RESEARCH LETTER

Pediatric Information in Drug Product Labeling

To the Editor: The dearth of information on drugs for children led to children being called "therapeutic orphans." In 1975, Wilson determined that 78% of drug labeling had inadequate pediatric information.[1] In 1999, Wilson summarized 25 years of efforts to get pediatric information into labeling and extended his analysis.[2] In the decade after Wilson's review, regulations and legislation have led to more pediatric studies and labeling.[3] We hypothesized that a higher percentage of labeling has information on use in children compared with the analyses by Wilson in 1975[1] and in 1999.[2]

Methods. We evaluated labeling in the June 2009 electronic Physicians' Desk Reference[4] (ePDR) using methods established by Wilson[1] in analyzing the 1973 print PDR. Labeling was categorized as adequate if it stated that the drug was approved for pediatric use, had been studied, or had safety, efficacy, or dosing information for all appropriate pediatric populations; and inadequate if labeling lacked data on dosing, safety, or efficacy in at least 1 pediatric subpopulation. Partially labeled was a subgroup of inadequately labeled and defined as adequate labeling for at least 1 but not all appropriate pediatric subpopulations.

Labeling in the ePDR was reviewed by 3 people (A.N.S., D.A., W.R.). Differences were reviewed by a fourth person who made final assignments (M.D.M.). The κ was 0.91. Topicals, nasal sprays and most over-the-counter products were excluded per the methods of Wilson. In products with multiple formulations, only 1 likely to be used in children (ie, oral formulation) was analyzed.

Because limitations in the ePDR may lead to an underestimate of pediatric labeling, 2 subanalyses were performed. First we excluded products on the US Food and Drug Administration's (FDA's) list of Products Deemed Not Relevant to Pediatrics.[5] Second, we compared the ePDR list with the FDA's Pediatric Labeling Changes Table (February 1998-June 2009), which reflects only pediatric legislative initiatives and is not comprehensive, to determine whether most new pediatric labeling changes were included in the ePDR.[3]

Similar to Wilson,[2] we also assessed the labeling for all new molecular entities (NMEs) approved between 2002 and 2008[6] to determine if the product might be used in pediatrics and the adequacy of the pediatric information.

Results. There were 1264 trade name products in the ePDR. After excluding 510 products (consistent with the approach by Wilson) and 194 multiple formulation products, 560 products in the ePDR were analyzed. Of these, 231 (41%; 95% CI, 37%-45%) were adequately labeled and 29 (5%; 95% CI, 3%-7%) were partially labeled for pediatric use. Therefore, 260 (46%; 95% CI, 42%-51%) products had some information on pediatric use in labeling.

If products deemed not relevant to pediatrics were removed, 231 of 461 (50%; 95% CI, 46%-55%) were adequately labeled for pediatric use, 29 (6%; 95% CI, 4%-9%) were partially labeled; and 260 (56%; 95% CI, 52%-61%) had some pediatric labeling. If 72 products with pediatric labeling from the Pediatric Labeling Changes Table that were not in the ePDR were added, 303 (57%; 95% CI, 53%-61%) products were adequately labeled, 29 (5%; 95% CI, 4%-7%) were partially labeled, and 332 (62%; 95% CI, 58%-66%) had some pediatric information.

Between 2002 and 2008, the FDA approved 142 NMEs; 105 (74%) were deemed to have potential pediatric use and 43 (41%) had pediatric information in the labeling (TABLE).

Comment. In 2009, only 46% of products in the ePDR had some information on pediatric use in labeling. Progress has been made since 1975, when only 22% were labeled.[1] Of NMEs with pediatric labeling, the increase from 20% in 1999[2] to 41% in 2009 is also an improvement. Our estimate of the true percentage of products with pediatric labeling information is probably an underestimate because many commonly used products were excluded from the analysis and not all products are listed in the ePDR.

Labeling with pediatric information in only 46% of products is still insufficient. Legislation to increase pediatric clinical trials and require the resulting information be added to labeling is necessary. The current legislation expires in 2012 without reauthorization.

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Author Contributions: Ms Avant had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Sachs, Avant, Murphy.
Acquisition of data: Sachs, Avant, Lee, Murphy.
Analysis and interpretation of data: Sachs, Avant, Lee, Rodriguez, Murphy.

Table. New Molecular Entities Approved Between 2002-2008[a]

	No. (%) of New Molecular Entities Approved							
	2002 (n = 17)	2003 (n = 21)	2004 (n = 31)	2005 (n = 18)	2006 (n = 18)	2007 (n = 16)	2008 (n = 21)	Total (N = 142)
Potential pediatric use	15 (88)	13 (62)	23 (74)	16 (89)	12 (67)	12 (75)	14 (67)	105 (74)
Pediatric labeling	9 (60)	6 (46)	10 (44)	8 (50)	4 (33)	4 (33)	2 (14)	43 (41)

[a] Data were accumulated from the time of the US Food and Drug Administration approval to June 2009.

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Drafting of the manuscript: Sachs, Avant, Lee, Murphy.
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CORRECTIONS

Names Misspelled: In the Original Contribution entitled "Moderate to Vigorous Physical Activity and Sedentary Time and Cardiometabolic Risk Factors in Children and Adolescents," published in the February 15, 2012, issue of *JAMA* (2012; 307[7]:704-712), the names for 2 contributors of data to the International Children's Accelerometry Database should have read, "L. B. Sardinha, PhD and L. B. Andersen, PhD." This article was corrected online.

Incorrect Figure Labels: In the Review entitled "Association of LDL Cholesterol, Non–HDL Cholesterol, and Apolipoprotein B Levels With Risk of Cardiovascular Events Among Patients Treated With Statins: A Meta-analysis," published in the March 28, 2012, issue of *JAMA* (2012;307[12]:1302-1309), the forest plot labels in Figure 1 and Figure 2 should have read: "Non–High-Density Lipoprotein Cholesterol," and not "High-Density Lipoprotein Cholesterol." This article was corrected online.

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