May 12, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-N-0745, Action Plan for the Collection, Analysis, and Availability of Demographic Subgroup Data in Applications for Approval of FDA-Regulated Human Medical Products, Public Hearing."

To Whom It May Concern:

It is with a deep sense of urgency that we as physicians of diverse American cultures join together to communicate our shared passion and resolve for addressing the critical need to improve "minority" representation in clinical trials data supporting marketing applications for products regulated by the Food and Drug Administration (FDA).

Section 907 of the FDA Safety and Innovation Act of 2012, commonly referred to as FDASIA, required a report to Congress on the clinical trial participation and inclusion of safety and effectiveness data by demographic subgroups including age, sex, race and ethnicity data in applications submitted to FDA. This report as issued August, 2013, disclosed that "whites represented a high percentage of clinical trial study participants for biologic, drug, and medical device applications and in many cases, other racial subgroups were underrepresented." We believe this underrepresentation which has been well-reported for many years, contributes to, and perpetuates the health disparities in our nation and thus require your immediate attention and deliberate action.

To this end, Section 907 also required the development of an "Action Plan for the Collection, Analysis, and Availability of Demographic Subgroup Data in Applications for Approval of Food and Drug Administration-Regulated Medical Products." We wish to take this opportunity to provide comments and recommendations regarding the development of this Action Plan.

Like our patients, we are physicians of diverse racial and ethnic origins with a common need. Many, if not most of us, provide care for patients who manifest a disproportionate share of disease burden in our American society. Many of our patients are parts of communities that are often underserved with respect to medical care and basic health resources. Furthermore, the underrepresentation of these patients in clinical trials of pharmaceuticals, biologics, and medical devices lead to a preventable lack of adequate data on the proper use of therapeutic innovations in this subsection of our population. These are but a few of the barriers to our ability to achieve equity in patient care and treatment of many diseases.

It is our patients who suffer the health consequences of a clinical research enterprise that does not routinely address their needs. However, it is we who are faced with little alternative but to administer treatments to our patients in the absence of adequate data to support safety and effectiveness for them. In doing so, not only do we risk untoward effects, we also risk the trust of our patients and their willingness to seek timely diagnosis, treatment, and regular preventive care. Unfortunately, for many of us this represents most of our patients. Therefore, it is we who must deal with the subsequent outcomes whatever they may be, and we who must advocate for change on behalf of our patients as essential to maintaining the trustworthiness of the relationship.

We join together with clarity and consistency of purpose to make the following recommendations to FDA as important steps in protecting the entirety of the American public and achieving the health equity that the American people have sacrificed for, and our patients deserve:

1. The FDA should take action to require, as a part of the relevant regulatory submissions, a summarized and annotated report of the available scientific and medical literature describing the age, gender, racial and ethnic prevalence of the disease for the target indications prior to allowing the clinical trial evaluation of a pharmaceutical, biologic, or medical device product.

2. FDA should take action to require a statement of goals, and a proposed method for achieving the goals for the inclusion of diverse populations in clinical trials supporting products to be approved for use in the United States (US). Goals for inclusion should be proportional to US disease prevalence by racial and ethnic subgroup. While many sponsors of US clinical trials are global organizations, given variances in genetics, nutrition, habits, standard of care, environmental exposures and a host of other factors, use of foreign data as a surrogate for data showing safety and effectiveness in American "minority" populations is **not acceptable**. The data must be sufficient to reach conclusions and inform the proper use of the product in the relevant diverse subgroups of American patients.

   We do not accept the premise of a general lack of feasibility for obtaining conclusive data in population subgroups. The medical and statistical literature provides guidance on how this might be accomplished with adequate planning and without the unreasonable expansion of the clinical trial population. [1,2]

   Delaying approval of new product applications may be an obvious tool to incentivize inclusion of data from diverse populations. However, this approach may be contrary to the interest of patients. Furthermore, it may not be consistent with the principles of the Hippocratic Oath to delay availability of important innovations in treatment that have been ***proven*** safe and effective for any part of our population. Thus, use of modest market exclusivity extension as an incentive for submission of inclusive data as a part of the **initial market application** may be appropriate. However, this consideration should be balanced with the potential for withdrawal of some significant amount of market exclusivity for the lack of inclusive data submission within a reasonable period of time (e.g., 2 to 3 years) post-approval. This is but one example of how one might address this conundrum.

   Any incentive/disincentive program must recognize the potential for negative contribution to morbidity and mortality in patients associated with the delay in acquisition of the proper data in a diverse population.

3. FDA should take action to require submission of a Comprehensive Outreach Plan. This Plan should include a process for educating and enrolling "minority" patients. (This is consistent with the intent of the National Institutes of Health Revitalization Act of 1993, PL 103–43 for federally funded trials.) This Plan should also recognize that most "minority" physicians tend to serve mostly "minority" patients.[3] These physicians represent an underutilized resource for gaining better access to "minority" patient enrollment. Therefore, we strongly recommend the Outreach Plan also include documentation of methods to develop and involve "minority" physician/investigators. This allows better opportunity for observation and documentation of the impact of clinically relevant cultural issues on the recruitment and execution of clinical trials and patient responses. Such information should be available to all physicians who provide care for diverse patients.

4. FDA should take action to require the review of clinical trial designs to assure that they do not directly, or indirectly through their specific criteria, exclude patients of diverse racial and ethnic origins unless strong medical and/or scientific rationale is provided.

5. FDA should take action to implement a system for sharing and comparing clinical trial data by names (brand and generic) of products to allow the health professionals, when they deem it necessary, to evaluate and compare human experience with the product and its relevance to the patient being treated.

We realize there has never been a statutory barrier to the inclusion of racially and ethnically diverse populations in clinical trials supporting the marketing of drugs, biologics and medical devices. However, the historical and cultural factors that have contributed to our predicament are many and complex. We believe the redesign of a system to address the shortcomings of our current clinical trial process does not need to be complicated and can operate within the parameters of past experiences at FDA and its "sister" organization, the NIH, regardless of the funding support for the clinical trials.

We have made an effort through our recommendations to focus on the most fundamental barriers to an equitable process for meeting the needs of our diverse society and we extend to FDA our sincere offer of assistance in an effort to move forward with all deliberate speed.

Sincerely,

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References

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3. Marrast, L, Zallman, L. et al. Minority Physicians' Role in the Care of Underserved Patients: Diversifying the Physician Workforce May Be Key in Addressing Health Disparities. *JAMA Internal Medicine.* 2014;174(2):289–291.
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