

Minutes of Meeting

February 25, 1985

10:00 am

Attendees: Industry and Press

Anthony R. Temple, M.D., McNeil Consumer Products
Company
Diane Thilman, Menley & James Laboratories
J. Greg Parkins, Burroughs Wellcome Company
Linda Harun, A. H. Robins Company
Leonard D. Fantasia, CIBA Consumer
Pharmaceutical Company
George Latyszoath, Bristol-Myers Products
Doris Mathis, Perito, Duerk, & Pinco
Liz Liperstein, FDC Reports
Bill Pawlson, FDC Reports

and

Food and Drug Administration

Patricia H. Russell, M.D., (HFN-160)
Philip G. Walters, M.D., (HFN-160)
Robert L. Donahoe, M.D., (HFN-160)
James R. Gebert, (HFN-160)
Gerald M. Rachanow, Esq., (HFN-210)
Saul Bader, Ph.D., (HFN-213)
Anne J. Mustafa, (HFN-213)

Subject: Changing Children's Dosage Schedules for OTC
Antihistamine and Nasal Decongestant Drug Products to Provide
More Age Intervals, to Add Weight-Based Dosages, and to Extend
OTC Package Labeling Dosage Schedules for Antihistamines Down
to 2 Years of Age

After brief introductions, Dr. Temple of McNeil presented
several concerns the company has regarding the children's
dosage schedules that were recently proposed by the agency in
the published tentative final monographs for OTC antihistamine
and nasal decongestant drug products. He said that he is
currently heading a subgroup of the Proprietary Association
(PA) that is working on developing consistency in the
marketplace for pediatric dosages for OTC drug product
categories such as internal analgesics, antitussives, nasal
decongestants, and antihistamines. Dr. Temple added that the
PA subgroup is developing comments on the agency's proposed

rules for these drug categories that will request changes in the proposed pediatric dosing schedule to provide consistency among the rulemakings.

Dr. Temple explained that to achieve a consistent approach to pediatric dosing of OTC drug products in the marketplace and in the agency's rulemakings, the dosage schedules should provide (1) relatively fixed dosage forms, (2) sufficient flexibility in the dosage schedules by basing the schedules on weight and age, (3) the ability to correlate dosing with a greater subdivision of standard age breaks, and (4) ease of physician and consumer use. He pointed out that there are significant differences between the pediatric dosing schedules recommended by the Advisory Review Panel on OTC Internal Analgesic and Antirheumatic Drug Products for internal analgesics and the agency's pediatric dosing schedules for cough-cold drug products such as antihistamines and nasal decongestants. The children's dosages for antitussives, nasal decongestants, and antihistamines provide two age ranges for children under 12 years of age (6 to under 12 years and 2 to under 6 years with professional labeling only for the use of antihistamines in the under 6 age group) whereas the children's dosages for internal analgesics provide five shorter age ranges for children under 12 years of age (11 to under 12 years, 9 to under 11 years, 6 to under 9 years, 4 to under 6 years, and 2 to under 4 years). McNeil believes that the pediatric dosage schedule for internal analgesics is better than the dosage schedules for cough-cold drug products because the internal analgesic dosage schedule correlates more closely with the practice of basing children's dosages on body weight. Dr. Temple stated that the use of body weight is widely accepted by pediatricians as a preferred method of determining drug dosages for children. In addition, it is well recognized that variations in weight have a significant impact on appropriate dosage levels for different individuals, and that body weight varies significantly with age for children between the ages of 2 and 12 years because this is a period of rapid growth. Therefore, it is appropriate to have a greater subdivision of age ranges in the recommended dosages for the 2 to 12 year age group so that the dosages correspond better to body weight variations due to rapid growth.

