

Appendix 1

Federal Register Notices And Comments Received

Dated: June 9, 1999.

Linda S. Kahan,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 99-15755 Filed 6-21-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Dermatologic and Ophthalmic Drugs Advisory Committee, Ophthalmic Drugs Subcommittee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Dermatologic and Ophthalmic Drugs Advisory Committee, Ophthalmic Drugs Subcommittee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on July 21, 1999, 8:30 a.m. to 5 p.m.

Location: Hilton Hotel, Salons A and B, 620 Perry Pkwy., Gaithersburg, MD.

Contact Person: Tracy Riley or Angie Whitacre, Center for Drug Evaluation and Research (HFD-21), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-7001, or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area), code 12534. Please call the Information Line for up-to-date information on this meeting. Current information may also be accessed on the Internet at the FDA Website "www.FDA.GOV".

Agenda: The subcommittee will discuss new drug application (NDA) 21-023 (cyclosporine ophthalmic emulsion, 0.05%, Allergan, Inc.), for treatment of moderate to severe keratoconjunctivitis sicca.

Procedure: Interested persons may present data, information, or views, orally or in writing, on issues pending before the subcommittee. Written submissions may be made to the contact person by July 16, 1999. Oral presentations from the public will be scheduled between approximately 8:30 a.m. and 9:30 a.m. Time allotted for each presentation may be limited. Those

desiring to make formal presentations should notify the contact person before July 16, 1999, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time requested to make their presentation. Notice of this meeting is given under the Federal Advisory Committee Act (5 U.S.C. app. 2).

Dated: June 16, 1999.

Linda A. Suydam,

Senior Associate Commissioner.

[FR Doc. 99-15752 Filed 6-21-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions; Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of meeting.

SUMMARY: The Food and Drug Administration (FDA) is announcing a meeting concerning the public availability of information on clinical trials for investigational devices intended to treat serious or life-threatening conditions and the availability of this information in a publicly available data bank. This meeting is being held to assist the agency in preparing a report to Congress required under the FDA Modernization Act of 1997 (FDAMA). Elsewhere in this issue of the **Federal Register**, FDA is inviting written comments and information that may assist FDA in this endeavor.

DATES: The meeting will be held on July 8, 1999, from 1:30 p.m. to 4:30 p.m.; registration will begin at 1 p.m.

ADDRESSES: The meeting will be held at 9200 Corporate Blvd., conference room 020B, Rockville, MD.

FOR FURTHER INFORMATION CONTACT: Robert R. Gatling, Center for Devices and Radiological Health (HFZ-404), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-594-1190, ext. 140, FAX 301-594-2977, or e-mail "rrg@cdrh.fda.gov".

Those persons interested in attending the meeting should fax or e-mail their registration including name, title, firm name, address, telephone, and fax number to Linda J. Lyons at 301-594-

1190, ext. 108 or by fax at 301-594-2977. There is no charge to attend this meeting, but advance registration is requested due to limited seating. If you need special accommodations due to a disability, please contact Linda J. Lyons at least 7 days in advance. Comments at the meeting may be limited in time depending on the number of presenters. Presenters should contact Linda J. Lyons by July 5, 1999.

SUPPLEMENTARY INFORMATION: FDAMA (Pub. L. 105-115) was enacted on November 21, 1997. Section 113(a) of FDAMA amends section 402 of the Public Health Service Act (PHS Act) (42 U.S.C. 282) by adding a new section 402(j). This new section directs the Secretary of Health and Human Services (the Secretary), acting through the Director of the National Institutes of Health (NIH), to establish, maintain, and operate a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions.

Section 113(b) of FDAMA (collaboration and report) directs the Secretary, the Director of NIH, and the Commissioner of Food and Drugs to collaborate to determine the feasibility of including device investigations within the scope of the data bank under new section 402(j) of the PHS Act. In addition, section 113(b) of FDAMA directs the Secretary to prepare and submit to the Committee on Labor and Human Resources of the Senate and the Committee on Commerce of the House of Representatives a report on the following:

1. The public health need, if any, for inclusion of device investigations within the scope of the data bank under section 402(j) of the PHS Act;
2. The adverse impact, if any, on device innovation and research in the United States if information relating to such device investigations is required to be publicly disclosed; and,
3. Such other issues relating to section 402(j) of the PHS Act as the Secretary determines to be appropriate.

Elsewhere in this issue of the **Federal Register**, FDA is inviting written comments and information that may assist FDA in preparing their report to Congress. Those questions should also be considered by those making presentations at the public meeting.

Dated: June 14, 1999.

Linda S. Kahan,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 99-15758 Filed 6-21-99; 8:45 am]

BILLING CODE 4160-01-F

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

Collection Activity	No. of Recordkeepers	Annual Frequency per Recordkeeper	Total Annual Records	Hours per Recordkeeper	Total Hours
Blood Establishments	2,800	5	10,000	40	112,000
Consignees	6,200	2.5	15,136	16	99,200
Total					211,200

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Maintenance costs were not estimated for the additional maintenance of records beyond the current 5 years to the recommended 10 years because modern storage technology has markedly reduced the space needed to store records.

In compliance with section 3507(d) of the PRA (44 U.S.C. 3507(d)), the agency has submitted the information collection provisions of this draft guidance to OMB for review. Interested persons may submit comments regarding this information collection by August 23, 1999, to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Wendy Taylor, Desk Officer for FDA.

IV. Electronic Access

Persons with access to the Internet may obtain the document using the World Wide Web (WWW). For WWW access, connect to CBER at "http://www.fda.gov/cber/guidelines.htm".

Dated: June 16, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy Coordination.

[FR Doc. 99-15754 Filed 6-21-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99N-1737]

Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA), Center for Devices and Radiological Health, is requesting comments concerning the feasibility of including information for device investigations for serious or life-threatening diseases and conditions in a

public data bank. This action is being taken to assist the agency in preparing a report to Congress required under the FDA Modernization Act of 1997 (FDAMA). Elsewhere in this issue of the **Federal Register**, FDA is announcing an open public meeting on this subject.

DATES: Written comments by August 23, 1999.

ADDRESSES: Written comments concerning this document must be submitted to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Robert R. Gatling, Center for Devices and Radiological Health (HFZ-404), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-594-1190, ext. 140 or e-mail "rrg@cdrh.fda.gov".

SUPPLEMENTARY INFORMATION: FDAMA (Pub. L. 105-115) was enacted on November 21, 1997. Section 113(a) of FDAMA amends section 402 of the Public Health Service Act (PHS Act) (42 U.S.C. 282) by adding a new section 402(j). This new section directs the Secretary of Health and Human Services (the Secretary), acting through the Director of the National Institutes of Health (NIH), to establish, maintain, and operate a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions.

Section 113(b) of FDAMA (collaboration and report) directs the Secretary, the Director of NIH, and the Commissioner of Food and Drugs to collaborate to determine the feasibility of including device investigations within the scope of the data bank under new section 402(j) of the PHS Act. In addition, section 113(b) of FDAMA directs the Secretary to prepare and submit to the Committee on Labor and Human Resources of the Senate and the Committee on Commerce of the House of Representatives a report on the following:

1. The public health need, if any, for inclusion of device investigations within the scope of the data bank under section 402(j) of the PHS Act;

2. The adverse impact, if any, on device innovation and research in the United States if information relating to such device investigations is required to be publicly disclosed; and,

3. Such other issues relating to section 402(j) of the PHS Act as the Secretary determines to be appropriate.

Section 520(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360j(g)) permits the investigational use of devices by experts qualified by scientific training and experience to investigate the safety and effectiveness of such devices. Part 812 (21 CFR part 812) contains the implementing regulations for section 520(g) of the act. In accordance with part 812 and the agency's public information regulations, FDA generally will not disclose the existence of an investigational device exemptions (IDE) application unless its existence has previously been publicly disclosed or acknowledged, until FDA approves an application for premarket approval (PMA) for the device, or until a notice of completion of a product development protocol (PDP) for the device has become effective. The establishment of a data bank intended to contain publicly available information about certain IDE's would require changes in these implementing regulations. Section 113(b) of FDAMA requires the Secretary to evaluate whether public disclosure of IDE information would adversely impact device innovation and research.

The provisions of section 113 of FDAMA apply to drugs for "serious or life-threatening diseases and conditions." Any consideration of inclusion of device trials within the scope of the data bank requires a definition of what types of devices would be covered. FDA does not currently have a definition for "serious" or "life-threatening," as those terms would apply to devices.

In the **Federal Register** of September 18, 1997 (62 FR 48940), FDA published a final rule for treatment use of an investigational device. The rule added § 812.36 (21 CFR 812.36). In the preamble to the final rule, FDA explained that it did not define "serious disease or condition" because the agency concluded that defining the term

could be unduly restrictive and limit the agency's discretion when determining whether certain stages of a disease or condition are "serious." Instead, § 812.36(a) applies the treatment IDE rule to "immediately life-threatening" diseases, and defines that as a stage of a disease in which there is a reasonable likelihood that death would occur within a matter of months or in which premature death is likely without early treatment.

This definition could be used to help define the category of device trials that could be included in a clinical trials data bank. The clinical trials data bank could contain a list of clinical trials, whether Federally or privately funded, of investigational devices for serious or life-threatening diseases, a description of the investigational device, eligibility criteria for patients, the location of clinical trials sites, and a point of contact for those wanting to enroll in the trial. In evaluating the public health need for a device trials data bank and the effects a mandatory public data bank would have on innovation and research, FDA is currently assuming the devices that would fall within the scope of the provision are those intended to treat such "immediately life-threatening" situations, but FDA invites public comment on this issue.

FDA is in the process of consulting with NIH on the feasibility of adding device trials to the data bank. In addition, through this notice, FDA is soliciting comments and information that will help the agency draft its report to Congress under section 113(b) of FDAMA. In particular, FDA seeks input in response to the following questions:

1. Is there a public health need for inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act?

2. If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?

3. Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients?

Will a public data bank create pressures to increase the size of device trials or number of sites in situations where such expansion may increase risk to patients?

4. IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?

5. If disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?

6. Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?

7. Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?

8. What other important information or issues should the agency consider?

FDA is planning a public meeting to give interested parties a chance to present their views on the feasibility, utility, and effects of a data bank for device trials. Information regarding the date and place of this meeting is published elsewhere in this issue of the **Federal Register**.

Interested persons may, on or before August 23, 1999 Dockets Management Branch (address above) written comments regarding this notice. Two copies of any comments are to be submitted, except that individuals may submit one 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 office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: June 14, 1999.

Linda S. Kahan,

Deputy Director for Regulations Policy, Center for Devices and Radiological Health.

[FR Doc. 99-15757 Filed 6-21-99; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[HCFA-1081-2N]

Medicare Program; Cancellation of the June 24, 1999, Meeting of the Competitive Pricing Advisory Committee and the Area Advisory Committee for the Kansas City Metropolitan Area

AGENCY: Health Care Financing Administration (HCFA), HHS.

ACTION: Notice of meeting cancellation.

SUMMARY: This notice announces the cancellation of the June 24, 1999, meeting of the Competitive Pricing Advisory Committee and the Area Advisory Committee for the Kansas City metropolitan area.

FOR FURTHER INFORMATION CONTACT: Sharon Arnold, Ph.D., Executive Director, Competitive Pricing Advisory Committee, Health Care Financing Administration, 7500 Security Boulevard C4-14-17, Baltimore, MD 21244-1850, (410) 786-6451 (for information about the CPAC).

Richard P. Brummel, Deputy Regional Administrator, Health Care Financing Administration, Richard Bolling Federal Building, Room 235, 601 East 12th Street, Kansas City, MO 64106, (816) 426-5233 (for information about the Kansas City metropolitan area AAC).

SUPPLEMENTARY INFORMATION: This notice announces the cancellation of the June 24, 1999, meeting of the Competitive Pricing Advisory Committee and the Area Advisory Committee for the Kansas City metropolitan area. The meeting will be rescheduled and announced in a subsequent **Federal Register** notice. (Section 4012 of the Balanced Budget Act of 1997, Pub. L. 105-33 (42 U.S.C. 1395w-23 note) and section 10(a) of Pub. L. 92-463 (5 U.S.C. App. 2, section 10(a))

(Catalog of Federal Domestic Assistance Program No. 93.773, Medicare—Hospital Insurance; and Program No. 93.774, Medicare—Supplementary Medical Insurance Program)

Requests for Extension of Comment Period
FDAMA Section 113(b)
Docket Number 99N-1737

Health Industry Manufacturers Association (HIMA)

Applied Research Ethics National Association (ARENA)



By messenger

July 14, 1999

Dockets Management Branch
Mail Code HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

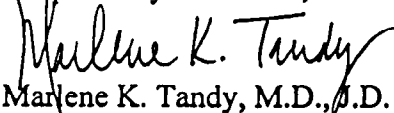
Re: Request for Extension of Comment Period for FDA Docket No. 99N-1737: Notice, Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions

Dear Madam or Sir:

The Health Industry Manufacturers Association (HIMA), pursuant to 21 C.F.R. §10.40(b)(3), hereby requests an extension of time to provide comments to the notice referenced above. HIMA is a Washington, D.C.-based trade association and the largest medical technology association in the world. HIMA represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. The notice [64 Fed. Reg. 33313 (June 22, 1999)] requires comments to be submitted to the agency by August 23, 1999. HIMA requests a 30-day extension of this comment period.

The subject of this notice is whether it is feasible to include medical device clinical trials in the public data bank that is required for pharmaceutical products under Section 113 of the FDA Modernization Act (FDAMA). This subject is one that has not been considered previously by HIMA and it raises many complex questions. In fact, the notice sets forth eight specific questions to be addressed by commentors. In view of the novelty of this issue, its importance to the medical device industry, and the need to accommodate summer business and vacation schedules, HIMA believes that sound public policy supports an additional 30 days to provide meaningful comment to FDA.

Respectfully submitted,



Marlene K. Tandy, M.D., J.D.
Director, Technology and Regulatory Affairs
and Associate General Counsel

cc: Linda S. Kahan, Deputy Director, Regulations and Policy, CDRH
Robert R. Gatling, Office of Device Evaluation, CDRH
Joseph M. Sheehan, Regulations Staff, CDRH

World Leaders in Health Care Innovation
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

July, 16, 1999

Marlene K. Tandy, M.D., J.D.
Director, Technology and Regulatory Affairs
And Associate General Counsel
Health Industry Manufacturers Association
1200 G Street, N.W.
Suite 400
Washington, DC 20005

Docket No. 99N-1737

Dear Dr. Tandy,

This is in response to your letter dated July 14, 1999 requesting an extension of the comment period on the notice on public availability of information on clinical trials for investigational devices intended to treat serious or life-threatening conditions. Because of the time constraints imposed by the statutory requirements of the Food and Drug Administration Modernization Act of 1997 (FDAMA), I must deny your request for an extension.

