

Testimony on OTC Cough and Cold Products for Children  
Docket # FDA-2008-N-0466

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Thank you for the opportunity to testify today. This Part 15 hearing marks the start of an important effort by the agency to change the monograph governing OTC cough-and-cold preparations for children.

The agency is re-opening the regulation because, in the words of Dr. Janet Woodcock, the director of the Center for Drug Evaluation and Research, “[T]his is an opportunity to apply modern science to evaluate these products.”<sup>1</sup>

There is no time to waste. As many as 10% of U.S. children are using these products in a given week, as companies are still widely marketing these products as safe, effective, and physician recommended.

These claims are untrue.

Many reports and scientific papers document safety risks, including associations with 123 deaths between 1969 and 2006 among children from birth to six years of age.<sup>2</sup> There are thousands of related poison control calls and emergency department visits each year.

No properly designed studies demonstrate that these products are effective in children. Since the advisory committee hearing last year, four more peer-reviewed studies have been published that further undermine the claim that these products are safe and effective for use in children. A summary of these studies is attached. (See Attachment 1.)

Numerous expert groups and professional organizations, including the American Academy of Pediatrics<sup>3</sup> and National Association of Pediatric Nurse Practitioners,<sup>4</sup> have recommended that parents not give cough-and-cold preparations to young children. FDA’s own advisory committee agreed with our petition and urged that OTC cough and cold preparations for children under age six be pulled from the market immediately.<sup>5</sup>

Unquestionably, these products fail to meet the statutory requirement of “generally recognized as safe and effective.”<sup>6</sup>

Today's hearing signals that FDA agrees with the fundamental premise of our petition. The agency is here because it cannot assure the public that these products are safe and effective for use by children. The products do not today meet the requirements of the law.

The public has a right to understand what we all understand.

As soon as possible, the FDA should counter the marketing exposing millions of Americans to misleading claims of effectiveness, safety, and support from physicians with a clear statement to the public: Cough-and-cold preparations for young children have not been shown to be safe and effective according to modern standards. FDA should recommend that parents not give these products to children under age six until they are shown to meet these standards.

FDA should call for a voluntary withdrawal of cough-and-cold preparations that are marketed for children under age 6, and companies should comply with the request.

Simultaneously, FDA must move quickly to amend the OTC monograph, to make products that are not generally recognized as safe and effective illegal under federal law.

By January 2009, after the close of public comment period in December, FDA should announce the principle that OTC cough and cold products indicated for pediatric use must meet the same modern safety and efficacy standards as the agency has applied to prescription medications. There should not be a lower bar for pharmaceuticals used by as many as 10% of U.S. children each week.

The process for obtaining data on pediatric uses of cough and cold products should be similar to the process used for prescription medications, namely:

First, FDA should publish a list of ingredients for which the evidence of risk to children is so compelling that it will move immediately to remove these products from the market.

For ingredients such as phenylpropanolamine, there is strong evidence of significant risk to children. There is no amount of reduction in nasal congestion that will balance out against the potential risk of stroke.

These products are not cures for cancer. The common cold is a self-limited illness. Where there is compelling evidence of potential life-threatening side effects – where the risk-benefit balance will never be favorable for the common cold -- FDA can and should make that very clear. Upon publication of this list, the agency should promptly amend the monograph using interim procedures using to exclude these ingredients.

Second, for other ingredients, companies should be invited to propose how to demonstrate safety and effectiveness with studies, and the agency scientists should

determine whether the proposal is satisfactory. The agency should set an April 2009 deadline for companies to propose which ingredients and combinations are planned for study, to have appropriate discussions about study design with FDA, to commit to do those studies, and to propose a schedule for completion.

As a result, by April of next year, FDA will know whether there is any chance of new evidence coming in on particular ingredients or combinations.

This leads to step three. If the industry fails to propose a study for a particular drug or drug combination, then, in April 2009, the agency should use interim procedures to amend the monograph to exclude its use. Similarly, if the agency and the industry cannot reach agreement on the appropriate study design for a particular drug or drug combination, then the agency should do the same.

Fourth, FDA should review the industry's progress on a quarterly basis. If studies of a particular drug or drug combination are not moving forward, the agency should take action to amend the monograph to exclude its use.

This four-step approach has the advantage of giving the industry the ability to make the case for particular ingredients or combinations, while at the same time not providing indefinite periods of time for delay.

