CHPA

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November 28, 2007

Dr. Charles Ganley
Director, Office of Nonprescription Products
WO22-5474
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

Dear Dr. Ganley:

Thank you for the opportunity to present our voluntary plan to address concerns surrounding the safety and efficacy of OTC oral pediatric cough and cold medicines. CHPA and its member companies who make oral pediatric cough and cold medicines strongly believe that the current data support the safety and efficacy of these medicines; however, we are committed to taking aggressive industry actions to better advance the science and enhance consumer safety around the use of these products. Based on our own thorough analysis of the data along with those concerns raised at the October 2007 advisory committee, CHPA, on behalf of its member companies, commits to the following initiatives:

Commitments Within the "Drug Facts" Label

1. **Label directions for children under age two.** Companies are changing "ask a doctor" to "do not use" for children under 2 years of age in the directions section of all OTC oral cough and cold medicines. Further, for products designed for use in children where current label directions read "ask a doctor" for children under 6 years of age, companies will add "do not use" for children under 2 years of age. While companies are beginning the label change process now, it will take several months before we anticipate these changes will be completed and products are shipped. Labels shipped will be changed through the next cough and cold season (i.e., the 2008/2009 season).

2. **Monograph products containing antihistamines for children age two to under six.** Companies are adding a warning to the warnings section of the label for OTC oral cough cold products containing a monographed antihistamine to read: "Do not use to sedate children" or "Do not use to make a child sleepy". While companies are amenable to working with the agency to test alternative wording of this statement (using the most consumer-friendly word among "sedate," "sleepy," or "sleep", for example), in the interest

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of moving ahead for the next cough and cold season, companies are beginning the label change process now.

3. **Monograph products containing antihistamines for children age two to under six.** Companies are adding an additional statement to the directions section of the label of products containing a monographed antihistamine to read: "do not use unless directed by a doctor," or "do not use unless under a doctor's supervision" in place of the existing direction to "ask a doctor" in children 2 to under 6 years of age. Again, label changes are beginning now, with completion in the next cough and cold season.

4. **Products containing label directions for children age two to under six.** Companies are adding an additional statement to the directions section of oral cough and cold medicines without an antihistamine to add "ask a doctor" to the existing directions for children 2 to under 6 years of age.

We firmly believe that all four of the label changes described above can make a positive impact on safe, responsible use of these medicines. Since these changes go *beyond* the label language required under the relevant cough and cold monographs, as opposed to departing from it, we trust in the agency's judgment to exercise enforcement discretion and not act against products labeled with these changes. Similarly, we trust in the agency's judgment to exercise enforcement discretion and not act against products labeled with these changes under new drug applications or abbreviated new drug applications. While NDA holders will, of course, file labeling supplements with the agency, NDA and ANDA holders are moving ahead now to make these changes.

Illustrations of labels with these changes are attached: one with a monographed antihistamine, and one without.

Additionally, all of these label changes will be reinforced through our national education campaign, as described below.

Additional Labeling Commitments

1. **Claims.** Companies intend to stop use of references to "doctor recommended" or similar language in children's OTC oral cough and cold medicine labeling. While such language is truthful and not misleading where appropriately substantiated, our member companies are aware of the criticisms of the advisory committee and are taking this voluntary step. Any reintroduction of similar terms would only be on the basis of substantiated, robust support. Label changes are beginning now, with completion by the next cough and cold season. Companies will also stop such references in advertisements, and advertising changes will begin immediately.

2. **Principal display panel.** Companies are adding the name of active ingredients in oral cough cold combination products to the principal display panel of packages, adjacent

to the purposes. Label changes are beginning now, with completion in the next cough and cold season.

Packaging Commitments

1. **Dosing devices.** For liquid products, companies plan to review any dosing devices packaged with their products to remove extraneous marking systems that do not correspond to a marking system on the label (i.e., "teaspoon" [tsp], or "ml"). In other words, for example, a dosing device would not have tablespoons, ounces, and milliliters where the label only had milliliters. Rather, it would only have milliliters in this example. Companies will also review and make any indicated changes to dosing devices packaged with their products to confirm dosing devices include markings for amounts directed in their labeling.