As you know, section 113(b) of FDAMA requires the Food and Drug Administration (FDA) to submit a report to Congress by November 24, 1999 on (1) the public health need, if any, for inclusion of device investigations within the scope of the data bank under section 402(j) of the Public Health Service Act; (2) the adverse impact, if any, on device investigations and research, if information relating to device investigations is made publicly available; and on such other issues relating to section 402(j) that FDA deems appropriate. In order to complete this mandatory report within the statutory timeframes, FDA believes that it is necessary to end the comment period on August 23 as planned.

FDA held a public hearing on this subject on July 8, 1999 and was able to hear from a number of stakeholders on these issues. In fact, HIMA participated in this public hearing. The agency will consider all the information and opinions that were presented in that forum. In addition, FDA expects the discussion at the public meeting to stimulate the submission of additional comments to the docket before August 23. The agency encourages HIMA to provide any additional comments it can offer by that date and will look forward to receiving HIMA's input.

Sincerely yours,

Linda S. Kahan
Deputy Director for Regulations and Policy
Center for Devices and
Radiological Health



August 23, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

1732 90 15 39 1150

RE: Docket No. 99N-1737: Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions

Dear Sirs;

On behalf of the Applied Research Ethics National Association (ARENA) we are writing regarding the above referenced public notice. ARENA is dedicated to promoting the ethical conduct of research. ARENA is a membership organization with nearly 1,000 members, including Institutional Review Board (IRB) chairs and administrators. ARENA promotes individual professional development opportunities and public policy awareness for those involved in the day-to-day application of ethical principles, government regulations, and other policies regarding research.

We believe that public availability of information on investigational device trials is an important issue that will greatly impact the public, research institutions, and Institutional Review Boards (IRBs). Unfortunately, we believe that the agency has not provided sufficient time for public response to the federal register notice. Therefore, we request a 60 day extension to the public comment period in order to provide comments on this important issue.

Thank you for consideration of our request.

Sincerely,

Gary L. Chadwick, PharmD, MPH
President

cc: Ada Sue Selwitz, ARENA Public Policy Committee Co-Chair
ARENA Public Policy Committee

Steven Peckman
Public Policy Sub-Committee Chair

99N-1737 Joan Rachlin
PRIM&R Executive Director

EXT 2

132 BOYLSTON STREET
BOSTON, MASSACHUSETTS 02116
617 423-4112



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

September 21, 1999

Gary L. Chadwick, PharmD, MPH
Applied Research Ethics National Association
132 Boylston Street
Boston, Massachusetts 02116

Docket No. 99N-1737

Dear Dr. Chadwick,

This is in response to your letter dated August 23, 1999 requesting an extension of the comment period on the notice on public availability of information on clinical trials for investigational devices intended to treat serious or life-threatening conditions. Because of the time constraints imposed by the statutory requirements of the Food and Drug Administration Modernization Act of 1997 (FDAMA), I must deny your request for an extension.

As you know, section 113(b) of FDAMA requires the Food and Drug Administration (FDA) to submit a report to Congress by November 24, 1999 on (1) the public health need, if any, for inclusion of device investigations within the scope of the data bank under section 402(j) of the Public Health Service Act; (2) the adverse impact, if any, on device investigations and research, if information relating to device investigations is made publicly available; and on such other issues relating to section 402(j) that FDA deems appropriate. In order to complete this mandatory report within the statutory timeframes, FDA believes that it is necessary to end the comment period on August 23 as planned.

FDA held a public hearing on this subject on July 8, 1999 and was able to hear from a number of stakeholders on these issues. The agency will consider all the information and opinions that were presented in that forum, as well as the written comments in the docket as it prepares its report to Congress.

Sincerely yours,

A handwritten signature in cursive script, reading "Linda S. Kahan", is positioned above the typed name.

Linda S. Kahan
Deputy Director for Regulations and Policy
Center for Devices and
Radiological Health

List of Comments Received
FDAMA Section 113(b)
Docket Number 99N-1737

Industry and Industry Trade Associations

Health Industry Manufacturers Association – James Benson
Medical Device Manufacturers Association – Stephen Northrup
The Innovation Factory – Carolyn George
Thermo Cardio Systems, Inc. – Tim Krauskopf
Baxter Healthcare Corp; Cardio Vascular Group – Patricia Garvey
Medtronic, Inc. – Chip Whitacre
Cook Group, Inc. – Stephen Ferguson
Abbott Laboratories – Frank Pokrop

Advisory Panel Consumer Representatives

Radiological Devices Panel – Marilyn Peters
Ear, Nose and Throat Devices Panel – Renee Middleton
Neurological Devices Panel – Anne Wojner
Circulatory Systems Devices Panel – Robert Dacey
Gastroenterology and Urology Devices Panel – Diane Newman

Consumers and Health Professionals

Stan Reynolds
Joyce A. M. Thomas

Health Organizations

National Organization for Rare Disorders – Abbey Meyers
AIDS Project Los Angeles – Ruben Gamundi
Oklahoma State Department of Health – Patricia Hawkins

Public Citizens

Steven Rohr
Steven Peckman

Comments
From
Industry
And
Industry Trade Associations



August 23, 1999

7 0 3 2 '99 AUG 23 11:24AM

Dockets Management Branch
Mail Code HFA-305
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. 99N-1737; Notice - Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions

Dear Madam or Sir:

These comments are submitted by the Health Industry Manufacturers Association (HIMA) in response to the Food and Drug Administration's (FDA's) notice concerning the feasibility of including information about clinical trials of investigational medical devices in a public data bank [64 Fed. Reg. 33313 (June 22, 1999).] HIMA is a Washington, D.C.-based trade association and the largest medical technology association in the world. HIMA represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. HIMA's members manufacture nearly 90 percent of the \$62 billion of health care technology products purchased annually in the United States, and more than 50 percent of the \$147 billion purchased annually around the world.

Background

Section 113(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) requires the Department of Health and Human Services (HHS), acting through the Director of the National Institutes of Health (NIH), to establish and maintain a data bank of information concerning clinical trials for drugs for serious or life-threatening diseases or conditions. [This requirement is codified in §402(j) of the Public Health Service Act (42 U.S.C. §282).]

Section 113(b) of FDAMA directs HHS, NIH and FDA to collaborate to determine the feasibility of including device investigations in this data bank. Section 113(b) also requires HHS, not later than two years after this section's enactment date, to submit to Congress a report regarding the public health need, if any, of including device clinical trial information in the data bank as well as the adverse impact, if any, on device innovation and research in the event that such information is publicly disclosed in a data bank. Unlike the terms of Section 113(a) for drugs, the provisions of Section 113(b) do not require or authorize the establishment of a clinical trial data bank for devices.

*HIMA Comments to FDA Docket No. 99N-1737**August 23, 1999**Page 2 of 8*

The HHS report to Congress is due by November 21, 1999. The FDA's notice referenced above seeks information to be used in assisting the agency in preparing the report to Congress.

HIMA's Position: It is Premature to Recommend a Data Bank for Device Investigations

HIMA supports the goal of making information about clinical trials of investigational medical devices more available to the public to enhance participation, as appropriate, in these studies. Nevertheless, HIMA believes that it is premature for HHS to recommend a data bank for clinical trials of investigational medical devices. The structure and intent of Section 113 of FDAMA makes clear that the data bank is intended to be established first for drugs, and then after experience with this data bank exists, the feasibility of extending the data bank to devices is to be considered and evaluated by the relevant agencies. This Congressional intent should be followed. The data bank for drugs should be operational for a period of time (2 years) after which consideration should be given whether to add devices within its scope.

The purpose of Section 113 of FDAMA is "to simplify the process through which individuals with serious or life-threatening medical conditions obtain information about opportunities to participate in clinical trials of experimental therapies." S. Rep. No. 105-43 at 67 (1997). As stated above, HIMA endorses this goal.

HIMA believes that Congress's plan for the data bank is intended to permit a thorough consideration of the experience with a data bank for drugs before deciding whether to extend it to devices. HIMA also appreciates Congress's concern, as expressed in Section 113(b), that an evaluation of whether to add devices to the data bank is to consider and protect sponsors' needs to maintain the confidentiality of proprietary information and refrain from hindering device innovation and research.

In HIMA's view, Congress wanted experience with a data bank for drugs before deciding whether or not to apply one to device investigations. To date, the data bank for drugs has not been implemented. Thus, at present there is no experience with a data bank for drugs that provides insight into the determination whether a data bank for devices is appropriate.

Important information from a data bank for drugs, such as its functioning, utility to the public, effects on sponsors and clinical investigators, effects on the conduct of clinical trials, costs, and efficiencies, is not yet available. Implementation of the data bank for drugs will define, among other items, the scope of the program and its effects, the diseases and conditions to be included as serious or life-threatening, whether or not both safety trials and effectiveness trials should be included or only those designed to evaluate effectiveness, and when information should be submitted to the data bank. Clearly, Congress recognized that obtaining this type of information would ensure an appropriate evaluation of the feasibility of including devices in the data bank.

HIMA suggests the HHS report to Congress recommend that the agency's evaluation of whether to implement a data bank for devices await two years of experience with the data bank for drugs, so that a more informed recommendation to Congress about a device data bank can be made. A

*HIMA Comments to FDA Docket No. 99N-1737**August 23, 1999**Page 3 of 8*

recommendation to Congress now about a device data bank will be as uninformed as Congressional action to establish a device data bank would have been 21 months ago when Section 113 of FDAMA was enacted. HIMA believes that adhering to Congress' original implementation concept would best benefit the public health.

HIMA's Response to the FDA Questions Posed in the Notice

(1) Is there a public health need for inclusion of device investigations within the scope of the data bank under Section 402(j) of the Public Health Service Act?

It is not clear whether such a public health need exists.

There has been suggestion that some types of medical device clinical trials have found recruitment difficult, resulting in delayed development of therapies that might benefit the public health. If appropriate subject recruitment is enhanced, some clinical trials might be completed faster with the likely result that safe and effective therapies could come to market faster.

On the other hand, a data bank of device clinical studies has the potential to create larger studies, particularly in response to a heightened public demand to participate in clinical research. Inappropriately large studies can needlessly slow down the conduct of clinical trials and ultimately slow the introduction of safe and effective therapies to the general public. In addition, excessively large clinical studies can result in an unmanageable number of investigational centers to monitor and an increase in the risk of significant protocol deviations. All of these results would be a net detriment to the public health.

A device clinical trial data bank may not be necessary because numerous sources of information about clinical trials currently exist through the Internet and, given the constant expansion of the Internet, more such listings of clinical trials can be expected in the future. Examples of such web sites include, but are not limited to, the CenterWatch Clinical Trials Listing Service (www.centerwatch.com), Oncolink (www.oncolink.upenn.edu), and the Dr. Koop web site (www.drkoop.com).

In addition, a device clinical trial data bank may not be necessary because there are programs currently in existence which facilitate public access to investigational medical devices for serious or life-threatening diseases or conditions. For example, there are programs for emergency use, compassionate use, treatment IDE, expanded access and continued access. (See FDA "Guidance on IDE Policies and Procedures," issued January 20, 1998.)

(2) If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?

*HIMA Comments to FDA Docket No. 99N-1737**August 23, 1999**Page 4 of 8*

If device trials are included in the public data bank, HIMA recommends that they be clinical trials involving investigational, critical life-supporting devices for serious, life-threatening illnesses or conditions, for which no comparable or satisfactory alternative exists.

Feasibility/pilot trials should not be included in a data bank. Feasibility/pilot trials are typically conducted at a minimum number of sites with very few subjects (e.g. less than 20). Their purpose is to assess the feasibility of conducting a safety and effectiveness trial in the target population. FDA often places significant restrictions on the target population for enrollment in the feasibility phase. Additionally, feasibility/pilot trials are generally intended as an initial evaluation of a device's safety and possible effectiveness. As such, they have yet to reach the threshold necessary to justify exposing larger numbers of people to the investigational device at this early stage. For these reasons, it would not be appropriate to include these trials in a data bank.

(3) Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients?

One potential negative impact would be the inability of a person to enroll in a device trial that he or she learns about from the data bank, because of the smaller number of subjects involved. There may be extensive pressure on sponsors, investigational sites, and perhaps even the FDA, by persons seeking to participate in device trials that have only a limited number of devices available for testing, resulting in difficulty conducting the clinical trial.

For example, lotteries might become necessary to determine which persons meeting the inclusion and exclusion criteria of the study protocol are going to be enrolled as subjects in the clinical trial. Or, there might be an overabundance of requests and pressure from patients' physicians for expansion of the clinical trial enrollment or, failing that, for enrollment of a patient under an emergency use procedure. There is the potential for sponsors to have great difficulty in dealing with such a volume of requests, both from a humanitarian perspective and a regulatory perspective.

Furthermore, a data bank might only increase patient access to clinical trial information at the expense of collateral damage to the research and development process. For example, with some devices (e.g. heart valves) there are relatively few clinical trial sites in the U.S. with sufficient patient populations for acceptable implant rates and with the necessary infrastructure to provide timely and accurate clinical trial data. If the public data bank includes clinical trial locations, then an abundance of companies seeking to start clinical trials on a particular type of device may approach the same sites. This could overwhelm the ability of a limited pool of clinical trial sites to conduct meaningful studies.

Also in those cases in which only a few investigational centers in the United States are qualified to participate in a clinical trial, potential subjects may seek to participate in trials well outside

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their immediate geographic location. There is evidence to suggest that many of these subjects become "lost to follow-up" during the course of the trial, due to difficulty in traveling to the investigational site. Posting a listing of all investigational sites in a data bank can draw subjects from many geographic locations that may increase the likelihood of enrollment of future "lost to follow-up" subjects. This can have a significant negative effect on the overall integrity of the study and can prolong the completion of the study.

(4) IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?

Device firms often conduct a single safety and effectiveness trial to support a marketing application, and many small device companies are developing only a single product. If two or more firms are developing similar products and one discloses the existence of its study by posting in the data bank, the other firm(s) may rush to post their information for fear that the initially disclosing firm will be viewed by the market as more innovative and "first to market" through its pursuit of a clinical investigation. For the small firm with a single product, this could have a negative effect on continued funding by venture capitalists of research and development, particularly if the firm is not the first to post information in the data bank.

(5) If disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?

Mandatory disclosure is likely to hamper innovations and investment in research and development due to the nature of device development. Firms go to great lengths to protect confidentiality of device research and development. Firms provide detailed information on this development to FDA under an IDE and this information is, by regulation, considered confidential.

Clinical trial investigators are routinely required to sign written confidentiality agreements, because the clinical protocol provides critical and detailed strategic elements of the firm's research and development plan. These confidential elements include the description of the device's design, the intended use, the indications for use, the identification of the target population, the enrollment criteria, and the clinical trial sites. The data bank for drugs is slated to include the description of the product, the inclusion and exclusion criteria, the location of trial sites, and a point of contact. This is the type of information that is routinely held confidential in device trials. Its disclosure could severely hamper a sponsor's competitive edge.