Finally, I would like to comment on what may be holding the FDA back from taking the decisive action called for by the agency's advisory committee: Fear that the removal of over-the-counter cough and cold preparations from the market will lead parents to give children inappropriate doses of other formulations, thereby increasing risk. This kind of overdose is called a therapeutic misadventure (as opposed to an accidental overdose, the kind where a child gets into the medicine cabinet).

The logic of this concern assumes parents will ignore safety warnings against use in children and give inappropriate products to their children. As a pediatrician, I find this scenario unlikely, because in my experience, parents of all backgrounds listen to warnings and generally do what is right for their kids. In addition, the history of medication use in children is that parents do respond to public health warnings and advise. The sharp decline in Reye Syndrome that coincided with new restrictions on aspirin use for children is a case in point.<sup>7</sup>

However, the best response to this concern is not just one pediatrician's experience or a historical analogy. The best response is data that is right under our noses.

In October 2007, companies withdrew, in the middle of much publicity, OTC cough and cold products marketed for use by young infants (under age 2).

According to clinical intuition and historical inference, this action should have led fewer parents to use these dangerous products, with fewer resulting problems.

According to the agency's worst-case scenario, however, the voluntary withdrawal last October should have led to even more problems as parents continued to give higher doses of products intended for older children.

We now have data from Maryland Poison Control to answer this question.

These data show that calls for cough-and-cold medications for children under age 2 declined 40%, from 99 to 60, in the first six months of 2008 compared to the first six months of 2007.<sup>8</sup> Looking just at calls for what we would call therapeutic misadventures, the drop was even greater, of 54%, from 41 to 19.<sup>9</sup> All of these declines were far greater than the modest declines for children ages 2 to 6, where the decline in therapeutic misadventures was 15% from 83 to 70.<sup>10</sup> More detail on these data is provided in an attachment. (See Attachment 2.)

The feared increase in poisonings simply did not happen. In fact, the opposite occurred. Infants in Maryland are safer because of the industry's voluntary withdrawal.

And I would also note that this positive outcome happened before companies made changes to the packaging of products for older children and without a major effort to warn parents of the risk of giving the products to infants.

Both of these steps would have reduced the risk further.

I urge FDA not to let fear without basis guide its decision-making. Parents deserve to know the truth about products for their children. A strong public health education campaign, led by FDA and CDC, will dramatically reduce the potential harm of these products and their adult counterparts to U.S. children.

Quick regulatory action will put these products on a firm, modern, scientific foundation.

I appreciate the important work of FDA to protect children, families, and the public health. Thank you for the opportunity to submit testimony.

## Endnotes

1. Stein, R. FDA to Revise Rules for Cold Medicines Meant for Children. *Washington Post*, 23 August 2008: A2.
2. Food and Drug Administration, Division of Drug Risk Evaluation. Nonprescription Drug Advisory Committee Meeting: Cold, Cough, Allergy, Bronchodilator, Antiasthmatic Drug Products for Over-the-Counter Human Use. 2007:29. Memorandum. Accessed on September 23, 2008 at <http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf>.
3. Testimony of David Bromberg, MD on behalf of the American Academy of Pediatrics before the Joint Meeting of the Food and Drug Administration Nonprescription Drugs Advisory Committee and Pediatric Advisory Committee, 19, October 2007. Accessed September 24, 2008 at <https://www.aap.org/sections/socpt/cough&cold-FINAL10-15.pdf>.
4. Patricia Jackson Allen, RN, MS, PNP, FAAN. National Association of Pediatric Nurse Practitioners Testimony before the FDA Advisory Committee. 17 October 2007. Accessed on September 24, 2008 at [http://www.napnap.org/userfiles/File/Testimony\\_of\\_Patricia\\_Jackson\\_Allen\(1\).doc](http://www.napnap.org/userfiles/File/Testimony_of_Patricia_Jackson_Allen(1).doc).
5. Food and Drug Administration. Over the Counter Cough and Cold Medications for Pediatric Use: Notice of Public Hearing. (Accessed on September 24, 2008 at [http://www.regulations.gov/search/search\\_results.jsp?css=0&N=0&Ntk=All&Ntx=mode+matchall&Ne=2+8+11+8053+8054+8098+8074+8066+8084+8055&Ntt=FDA-2008-N-0466&sid=11C95A2EA574](http://www.regulations.gov/search/search_results.jsp?css=0&N=0&Ntk=All&Ntx=mode+matchall&Ne=2+8+11+8053+8054+8098+8074+8066+8084+8055&Ntt=FDA-2008-N-0466&sid=11C95A2EA574)).
6. Code of Federal Regulations. Volume 5, Title 21, Subchapter D, Part 330 – Over-the-Counter (OTC) Human Drugs which are Generally Recognized as Safe and Effective and Not Misbranded. Accessed on September 24, 2008 at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=330.1>.
7. Belay, ED, et al.. “Reye’s Syndrome in the United States from 1981 through 1997.” *New England Journal of Medicine*. 1999;340(8): 1377-1382.
8. Correspondence from Suzanne Doyon, MD, ACMT, Medical Director, Maryland Poison Center, to the Baltimore City Health Department (September 17, 2008). See Attachment 2.
9. Correspondence from Suzanne Doyon, MD, ACMT, Medical Director, Maryland Poison Center, to the Baltimore City Health Department (September 17, 2008). See Attachment 2.