Dr. Temple proposed that a standard pediatric dosing unit be established based on both weight and age considerations and suggested that a good standard pediatric dosing unit would be one-eighth of the adult dose. This standard pediatric dosing unit would correlate with 6-pound increments as a child grows and could be used with the 50th percentile weights for age ranges to produce the following dosing increments for the given age and weight ranges:

<u>Age Range</u>	<u>Weight range</u>	<u>Appropriate Number of Dosing Units</u> (1 dosing unit = 1/8 adult dose)
4 to 11 months	12-17 lbs.	1
1 to under 2 years	18-23 lbs.	1.5
2 to under 4 years	24-35 lbs.	2
4 to under 6 years	36-47 lbs.	3
6 to under 9 years	48-59 lbs.	4
9 to under 11 years	60-71 lbs.	5
11 to under 12 years	72-95 lbs.	6
12 years and over	96 + over lbs.	8

Dr. Temple pointed out that applying the above dosing schedule to OTC drug products would not result in doses that exceed the currently proposed doses for internal analgesics where toxicity is a real concern, and yet would prevent underdosing of older children at the top end of the cough-cold dosing age range of 6 to under 12 years. He added that OTC drug labeling should consider the needs of children who are in the tenth or ninetieth percentile ranges for weight by including weight ranges in addition to age ranges for dosing.

Dr. Donahoe of FDA said that McNeil's basic premise that pediatric doses for cough-cold drugs should be more closely related to weight-based and age-related parameters is sound; however, we still need to be sure that the doses are effective. For example, in the case of the antitussive dextromethorphan the data to support revising children's dosages is scant. Dr. Temple replied that not much data are available for many OTC drug products, but that the basic premise of McNeil's request to revise the pediatric dosage schedules still applies and would make pediatric dosing consistent in the marketplace.

Dr. Temple then presented some data from a survey of 200 pediatricians concerning their use in children of OTC cough-cold and internal analgesic drug products as well as their preferences for the pediatric labeling of these drug products. When asked whether they recommend the use of these products in children in the age ranges of 2 to 5 years and 6 to 14 years, over 90 percent said that they did recommend use in both age ranges with the exception of aspirin (51 percent in favor of use in the 2 to 5 year group and 60 percent in favor of use in the 6 to 14 year group). Responses to how the pediatricians determine the dose of cough-cold or internal analgesic drugs for children varied widely from using the "Physician's Desk Reference" (PDR) or other pediatric handbooks to personal experience in using the drugs in children. Dr. Temple pointed out that these wide variations in determining

pediatric doses lead to inconsistent dosing of children. Although the proposed OTC drug labeling provides a basis for consistency in dosing for children 6 years of age and over, dosing for children under 6 years is less consistent if the OTC labeling, e.g., the proposed antihistamine labeling, does not provide dosages for children in this age group. When asked what dosing parameters, i.e., age, weight, age and weight, body surface, or other parameter, the pediatricians would prefer in the labeling of OTC drug products, the majority (61 to 63 percent) said that they would prefer age and weight dosing parameters in the OTC labeling of antihistamines, antitussives, nasal decongestants, and internal analgesics. The survey revealed that the majority (51 percent) of the pediatricians believe that pediatric dosing information for children under 2 years of age in OTC drug labeling would be "very beneficial" and an additional 34 percent believe such labeling would be "somewhat beneficial." Mr. Rachanow asked whether the survey sought information as to where the pediatricians would prefer pediatric dosing information, e.g., in OTC drug labeling or in the PDR. Dr. Temple replied that a specific question on preference of the source of pediatric dosing was not included in the survey. However, in response to a question concerning the comfort level of including pediatric dosing information in OTC drug labeling, most pediatricians expressed a "high comfort level" with such labeling. Mr. Rachanow asked if the survey had determined how pediatricians feel about parents using OTC drug products (specifically antihistamines) in their children ages 2 to 5 years without contacting a doctor first. Dr. Temple replied that McNeil doesn't have any information on this, but that he believes it is better to have the information on the label to provide consistency in dosing even though parents may use the product in children without contacting a doctor.

Dr. Temple summarized the following points that McNeil is asking FDA to consider:

1. There should be a greater subdivision of pediatric dosing age ranges for OTC cough-cold products than the 2 to under 6 years and the 6 to under 12 years ranges proposed by FDA, and that the age ranges should be more consistent with the dosing age ranges for OTC internal analgesics.
2. Body weight should play a significant role in determining pediatric dosages.

3. There is a need to provide more consistency in OTC pediatric dosage labeling. This can be accomplished by using McNeil's proposed standard pediatric dosing unit of one-eighth of the adult dose and age ranges based on 50th percentile weights to establish pediatric dosage schedules.

