRU: Penelope A. Fenner-Crisp, Ph.D.
Director *PAC 3/5/91*
Health Effects Division (H7509C)

TO: Vic Warner
HFD-300
FDA

EPA has previously responded to requests from FDA concerning the finding of pesticide residues in Lanolin (memo, T. Levine to T. Farber, 10/17/88). In that memorandum we commented on 16 pesticides and our conclusion was that, given worst-case exposure scenarios, "few pesticide contaminants (of the 16) present an immediate concern to nursing infants". This was qualified by our concern for certain pesticides not registered in the U.S., those with no tox data available, or those which were identified frequently and at high levels. We recommended that, as a general principle, pharmaceutical products (such as lanolin) should be free of pesticide contaminants.

We wish to reiterate our previous recommendations/conclusions, particularly as they relate to the latest In-Process Revision to the U.S. Pharmacopeia for lanolin, dated Jan.-Feb., 1991, pgs 1357-1365 [FAX received 1/24/91, V. Warner (FDA) to B. Jaeger (EPA)].

We believe it is important to note that the proposed Table 1, pg 1360 of this In-Process Revision, includes more pesticide contaminants than the original 16. These now include: TCNB, HCB, Propetamphos, Ronnel, Malathion, Chlorfenvinphos Z, Stirophos, Endrin, Aldrin, Endosulfan (a, B), Ethion, and Methoxychlor. Thus, our 10/17/88 comments should not be interpreted loosely to include these as well. Also, two pesticides, cypermethrin and permethrin, found in FDA samples at levels up to 13.6 ppm (cypermethrin) are not listed in Table 1. There is no indication why they are not included.

A few additional comments also seem warranted, particularly when the USP is recommending setting specific limits for pesticide contaminants in lanolin. Setting a limit of 10 ppm for diazinon in lanolin seems excessive when you consider there is presently no U.S. tolerance in foods intended for human consumption in excess of 0.75 ppm for any specific commodity, and in particular, no tolerance in milk or dairy products. Similarly, there is only one CODEX CXL with a limit of 2 mg/kg; all others for diazinon are 0.7 or less. These levels are "farm gate" limits and are frequently greater than actual residues which may be consumed in/on a particular food commodity. They are intended solely to control a specific registered use. Although this relationship is highly unlikely for diazinon in lanolin, an equally conservative limit appears justified for a product intentionally applied to human skin and which is likely to be ingested by nursing infants.

Furthermore, HED looked closely at the cholinesterase inhibiting pesticides identified in the original list of 16 pesticides because of a concern for acute toxicity. Of the seven ChE inhibitors (bromophos ethyl, carbophenothion, chlorfenvinphos, chlorpyrifos, diazinon, dichlofenthion, and pirimiphos ethyl), three have no U.S. EPA registration (bromophos ethyl, dichlofenthion, and pirimiphos ethyl). A quick comparison of NOAELs, where known, to the maximum contaminant level found by FDA, demonstrated margins of safety (or "uncertainty") ranging from 15 (diazinon) to 3900 (carbophenothion). Although HED would prefer the previously proposed language which limited the amount of diazinon to 4 ppm and each additional individual pesticide to 1 ppm (from a total limit of 40 ppm for all pesticides), particularly for the ChE inhibitors, the proposed limits do not appear to pose a problem. However, this is based on an exposure estimate determined by FDA, wherein it was calculated that the maximum oral exposure to lanolin for nursing infants ranged from 0.1 gm to 0.6 gms per infant per day, based upon one to six applications per day. We used 0.2 grams in our calculations (representing two applications daily) and 10 Kg for the infant body weight. An example of our calculations for diazinon follows:

NOAEL = 0.36 ppm (or 0.009 mg/kg bw) (dog)

Max. Contaminant Level = 29.2 ppm (or mg/kg)

<u>EXPOSURE</u>	<u>vs</u>	<u>NOAEL</u>
29.2 mg/kg x 0.0002 kg = 0.00054 mg/kg bw	<u>vs</u>	0.009 mg/kg bw
10 kg bw		[equals 15.4 Margin of Safety]

Finally, pesticides which have been banned in foods or severely restricted by EPA in order to reduce or remove potential human exposure to them (e.g. aldrin, dieldrin, heptachlor, etc.) should not be permitted as contaminants in emollients which can be directly applied to human skin or result in direct oral exposure to infants from nursing. Setting a limit of 40 ppm total residue for all pesticide contaminants in lanolin (many of which are carcinogens) seems contradictory to this regulatory concern.

In this regard we believe the language regarding "Foreign Substances" should be clarified. As presently drafted it clearly is only an analytical process, in that it states that pesticides not approved for use in the country of origin of Lanolin, if included in Table 1, may be omitted from the Standard preparation mixture. Thus, an effort to simplify the analytical process without regard for those pesticides which are a health concern. In other words, there should also be language which relates to identification of those pesticides in Table 1 which are banned or not authorized in the country which imports the Lanolin. Unless this concern is also similarly identified under this heading it is going to be a difficult concept to sell to the American users (or to Congress), particularly when one considers the concern expressed for carcinogenic pesticide residues in food and exposure to children. This does not lend itself to risk/benefit analyses since there are probably several emollients which are suitable pesticide-free substitutes for lanolin, and thus would be preferred.

These comments are provided to clarify our position and our concern regarding this In-Process Revision to the USP Standard for Lanolin. We believe there should be a consistent approach by government agencies toward pesticide exposures to the U.S. population. We appreciate the opportunity to comment on this latest USP revision.