

DDM

Display Date 1-12-09
1-13-09
SReese

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2009-N-0674]

Participation of Certain Population Subsets in Clinical Drug Trials; Request for Comment

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is seeking information and comments on issues related to the enrollment of certain populations in clinical drug trials. Particularly, we are requesting information and comments from medical product manufacturers, institutional review boards (IRBs), patient groups, universities, researchers, community groups, and other interested parties. This request is related to FDA's implementation of the Food and Drug Administration Amendments Act of 2007 (FDAAA) section 901, which requires recommendations be included in a report to Congress addressing best practice approaches on increasing the participation of elderly populations, children, racially and ethnically diverse communities, and medically underserved populations in clinical drug trials. FDA requests that those with information on possible approaches to increase participation of these groups in clinical drug trials submit comments.

DATES: Submit written or electronic comments by *[insert date 45 days after date of publication in the Federal Register]*.

ADDRESSES: Submit electronic comments to *http://www.regulations.gov*.

DC08310 FDA-2009-N-0674

N

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Brenda Evelyn, Office of Special Health Issues, Office of the Commissioner, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4460.

SUPPLEMENTARY INFORMATION:

I. Background

Section 901 of FDAAA requires that FDA submit a report to Congress that includes “recommendations regarding impediments to the participation of elderly populations, children, racially and ethnically diverse communities and medically underserved populations in clinical drug trials” and recommendations that address “best practice approaches for increasing the inclusion of such subsets of the general population” in clinical drug trials (FDAAA, section 901(d)(5)). In developing this report, FDA seeks comments that may help to develop these recommendations.

Participation of all segments of the population in medical research is critical to public health. The ability to develop drugs that are safe and effective for diverse groups hinges on the availability of clinical drug trial participants from these same groups. Some researchers and public health experts argue that inconsistent representation of certain communities can potentially lead to health disparities and insufficient data for risk assessment. FDA has previously identified the need for inclusion of children, both sexes, the elderly, racially and ethnically diverse communities, and other populations in clinical trials so that data are available to evaluate the potential differences among these subgroups (63 FR 6854, February 11, 1998). According to the Department of

Health and Human Services (HHS) Office of Minority Health, in a recent prostate cancer study, only 8 percent of the 18,000 participants were minorities (www.omhrc.gov/templates/content.aspx?ID=5147). Increased participation from all of these sub-groups may help assure that data relevant to the entire treatment population are obtained.

In addition, statutory mandates and incentives such as the Pediatric Research Equity Act (PREA) (Public Law No. 108–155 as amended by FDAAA) and the Best Pharmaceuticals for Children Act (BPCA) (Public Law No. 107–109 as amended by FDAAA) require and encourage medical research to consider implications for pediatric populations.

For over 20 years, FDA has worked to encourage broad participation of all groups in clinical drug trials. Under FDA regulations (21 CFR 312.33), all investigational new drug (IND) applications must include in annual reports the number of patients tabulated by age, gender, and race, and under 21 CFR 314.50(d)(5)(v) and (d)(5)(vi), new drug applications (NDA) are required to include analyses of efficacy and safety by demographic subgroups. Biologics license applications typically include analyses of efficacy and safety by demographic subgroups. The International Conference on Harmonization (ICH) guidance on the common technical document also calls for such analyses (see M4E: The CTD—Efficacy (August 2001) available at <http://www.fda.gov/cber/gdlns/m4ectd.pdf>).

FDA has issued labeling recommendations for specific sub-populations (Guidance for Industry: Content and Format of the Adverse Reactions Section of Labeling for Human Prescription Drugs and Biological Products, January 2006, available at <http://www.fda.gov/cber/gdlns/cfadvers.htm>) and guidelines for studying gender differences in clinical drug studies (Guideline for the

Study and Evaluation of Gender, July 1993, available at <http://www.fda.gov/cder/Guidance/old036fn.pdf>). FDA has made recommendations for minimum standards for the collection and use of race and ethnicity information to assist in the reporting of the 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. (Guidance for Industry: Collection of Race and Ethnicity Data in Clinical Trials, September 2005, available at <http://www.fda.gov/CBER/gdlns/racethclin.htm>; see, also ICH E-7 Guideline for Industry, Studies in Support of Special Populations: Geriatrics (August 1994) available at <http://www.fda.gov/cder/guidance/iche7.pdf> and Reviewer Guidance: Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review (February 2005) available at <http://www.fda.gov/cder/guidance/3580fnl.pdf>.)

Other agencies have also issued guidelines for the participation of diverse groups in clinical trials. For example, the National Institutes of Health (NIH) requires the inclusion of women and minority groups in NIH-funded trials unless an exception is warranted (NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research as amended October 2001, information is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm). NIH also has issued guidelines for inclusion of children as research subjects (March 1998 NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects, available at <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>).