Disclosure of clinical trial investigations may compromise the clinical development programs of companies whose competitors decide to shift resources in an attempt to "beat" the other company to market. This may disproportionately disadvantage smaller companies compared to larger companies with more financial resources.

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The medical device industry is innovative, fast-paced and highly competitive. Success is typically a function of rapid, well-controlled product development and being first to market with a safe and effective device. Mandatory disclosure of strategic elements of the research and development plan may drive medical device research outside the United States, where no such requirements currently exist. This would be a net detriment to public health in the United States.

Given these considerations, any device clinical trial data bank should be a voluntary program. The existence of a voluntary device clinical trial data bank may offer people with critical life-threatening diseases or conditions another source for information about alternative experimental therapies. A voluntary data bank can also offer sponsors an opportunity to accelerate clinical trial enrollment, if necessary, for particular device trials. A voluntary data bank may also avoid the wholesale disruption of existing confidentiality protections and prevent damage to the competitive innovation necessary for continued successful medical device research and development.

(6) Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?

The ethical principles of the trial must be maintained, regardless of its inclusion in a public data bank. In addition, the statistical restrictions in the protocol must also be maintained. This mitigates against potential financial pressures to inappropriately increase trial size.

In HIMA's opinion, FDA should always be concerned about improper promotion and commercialization of investigational devices. The creation of a data bank for information on investigational devices yields yet another avenue for improper promotion and commercialization of investigational devices. If a data bank for device trials is established, there should be clear guidance issued by FDA regarding the criteria for deciding whether information provided to the data bank constitutes improper promotion and commercialization. FDA will also need to monitor the data bank for improper promotion of investigational devices.

(7) Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?

Third party payers may see an opportunity to influence sample size upward for purposes of determining reimbursement. Although health outcome studies are not within FDA's purview, if IDE trial information is publicly disclosed, third party payers may exert pressure on sponsors during trials to include outcome measures or move to withhold reimbursement.

(8) What other important information or issues should the agency consider?

HIMA Comments to FDA Docket No. 99N-1737***August 23, 1999******Page 7 of 8*****Institutional Review Board (IRB) Issues**

Section 113(a) requires the data bank for drugs to contain the following information: a description of the purpose of each experimental drug, the eligibility criteria for participation in the trial, a description of the location of trial sites, and a point of contact for those wanting to enroll in the trial. This information is intended to be communicated through the data bank directly to persons who may participate in clinical trials. One possible regulatory interpretation would be that this disclosure is within the scope of the informed consent requirements in 21 CFR Part 50. Another possible regulatory interpretation is that this information constitutes recruitment material for study subjects under the FDA's "Guidance for Industry and FDA Staff on Preparing Notices of Availability of Investigational Medical Devices and for Recruiting Study Subjects," issued March 19, 1999 and the FDA's "Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators," 1998 Update. IRB approval is required for informed consent materials and for study subject recruitment material.

Adding review of data bank disclosures to the workload of the already overburdened IRBs in the United States would not be good policy for the conduct of human subject research to develop new diagnostic and treatment products. It would take IRBs away from the critically important priority of reviewing and approving protocols and informed consent documents. It also would make submission of information to the data bank more cumbersome. Review of this information would not be an IRB priority and it would delay the posting of information in the data bank. Accordingly, HIMA recommends that any data bank program established under Section 113 of FDAMA be specifically exempted from any type of informed consent procedures and IRB review.

Intellectual Property Issues

Intellectual property issues are key concerns to every company developing a medical device. Without strong protection of intellectual property rights, new product development to advance the public health is inhibited.

The information likely to be included in a clinical trial data bank (device description, patient eligibility criteria, clinical trial site location) can provide a company's competitors with important confidential information. From this, a competitor can obtain information about a new device's characteristics and intended use.

One particular concern with posting this type of information in a public venue is the statutory provision in 35 U.S.C. §102(b), which states that a person is not entitled to a patent if the invention has been described in a printed publication more than one year prior to the date of the person's application for a U.S. patent. If the data bank includes a description of the device that enables another person (with ordinary skill in the art) to make the device, then the data bank may become a "printed publication" that prevents the original inventor from obtaining a patent on that device. Thus, a data bank should contain only a very limited, general description of the device and/or the conditions for which it is being investigated in the clinical trial.

HIMA Comments to FDA Docket No. 99N-1737
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Another concern with including information in a public data bank about a device under development is that another company could use it to "engineer around" that device and dilute the value of the company's patent protection. At present, investigational devices are not so readily available for reverse engineering by competitors. To maintain this protection, the information provided about a device to a public data bank must be as basic and general as possible.

Clinical Trial Control Group Issues

Device trials are often conducted with a control group that does not receive a medically or surgically active intervention. People that volunteer for clinical trials, even when informed that the trial has such a control group, may agree to participate in order to obtain a chance at receiving the active investigational device. If randomized to the control group in a non-masked study, the subject may become agitated and drop out of the trial to seek another opportunity at a different clinical trial site to obtain the investigational device. This practice jeopardizes study results because it contributes to bias in subject selection. Although this happens today without the existence of a data bank, there is increased likelihood of this practice occurring when clinical trial site information is widely available through a data bank.

Timing of Submissions to a Data Bank

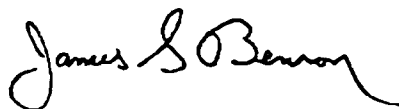
If a device data bank is established, sponsors will need to know when to submit the required information. Some possible options include a defined time period after IRB approval of the protocol, a defined time period after IDE approval, or a defined time period after the first subject's enrollment at individual study sites.

Definition of Life-Threatening Diseases or Conditions

If a device data bank is established, a definition will be necessary for "serious, life-threatening conditions" and FDA will need to clarify any differences between this definition and the criteria used to determine significant risk/non-significant risk device studies, class II and class III devices, and devices appropriate for treatment IDE status.

HIMA appreciates the opportunity to comment on these issues.

Respectfully submitted,



James S. Benson
Executive Vice President
Technology and Regulatory Affairs



August 23, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, room 1061
Rockville, Maryland 20852

Subject: Docket No. 99N-1737 – Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions; Request for Comments

Dear Sir or Madam:

The Medical Device Manufacturers Association (MDMA) appreciates this opportunity to comment upon the above-referenced notice published June 22 by the FDA's Center for Devices and Radiological Health (CDRH).

MDMA, based in Washington, D.C., is the national association for the innovators and entrepreneurs in the medical device industry. Representing 130 independent manufacturers of medical devices, diagnostic products, and health care information systems, MDMA seeks to improve the quality of patient care by encouraging the development of new medical technology and fostering the availability of beneficial innovative products in the marketplace.

Section 113(b) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) directs the National Institutes of Health (NIH) and the FDA to examine the feasibility of including medical device investigations within the scope of the NIH's public database of information on clinical trials of drugs for serious or life-threatening diseases and conditions. In response, the FDA has invited public comment on whether such a public database of clinical trials of medical devices is in the best interests of the public health.

MDMA Position

MDMA does not believe the establishment of a general public database of clinical trials of medical devices is in the best interests of the public health. Moreover, we believe the existence of such a general public database would be detrimental to the public health by chilling the process of continuous, incremental innovation that is the hallmark of the medical device industry. However, MDMA recognizes that patients may be frustrated by the lack of a central repository of information about clinical trials that have been disclosed by companies. To respond to this concern, MDMA believes the FDA should consider establishing or supporting a central Internet clearinghouse use of clinical-trial information volunteered by manufacturers.

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Rationale

The mere existence of a clinical trial of an investigational device is sensitive, proprietary information for the company sponsoring the trial. The FDA currently recognizes this sensitivity by not disclosing the existence of investigational device exemption (IDE) applications except under certain limited circumstances.

MDMA believes that this policy is still appropriate, particularly since entrepreneurial companies with limited resources continue to set the pace of innovation in most sectors of the medical device industry. If forced to disclose the nature and thrust of their research and development efforts, small and entrepreneurial companies may choose not to investigate (at least in the United States) the potential of innovative ideas in fear that other companies will begin their own investigations along the same or similar lines. Unlike drugs, medical devices have effective product lives that, in many cases, are measured by the months, rather than years, before the next incremental advances are brought to market. MDMA believes that, without the possibility of being "first to market" with innovative devices, entrepreneurs would find much less incentive to innovate.

Furthermore, MDMA believes that the investment community could inadvertently harm innovators by misinterpreting the specifics of device trials listed in a public database. Most public medical-technology firms have very small market capitalizations and are extremely vulnerable to the exigencies and vicissitudes of the equity markets. One equity analyst's public misinterpretation of public information can send a small public company's stock into a tailspin that saps the resources it needs to bring its technology to market. Surely, the untimely demise of a small public (or private) company with a promising medical technology is not in the best interests of the public health.

MDMA does not believe that the existence of a public database of device investigations would lead to improper promotion or commercialization of clinical trials or undue pressure to expand the number of patients or sites involved in a particular clinical trial. Despite the potential for recovering some research and development costs, most device manufacturers cannot afford to stage huge, multi-center clinical trials. Instead, one of the main challenges for device manufacturers is to find a handful of capable physicians and medical institutions to serve as investigators and sites.

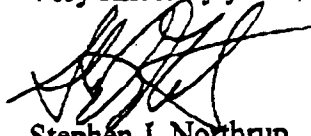
As a result, clinical trials of medical devices are usually smaller than trials of pharmaceuticals, which depend much less on the physical skills and specific training of the health professionals involved in the trial. To protect both the company and the patients it hopes to serve, device manufacturers clearly would prefer to gather promising safety-and-effectiveness data through limited clinical trials before adding scores of new subjects to their trials.

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In sum, MDMA believes the establishment of a public database of clinical trials of medical devices is not in the best interests of the public health. The public disclosure of proprietary information about device investigations would be a major disincentive to the process of medical device innovation. However, MDMA recognizes that patients seeking information on clinical trials are undoubtedly frustrated by the absence of a central repository of information on clinical trials that have been acknowledged or disclosed by sponsors. MDMA recommends that the FDA consider establishing or supporting a central Internet clearinghouse of clinical-trial information volunteered by manufacturers, including links to manufacturers' Web sites. However, MDMA cannot reiterate strongly enough that inclusion of a clinical trial in this or any other database should be voluntary and at the discretion of the sponsor.

Thank you for the opportunity to comment on this important subject.

Very sincerely yours,



Stephen J. Northrup
Executive Director

August 20, 1999

Docket No. 99N-1737

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Dear Sir or Madam:

TCI is submitting two copies of these comments in response to the June 22, 1999 Federal Register (FR) notice requesting input on the feasibility of including information on device investigations for serious or life threatening conditions in a public data bank. TCI is opposed to this public disclosure of information which was previously held confidential by the Agency. Our opposition is based on the adverse risk to public health that such a data bank may entail, and the incentive such a data bank would create to conduct clinical trials outside the United States.

In the FR notice, the Agency stated eight general issues for which it is requesting public comment. The questions focused on the logistics and risks of implementing the proposed data bank, but failed to present the global issue. TCI believes that the first question to ask is "what need is currently not being met?" The disclosure of device trial data to the general public has no inherent benefit unless the public can affect the trial progress. This affect could be as little as increasing the pool of potential patients presented for screening, or as significant as altering the trial population sufficiently to void any outcome. The implication that a patient may benefit by being enrolled into these types of trials must be offset by the realization that this same patient may be harmed by his/her enrollment. If the purpose of disclosure is to make a benefit more readily available to the public, then the "benefit" must be clearly defined.

Is there a benefit to a patient with a serious or life threatening condition in being enrolled into a device trial? The answer of course is that any benefit is unknown, but potential benefits may be postulated. Good clinical practice requires that a known benefit should be made available to any suitable patient. Withholding known beneficial therapies is inappropriate. If a benefit is known to exist then the purpose of the trial must be brought into question. Therefore, clinical trials of devices to treat these serious conditions must be done only when the benefit is not known. Indeed the primary purpose of an IDE trial is to *establish* the safety and efficacy of the device. Claiming or implying an unproven benefit is prohibited. A risk comes from the implication that a government "sponsored" data bank implies some level of safety, yet none can be claimed.

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August 20, 1999

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Without a clear benefit to wide publication of the existence of device clinical trials, TCI is concerned that a public health risk may be created by this data bank. This risk comes from the increased likelihood that patients will have access to information that allows them to falsely meet the enrollment criteria. Patients are currently screened for enrollment in these trials by trained health care professionals. If the patient can "self diagnose" their eligibility for a trial, they will be able to use this knowledge when they present themselves for enrollment. The risk to their health comes from the incentive to alter their current prescribed treatment(s). For example, if a study requires that patients not take a particular medication in order to qualify, a patient seeking to be enrolled may stop his/her medication just to qualify. The potential patient can further increase their chance of this deception being missed by "shopping" for a site willing to enroll them from among all the sites listed in the database. This self diagnosis and treatment is a public health risk that is controlled in current device trials by the screening of patients in a very regulated manner.

These same patients are very adept at pressuring clinicians to use the experimental device outside the scope of the trial. With serious and life threatening conditions creating the urgency, patients have a strong incentive to push for the treatment. The clinicians can thwart much of this pressure by explaining the risks associated with the device. However, the patients often have the perception that a trial would not be underway unless the potential benefits outweigh the risks. These patients can be better protected and still provided with unapproved devices through application of either the emergency use process or the treatment use IDE process.

Will the Agency allow sponsors to enroll more patients if the data bank increases demand? If the number of patients is set by the statistical rationale for the hypothesis being tested, then increasing the demand only increases the likelihood of pressure on the investigational sites to perform deviations from the protocol or apply emergency use criteria.

Another issue the Agency must consider in reviewing a potential data bank is; "are clinical investigations of medical devices in the United States not being completed due to a lack of public disclosure?" The Agency has at it's disposal the data concerning the number of Investigational Device Exemption (IDE) trials being conducted and the number of patients expected to be enrolled. If one assumes that only a device used in an IDE trial could qualify as being to treat "serious or life threatening conditions," the current need for patients is clearly identified.

Many factors go into the rate at which patients are enrolled into device trials. The availability of the device during a clinical trial is typically very controlled by the sponsor. In fact the pace of enrollment is often dictated by the desire of a sponsor to limit their exposure to risks of device problems by limiting the number of devices in distribution. The clinical trial is the time when one expects to uncover problems with the product. Expanding the number of patients put at risk from these problems has a negative health impact.

