Action Plan to Address Demographic Subgroup Data in FDA Product Applications

The Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) (FDASIA), in Section 907, directed the US Food and Drug Administration (FDA) to report on the extent to which demographic subgroups (sex, age, race, and ethnicity) participate in clinical trials in marketing applications for drugs, biologics, and devices[1]. This assessment report, issued in August 2013, provides a review of information derived from sponsor applications, FDA reviews, and product labelling on the status of this data in product applications. Section 907 also requires that FDA develop an action plan no later than one year following publication of the report. The legislation directs that the content of the action plan includes recommendations as appropriate for different product types on the following topics/issues/concerns:

- Ways to improve the completeness and quality of analyses of data on demographic subgroups in summaries of product safety and effectiveness data, and in labelling
- The inclusion of demographic subgroup data, or the lack of availability of such data, in labelling
- Improve the public availability of subpopulation data to patients, healthcare providers, and researchers.

At a public meeting on April 1, 2014[2], various stakeholders presented their comments to an FDA panel. The FDA framed the meeting by asking several questions pertaining to issues and challenges associated with the collection, analysis, and availability of demographic subgroup data in applications for approval of FDA-regulated human medical products. The comments and discussions, in addition to comments to the public docket, will be used to assist in developing the action plan mandated by FDASIA. These regulatory activities are a likely precursor to more stringent requirements regarding the inclusion of demographic subgroup analysis in product applications.

The overwhelming recommendation made at the public meeting focused on the need for the FDA to initiate mandated requirements for product sponsors regarding the inclusion of appropriate demographic subgroups in clinical trials, and the information on any related analysis. Further, stakeholders recommended that the FDA develop and maintain a formal system to monitor compliance, track clinical trials, and make the results of studies of demographic subgroups readily available to the public. The stakeholder recommendations for mandating requirements were cross-cutting, extending to devices as well as drugs and biologic products. Many presenters also recommended an incentive plan, either similar to other expedited review pathways (i.e., *fast track*) or with some sort of "conditional approval" elements applied.

The stakeholders presenting at the meeting also urged the FDA to complete guidance on recommendations for providing subgroup information and analysis in clinical studies. There are some general FDA guidance documents to direct sponsors on providing demographic subgroup information, but in many instances these documents have not been recently updated or finalised. Many of these are listed in the FDA's August 2013 report *Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products*[3].

One of the more recent guidances - the 2011 *Draft Guidance for Industry and Food and Drug Administration Staff, Evaluation of Sex Differences in Medical Device Clinical Studies*[4] - targets device applicants. Another guidance document - the *Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials*[5] - issued in 2005, describes the FDA's recommendations for sponsors of new drug applications (NDAs) on presenting a summary of safety and effectiveness data by demographic subgroups (age, gender, race), as well as an analysis of whether modifications of dose or dosage intervals are needed for specific subgroups.

The public also made recommendations on ways to improve the available data on demographic subgroups, and on communicating information to the public. Comments on the latter point often focused on

information in product labelling. Many participants recommended that the FDA establish standardised requirements in labelling for medical products that would detail subgroup demographic information and analysis. Such labelling information would also include a statement that noted whether or not the population studied could support efficacy and safety. Alternatives to labelling were also offered as recommendations. These included using experts on public communication to make recommendations, use of internet-based tools, and possibly a "demographic guide" that would provide information to patients on the use of products for specific subgroups. Additional public comments on this topic are available at regulations.gov by accessing the FDA docket: FDA-2013-N-0745-0022.

References

1. Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) (FDASIA) http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/default.htm. Accessed April 15, 2014.
2. Federal Register: Action Plan for the Collection, Analysis and Availability of Demographic Subgroup Data in Applications for Approval of Food and Drug Administration-Regulated Medical Products; Notice of Public Hearing; Request for comments (Notification of public hearing; request for comments), March 4, 2014 (Volume 79, Number 42) (Pages 12134 – 12135).
3. Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products. FDA Website. http://www.fda.gov/downloads/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm365544.pdf August 2013. Accessed April 14, 2014
4. Guidance for Industry and Food and Drug Administration Staff, Evaluation of Sex Differences in Medical Device Clinical Studies (draft). FDA Web site. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm283453.htm December 2011. Accessed April 14, 2014.
5. Guidance for Industry, Collection of Race and Ethnicity Data in Clinical Trials for FDA Regulated Products. FDA Web site. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126396.pdf September 2005. Accessed April 14, 201

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