Currently, healthcare professional organizations, various universities, foundations, and industries are taking steps to encourage broad participation of all populations in clinical drug trials.

Since 1998, the National Medical Association has administered Project IMPACT, a program initially funded by HHS designed to train African American physicians on being clinical investigators and to increase knowledge and raise awareness about clinical trials among African American physicians and consumers. (Information is available at <http://www.omhrc.gov/assets/pdf/checked/Project%20IMPACT--Increasing%20Minority%20Participation%20and%20Awareness%20of%20Clinical%20Trials.pdf>.) The program is currently being funded by AstraZeneca and has expanded to include the Interamerican College of Physicians and Surgeons, an Hispanic health professional organization. (Information is available at <http://www.astrazeneca-us.com/community-support/?itemId=1338629>.) Further, some foundations have supported studies and programs designed to increase participation (e.g., the Lance Armstrong Foundation's support of the Education Network to Advance Clinical Cancer Trials, intended "to foster awareness about cancer clinical trials, enhance their acceptability and improve access to them." Information is available at <http://www.livestrong.org/site/c.khLXK1PxHmF/b.2662065/k.C0D9/ENACCT.htm>). Industry has partnered with academia to fund similar programs (e.g., Genentech's and Baylor College of Medicine's research initiative with the Intercultural Cancer Council, "Project addresses underrepresentation of minorities, underserved patients in clinical studies." Information is available at <http://www.bcm.edu/news/item.cfm?newsID=420>).

We are seeking information to determine if additional approaches are necessary to increase participation of certain subsets of the general population

(elderly populations, children, racially and ethnically diverse communities, and medically underserved populations) in drug clinical trials.

II. Request for Comments and Information

In providing comments, we are particularly interested in responses to the following questions regarding the participation of certain population subsets in clinical drug trials.

A. Communication and Knowledge Barriers

1. To what extent do differences in native language, educational level, and literacy interfere with members of some populations' participation in clinical trials:

- Finding out about the existence of trials and how to enroll
- Understanding informed consent documents and procedures
- Adhering to clinical trial instructions and drug regimens
- Completing clinical trials

2. To what extent do limitations in access to technology and to medical care in general decrease the chance that members of some populations will know about the existence of clinical trials and how to participate in them?

- Are these subsets of populations aware of *www.ClinicalTrials.gov*?

3. What proven methods, i.e., best practices, are available to address the impact of these potential barriers to communication about the existence of, and how to participate in, clinical drug trials?

4. To what extent are health care providers aware of *www.ClinicalTrials.gov*?

B. Trust and Cultural Sensitivity

1. To what extent do culturally-bound beliefs or traditions, or trust or stereotypes about the medical research community, interfere with group members' willingness to participate in clinical drug trials?

- Are particular populations significantly more or less trusting of those who conduct medical research?

2. What approaches to address cultural sensitivity and trust issues, including increased collaboration with community-based organizations, have been shown to increase successful clinical trial participation?

3. To what extent do the beliefs of clinical trial personnel about the commitment or ability of members of some populations to follow through with a protocol influence willingness to recruit and enroll such individuals in clinical drug trials?

4. What approaches, i.e. best practices, have been shown to improve trust between potential participants and clinical drug trial researchers and healthcare providers who can provide referrals?

C. Costs of Clinical Trial Participation

Note: The term "cost" may vary from participant to participant and is intended to include time lost (i.e. wages, childcare, etc), effort expended, and other sacrifices that may be necessary to participate in clinical drug trials.

1. To what extent do data show that the "costs" of participation, to either potential participants or to those who conduct clinical drug trials, prohibit participation or enrollment of particular populations?

2. To what extent do data address the following?

- Do particular populations understand the potential public benefit from participating in clinical drug trials as compared to the “cost” to the participant?

- Is the belief that there is a public benefit from participating in clinical drug trials a sufficient incentive for participation for some populations?

3. To what extent do data show that limited health insurance coverage is an impediment to clinical drug trial participation?

4. To what degree is the geographical accessibility to clinical trials a significant cost that affects the participation of some populations?

5. What are the “costs” of participating in clinical drug trials that are most relevant to some populations? How might these be reduced?

6. What approaches, i.e. best practices, have been shown to decrease “costs” with resulting increased participation in clinical drug trials?

D. Other

1. Please describe any other barriers, or best practice approaches, that HHS should consider in striving to increase participation of certain population subsets in clinical drug trials.

III. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at *<http://www.regulations.gov>*.

Dated: 1/6/09
January 6, 2009.



Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

1/7/09

[FR Doc. 08-⁰⁹????? Filed ??-??-⁰⁹08; 8:45 am]

BILLING CODE 4160-01-S

CERTIFIED TO
COPY OF THE