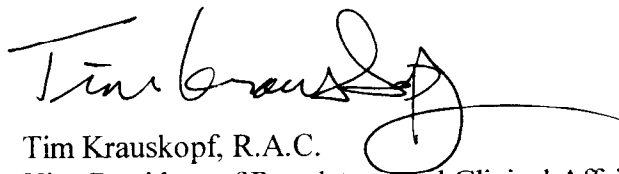
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The other concern such a data bank raises for TCI is the possible incentive to conduct trials where such disclosure is not mandated. This incentive is due to the competitive advantage that will be lost if the proposed data bank is established. The data bank can be used by a potential competitor to glean information regarding future marketing strategy and product development. A competitor can review the public data bank for information on indications for use and learn the target population for future marketing efforts. These competitors can also get a list of the investigational sites to target in efforts to derail the sponsor's clinical trial plans. The risk of these competitive disadvantages must be weighed by sponsors against the benefit of having a clinical trial performed in the United States. If the same trial can be conducted in a country without the need to disclose this information to competitors, the movement of sponsors to off-shore trial sites would deprive the U.S. population of a potential benefit.

Feeding this competitive risk is an expectation the public would have for an update to the data in this data bank as any information changes. Therefore sponsors will be required to continuously submit corrections as study sites are added or indications for use change. Doing this allows a competitor up-to-date information regarding changes in marketing plans or hospital affiliations. Sponsors may find the risk from this early disclosure of critical data to be so large that clinical trials in the U.S. would be limited or eliminated.

Due to these risks to public health and availability of experimental devices, TCI recommends against establishing the proposed data bank. Without any clear presentation of the current unmet need, review of the proposal for adequacy in meeting the need cannot be completed. If the Agency presents further explicit data in support of establishing that a need for such a data bank exists, TCI requests that the comment period be reopened.

Sincerely,



Tim Krauskopf, R.A.C.
Vice President of Regulatory and Clinical Affairs

TCI

Thermo Cardiosystems, Inc.
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Baxter

August 20, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852**Subject: [Docket No. 99N-1737]****Notice: Public Availability of Information on Clinical Trials for Investigational
Devices Intended to Treat Serious or Life-Threatening Conditions**

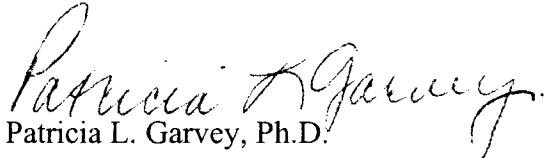
Dear Madam or Sir:

The enclosed comments are being submitted by Baxter Healthcare Corporation, CardioVascular Group, in response to the Food and Drug Administration's Request for Comments to the *Federal Register* notice dated June 22, 1999 (Volume 64, Number 119). Baxter's CardioVascular Group (CVG) is a leader in providing a comprehensive line of therapies and services to treat late-stage cardiovascular disease. Marketed cardiovascular devices include heart valves, vascular grafts, cardiac monitoring catheters, cardiopulmonary bypass equipment and devices, and left ventricular assist systems. Many of these devices are intended to treat serious or life-threatening conditions.

CVG's basic position: CVG is deeply concerned that the proposed publicly available data bank will have a negative impact on innovation and rapid medical device development in the U.S. due primarily to the loss of confidentiality of intellectual property. However, if medical device information is to be included, posting of clinical trial information should be strictly voluntary. Further, specific information posted should be at the discretion of the sponsor to protect trade secret information, and information to be posted should be reviewed in advance by the affected investigators and institutional review boards.

CVG respectfully submits these comments to FDA.

Sincerely,


Patricia L. Garvey, Ph.D.Vice President
Regulatory and Clinical Affairs
CardioVascular Group

99N-1737

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Baxter

***Comments on Public Availability of Information on Clinical Trials for
Investigational Devices Intended to Treat Serious or Life-
Threatening Conditions***

1. *Is there a public health need for the inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act?*

It is unclear whether a specific public health need exists for inclusion of device investigations within the scope of the data bank. The data bank could conceivably facilitate study enrollment. Study enrollment rate may be affected in part by limited availability of information about the trial and therefore might be accelerated by including this information in the proposed data bank. Enrollment of subjects during a clinical trial of an investigational device intended to treat a serious or life-threatening condition can be slow in some circumstances and can ultimately delay the public availability of a marketed safe and effective therapy option. However, within the limits of current IDE regulation, recruiting for subjects through public announcement is now available to investigators and sponsors on a voluntary basis. Baxter CVG believes this currently available mechanism to recruit subjects is sufficient, as this can be applied to the local geographic area where the studies are being conducted. Local recruitment has the greatest opportunity to attract locally-available subjects, thus enhancing study management and minimizing potential "lost to follow-up."

2. *If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for the IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?*

The medical device industry is innovative, fast-paced and highly competitive. Success is typically a function of rapid, well-controlled development and first to market. Firms go to great lengths to protect confidentiality of device research and development, and provide detailed information on this development to FDA under an IDE with confidence that this information is protected from public disclosure under the regulations. Most often a device firm will conduct a single IDE trial for support of a marketing application. Clinical trial investigators are routinely required to provide

marketing application. Clinical trial investigators are routinely required to provide written agreement of nondisclosure, as the clinical protocol provides critical and detailed strategic elements of the firm's research and development plan. These elements include description of the device design, intended use/indication for use, identification of the target population, and all eligibility criteria defined. As listed in the *Federal Register* notice, data elements to be provided in the databank would include confidential and proprietary information in the form of a device description, eligibility (i.e., inclusion and exclusion) criteria for patients, location of trial sites, and an investigational site point of contact.

Currently, promotion of investigational devices is prohibited under IDE regulation 21 CFR 812.7. In an attempt to recruit either investigators or subjects, sponsors can announce publicly that a clinical study is being conducted if no claim is made that the device is safe and effective for the purposes for which it is being investigated. However, this recruiting practice is voluntary and highly dependent upon agreement with the investigator and prior review and approval by the associated IRB. Inclusion in the databank should therefore be voluntary and subject to investigator and IRB review and approval.

Pilot trials are typically conducted at a minimum number of sites with very few patients (less than 20). The purpose is to assess the feasibility of conducting and safety and effectiveness trial in the target population. However, FDA may place significant restrictions on the target population for enrollment in the feasibility phase. For example, the patients may be higher risk than those targeted for the safety and effectiveness trial. The device pilot trial is, therefore, not analogous to a drug phase 1 trial that is performed with healthy volunteers and should not be included in the databank.

Many devices designed to treat serious or life-threatening conditions require concomitant surgery. The device itself may be implantable. Investigators must document study-specific skills and training and often require additional training by the sponsor as a requirement for participation in the clinical trial. In those cases where only a few investigational centers are qualified to participate in the trial (e.g., open-heart centers trained for LVAD implantation), potential patient candidates may seek to participate in trials well outside their immediate geographic location. They may agree initially to return for all required follow-up visits, however, there is evidence that many patients do not return and become "lost to follow-up" due to difficulties in traveling to the investigational sites. This can have a significant effect on the overall integrity of the study and can prolong the completion of the study and submission of the marketing application. Posting a listing of all investigational sites on a website can draw subjects from many geographic locations that may not be well served by the investigation and may increase the likelihood of lost to follow-up patient enrollment. For this reason, when sites choose to use public announcement as a recruiting tool, it is restricted to the

immediate geographic location. Investigational sites should therefore not be identified on the databank website.

3. *Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients? Will a public data bank create pressures to increase the size of device trials or number of sites in situations where such expansion may increase risk to patients?*
4. *IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of public health?*

Device firms typically conduct a single safety and effectiveness trial to support a marketing application. If two or more firms are developing similar products and one discloses the existence of their study by posting this information on the data bank, the other firms will likely post their information as well against their better judgment for fear that the initially disclosing firm will be viewed by the market as more innovative and “first to the market” through its clinical investigation. For the small firm with a single product, this could have a negative effect on continued funding through venture capitalists, particularly if they are not first to post the information on the data bank website. As stated earlier, first to market is often associated with market success and share as well as being perceived by the market as most innovative.

5. *If disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?*

Mandatory disclosure is likely to hamper innovations and investment in research and development due to the nature of device development. That is, trade secrets are protected throughout a very rapid development cycle. Mandatory disclosure of strategic research and development elements, as well as financial disclosure requirements recently imposed, will continue to drive medical device research offshore where no such regulatory requirements exist. Because foreign data can be used to support marketing applications, there are increasingly more incentives to do research outside the U.S.

6. *Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsor to add subjects to the trials without appropriate*

consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?

7. *Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?*

Third party payors may see an opportunity to start influencing sample size upwards for purposes of determining reimbursement. However, the purpose of the IDE trial is to determine safety and effectiveness of a device for its intended use. Sample size requirements for an IDE trial are significantly lower than that for a economic study, and it should be the sponsor's decision alone to combine or not combine these two purposes. Health outcome studies for devices are not under FDA purview, but if IDE trial information is publicly disclosed, third party payors may exert pressure on sponsors during trials to include outcome measures or move to withhold reimbursement.

8. *What other important information or issues should the agency consider?*

- **Definitions are essential for "serious, life-threatening conditions," and differences should be clarified and relationships identified by FDA between these definitions and significant/nonsignificant risk, class II and III, and treatment use IDE criteria.**
- **How will the databank be maintained and by whom? Who will ensure its integrity? How long will information remain on the databank, and how will up-to-date information be assured?**
- **From a retrospective view, which currently commercially available devices would have been identified for inclusion in this databank?**
- **The public health need is best served by bringing good, innovative medical devices of the highest quality to the market quickly at the lowest cost. The fastest, cheapest, most controlled trials are conducted at the smallest number of sites with the fewest number of patients determined to meet preestablished primary study endpoint criteria. How would prolonging such trials, increasing their costs and potentially losing some control over larger studies (that are harder to manage, monitor and audit) better serve the public health need?**
- **How could this disclosure of information possibly not have a negative influence on small or start-up device companies?**

- **Device trials typically are not blinded. In many, the control is a surgical procedure. Using information obtained from the databank, patients will pursue participation in a trial and be motivated by assuming that they will be treated with the investigational device. Patients may refuse to participate in randomized trials for this reason. But even if they agree to participate and then are randomized to the control, patients may then refuse to participate and seek another opportunity at another site identified on the databank website to improve their chances for being “randomized” to the treatment arm. This will add study bias to the patient selection thus jeopardizing the study results.**
- **Inclusion in the databank of the device description, eligibility of patients, and location of sites reveal critical strategic elements of the sponsor’s research and development and marketing plans. This also provides proprietary, trade-secret information to competitors.**



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August 20, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 99N-1737; Notice – Public Availability of Information on Clinical Trials for Investigational Devices Intended to Treat Serious or Life-Threatening Conditions

To Whom It May Concern:

These comments are submitted by Medtronic in response to the Food and Drug Administration's notice (64 FR 33313 - June 22, 1999) concerning the feasibility of including information about clinical trials of investigational devices in a public database.

The Health Industry Manufacturer's Association, HIMA, has responded to the FDA notice on behalf of the medical device companies constituting its membership. We agree in principle with those comments and wish to stress some additional points of specific concern to Medtronic. In particular, we believe that FDA should heed the direction established in the act to wait for a period of time after the establishment of the database for drug trials before initiating a similar database for medical devices.

In general, Medtronic believes that there are times when it would be in the interest of the public health to make information about on-going trials available to those in need of medical device therapies. However, we believe that the public health interest would be best served if the information to be disseminated related only to those studies of devices that treat conditions for which there are no approved alternative therapies. This would represent only a fraction of the studies being conducted under the IDE at any one time. We are concerned that the inclusion of all IDEs would place additional burden on all study centers to respond to requests for information while not creating benefit for patients.

Medtronic considers the information contained in the investigational plans for its clinical studies to be proprietary, including the inclusion and exclusion criteria and the indications for use. This information, if made available to the public, would provide valuable insight to our competitors regarding our regulatory and clinical strategies for new products. Also, disclosing this type of information to the general public would not help patients determine their suitability as study participants.

99N-1737

When Life Depends on Medical Technology

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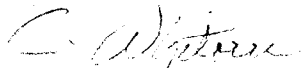
FDA should look for other avenues by which to disseminate this information if it decides to proceed. For example, information that is disseminated could be made available only to qualified health professionals rather than the general public. This would allow someone who understands the medical implications of the study and the therapeutic needs of a particular patient to make a determination of whether or not the device being studied in the trial might offer some benefit to that patient.

In summary, Medtronic believes there might be some public health benefit from making information available to the medical community on clinical studies of devices that treat conditions for which there are no alternative therapies. However, FDA should seek methods other than release to the general public and any information that is released must not compromise the competitive position of the study sponsor.

FDA should see what the results of the proposed drug trial database are before proceeding with a device database. The experience with drug studies could provide valuable insight into the feasibility of a similar database for devices.

Medtronic appreciates the opportunity to comment on this issue.

Sincerely,



Chip Whitacre
Director, Corporate Regulatory and
Clinical Affairs
tel 612-514.8556
fax 612.514.6459

COOK[®]**Cook Group Incorporated**

August 23, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket No. 99N-1737

Dear Sir or Madam:

The Cook Group ("Cook") submits this comment in response to the Food and Drug Administration's ("FDA") June 22, 1999 *Federal Register* publication regarding public availability of information on clinical trials.

Cook is a holding company of an international corporation engaged in the manufacture of diagnostic and interventional products for radiology, cardiology, urology, gastroenterology, emergency medicine and surgery services. Cook has pioneered numerous products to improve patient treatment and care, including devices used in the Seldinger technique of angiography and in techniques for interventional radiology and cardiology. Many Cook products benefit patients by providing doctors with the means of diagnosis and therapeutic intervention without necessitating open surgical procedures. Cook sells over 15,000 different products which can be purchased in 130,000 different combinations.

Section 113 of FDAMA directed that the National Institutes of Health (NIH) establish, maintain and operate a data bank of information on clinical trials for serious and life-threatening diseases and conditions. It also instructed the Secretary of Health and Human Services (HHS), the Director of NIH and the Commissioner of the Food and Drug Administration (FDA) to collaborate and determine the feasibility of including device investigations within the scope of the data bank.

We are not familiar with what has been learned in assembling the data bank for drugs. However, it is Cook's view that HHS should utilize the experience gained in setting up that data bank to determine whether and how to move forward in the case of devices. If indeed it is found that there has been significant patient benefit by establishing this data bank for drugs, we believe it should be explored for medical devices.

Dockets Management Branch (HFA-305)

August 23, 1999

Page 2


In analyzing this issue as it pertains to medical devices, it is important that HHS recognize the device industry is quite distinct from the pharmaceutical industry. Devices are manufactured by thousands of companies, most of which are very small. These small companies are responsible for much of the innovation in the industry. Many of them are privately held and were created to develop one particular product. Further, while most of the larger, publicly held device companies publicly disclose clinical trials as a matter of practice, the smaller, privately held companies generally do not. Confidentiality is particularly important for them. If potential competitors are aware of the developmental activities of a one product company and beat it to the market place, that will usually destroy the small enterprise.

