January 23, 2015

The Honorable Margaret Hamburg, M.D.
Commissioner of Food and Drugs
Food and Drug Administration
Division of Dockets Management (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: [Docket No. FDA--2014-N-1818] Comments on FDA Drug Trials Snapshots

Dear Dr. Hamburg:

On behalf of the undersigned organizations, we thank you for the opportunity to comment on the newly launched Food and Drug Administration (FDA) Drug Trials Snapshots, an initiative of the *FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data*, as required by Section 907 of the Food and Drug Administration Safety and Innovation Act (FDASIA). We support the FDA's efforts to ensure that women, the elderly, and people of color are proportionately represented in clinical trials for FDA approved drugs and biologics and that the results of their participation are publicly available and easily accessible on the FDA website.

We commend the FDA for creating the Drug Trials Snapshots. This tool heightens the transparency, availability and accessibility of demographic data about clinical trial participants. Millions of people use FDA approved drugs, biologics, and medical devices every day. Accessible and consumer-friendly health information is vital for women to make informed health care decisions for themselves and their families. While we would prefer that information about the safety and efficacy by demographic subgroup be made available through the product labeling, the Snapshot website is a strong first step toward making this information more readily accessible to consumers and healthcare providers.

However, improvements are needed to make the Snapshots as helpful as possible. We make the following major recommendations for improving the Snapshots website, and we will expand on these and other recommendations later in our letter:

- We strongly recommend expanding the effort to include complete demographic data for drugs and biologics approved prior to 2014, as well as information on Phase 0, I, II, and IV studies for these products. We urge FDA to make similar Snapshots available for medical devices, including devices approved prior to 2014 and also including data from early phase studies.
- We urge you to include clinical trial data related to the intersection of age, race, and sex to provide consumers a thorough understanding of their risks and benefits as individual users of a certain drug or biologic.
- Access and use of this tool needs to be as easy as possible for consumers. Therefore, we urge FDA to ensure that the Snapshots can be readily accessed by consumers from the FDA homepage and other FDA web pages frequented by consumers.
- We urge you to make the content available in multiple languages to ensure non-English speakers can access the information. Translating the website content into Spanish should be the first priority.

- Finally, the information in the Snapshots related to age subgroup data is lacking, and we have a number of recommendations for improving that information.

Complete and accurate information about medical products, particularly the specific benefits a drug or device might offer and the risks it might pose to women, the elderly, or those of African heritage, is of critical importance. It is essential that FDA strengthen the Drug Trials Snapshots by implementing the following improvements.

Priority I. Completeness and Quality of Data

We urge you to include **all** drugs and biologics approved by the Food and Drug Administration since 1998 on the Drug Trials Snapshots website, rather than limiting the website to drugs approved prospectively. It is critical that health care consumers have access to subgroup data about as many FDA approved medical products as possible, not just those that were approved after 2013. Also, to the maximum extent possible, we urge FDA to include data on earlier phase studies, which may offer critical insight into the safety of approved medical products. Finally, in addition to drugs and biologics, we urge you to include retrospective and prospective information for FDA approved medical devices by subgroup. The maximum number of FDA approved drugs, biologics, and medical devices needs to be included in order for the Snapshots to be effective and valuable for health consumers.

Priority II. Greater Transparency of Data

The Drug Trials Snapshots currently provide complete clinical trial demographic information only for race and sex, while the information for age subgroups is more limited. We found the figures (charts) illustrating trial composition by sex and race to be very helpful and encourage the FDA to include similar figures showing the composition by age.

We also strongly urge the agency to provide efficacy, effectiveness, and safety information related to the intersection of sex, age, race, ethnicity, and the intersection of these subgroups for each drug and biologic listed on the Drug Trials Snapshots. The influence of age, gender, race, ethnicity, and especially the intersection of these characteristics, on a body's response to medical products can be profound. Consumers assessing the benefits and risks of a particular medical product across multiple subgroup variables could use more complete data demonstrating the varied safety and effectiveness of medical products due to critical demographic subgroup distinctions. Therefore, FDA should present the participation data in a format that allows the public to access and query a searchable database where multiple demographic variables can be examined simultaneously in order to allow for meaningful analysis of specific subgroups by sex, race, ethnicity, and age. For example, subgroups on sex should be easily cross-referenced with subgroup data on race/ethnicity to determine how many African-American women are included in a specific drug's clinical trials. Doing so would help illustrate that these subgroups are often disproportionately underrepresented. This underrepresentation makes it difficult, if not impossible, to assess the efficacy, effectiveness, and safety of specific drugs and biologics for patients who span multiple subgroups. Consumers of FDA approved medical products deserve to know if they are more likely to experience adverse effects, or elicit no response, from prescription drugs and medical devices because of these characteristics.

When there are disparities found in sex, age or race subgroups for either the safety or the efficacy of a drug, this needs to be consistently and clearly noted in the Snapshots and ideally in the label as well. Similarly, when there is insufficient data to conduct appropriate subgroup analyses for group differences in safety or efficacy, this should also be noted in all appropriate documents available to the consumer, including the label. A simple statement such as "There were not enough (sex- or age- or race group) participants in the study to conduct a meaningful analysis." could be included in the labeling. We

recommend that sex and race subgroups should be a standard section on all drug, device and biologics labels, as is the case for age in drug and biologic labels. This would help ensure that demographic subgroup information is collected, analyzed and made openly available to the public.

Our organizations have previously commented on the low rates of participation by women, the elderly, and people of color, in clinical trials and have been strong proponents of the FDA Action Plan to reverse this. Adequate representation of patient subgroups in clinical trials is critical to ensuring that products are safe and effective for all who might use them. It was particularly concerning that five of the six Snapshots had insufficient numbers of non-whites to allow for any subgroup analysis, and half of the Snapshots had insufficient numbers of older adults to allow for meaningful analysis. This should be a clarion call to the FDA to create a dedicated oversight process to improve the inclusion of underrepresented groups.

