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The Globalization of Pediatric Trials: Should We be Worried?

Julia Dunne, MD, **Dianne Murphy, MD**, **Gerold Wharton**

Office of Pediatric Therapeutics, Office of the Commissioner, Food and Drug Administration, Silver Spring, MD 20993

In "Globalization of Pediatric Research: Analysis of Clinical Trials Completed for Pediatric Exclusivity," Pasquali et al[1] reported that 65% of the studies conducted for pediatric exclusivity took place in at least 1 non-US country, and 38% of trials enrolled patients in more than 1 site located in a developing/transition country, including more than one-third of infectious disease, cardiovascular, and allergy/immunology trials. The authors concluded that pharmaceutical companies may be using "developing" countries to both meet enrollment needs and avoid the regulatory requirements of more developed countries. The article relied on published data that did not provide patient-level information.

The Food and Drug Administration has analyzed the patient-level data for all pediatric studies submitted to it between 2002 and 2007 in response to a written request issued under the pediatric exclusivity program. These data represent more than 257 pediatric trials involving 46 000 subjects. Of these, we obtained country, center, and patient-level data for 119 trials.

Table 1 provides patient-level data for 2 conditions of concern in the Pasquali et al article: cardiovascular disease and juvenile rheumatoid arthritis. Data for allergy/immunology and atopic dermatitis studies were omitted. These studies were conducted solely within the United States during this period.

Relatively few patients in the studies came from "developing" countries. For example, of 1539 pediatric patients involved in the cardiovascular studies, only 53 were from Africa. Most of these studies were for pediatric hypertension, which has a growing prevalence in Africa. Also, of the 146 children from developing countries, most were from Latin America, and few were from 1 country.

Large numbers of children were not recruited from countries in which the prevalence of the condition under investigation is low. And, all but 5 trials with centers in developing countries also had centers (and therefore protocol and ethical approval) in the United States, Canada, or Western Europe. The country locations for the 5 exceptions were appropriate choices in terms of the prevalence and seriousness of the condition studied.

Using the United Nations criteria of Human Development Index (HDI) for defining level of development, patient distribution for these clinical trials shows that most children (96%) were recruited in high and very-high HDI countries; only 4% were recruited in medium-HDI countries, and none were recruited in the least-developed countries.

Last, the authors stated that companies have made “more than $14 billion in profits” from pediatric exclusivity; our data indicate that companies have $14 billion projected sales over 20 years.

REFERENCE

1. Pasquali SK, Burstein DS, Benjamin DK Jr, Smith PB, Li JS. Globalization of pediatric research: analysis of clinical trials completed for pediatric exclusivity. Pediatrics. 2010;126(3):e687–692. Available at: www.pediatrics.org/cgi/content/full/126/3/e687 [PubMed: 20732941]

TABLE 1

Location of Pediatric Subjects in Clinical Trials 2002–2007

	Patient No. (%)
Cardiovascular trials (N = 1539)[a]	
Developed countries[b]	
United States	798 (51)
Netherlands	398 (26)
Canada	61 (4)
Hungary	36 (2)
Norway	35 (2)
New Zealand	16 (1)
Developing/transition countries[b]	
South Africa	53 (3)
Argentina	22 (1)
Chile	20 (1)
Russia	20 (1)
Brazil	16 (1)
Peru	11 (1)
Juvenile rheumatoid arthritis trials (N = 556)	
Developed countries[b]	
United States	180 (32)
Israel	52 (9)
Germany	42 (8)
Australia	42 (8)
Norway	30 (5)
Austria	22 (4)
Portugal	21 (4)
Italy	9 (2)
Developing/transition countries[b]	
Peru	47 (8)
Argentina	42 (8)
Brazil	40 (7)
Mexico	21 (4)
Chile	8 (1)

[a] Cardiovascular conditions studied included hypertension, heart failure, arrhythmia, and heterozygous familial hypercholesterolemia.

[b] This delineation is subjective and based on a United Nations reference that indicates that the delineation is not an established convention and should be viewed as a generalization.