Nonetheless, if it is demonstrated that disclosure of clinical trials for a device will significantly help patients who are very ill, it should be made. We recommend that any such disclosure in the device area be limited strictly to products used in treating serious or life-threatening diseases and conditions. The appropriate clinical trials for disclosure should be determined according to whether the Agency would engage in an expedited review of the product. The products that receive an expedited review are the types of products to which Congress felt patients need access. Patients who are not seriously ill or who have effective alternative therapies available to them are not interested in finding clinical trials.

It is also recognized that in some situations companies may want to have information on a clinical trial listed in the data bank, and should be permitted to add it if they elect. The data bank may assist in obtaining patients for some conditions with small populations.

We appreciate the opportunity to offer these comments. We believe that confidentiality of information regarding product development is important for innovation in our industry. However, if the experience with the drug data bank indicates that there is significant benefit to patients, disclosure of clinical trials for devices in limited types of cases is appropriate, in our judgment, and good public policy.

Respectfully,



Stephen L. Ferguson

SLF:clw



Corporate Regulatory Affairs

Abbott Laboratories

D-387, Building AP6C
100 Abbott Park Road
Abbott Park, IL 60064-6091

August 23, 1999

Dockets Management Branch (HFA-305)
The Food and Drug Administration
5630 Fishers Lane Room 1061
Rockville, MD 20857

RE: Public Availability of Information on Clinical Trials for Investigational Devices
Intended to Treat Serious or Life-Threatening Conditions
[Docket No. 99N-1737]

Dear Sirs or Madams:

Abbott Laboratories submits the following remarks in response to the Agency's request for comments on the above-named subject and docket. Abbott is an integrated worldwide manufacturer of healthcare products employing more than 56,000 people and serving customers in more than 130 countries.

I. GENERAL REMARKS

1. HIMA. Abbott generally supports the August 23, 1999 response to this same subject sent to the FDA by the Health Industry Manufacturers Association (HIMA).
2. Access by Individuals and Overall Goals Support. One purpose of Section 113 of FDAMA is "to simplify the process through which individuals with serious or life-threatening medical conditions obtain information about opportunities to participate in clinical trials of experimental therapies." While we endorse this goal, there are two other goals which must also be supported, namely, (1) maintaining the integrity of the clinical trials process, and (2) protecting the competitive advantages of those medical device firms involved in clinical research.

99N-1737

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3. Experience from the Drug Database. One intent of Congress was that the FDA and other government agencies get at least two years' experience with the drug data bank for clinical trials before proceeding with the device clinical trials database. While the drug data bank has yet to be established, we believe that experience with the database for drugs would be a worthwhile consideration in designing and developing a clinical trials database for medical devices. It would be best to wait, however, until all parties gain experience and knowledge operating the drug database.
4. Development and Communication. We recommend a series of ongoing discussions and communications between the Agency, industry and other parties concerning the development of any device clinical trials database. A key consideration in the development process is how the database would accomplish many of the following potentially conflicting objectives:
 - Be accountable to individuals yet maintain privacy on a national level.
 - Meet broad national objectives such as FDAMA but also remain accessible to all parties, including those who may not have access to the Internet.
 - Stimulate individuals to participate yet maintain the privacy and technical advantage of the company conducting the research.

II. SPECIFIC COMMENTS

The FDA asked for comments on eight specific question. The questions and our comments are shown below:

1. *Is there a public health need for inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act?*

Comment: It is our opinion that a public health need does exist. Several historical examples bear this out. For instance, the many early attempts to develop an artificial heart and associated replacement parts were hindered due to a lack of suitable patients. Similarly, early tests on many of today's commonly used devices for cardiovascular surgery had to be delayed or taken overseas due to the inability to attract and identify suitable candidates for human trials. Finally, we must recognize that these trials may be the only potential source of help for some patients.

2. A. *If there is a public health need, what category of device trials should be made publicly available and how should this category be defined?*

Comment: We would recommend that trials involving the more critical or life-dependent devices be made publicly available. This typically includes Class III and PMA-type devices.

- B. *FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted?*

Comment: No. We would encourage the Agency to act positively on these provisions and not to "restrict" any information other than to blind selected data. Certain data must be blinded so that original research is not compromised and company identification remains known only to the Agency.

The Agency should not restrict this work to treatment IDE's since it would limit the intent of FDAMA; it would limit the availability of potentially life-enhancing procedures to the public; and it would prevent the identification of suitable candidates, a major factor in preserving national competitiveness.

- C. *Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?*

Comment: The FDA should use its scientific knowledge base to resolve this question. Historically, pilot testing has been closely controlled when humans are involved so as to prevent unintended harm to healthy subjects. When the device has shown some degree of reliability, only then should the trials be made public through this proposed database.

3. *Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients?*

Comment: Historically the FDA has closely controlled these trials, including the associated statistical rationales for selecting population and sample sizes. We would not expect the FDA to change this oversight function despite a wider public awareness of the many ongoing device clinical trials. Nevertheless, certain impacts could be experienced by all parties involved with device clinical trials if, or when they are generally better known to the public.

Positive Impact: Both the public and the Agency would have greater assurance that the device in question is safe since the clinical trials could be carried out with a larger and perhaps a more statistically significant population and related sample size.

Negative Impacts: If the Agency develops a database as described above, the public's greater desire or ability to participate in a certain trial should still be limited to the formal inclusion criteria as specified in the company's clinical protocol. The other issue is the possible management of a trial in which a limited number of devices are available for life-threatening diseases. For example, a drug company was recently confronted with the necessity of having to run a lottery for including a specific type of patient for a possible cure to a specific type of cancer. This scenario stemmed from a limited supply of the drug used to treat a life-threatening disease.

4. *IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?*

Comment: We again defer to a blinding of data by the Agency which would maintain the integrity of research while allowing individuals to pursue specific treatments. The database might be tailored to list treatments and contact persons only. Multiple "hits" or listings under one specific treatment should not compromise the identity of the company. In all cases, competitive advances, specifically related to the overall national competitiveness, must also be maintained.

5. A. *If disclosure is mandatory, is it likely to hamper innovations and investment in research and development?*

Comment: Yes. The company undertaking the research along with the specific information about the product and possible course of treatment should not be disclosed.

- B. *Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?*

Comment: As described in #3, given the potential for larger populations and an increased number of test subjects, the outcomes would be more reliable.

6. A. *Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk?*

Comment: The statistical and ethical principles of the trial must be maintained, and the Agency and the sponsor must communicate their statistical needs and material expectations to one another in these instances.

- B. *Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?*

Comment: This is a possibility if too much data are made available and an uncontrolled format is allowed to be made public. The Agency has already stated that it would consider improper promotion in this format as a basis for possible enforcement actions.

7. *Will public disclosure of information about device trials for products to treat serious or life-threatening disease or conditions affect reimbursement policies of third party payers?*

Comment: Possibly. But this issue goes beyond FDAMA and should be resolved through joint efforts with HCFA, industry and other parties.

8. *What other important information or issues should the agency consider?*

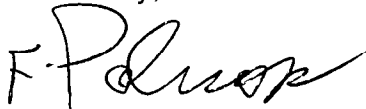
Comment: The Agency should consider in what format this information will be displayed and how it will be made available to the public. By providing too much information, research integrity and clinical trial data may be unduly pressured. Issues of competitiveness should be resolved through consultation with industry trade associations and individual companies as this remains a viable concern for this issue. Finally, the Agency should develop operating principles to ensure proper operation of the database including data input, data display, when to remove data and how to maintain confidentiality.

III. CLOSING COMMENTS

The implementation of the proposed database should be undertaken with the following criteria in mind:

- A. Consensus based. There exists a real potential for conflicting goals involving private citizens, national companies, various privacy issues and the involvement with companies which vary greatly in size. Because of the broad scope of this proposal, further development on this database should be undertaken with these various parties on a consensus basis.
- B. Privacy. Patient confidentiality will be a concern, and in this instance the Agency must also deal with national competitiveness and the proprietary issues affecting the companies carrying out the research.

Yours truly,



Frank Pokrop
Director, Corporate Regulatory Affairs
(847) 937-8473
FAX: (847) 938-3106

cc: Robert R. Gatling, FDA (HFA-404)

Comments
From
Advisory Panel Consumer
Representatives

Gatling, Bob

From: Peters, Marilyn R. [Marilyn.Peters@med.va.gov]
Sent: Friday, August 20, 1999 10:50 AM
To: 'RRG@CDRH.FDA.GOV'
Subject: Response to Questions



FDAMA Section
113.doc

Attached is the brief response to questions 1 & 2. This is the consensus from my consumer contacts as well as my own view.

<<FDAMA Section 113.doc>>

FDAMA Section 113(b) Questions

Question 1: Is there a public health need...

The current trend in the health care arena is for all consumers to become partners with their providers and be informed participants in healthcare decisions. The emphasis is on self-care and knowing when to seek the assistance/support of healthcare providers. With that in mind, one needs to have access to information in order to make appropriate decisions.

A data bank (although public) would probably not be accessed by the masses. The need for this type of information would be generated by the critical nature of one's illness. Therefore, I believe it to be in the best interest of the public to have information available about potential devices that demonstrate reasonable assurance of safety and effectiveness that may ease suffering/prolong life/restore health.

Question 2: The adverse impact...

If researchers stop investigating/testing because the public can have access to what is being done, then maybe the research is not appropriate. Or the methods are questionable. Special interest groups have been very vocal in the past. Some have had profound effect on the public. The effect on the public, I believe, has not always been the groups' intention but rather is an outcome of how the media has presented the groups' message. Our present culture of lawsuits would make one reticent to have the public knowledgeable about device innovations and research/investigation. However, how can one solicit subjects without some knowledge being available? If knowledge needs to be available why not have a systematic format with guidelines that will cover all such devices? I believe that the establishment of a data bank will not unduly affect credible innovations and device research.

Gatling, Bob

From: Renee Middleton [middle@groupwise1.duc.auburn.edu]
Sent: Tuesday, August 24, 1999 4:32 PM
To: rrg@drh.fda.gov
Subject: FDAMA Section 113(b) Questions

I am Faxing you a copy of the Request to Be Paid for Agency-Directed Assignment (Homework) Form...Please confirm your receipt of this E-mail. Thank You!

Responses to Questions 1-8...

1. Yes, there is a public health need for inclusion of device investigations...

2. Device trials should be made publicly available. Unless there is a plausible reason for not doing so, why can't the categories be "serious" and "life threatening" utilizing the same definitions applied to IDE i.e., "as a stage of a disease in which there is a reasonable likelihood that death would occur within a matter of months or in which premature death is likely without early treatment"... Just extend the definition...YES< a data bank for IDE's should be similarly restricted. I believe the bank should include ONLY those studies that are intended to demonstrate reasonable assurance of safety and effectiveness.

3. Industry may decide they want to have "larger" numbers of subjects so that their data is seen in the most positive light, HOWEVER, if they do so, they do so for their own reasons. FDA should not establish this as an expectation...It should be left up to the industry. I believe the release of information will help "wise" consumers to be more aware of those devices and drugs that are likely to be of benefit to them in the future...They will also be more aware of the "real" and/or "potential" risks involved in their participation in clinical trials...FDA should set limitations or standards for increases in the size of device trials or number of site situations ONLY when it is BELIEVED that doing so would increase risks to patients...

4. I have no problem with making public disclosure voluntary on the part of the investigators/sponsors (this would help to control for those instances where expansion might increase risk to patients)...If disclosure by one sponsor puts pressure on similar investigations to disclose the existence of their studies, so be it! I still believe it is in the best interest of the public and participants to have the information made public.

5. I wouldn't want to make disclosure mandatory, investigators would then find ways to manipulate their data unfairly to produce desired results (sorry, but that's what I believe)...If you make it voluntary, it creates more of a competitive environment, a healthy competition...

6. FDA should NOT BE CONCERNED with the supposedly "undue" financial pressure or incentives on the trial sponsors...As you say, they will be able to recover the burden of the costs... FDA should be concerned about improper promotion and commercialization, but I think this will be less of a problem if you make it voluntary. Additionally, I believe FDA should be able to control for this with requiring some sort of disclaimer statement being included by those who use the data bank.

7. Not sure how it would....

8. I think you should certainly use The Tuskegee University Carver Reserach Foundation and their Center for Bioethics in Research & Health Care...If you have not already sought their input, I would encourage you to foward these questions to them---Dr. Marian Secudy (334) 727-8287; E-mail" WSapp@acd.tusk.edu

Renee A. Middleton, Ph.D.
Assistant Professor and Director
Auburn University
College of Education
Department of Counseling and Counseling Psychology
Auburn University, AL 36849-5218
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middlre@auburn.edu

***** "It is when we are at our lowest that we are called to rise,
and then,
if we are true to plan, our statures touch the skies" ***** (Emily
Dickenson).

Gatling, Bob

From: Anne Wojner [anne.wojner@aacn.org]
Sent: Thursday, August 19, 1999 12:36 PM
To: RRG@CDRH.FDA.GOV
Subject: Homework Assignment

After consulting with some other consumers, here are my responses to your request for information.

*It was generally agreed by all, that patients in the defined category should have access to devices which may improve their health, and/or quality of life. All seemed to feel that these patients have, "nothing to lose," and indeed, "may gain," from inclusion.

*General consensus was that "reasonable" evidence of efficacy/safety should be established prior to making devices accessible for this patient population. "Reasonable" was defined as, 1) animal evidence of safety & efficacy, 2) evidence that suffering (pain specifically) was not exacerbated by use of the device, and 3) evidence that use of the device would not promote social isolation from significant others/loved ones, caused by fear, inaccessibility, or increased risk/vulnerability to infection.

*There was concern that enrollment in device trials be governed by an informed consent process that clearly defines the objectives of the trial, and what has been found to date; in other words, if you are seeking 20 subjects, and the patient to be enrolled is number 20, then they wanted to know what has been found thus far. I'm not sure how realistic this is, but the consumer that brought it up quoted a recent U.S. News & World Report that discussed how to be research savvy.

*No other concerns were identified; there was a general feeling of trust for the FDA decision-making bodies, and a belief that the consumer would not be "harmed" by inappropriate management of the process by the FDA. Thank you for the opportunity to contribute.

Anne Wojner
Consumer Rep
Neurologic Device Panel

A Consumer Representative's Perspective

FDA Modernization Act (FDAMA) of 1997

**Including Device Clinical Trials for Serious or Life-Threatening
Conditions in a Data Bank under 402(j) of the PHS Act.**

By

Robert A. Dacey

Consumer Representative

Circulatory Systems Devices Panel

August 20, 1999

The following is my response to the FDMA Section 113(b) questions regarding inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act.

Please understand that I have, at this time, only limited knowledge of, and experience with, the legal and regulatory issues of these sections of the PHS Act. Consequently, my comments as a consumer representative may be general and lacking in technical expertise.

I. Overview

As our world, and our diverse communities, make the transition from the modern era into the postmodern era, many of our beliefs, values, institutions and infrastructure systems face new challenges for dominance and survival. Beliefs, values and problem-solving systems that were formerly simple and uncomplicated may now be complex and difficult to comprehend by the general ("consumer") public. For many consumers, the power and velocity of change is overwhelming at times.

