October 4, 1988

H. W. Dietz

ACTIVITIES REPORT FOR SEPTEMBER, 1988

1. Hydrophilics

After approximately five years and many proposals and reproposals, the carbomer monographs have been published in the 8th supplement to the USP-NF. The monographs are for Carbomers 910, 934, 934-P, 940, 941 and 1342. The monographs correspond to the respective Carbopol resins.

Formal publication of these monographs recognizes the use of the cross-linked polyacrylic acid resins as pharmaceutic ingredients. Such recognition should make it easier to obtain FDA clearance for use of the Carbopol resins in pharmaceutic preparations. Also, the FDA Division of Cosmetic Technology has never formally accepted the generic name "Carbomer" for labeling purposes. Since USP-NF is an official compendium by law, inclusion of the carbomers adds authority for the use of this name for labeling purposes.

The Cosmetic, Fragrance and Toiletry Association (CTFA) had adopted the name Carbomer 1342 for Carbopol 1342, but later rescinded it to reevaluate the nomenclature for all acrylic based resins. This left our C-1342 cosmetic customers without a solid basis for labeling. I have talked to CTFA about the NF carbomer monographs and have sent them a copy. Hopefully, the NF monograph should resolve CTFA's dilemma.

EPA had expressed concern about applicator exposure to residual benzene and acrylic acid from pesticides containing Carbopol 1342 as an inert ingredient. EPA has evaluated and concurred with the information I submitted that demonstrates that applicator exposure to residual benzene and acrylic acid would be essentially nil under foreseeable use conditions. A Federal Register notice is being prepared to permit the use of Carbopol 1342 as an inert ingredient in pesticide applications.

There is current interest in the use of polycarbophil in opthalmic and bioadhesive applications. We have petitioned the USP to reactivate the polycarbophil monograph with some revisions. Polycarbophil was omitted from USP-XXI when the calcium polycarbophil monograph was adopted. Both polycarbophil and calcium polycarbophil were evaluated as safe and effective by the FDA Over the

Counter (OTC) Panel for use as bulk laxatives and antidiarrheals. However, since the calcium form is the actual dosage form used in such products, the monograph for the acid form was not retained.

Since polycarbophil is a cross-linked polyacrylic acid, USP has proposed to change the name and issue a carbomer NF monograph for it. NF monographs are for drug ingredients (i.e. inactives) not drugs. Some of the current interest is for use as an active ingredient. Therefore, the proposed change could not only hurt BFG marketing efforts but could pose a variety of problems for the current proposed uses. We have enlisted Dr. J. Robinson (U. of Wisconsin), who has several vital interests in the use of polycarbophil as a drug, to help maintain its USP status. Dr. Robinson is on the USP General Revisions Committee, the USP Pharmaceutical Ingredients and Pharmaceutics committees.

2. No Foul

The Organotin Antifouling Paint Control Act of 1988 establishes a certifying program for antifouling paints, coatings or treatments under which only those that do not exceed a release rate of 4 micrograms organotin per square centimeter per day may be sold and used. Companies who had not submitted release data to EPA had 30 days to submit the data or lose FIFRA registration. The required release rate method is not usable for No Foul. I discussed the situation with the EPA Special Organotin Manager. She felt we could use the calculated average release rate, but would confirm it and let me know within the week.

As a consequence of unanswered, unreturned phone calls and expiring time, I submitted a written explanation along with a request for exemption from the data requirements. I requested the BFG Washington, D. C. office to follow up. Marie Taylor reported that EPA was too busy to talk on the phone until after Oct. 1. They felt that the information sent would suffice and would call the week of October 3rd.

3. Geons

I reviewed the status of the use of lead and cadmium based pigments and stabilizers in food contact articles, drugs, cosmetics, medical devices and water in the U.S. for the Geon Division. There are no specific regulations which prohibit the use of these materials in food contact articles, however FDA has set action levels for leachable lead and cadmium from ceramic ware of 2.5-7 ppm and 0.25-0.5 ppm respectively. EPA has set an MCL for water of 50 ppb lead (to be reduced to 10 ppb) and 10 ppb cadmium. Except for lead in paint, there are no other

regulations limiting these substances in other consumer products, drugs, cosmetics, etc. California Proposition 65 lists lead as a reproductive toxin and cadmium as a carcinogen and therefore the provisions of this law would apply. In Europe a total of 0.010% lead is allowed in food contact articles and consumer products; a range of 0.01 to 0.2% cadmium solubles in hydrochloric acid, as an impurity.

Kessler Products, Youngstown, Ohio, has been using Geon 87446 trans 001 in the manufacture of toys. They wanted a PVC compound that had FDA clearance for food contact for this purpose but were reluctant to pay a premium for it. Bob Littel, Geon, requested that I review 87446 trans 001 to determine why it was not listed as an "FDA" compound. My review revealed that 87446 trans 001 is acceptable for use in contact with all food except liquid milk. Consequently, Kessler Products has been unknowingly using an FDA acceptable compound all along, while apparently paying for a general purpose one.

Geon 87403 trans 002 has been listed as an FDA acceptable compound since 1985. I had not been requested to review the FDA status of this compound until recently. My review showed that although the ingredients in 87403-002 had some FDA clearance, they were not being used in accord with the use condition limitations set by FDA. Therefore, Geon 87403 trans 002 is not in compliance and hence not acceptable for food contact applications. As a result of this finding, marketing has requested ALTC to submit all Geon compounds now listed as "FDA cleared" for my review. Apparently there are a number I have never reviewed so listed.

4. Estanes

Additional information on Estanes 58311 and 58630 was submitted to the FDA for inclusion in Drug Master File #5361. This information was requested by the FDA to help support Wisconsin Pharmacal's use of these polyurethanes in their "female" condom application. The information submitted included: the molecular rations of monomers; raw materials specifications and control; molecular weight distribution of polymeric raw materials; specifications and typical properties of the Estane compounds; typical molecular weight distribution of the polyurethane resin; and toxicity data on the raw materials and polyurethane.

Ortho Pharmaceuticals, Canada, is considering the use of Estane polyurethanes to fabricate male condoms. A tentative meeting with Ortho has been set for October 20 to review various aspects of this use including toxicity tests that may be needed.

Two European Estane masterbatches were reviewed for their FDa status. One was acceptable, while I could not find information to determine the FDa status of the polyurethane resin in the other.

5. SP&C

I reviewed the FDA status of ethylene-vinyl acetate, ethylene-vinyl chloride and vinyl chloride-vinyl acetate copolymers last month. In a discussion with John Cavanaugh, it was evident that SP&C was interested in what the industry calls "ethylene-vinyl acetate" polymers. These are terpolymers, etc. Consequently, I reviewed the FDA status of copolymers of various combinations of ethylene, vinyl acetate, vinyl chloride, acrylic acid, itaconic acid, acrylamide and n-methylol acrylamide. The review included 13 regulations of over two dozen different copolymer compositions.

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