4. There is not a good reason to exclude dosing information in OTC drug labeling for children under 6 years of age for antihistamines and for children under 2 years of age for antitussives, nasal decongestants, and internal analgesics. Although parents may use these drug products in young children without first contacting a doctor, McNeil believes that it is better to have consistent information available to the physician and to the parent in the labeling. This should reduce the possibility of inappropriate dosing in the younger age groups.

Dr. Temple asked for feedback on what appropriate information concerning the above matters McNeil should include in its comments to the published rulemakings for OTC antihistamines and nasal decongestants. Agency staff gave Dr. Temple the following feedback:

1. McNeil needs to present data demonstrating the safety of using OTC antihistamines in children under 6 years of age. OTC antihistamines are comprised of several drug classes that may be different with respect to the safety of use in children. Therefore, it would be appropriate to provide data for specific ingredients and/or classes of ingredients because differences in safety may support OTC use in the younger age group for some ingredients, but not for others.

2. Because children under 6 years of age may be particularly vulnerable to adverse reactions and possible inadvertent overdosing, McNeil needs to strongly support the safety of any requested dosage revisions in this age group.

3. Suggested sources of safety data included FDA adverse reaction reports and the open literature. Although safety data within recommended dosage ranges are particularly pertinent to supporting safe use of a drug in young children, some attention should be given to the seriousness of the effects of overdoses of the drugs in children.

4. McNeil should consider the need for requiring calibrated measuring devices in the packaging of products with labeling for use in young children. This will insure accurate dosing in an age group that may be particularly vulnerable to adverse effects due to inadvertent overdosing.
5. McNeil should consider the impact of revised dosing schedules on combination drug products.
6. McNeil should consider the need for and suggest appropriate additional labeling directions and warnings for antihistamines that could address possible safety concerns when these drugs are used in children under 6 years of age.
7. McNeil should seek the concurrence of organizations such as the American Academy of Pediatrics for its proposed pediatric dosing schedules. Working with PA may help manufacturers to develop consistent pediatric dosage schedules.
8. Although weight-based and age-related pediatric dosage schedules are preferred in general, issues concerning the safety and effectiveness of particular ingredients at revised dosage levels cannot be ignored.

Mr. Rachanow suggested that McNeil submit comments on the above matters to the rulemakings for antihistamine drug products and for nasal decongestant drug products before the May 1985 closing date of the administrative records for these rulemakings. If all the necessary data and information are not ready for submission before the May 1985 closing date, the company can indicate its intention to submit further data during the 1-year period provided for submitting data.



Anne J. Mustafa

McNEIL

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February 6, 1985

William E. Gilbertson, Pharm. D.
Center for Drugs and Biologics
Food and Drug Administration
5600 Fishers Lane HFN 210
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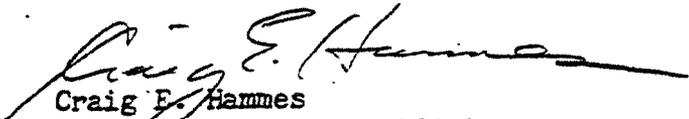
Re: Docket No. 76N-052A

Dear Dr. Gilbertson:

We intend to submit written comments to the above referenced docket before May 15, 1985. Before completing these written comments, we would like to meet with you to discuss the content and format of our submission. Ms. Ann Mustafa of your office has confirmed by telephone your intent to meet with us on Monday, February 25, 1985 at 10:00 a.m.

The specific items which we wish to discuss are 1) pediatric dosage breakdowns by weight as well as by age, 2) greater subdivision of dosing ranges (by both age and weight), and 3) consumer labeling for use by children under 6 years of age. Attending this meeting for McNeil Consumer Products Company will be Craig E. Hammes, Director, Regulatory Affairs and Anthony R. Temple, M.D., Medical Director, Pediatrics.

Sincerely,


Craig E. Hammes
Director Regulatory Affairs

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0065d



Memorandum

MARK 5 1985

Date

From Director
Division of OTC Drug Evaluation (HFN-210)

Subject Material for Docket No. 76N-052N

To Dockets Management Branch (HFA-305)



The attached material should be placed on public display under the above referenced Docket No.



This material should be cross-referenced to Comment _____.

William E. Gilbertson, Pharm. D.

Attachment