This sense of being overwhelmed by information and technology is especially evident in the realm of health care, medicine and medical treatment. Generational differences and rapidly changing demographics further add to the social, economic, cultural, educational, political and ethical dilemmas spawned by the power and velocity of change. These generational differences and demographic changes also impact health care, medicine and medical treatment.

Public health policy and regulation are not immune from all the influences and indicators of these powerful and evolving changes.

However, certain foundations of beliefs remain on solid ground. To the best of my knowledge, the definition of *medicine* is still "...*science-based remedy*."

While other words, such as *hope*, *healing*, *wellness*, and *cure* have been transformed into marketing terms, *science* remains as a noun with profound meaning. With genuine respect and appreciation for the beliefs of the faith communities and other value systems, scientific methodology is still the foundation upon which medical knowledge resides.

Consumers, when they become *patients*, ultimately must trust the science of medicine, and in the science-trained providers of medical treatment. After all the health care marketing hype that consumes every media-driven day is discharged, consumers ultimately must rely on the science of medicine when confronted with a serious or life-threatening condition.

Consumers may, with personal justification, express profound confidence in a faith-based belief, or in other personal value systems, that provide special comfort during times of serious or life-threatening conditions. Health care and medical treatment providers may share or encourage such beliefs. But, the safety and efficacy of a medical intervention is still science-based.

Public health policy and market regulation is based on scientific knowledge. Consumers, for the most part, trust such science-based public health policy. When faced with a serious or life-threatening condition, consumers usually put abundant faith in the science, and in their medical treatment providers. Public health policy and regulation must, therefore, reinforce the consumer's trust and faith in the science.

Helping consumers to understand the science, via sharing information and knowledge, and via ongoing self-care skill training, is a special public health challenge. Certain consumer populations are more difficult to reach effectively, making the challenge even more complex.

However, allowing only the marketplace to dictate the science, and to inform the public, spawns awesome moral hazards and ethical dilemmas.

Consumers, when they become patients faced with a serious or life-threatening condition, are not merely customers of a market-driven medical treatment system. They are, individually and collectively, human lives, complete with all the complexities of a natural existence. They are collaborative partners (not just stakeholders), in the quest for safe, beneficial, and cost-effective medical interventions, with...

- medical treatment providers,
- medical device and drug manufacturers,
- third-party payers,
- and the regulatory agencies.

Consumers are people, not just demographic indicators in a strategic marketing plan. Knowledge of the demographic indicators does, however, help design the methods, materials and mediums for communicating with consumers.

From this consumer's perspective, investigational medical devices and investigational drugs are in equal general domains.

II. A Perspective on the Eight Questions

All of the eight questions provoke two general responses.

1. In addition to risk/benefit issues, there appears to be an implicit issue of cost/benefit analysis. Not simply economic cost to a business or to society, but also the costly risk of creating public demand for a device that could prove harmful or ineffective. This is especially true with Class II and III devices.
2. Public disclosure policy should be evaluated on a case-by-case basis for Class II and III devices.

Investigational medical devices can range from very simple to extremely complicated and sophisticated. A "one size fits all" policy would not work across the entire spectrum of potential Class II and III devices. This suggests that each device must be evaluated on its particular merits and intended use, with special emphasis on the potential consequences of public disclosure.

Mechanisms, especially in the areas of quality assurance and risk management, appear to already exist to address some of the above concerns.

III. Specific Answers to Each of the Eight Questions.

1. Yes! The public health mission of safeguarding America's health should not be perceived, in any way, as being shrouded in secrecy. Consumers are entitled to know what is on the science-based medical horizon. This horizon includes investigational medical devices.

With the proliferation of websites, offering misinformation as well as valid information, and displaying unrelenting marketing hype as well as valuable research data, it is imperative that responsible information and data be made available to the public via the Internet. The format for reporting investigational medical device information and data via the Internet must avoid any appearance of marketing hype or sales promotion.

For those consumers who are unable to access Internet-based information sources, efforts must be made to make such information and data available, on request, in non-electronic formats.

2. I'm really not qualified, at this time, to answer this question. However, as the Federal

Register notice points out, a definition of a “serious” or “life-threatening” condition, as the terms relate to medical devices, is needed. (“Sources of Risk From Medical Products,” as diagramed on Page 8 of the “Managing the Risks From Medical Product Use” Executive Summary, is a useful graphic for consumers.)

Not only do regulatory agencies and device manufacturers need to understand the scope of these terms, consumers need to know what “serious” and “life-threatening” mean. On a personal and professional level, I’ve struggled with this issue for many years. Crafting clear and useful definitions, for consumers, confronts an array of public perceptions. This is one area where the public looks to science for answers and clarification. This is one area where the public will ultimately trust the science.

3. My response to this question is again limited by my qualifications and experience. Positive and negative impacts are unavoidable, and the risk of unintended consequences and adverse events is always present.

A public data bank *should* put pressure on sponsors, investigators, and regulators to design and monitor the most effective investigational trials. All investigational trials involving medical devices must be bioethically and legally scrutinized. Consumers (often via their advocates) expect good science to seek such scrutiny.

If a device trial size or number of sites must be increased to satisfy the science of the investigation, allow consumers and patients to participate in the process that evaluates and defines the risks to the patient population. Allow consumers and patients to participate in the science. If the risk to patients is well understood, patients are then free to make a personal choice about participation in an investigational trial. This is a process that goes beyond the standard informed consent event.

Clearly, patients (and their representatives) who are incapable of understanding the implications of any risks should be excluded from any expanded investigational trial.

Based on the FDA Executive Summary, “Managing the Risks From Medical Product Use,” which I received in today’s mail (8/19), the risk management issue is well understood.

4. Is this a question of science or marketing?

The marketplace is intensely competitive. Allow market competition to serve the interests of science and public health.

5. Regardless of regulation and scrutiny, innovation and investment always finds ways to create new opportunities for profits. Mandatory public disclosure would, in the final analysis, promote improved science. The disclosure process may be painful to business interests, but public health will benefit.

6. Science must determine the size and scope of investigational device trials. If the science does not support R & D development, investment capital will look elsewhere for opportunities. Let science guide future investment and marketing. Marketing should not dictate the science.

The FDA should *always* be concerned about improper promotion and commercialization of medical devices, especially during investigational trials. The consumer/patient public is already overwhelmed with conflicting messages that promote questionable health care products.

For the most part, the public trusts the science when the science is not cloaked in marketing and advertising hype.

7. Yes, of course.

Third party payers are at the center of the cost/benefit and moral hazard storms. However, public disclosure of information about device trials to treat serious and life-threatening conditions can help payers project cost/benefit decisions into the future. They will not be able to ignore good science during the process of investigational medical device trials.

8. One of the greatest moral hazards is the temptation to put a price tag on human life. This was once an unthinkable subject in biomedical ethics. Under the traditional medical model, the patient is blameless for any serious or life-threatening condition. Market-driven forces are tilting the perspectives around this once unthinkable subject.

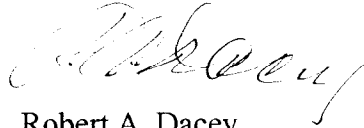
The FDA must not become embroiled in this debate, and I salute the FDA for the professionalism that it employs in carrying out its mission.

As a consumer representative, I have a special interest in developing more collaborative partnerships that include the “People Sector” as equal partners with the Public Sector and Private Sector. At some levels of discussion, consumers may be considered “stakeholders” in protracted decision-making processes. Eventually, however, the consumer must be considered a collaborative partner with the Public and Private Sectors.

I’m honored to be an FDA consumer representative. The learning curve is steep and intense. Perhaps, as part of my own learning process, I can help contribute to the public’s understanding that *medicine* is a *science-based* remedy.

Public health policy needs a science-literate public.

Thank you for requesting my comments.



Robert A. Dacey
Consumer Representative
Circulatory Systems Devices Panel

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DKN & ASSOCIATES, INC.

Rec 9/20/99
Postal Delay

Donald W. Wallace, M.D., Medical Director

Diane K. Newman, Adult Nurse Practitioner
Gina Amato, Geriatric Nurse Practitioner
Judith Ikpah, Adult Nurse Practitioner

August 22, 1999

Robert R. Gatling, Jr.
Director, Program Operations Staff
Office of Device Evaluation
Food & Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

Dear Mr. Gatling:

I would like to respond to the FDA MA Section 113(6) Questions.

1. Is there a public health need for inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act?

Yes, there is a public health need for inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act. There is increasing development of technology for devices and products that are being used to treat and manage life threatening diseases and conditions. This is especially true in elderly patients whose diseases are not being cured but managed. I believe the FDA needs to track usage, side effects, mortality, etc. as the devices are developed.

2. If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility / pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?

I believe all clinical trials of all devices should be publicly available. This should be for devices where no alternative device exists. The data bank should be restricted.

3. Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients? Will a public data bank create pressures to increase the size of device trials or number of sites in situations where such expansion may increase risk to patients?

I believe the current number of subjects for investigational device trials is too small. However, I do not believe subjects number need to be as large as drug studies. I do not believe a public data bank will create pressures to increase sites of trials but it may increase pressure to increase the size of subjects.

4. IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?

I believe public disclosure on device clinical trials should be mandatory. If it is voluntary I am unsure if industry would disclose their information. Remember, we are talking about life threatening diseases and conditions. Does the FDA know the number of current devices that fall into this category?

5. If the disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?

It depends when disclosure occurs. It should not be during feasibility or pilot trials. It should only be during actual clinical trials.

6. Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?

I do not believe that disclosure would increase commercialization. However, there is great interest from the investment community in device development and research because of increasing health care needs.

7. Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?

No, because most insurers want to see the outcomes of the clinical trials. At that time, information is disclosed.

8. What other important information or issues should the agency consider?

In discussions, with device companies, it is evident that they want separate regulations from the drug regulations. Many are small companies, with limited research dollars, unlike the pharmaceutical industry. However, I believe it is in the public's best interest to disclose information about developing devices for life threatening diseases and conditions as soon as possible.

Please let me know if you have any questions.

Sincerely,



Diane K. Newman, RNC, MSN, CRNP, FAAN

Comments
From
Consumers
and
Health Professionals

Date: August 24, 1999
To: Patricia M. Kuntze
From: Stan Reynolds
Subject: Public Availability of Data on Clinical Trials

I am sorry about the delay in this response. I was in the field for a week, trapping mice for hantavirus testing. I have spoken with several clinical microbiologists, as well as members of a Lyme disease advocacy group, several cancer patients, and a friend with CREST. All of these individuals have direct interest in clinical tests and the devices and kits used for those tests. When I reviewed the request for comments from the FDA, I concluded that there were three major issues to be considered. These are: 1) right to know, 2) need to know and finally, 3) the burden upon the manufacture.

All of us agree that the right to know was universal among all users and consumers. However some of the microbiologist feel more strongly about the need to know of any and all clinical trial results as soon as the were completed. When the patient groups were questioned as to whether the possibility that a test might become available at a future date would have any immediate impact on their decisions for being tested, the answer was "no".

To give an example of how I perceive microbiological devices to be different from medical and radiological devices, biological and pharmaceuticals allow me to give two examples.

If any individual was contemplating elective joint replacement surgery, and learned that a new type of polymer joint was available, he or she would quite likely investigate the new joint before proceeding with the surgery. If the individual learned that there might be substantial advantage to have the new joint, he or she might delay the surgery, pending the outcome of the clinical trials. In such a circumstance, the individual would want to know about the outcome of each stage of the trials as soon as possible. This would allow an intelligent choice as to whether to wait for the new joint to be release or to opt for the current surgery.

If an individual suspected that they had Lyme disease, or was told by their doctor that he or she might have Lyme disease, the individual would want to be tested as soon as possible. If you informed that patient, his physician or the laboratory personnel performing the test that a new Lyme disease test was in clinical trials, that information would have no effect on the testing. All or some of the parties involved may conclude in the future that the new test is better. At that time they

would opt to use that test, re-testing the patient if that was deemed appropriate or necessary.

So I see these as the situations that currently exist. In the first, the actions of consumers may be driven by ongoing clinical trial results. In the second they are not. I do not perceive the same need to know in the area of microbiological devices that exist in other area. Now we must consider the third issue, the burden on the manufacture. I am not an expert in this area. However it is obvious that there will be some burden to the manufacture. In the absence of some clear-cut benefit to the consumer, I can see little justification in requiring public availability of this information. Conversely if there is clear evidence of benefit, as I would expect to be in the case devices used in life threatening conditions, all trial information should be made available to the public.

Sincerely

Stanley M Reynolds

DR. JOYCE A. M. THOMAS
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O: 202.466.1111 H: 301.949.4050 F: 301.949.2627
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FACSIMILE TRANSMITTAL SHEET

TO:	Brenda Lee Evelyn	FROM:	Dr. Joyce A. M. Thomas
COMPANY:	US Food and Drug Administration	DATE:	08/21/99
FAX NUMBER:	301.443.4555	TOTAL NO. OF PAGES INCLUDING COVER:	2
PHONE NUMBER:	301.827.4460		
RE:	Docket No. 99N-1737 Public access to clinical trial information		

URGENT FOR REVIEW PLEASE COMMENT PLEASE REPLY PLEASE RECYCLE

The following response is submitted as public commentary to Section 113(b) of the Public Health Service Act.

1. Yes. There is a critical public health need to include medical device investigations within the scope of the data bank under 402 (j). The publicly provided resource will ensure accessibility to current drug and medical device trial information for all Americans, particularly the chronically ill and their family members or care takers.
2. The category of device trials should be defined to include feasibility/pilot trials and studies that are intended to demonstrate reasonable assurance of safety and effectiveness.
3. Where investigational device trials sites are made known to the public through data banks, there is an educated and involved public participant in the research processes.
4. If public disclosures are regulated under the FDA, all sponsors of a particular study should be required to inform the public of their research findings.
5. Mandatory disclosure of innovations in research and development would further research goals by extending enrollment participation opportunities.

DR. JOYCE A. M. THOMAS

6. The FDA should be concerned about improper promotion and commercialization of device trials, however the public has a right to know where the costs of the device are occurring.
7. I am not aware of how payment to third-parties would be affected by making device trial information publicly available.
8. It is commendable that the FDA is planning a public meeting to give interested parties a chance to present their views on the feasibility, utility, and effects of a data bank for device trials. It is important that individuals with life threatening diseases or conditions to know that research remains on the cutting edge and that hope for a cure is imminent. Information regarding the date and time of the meeting should be submitted to all of the respondents and published beyond the federal register.

Comments
From
Health Organizations

National Organization for Rare Disorders, Inc.®

NORD • 100 Rt. 37, P.O. Box 8923 • New Fairfield, CT 06812-8923

(203) 746-6518 • FAX : (203) 746-6481

http://www.rarediseases.org • e-mail: orphan@rarediseases.org



out of the darkness,
into the light...