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**Attachment 1:**      Original Research on Over-the-Counter Cough and Cold Medications, Published since October 2007

- 1) Paul, I, et al. “Effect of Honey, Dextromethorphan, and No Treatment on Nocturnal Cough and Sleep Quality for Coughing Children and Their Parents.” *Archives of Pediatrics & Adolescent Medicine*. 161:12 (December 2007) 1140-1146.
  - The authors compared the effects of dextromethorphan with no treatment on cough frequency, cough severity, bothersome nature of cough, and child and parent sleep quality among the 105 children, aged 2-18 years. They found that dextromethorphan “was not better than no treatment for any outcome.”
  
- 2) Schaefer M, et al. “Adverse Events from Cough and Cold Medications in Children” *Pediatrics*. 121:4 (April 2008) 1-5.
  - A two-year survey of 63 US emergency departments found that an estimated 7091 patients under age 12 were treated annually for adverse drug events from cough and cold medications, “accounting for 5.7% of emergency department visits for all medications in this age group.” 64% of these visits were for children aged 2 to 5 years.
  
- 3) Rimsza ME and Newberry S. “Unexpected Infant Deaths Associated with Use of Cough and Cold Medications.” *Pediatrics*. 122:2 (August 2008) e318-e322.
  - According to autopsy reports, ten unexpected infant deaths in Arizona in 2006 were associated with use of over-the-counter cold medication. The authors conclude, “... these findings suggest that warnings on these medications ‘to consult a clinician’ before use are not being followed by parents.”
  
- 4) Vernacchio L, et al. “Cough and Cold Medication Use by US Children, 1999-2006: Results from the Slone Survey.” *Pediatrics*. 122: 2 (August 2008) e323-e329.
  - The authors found that in a given week, 10.1% of US children used cough and cold medication. Exposure was highest among 2- to 5-year-olds, followed by children younger than 2 years of age.
  
- 5) Pitetti RD, et al. “Accidental and Nonaccidental Poisonings as a Cause of Apparent Life-Threatening Events in Infants.” *Pediatrics*. 122:2 (August 2008) e359-e362.
  - The authors examined toxicology reports for infants under two years of age who were brought to a pediatric emergency department showing signs and symptoms of a life-threatening event. 13 of the 274 toxicology screens performed (4.7%) were positive for over-the-counter cold medications.

**Attachment 2:**      Maryland Poison Center Data: 2007 and 2008

The Maryland Poison Center collected data on the number of calls received during the first six months of 2007 and 2008, related to the use of over-the-counter cold preparations in children age five and younger. These data are shown in the tables below.

Definitions:

- “Unintentional General” refers to accidental ingestion of a product by a child.
- “Unintentional Therapeutic Error” refers to accidental administration of the wrong product *or* the accidental administration of the right product in the wrong dose.

<b>Unintentional General Exposures</b>		
Age	1/1/2007- 7/1/2007	1/1/2008- 7/2/1008
< 1 year	7	5
1 year	48	35
2 years	118	79
3 years	64	67
4 years	31	27
5 years	8	8
<b>Total</b>	<b>276</b>	<b>221</b>

<b>Unintentional Therapeutic Error Exposures</b>		
Age	1/1/2007- 7/1/2007	1/1/2008- 7/2/1008
< 1 year	15	6
1 year	26	13
2 years	28	26
3 years	24	17
4 years	22	16
5 years	9	11
<b>Total</b>	<b>124</b>	<b>89</b>

*Source:* Correspondence from Suzanne Doyon, MD, ACMT, Medical Director, Maryland Poison Center, to the Baltimore City Health Department (September 17, 2008).