The section in each Snapshot titled "Who Was In The Study(ies)?" is very helpful for consumers. However, FDA should use surveillance data from the Centers for Disease Control and Prevention (CDC) or other federal sources to describe disease prevalence among subgroups in order to put the trial participation information into context. Other independent sources of data, such as voluntary health organizations like the American Heart Association, also regularly update and publish statistics on disease prevalence that can help to inform the FDA. Without this type of contextual information, it would be very difficult for consumers to accurately assess whether a particular subgroup is over- or underrepresented. In addition to providing more detailed information on the subgroup demographics to patients and clinicians, this will also highlight the underrepresentation and exclusion of certain demographic subgroups from these clinical trials. This will encourage trial sponsors to continue to make greater efforts to include historically excluded or underrepresented groups in clinical trials for life-saving drugs, biologics, and medical devices.

Priority III. Accessibility of Information

We are pleased to see that the Drug Trials Snapshots have been designed with an eye toward expanding consumer accessibility. We recommend the FDA continue their efforts to strengthen consumer usability of the website by first ensuring that the Drug Trials Snapshots webpage is clearly locatable from its main home webpage and on other pages through which consumers access information at the FDA. An identifiable visible icon will help consumers locate this information. We also suggest that FDA develop widgets and badges that organizations such as ours could add to our websites to help promote the availability of this information.

Second, we have a number of recommendations for including more consumer-friendly language on the Snapshots pages. A clearer explanation at the top of the Drug Trials Snapshots page, indicating the intents, limits and extent of information contained on the page, would be very helpful to consumers. We recommend including an explanation of why these drugs were initially selected and an explanation of terms used such as "stand-alone conclusions". We also suggest that the FDA create a glossary and a "How to use this page" tab to assist consumers to navigate the page more expeditiously and productively. We encourage adding a search feature and a link to already existing information from FDA on its website on "Inside Clinical Trials: testing medical products in people" as this page has important consumer information. The disclaimer included at the top of each drug's Snapshot should clearly state that individuals should speak with their healthcare providers to have drug information interpreted for their specific clinical needs and that they should not stop taking a medication unless advised by their healthcare provider.

The button for "More Information" at the end of each drug's Snapshot, which links to technical information more helpful for clinicians and researchers, should indicate that this information is intended for a professional audience such as researchers and clinicians. Finally, we would encourage the inclusion

at the bottom of each drug's Snapshot of a direct link to the FDA's MedWatch website so that consumers know where and how to report adverse event information.

Priority IV. Content Availability in Multiple Languages

The United States is currently the fifth largest Spanish speaking country in the world.[1] Research shows the number of Spanish speaking peoples continues to rise each year and in 2013, almost 13 percent of the US population reported speaking Spanish at home. It is imperative that non-English speakers have access to the same health information as native English speakers. When people are unable to read or understand crucial health information, such as the demographics of clinical trial populations, they are unable to make informed health care choices. While we acknowledge that providing the Drug Trials Snapshot in multiple languages will require more resources, it is a matter of heath equity and as such, should be considered a high priority for the FDA. This effort must also include the ability to locate the Snapshots from the FDA homepage in another language.

To increase accessibility of the website and make it more inclusive of diverse peoples, we recommend that multiple language options be added to the top of the main landing page of the Drug Trials Snapshot (http://www.fda.gov/Drugs/InformationOnDrugs/ucm412998.htm). Though translating the content into Spanish should be considered high priority, we also urge you to make the content available in French, Mandarin, and Portuguese. Many people who are non-native English speakers belong to communities that are already disproportionately underrepresented in clinical trials. We urge you to end this trend by allowing diverse peoples to access vital health information through the Drug Trials Snapshots.

Priority V. Improved Age Subgroup Data

Finally, the age subgroup information included between and within the six exemplar drug Snapshots is inconsistent and should be improved. Of the six examples of drug Snapshots, only Zontivity included an age breakdown for the elderly over age 75. Others included only older than 65 and younger than 65, which is insufficient to characterize the older adult population in the United States. The Zontivity Snapshot displayed age subgroup analysis broken down by "<65," "≤65 as well as <75" and "≥75". It would be preferred to use a consistent analysis of age data using the breakdowns "<65", "65-75" and ">75".

The manner in which the Zontivity example displayed the results for both the primary endpoint and for bleeding by age decile was helpful, but the risk table then displayed risk using a cutoff of age 69 and older for unclear reasons. With respect to age, we recommend including outcomes of particular interest to older adults (falls, incontinence, delirium, cognitive impairment, etc.) by age group.

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In conclusion, the FDA has an important opportunity to improve public health by requiring product sponsors to include adequate numbers of women, minorities, and the elderly in clinical trials, evaluate the evidence based on sex, race and ethnicity, and age, and make that information available to patients and

[1] http://nbclatino.com/2013/08/07/us-is-5th-largest-spanish-speaking-country-new-census-interactive-map/

consumers. Women and their families rely on the FDA to provide clear and complete information regarding the risks and benefits of approved drugs and biologics. Therefore, we urge you to revise the Drug Trials Snapshots in accordance with the recommendations above.

Sincerely,

Nancy A. Brown
Chief Executive Officer
American Heart Association

Cynthia A. Pearson
Executive Director
National Women's Health Network

Phyllis Greenberger
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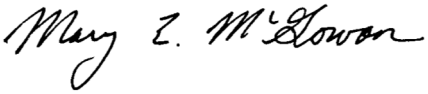

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