August 18, 1999

Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 99N-1737
Public Availability of Information
on Clinical Trials for Investigational
Devices Intended to Treat Serious
or Life-threatening Conditions

Dear Sirs:

In response to the agency's request for comments (*FR June 22, 1999: Docket No. 99N-1737*), the National Organization for Rare Disorders (NORD) feels very strongly that information about clinical trials with investigational medical devices for serious or life-threatening diseases should be made available to the public through an accessible database of clinical trials.

NORD is a national non-profit voluntary health organization representing an estimated 20 million Americans with rare "orphan diseases." Under the Orphan Drug Act of 1983, a rare disease is a health condition that affects fewer than 200,000 Americans. There are more than 6,000 of these disorders according to the National Institutes of Health (NIH).

Because economic analysis of research and development (R&D) of pharmaceuticals is different from economic R&D factors affecting medical devices (including patents), orphan devices were not integrated into the Orphan Drug Act. Instead, FDA's Humanitarian Device Exemption provides incentives to promote development of medical devices for populations under 4,000 Americans.

NORD was the primary advocate for inclusion of the Clinical Trials Database provisions of FDAMA (P.L. 105-115), which was enacted on November 21, 1997. NORD remains convinced that FDA's primary mission should be to enhance and protect the public health. The public is not well served when drug and device manufacturers shroud development of new products in a cloak of secrecy while patients with serious and life-threatening diseases are desperately searching for clinical trials they can participate in.

CH

MEMBER ORGANIZATIONS
Alliance of Genetic Support Groups
Alpha 1 Antitrypsin Deficiency National Association
ALS Association
American Brain Tumor Association
American Laryngeal Papilloma Foundation
American Porphyria Foundation
American Society of Adults with Pseudo-obstruction, Inc. (ASAP)
American Syringomyelia Alliance Project
Aplastic Anemia Foundation of America
Association for Glycogen Storage Disease
Batten Disease Support & Research Association
Benign Essential Blepharospasm Research Foundation, Inc.
Charcot-Marie-Tooth Association
Chromosome 18 Registry and Research Society
Cleft Palate Foundation
Cornelia de Lange Syndrome Foundation, Inc.
Cystinosis Foundation, Inc.
Dysautonomia Foundation, Inc.
Dystonia Medical Research Foundation
Dystrophic Epidermolysis Bullosa Research Association (D.E.B.A.)
Ehlers-Danlos National Foundation
Epilepsy Foundation of America
Families of Spinal Muscular Atrophy
Foundation Fighting Blindness
Foundation for Ichthyosis & Related Skin Types (F.I.R.S.T.)
Guillain-Barre Syndrome Foundation International
HHT Foundation International, Inc.
Hemochromatosis Foundation, Inc.
Hereditary Disease Foundation
Histiocytosis Association of America
Human Growth Foundation
Huntington's Disease Society of America, Inc.
Immune Deficiency Foundation
International Fibrodysplasia Ossificans Progressiva (FOP) Association, Inc.
International Joseph Diseases Foundation, Inc.
International Rett Syndrome Association
Interstitial Cystitis Association of America, Inc.
Lowe's Syndrome Association
Malignant Hyperthermia Association of the United States
Mastocytosis Society
Myasthenia Gravis Foundation
Myeloproliferative Disease Center
Myositis Association of America
Mucopolidosis Type IV Foundation (ML4)
Narcolepsy Network, Inc.
National Adrenal Diseases Foundation
National Alopecia Areata Foundation
National Ataxia Foundation
National Chronic Fatigue Syndrome and Fibromyalgia Association
National Foundation for Ectodermal Dysplasia
National Hemophilia Foundation
National Marfan Foundation
National Mucopolysaccharidoses Society, Inc.
National Multiple Sclerosis Society
National Neurofibromatosis Foundation
National PKU News
National Sjogren's Syndrome Association
National Spasmodic Torticollis Association
National Tay-Sachs & Allied Diseases Association, Inc.
National Tuberosclerosis Association, Inc.
National Urea Cycle Disorders Foundation
Neurofibromatosis, Inc.
Obsessive Compulsive Foundation
Osteogenesis Imperfecta Foundation
Parkinson's Disease Foundation, Inc.
Prader-Willi Syndrome Association
Pulmonary Hypertension Association
PXE International, Inc.
Reflex Sympathetic Dystrophy Syndrome Association
Scleroderma Foundation, Inc.
Sickle Cell Disease Association of America, Inc.
Tourette Syndrome Association, Inc.
Trigeminal Neuralgia Association
United Leukodystrophy Foundation, Inc.
United Mitochondrial Disease Foundation
VHL Family Alliance
Wegener's Granulomatosis Support Group, Inc.
Williams Syndrome Association
Wilson's Disease Association

99N-1737

Associate Members

Acid Maltase Deficiency Association
Aicardi Syndrome Newsletter, Inc.
ALS Association/Greater Philadelphia Chapter
American Autoimmune Related Diseases Association
American Behçet's Disease Association, Inc.
American Pseudo-obstruction & Hirschsprung's Disease Society, Inc.
American Self-Help Clearinghouse
Androgen Insensitivity Group
Angel view Crippled Children's Foundation

A-T Project
Ataxia Telangiectasia Children's Project
CDGS Family Network
Canadian Organization for Rare Disorders
Children's Hospital Medical Center, Akron Ohio
Children's Leukemia Foundation/Michigan Children's Medical Library
Children's PKU Network
Chromosome Deletion Outreach, Inc.
Chronic Granulomatous Disease Association, Inc.
Consortium of Multiple Sclerosis Centers
Contact A Family

Cooley's Anemia Foundation
Cushing Support & Research Foundation
Earl Goldberg Aplastic Anemia Fountain
Family Caregiver Alliance
Family Support System for North Carolina
Freeman-Sheldon Parent Support Group
Hydrocephalus Association
International Foundation for Alternating Hemiplegia of Childhood
JUMP Foundation
Klippel-Trenaunay Support Group
Late Onset Tay-Sachs Foundation
Les Turner ALS Foundation, Inc.

National Association for Pseudoxanthoma Elasticum
National Coalition for Research in Neurological & Communicative Disorders
National Gaucher Foundation
National Incontinentia Pigmenti Foundation
National Niemann-Pick Disease Foundation
National Oral Health Information
National Patient Air Transport Hotline
National Spasmodic Dysphonia Association
Neurotopia Support Association
Organic Acidemia Association
Osteoporosis and Related Bone Diseases

National Resource Center
Parents Available to Help (PATH)
Parent to Parent of Georgia, Inc.
Parent to Parent of New Zealand
Recurrent Respiratory Papillomatosis Foundation
Research Trust for Metabolic Diseases in Children/United Kingdom
Restless Legs Syndrome Foundation
Sarcolid Networking Association
Shwachman Syndrome Support Group
Sickel Cell Disease Association of Texas
Gulf Coast Society For Supranuclear Palsy, Inc.

Sotos Syndrome Support Association
Sturge-Weber Foundation
Treachler Collins Foundation
Vaincre les Maladies Lysozymales/France

* Associations are joining continuously.
For newest listing, please contact the NORD office.

Dedicated to Helping People with Orphan Diseases

The congressionally mandated report of the *National Commission on Orphan Diseases* (DHHS 1989) found that 47 percent of biomedical researchers said they could not find a sufficient number of rare disease patients to participate in clinical trials, while 76 percent of rare disease patients said they wanted to participate in clinical trials but could not locate scientists studying their disease. The FDAMA mandated *Clinical Trials Database* is aimed at solving this serious obstacle to research progress and engendering hope in patients with hopeless diseases.

Listed below are direct responses to the *Federal Register* questions:

1. **Public Health Need:** There is an intense public health need for information about device investigations. Information about experimental medical devices is even more difficult to locate than information about investigational drugs. Both patients and physicians need, but do not have access to this information. Thus patients who might benefit from experimental devices may be unfairly prevented from learning about opportunities to enhance scientific knowledge and promote development of new treatments.

Moreover, the rapid changes in modern technology may render new breakthrough treatments as "devices" rather than drugs. For example: implanted drug/device combinations, xenotransplanted tissues and organs, etc. These are products that do not technically fit either the current "drug" or "device" categories. If FDA classifies them as "devices," public knowledge of clinical trials will be even more imperative than it is today.

2. Will there be an adverse impact on device innovation if information on device investigations is required to be publicly disclosed? Firstly, we believe FDA's primary responsibility is consumer protection, not company protection. Therefore, it is FDA's responsibility to make and enforce policies that benefit the public health. Secondly, although companies often claim that secrecy is necessary to protect their products from competitors ("trade secrets"), one need only talk to a stock broker to learn which products each company is developing. Thus device companies cannot ethically claim that public secrecy is necessary while Wall Street secrecy is unnecessary.

It is a public health disgrace that Wall Street knows the products that device companies are developing, but patients and physicians don't know. Therefore, public access to this information can be no threat to innovation as long as FDA does not release the blueprints for the device and other detailed factors that might enable a competitor to duplicate the product.

3. **Other Factors:** The Secretary should be sensitive to the fact that patients simply want to know, especially when they have a serious or life-threatening disease without satisfactory treatment alternatives, that a clinical trial on a drug or device for their health condition is underway, where the clinical sites are located, and how they can obtain further information that can help them decide whether they want to participate in the clinical trial. This is all they want. Patients do not want to see the design of the device, the materials it is made out of, nor its marketing plans, nor wiring blueprints. If device manufacturers understand that their real trade secrets will be protected perhaps they will be more willing to cooperate in this public health venture.

On page 33314, the Federal Register notice asks another series of questions. Listed below are NORD's answers to those questions:

1. **Is there a public health need for inclusion of device investigations within the scope of the data bank under 402 (j) of the PHS Act?**

There is an absolute and critical need for public access to information about medical device investigations for serious and life-threatening health conditions. It is also critically important that information about pediatric devices is made available because there is a desperate need for small devices that can be used on infants and children.

2. **If there is a public health need, what category of device trials should be made publicly available and how should this category be defined? FDA's treatment IDE regulation applies only to devices for which no comparable or satisfactory alternative exists. Should a data bank for IDE's be similarly restricted? Should the trials that become part of the data bank include feasibility/pilot trials or only studies that are intended to demonstrate reasonable assurance of safety and effectiveness?**

There is probably minimal or no need for information about "me-too" medical devices (e.g., pacemakers similar to those already on the market). Unfortunately, much of the medical device industry conducts R&D on devices that vary only slightly from those that are already commercially available. The critical need is for information about devices for untreatable (or unsatisfactorily treatable) health conditions, pediatric devices, as well as truly innovative products that are improvements over currently available devices. Limiting mandatory disclosure to the truly innovative products (when no comparable or satisfactory alternatives exist), and pediatric devices, would be in the best interest of the public health.

We also suggest that clinical trials should be added to the database when they are in the more advanced investigational stages (the equivalent of phase III for drug trials). This is because earlier trials (while the product is in phase I or II) are more likely to fail; therefore, there is a higher risk to patients that the product will not be safe or effective. On the other hand, if a device manufacturer voluntarily asks for a product to be added to the database at an earlier stage of development, FDA should agree to do so if there are no significant safety or ethical questions.

3. **Investigational device trials have historically been smaller in numbers of subjects and numbers of investigational sites than investigational drug trials. What impact, both positive and negative, would the release of information have on these device trials, the sponsors, the investigators, the investigational sites, and the patients? Will a public data bank create pressures to increase the size of device trials or number of sites in situations where such expansion may increase risk to patients?**

Understanding that device trials are usually small and the clinical trial sites for devices are usually limited, there are factors that FDA and manufacturers should be sensitive to. Most importantly, patients will have difficulty traveling to the sites, and they may ask for travel assistance to cover costs. We do not believe the patient community will demand more

clinical trial sites so that participation will be more convenient to them. Rather, it has been our experience that patients are pleased to know research is being pursued, but the onus is on them to get to the clinical trial site rather than expect the site to come to them. Moreover, if too many patients wish to enroll in the study, FDA should monitor a fair and equitable rationing system such as a computerized random selection process.

4. **IDE information is generally protected from public disclosure under FDA regulations. If public disclosure were voluntary, would disclosure by one sponsor put pressure on sponsors of similar investigations to disclose the existence of their studies against their better judgment? Is this in the interest of the public health?**

It is in the best interest of public health to have as many device investigations disclosed on the database as possible. If FDA decides that only the truly innovative products should be listed (not the "me-too" devices), it is reasonable to expect that all manufacturers will want their products listed lest their product gains a reputation as not being a true innovation.

5. **If disclosure is mandatory, is it likely to hamper innovations and investment in research and development? Would disclosure of these investigational device trials help or hinder research by increasing patient enrollment?**

It is impossible to believe that mandatory disclosure would hamper investment in R&D. Indeed, it is only logical to expect that disclosure will speed innovation because it will enhance patients' and physicians' expectations, speed recruitment of patients for clinical trials, enable physicians to locate clinical sites that might be appropriate for their patients, and enable investors to analyze the potential for growth of the company. Indeed it is difficult to believe that investors would have any interest in a company that is unwilling to reveal information about future products in its pipeline.

6. **Because sponsors can recover some of the costs of the device research and development under the investigational device regulations, should FDA be concerned that publicly available information concerning investigational device trials will result in undue financial pressure or incentives on the trial sponsors to add subjects to the trials without appropriate consideration of risk? Should FDA be concerned about the possibility that improper promotion and commercialization will occur as a result of a public data bank for IDE trials?**

Will there be a financial incentive to manufacturers who can recover the costs of R&D under the Investigational Device regulations? Our experience with investigational orphan drugs (for which some manufacturers are allowed to charge a fee) proves otherwise. Many health insurers will not pay for investigational treatments so many patients must pay out-of-pocket when a drug is not yet approved for marketing. Therefore, only a small number of patients will be able to pay (depending upon the cost of the device) and to afford travel to distant trial sites. Any manufacturer who believes he will be able to make large profits on an investigational device is out of touch with today's managed care health system. Instead, we would urge FDA to require that a percentage of product be reserved for needy patients who want to participate in the trial but cannot afford to do so.

Should FDA be concerned that improper promotion and commercialization will occur because of the data bank? If FDA and NIH control the wording of clinical trial information in the database, claims will be truthful and non-commercial. Similarly, FDA must maintain control over written information about the investigational product, including informed consent documents.

7. **Will public disclosure of information about device trials for products to treat serious or life-threatening diseases or conditions affect reimbursement policies of third party payers?**

Unfortunately, public disclosure of information about investigational devices will not affect reimbursement policies of private third-party payers, but it may affect government payers (Medicaid & Medicare). Since there is no federal law governing private health insurers, many reimbursement problems have plagued investigational drugs, and they will similarly affect devices. We caution the FDA and NIH, however, not to create categories of specific diagnoses for which government insurance will reimburse (e.g., right now Medicare will reimburse for certain investigational cancer drugs, but not investigational drugs for other diseases). Instead, if FDA and NIH wish to advise HCFA about Medicare/Medicaid reimbursement for investigational devices, we implore you to negotiate reimbursement for all serious and life-threatening diseases for which alternatives are not satisfactory.