Looking ahead, for liquid products, companies are interested in moving from the current situation with a mix of "teaspoon" and "ml" dosing directions toward the use of "ml" only. However, we do not believe there is sufficient acceptance of "ml"-only at this time, and we believe changing all labels and dosing devices to solely using "ml" now has the potential to increase confusion rather than decrease it.

We look forward to opportunities to work with the agency should the agency want to remove "teaspoon"-based directions and use only "ml"-based directions in the future.

The process of changing dosing devices will begin immediately, with shipments during the next cough cold season.

2. **Child-resistant packaging.** While many pediatric cough and cold products already use child-resistant packaging, either as required by Consumer Product Safety Commission regulations or voluntarily, depending on the ingredients in the product, companies will now plan to use child resistant-packaging on all OTC oral pediatric cough and cold products.

We recognize child-resistant packaging issues are under the jurisdiction of CPSC, rather than FDA, but believe this is an important element in the safe use and safe keeping of these medicines.

Companies plan to move ahead expeditiously on this front, targeting changes in packaging during the next cough and cold season. Because testing of packaging is required to meet CRP standards, we anticipate a few products in non-CRP packing will remain at the beginning of the next cough and cold season.

Science and Surveillance Commitments

1. **Pharmacokinetic studies.** Companies plan to conduct pharmacokinetic studies for single ingredient phenylephrine, dextromethorphan, brompheniramine, diphenhydramine, and doxylamine in children 2 to under 12. Companies wish to discuss with FDA any perceived additional needs beyond existing PK studies conducted for pseudoephedrine and chlorpheniramine in children 2 to under 12.

We ask that a team of member company scientists have the opportunity to meet jointly with FDA officials as soon as possible to review study methodologies and to discuss expectations on these PK studies. While we want to plan these trials and share their results jointly, the PK studies themselves will be conducted by individual companies on the named ingredients. The process to begin PK studies will begin immediately.

2. **Efficacy program.** We ask that a team of member company scientists have the opportunity to meet jointly with FDA officials in early 2008 to discuss appropriate situations for extrapolation (among different pediatric age groups, for example), study methodologies, and endpoint validation expectations where efficacy studies are needed.

3. **Safety surveillance.** Companies plan to establish a safety surveillance program through the Rocky Mountain Poison and Drug Center to track, evaluate, and determine risk scenarios and root causes of: (a) any new fatal and non-fatal serious adverse events pooled from companies' databases and FDA's AERS; (b) any new moderate, major, or fatal poison control center cases; and (c) new cases in English language medical literature and news reports. This program using real-time surveillance methods will begin in January 2008. An independent expert panel will review all of these cases quarterly. We will provide reports to the agency on our findings.

We would welcome the opportunity to describe our safety surveillance program plans to agency officials in more depth.

Advertising and Education Commitments

1. **Advertising.** To further underscore our commitment to the safe use and safe keeping of pediatric cough cold medicines, companies intend to add an additional statement in their advertising that underscores a key educational message. OTC medicine advertisements already voluntarily include a statement encouraging consumers to read and follow the label. Examples of an additional message could include:

- Always read and follow the label exactly
- Ask a doctor or pharmacist with questions about appropriate use
- Do not use two products for the same symptom
- Keep all medicines out of reach of children

Member companies will begin adding one or more messages of these types to their advertising immediately.

2. **Education campaign.** We have already begun our "Safety First" education campaign to educate caregivers, particularly parents, about safe pediatric dosing. A copy of this plan is attached, describing the campaign's mission, strategies, and planned educational materials.

These strong steps will have a positive impact on the safe and responsible use of these medicines and, working with the agency, advance the science that supports their safety and effectiveness. We look forward to moving ahead.

Sincerely,

Linda A. Suydam

Linda A. Suydam, D.P.A.
President

Attachments: Label illustration – combination, no antihistamine
Label illustration – monographed antihistamine
National education plan

cc: Dr. John K. Jenkins, Office of New Drugs, FDA

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