8. **What other important information or issues should the agency consider?**

Other issues the agency should consider are the impact on the public health that secrecy has historically had and the implications of not making clinical trial information available to the public. The agency should define "trade secret" not as blanket secrecy, but rather protection of the plans, designs, ingredients, components, etc., of a medical device that might enable a competitor to copy the product. Public information about the location of clinical trials should clearly not be considered a trade secret, but a matter of public health.

Thank you for the opportunity to comment on this public notice.

Very truly yours,



Abbey S. Meyers
President

ASM:aa

cc: Stephen Groft, Director, NIH Office for Rare Diseases
Marlene Haffner, M.D., FDA Office for Orphan Products Development



August 17, 1999

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

[Docket No. 99N-1737]

To Whom It May Concern,

AIDS Project Los Angeles is the nation's second largest provider of direct services to people living with HIV/AIDS, serving approximately 8,000 Clients in Los Angeles County. Since we serve people with a life-threatening condition, it is our position that it is of great importance to expedite the approval of medications and devices to help those in need.

Consequently, information regarding clinical trials for medications and devices should be readily available to people in need. Although the inclusion of devices in a database of clinical trials would greatly increase the size of a database for an area that is perceived to be underused, devices such as the Ganciclovir Implant would not have been as readily available to people with AIDS-related CMV Retinitis if they had not been included in clinical trials listings.

Finally, it is our position that while clinical trials and the proper inclusion of medications and devices in such databases are important, ongoing safety and follow-up data are necessary to ensure the health and quality of life for people with life-threatening conditions such as HIV/AIDS.

Thank you.

Sincerely,


Ruben Gamundi
Client Health Advocacy Program Manager

C 8

99N-1737

To: Dockets Management Branch (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD. 20852

SEP 15 11 29 AM '99

From: Patricia Hawkins
Local Health Services
Oklahoma State Department of Health
1000 N. E. 10th Street
Oklahoma City, Oklahoma 73117-1299

Subject: Docket No. 99N-1737

1. There is a public health need for inclusion of device investigations within the scope of the data bank under 402(j) of the PHS Act.

According to FDA's classification of devices, Class III devices include ligament replacements and bone substitute. Class III includes those devices for which general regulatory controls are not sufficient to assure safety and effectiveness and there is not sufficient information to establish a performance standard. Class III devices are generally considered investigational and have generally not been cleared for marketing for a particular purpose by the FDA. Class III devices also include all devices introduced after the enactment of the 1976 Amendments that are not substantially equivalent to a device marketed prior to enactment.

Class III devices may present a substantial risk to the public.

Upon a manufacturer's petition to FDA, a medical device may be reclassified from Class III to Class II or I.

It is legally permissible for a physician to use a commercially available and marketed medical device according to the physician's best medical knowledge and judgment, even if the medical device has not been cleared for that particular use by the FDA.

The decision rendered by U. S. District Court Judge Louis C. Bechtle and Judge Sandra Mazer Moss of the Court of Common Pleas of Philadelphia County mandates that in the litigation and for all further pedicle screw cases presented in Philadelphia, the law of informed consent does not require a physician to disclose to a patient whether or not a device has been given a regulatory or administrative label by the FDA. "A physician is free to use a medical device for an off-label purpose if, in the physician's best medical judgment, he or she believes that the use of the device will benefit the patient," the judges wrote in the decision. "Because the off-label use of a medical device is a matter of medical judgment, a physician may be subject to medical malpractice liability for the exercise of that judgment. That physician cannot, however, be held liable under the doctrine of informed consent for failing to advise a patient that a particular device has been given an administrative or regulatory label by the FDA."

99N-1737

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The ruling essentially nullifies the physician's duty to tell a patient that a particular medical device has been labeled by the FDA as a "Class III" device, an "investigational device" or a "significant risk" device. The ruling has significant implications for other states.

In 1995 Medicare extended its coverage to pay for new generations of medical devices while they are still being studied for marketing approval. This policy means that Medicare will pay for most medical devices prior to marketing approval, when they are used as a part of an approved clinical trial. Medicare rates are the same for comparable approved devices. Medicare coverage for devices in clinical trials accelerated the use of these devices for older persons. The continued growth of the older adult population means that the use of medical devices will increase dramatically as older adults search for ways to deal with arthritis and osteoporosis.

Hip and knee replacement arthroplasty are by far the most commonly performed replacements. Shoulder, elbow, finger, and toe joint replacements are showing steady increases.

The success rate of ligament replacement operations is difficult if not impossible to access. However, faulty replacements are occurring. The literature consistently ties success rates to the experience of the physician. Personally, I know of one 51 year old Oklahoma woman who has had three hip replacement operations within the last 10 years.

The ethics of reuse of single-use devices of medical devices, which appears to be a legitimate question, is being debated at medical conferences. These discussions have centered around informed patient consent, cost versus benefits of reuse, and the need for further scientific studies and patient tracking. For patients covered by Diagnosis Related Groups, billing is not affected by the lower cost of a reprocessed single-use device.

Throughout its history, FDA has been overly cautious about the intersection of its legal authority to protect the public health and ability of physicians to practice medicine and surgery as they believe is most appropriate and in the best interest of their patients. This hesitation has resulted in increased patient risks and abuse, as well as increased costs and fraud.

2. Because a public health need does exist, categories I, II, and III, as well as all seven categories which relate to the 1976 amendment, medical device trials should be made publicly available and communicated in a consumer-oriented manner. Data banks for IDEs should not be restricted and data bank must be inclusive of all studies.

Public disclosure of this information is vital to patient decision-making. Fully informing patients of the risks and benefits of treatment options tends to improve patient outcomes and reduce costs, as well as fraud. The Foundation for Informed Medical Decision-Making, along with other consumer groups, supports the shared decision-making theory.

To transform this theory into shared decision-making practices, consumers must be empowered to make the types of decisions that makes it possible for a physician and a patient to make a treatment selection that reflects, not only important clinical considerations, but also the values and preferences of the patient.

Many consumers agree with the bodies that several major trends in health care today create the need for a more informed and empowered medical consumer. Primarily,

- 1) The need to reduce medical care costs. Thus far most efforts have focused on managed care efforts to reduce supplier demands, with little concern for services that appear to be neither needed nor consistent with patients' preferences.
- 2) Public dissatisfaction with the health care system is growing. This dissatisfaction can be traced to patients' frustration with the paternalistic system of both fee-for-service and managed care.
- 3) Consumers want more information and want to be involved in managing their health and health care. More and more consumers are turning to the media for answers about their health care needs, and this has resulted in increased media coverage and publications related to health care. Too often much of the information they receive may not be evidence-based and thusly inadequate for medical decision making.
- 4) The Internet is providing unparalleled information access. According to Cyber Dialog, an Internet research firm, more than 17 million U. S. adults searched 20,000 web sites for health and medical information in 1998. Increased access to information shows that medical opinion and treatment practices vary from physician to physician and region to region. As a result, there is an increased demand for unbiased evidence-based material.

Comments
From
Public Citizens

August 16, 1999

Steven Rohr
5786 General Washington Blvd.
Alexandria, Virginia 22718

Dockets Management Branch (HFA-306)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 99N-1737
Request for Comments
Public Availability of Information on Clinical Trials

To whom it may concern:

I am respectfully submitting comments regarding the public health need for inclusion of device investigations within the scope of the data bank under section 402(j) of the Public Health Service Act (PHS Act) and the impact of such an inclusion on device innovation and research in the United States. The importance of this issue must be underscored given the discrete possibility that such a data bank could directly conflict with the agency's statutory mission to "encourage" the development of useful devices in the U.S.

Before offering specific comments, I want to urge the Food and Drug Administration (FDA) to request a 2 year extension of time to prepare the report to Congress that is required under the FDA Modernization Act of 1997 (FDAMA). It is simply irresponsible for FDA to attempt to prepare this report without offering all interested parties ample opportunity to provide input. It appears that the FDA has totally neglected its responsibility to seek input for the first 19 months since the passage of FDAMA. Yet, the FDA insists that a 60-day comment period following the publication of an obscure notice in the Federal Register (FR) is adequate to gather information required for the task. Even the agency's attempt to convene a public meeting appears disingenuous. Although I have not been successful in getting transcripts of the meeting, I suspect that a 2-week notice announced in the FR went largely unnoticed by the parties with an interest in the issue and the eventual outcome.

I will not offer comments regarding the "feasibility" of including information on device investigations in a public data bank. My interpretation of section 113(b) of FDAMA places this responsibility with the FDA. I must admit that I find it quite surprising that FDA is soliciting public input on this issue as stated in the "Summary" section of the FR notice. I cannot imagine any non-governmental entities offering input of value in this area. It occurs to me that the FDA would, however, be in a much better position to assess the feasibility of incorporating device investigations if the agency had fulfilled its obligation to establish the data bank for drugs under Section 113(a).

For your consideration, I offer the following comments:

(I) **Public Health Need**

Comment 1: There is little information readily available to determine whether there is a true public health need to disclose information regarding device trials in a Department of Health and Human Services (DHHS) data bank.

Without information upon which a conclusion can be based, one can only offer an opinion. In order to determine whether a true need exists, one would have to be able to identify probable public health benefit that would likely be realized by patients having access to such information. Given that there are very few investigational devices used in the diagnosis or treatment of serious or life threatening conditions where no alternatives

exist. any espoused need for greater access to device trial information is likely not genuine.

The FDA must resist the temptation to conclude that the existence of complaints by a few sponsors of device trials regarding the difficulty of enrolling patients is evidence of public health need. In most instances, the desire to expand the scope of device trials is simply related to a sponsor's desire to increase their rate of patient enrollment, to secure additional revenue and to build an expanded customer base, i.e., prescribing physicians.

Comment 2: It is impossible to generate the information necessary to determine whether there is a public health need to include device trials in the data bank without being given a definition of "serious and life-threatening conditions".

The inclusion of the discussion regarding treatment IDEs in the FR suggests that only the FDA is capable of recognizing a serious disease or condition when one exists. In the case of treatment IDEs, the FDA has admitted that it avoided defining "serious disease or condition" to preserve its discretion to determine which device trials are eligible. Unless the FDA provides insight into what criteria it uses to determine what conditions are serious, no meaningful assessment of public health need can be provided.

Comment 3: Any effort by the agency to restrict the definition of "serious and life-threatening conditions" only serves to diminish any benefits realized by the agency's eventual efforts to establish the data bank.

Should the FDA choose to use its current definition of "immediately life-threatening" diseases to identify the "serious and life-threatening conditions" for purposes of section 113(b), the public health need for any data bank will be severely minimized. Although I am not aware of the numbers of "treatment IDEs" in existence for devices, I suspect that they are extremely few. If the numbers are as low as I suspect, FDA need only look in its own administrative records to observe the rather scanty public health need for disclosure.

Comment 4: The concept of public health need suggests that there is a segment of the American population that is disadvantaged by not knowing of the existence of certain device trials. Knowledge of the existence of device trials is likely a minor determinant of enrollment eligibility and an individual's ability to participate in any given trial.

It is universally recognized that a patient's socioeconomic status is the major determinant of whether they can participate in a device trial, assuming they meet the eligibility criteria for enrollment. Information dissemination will negligibly contribute to satisfying any public health need. If a true public health need exists, DHHS would be better off rerouting the funds and resources needed to create and maintain the data bank to a program providing financial assistance to those patients unable to participate in a device trial.

(II) **Impact of Device Innovation and Research in the United States**

Comment 5: The FDA suggests that there may be an option for "voluntary disclosure" rather than a system of "mandatory disclosure". Any system based on voluntary disclosure will not insure that patients receive complete information upon which they can base decisions. Any system that does not require sponsors of studies to disclose information on their studies will not satisfy any public health need should one be determined to exist.

Comment 6: The FDA indicates that information regarding device trials is "generally protected from public disclosure under FDA regulations". While this is correct, it is more

appropriate for the FDA to consider the protection from disclosure afforded to sponsors of device trials under the Federal Food, Drug, and Cosmetic Act (the Act).

Perhaps a review of the legislative history of the Act may provide insight into why Congress believed that it was important for the FDA to respect the privacy of developers of innovative devices while they are pursuing their developmental activities. Since sponsors of device trials are likely small entrepreneurial start-up companies, individual physician-investigators, or privately held corporations, it is best to allow them to approach device development without the pressures that disclosure of their activities in a DHHS data bank will create.

Comment 7: Disclosure of information on device trials in a DHHS data bank will place considerable pressure on sponsors, investigators, institutional review boards (IRBs) and the FDA to prematurely, or unnecessarily, expand the scope of studies.

Consumers who believe that they are appropriate candidates for a given study will put pressure on investigators and sponsors to include them in the trial. Desperate and demanding consumers are likely to insist that (1) they be included, even if they do not meet eligibility criteria, (2) they be given the device and not the control, thereby jeopardizing the study design, and (3) they receive follow-up from their own physician and not the investigator. Hospitals will be pressured to accept patients from outside their geographic areas and IRBs will inherit much of the responsibility for monitoring and judging the issues that increased consumer demand will create. Given that the Health Care Finance Administration authorizes reimbursement for many investigational devices, it is likely that this increased patient pressure will also impact our nation's health care cost-containment activities.

Comment 8: FDA and the device industry should consider how the systematic disclosure of the existence of a device trial would affect the disclosure of more detailed information within an IDE under the Freedom of Information Act.

Patients interested in participating in device studies are likely to request information regarding the regulatory history and the progress of the trial before pursuing enrollment. This has major cost implications for sponsors, investigators and the FDA. Who will handle the requests, prepare and distribute responses and monitor the activities to insure that consumers are not misled?

Comment 9: Should the Congress decide to mandate through legislation that DHHS administer a data bank which includes information on device trials, the FDA will require additional funding and resources. Any data bank of public health information for consumers must be maintained and closely monitored for accuracy by the FDA. A lack of agency oversight in this regard will result in a potential for considerable public deception.

The FDA should not simply consider the cost implications for the agency, but rather consider the cost implications for the device industry, IRBs and investigators. Should a data bank be established, mechanisms would need to be developed and instituted for patients and their doctors to obtain information from all sources.

Comment 10: Although directly dependent on how "serious and life-threatening" is defined by the FDA, there is the distinct likelihood that consumers will not understand the information posted in a data bank.

With the exception of devices eligible for a humanitarian device exemption (HDE), there are usually alternative therapies to devices undergoing clinical study. In the case of HDEs, there is usually no clinical study to include in a DHHS data bank. This will be

extremely confusing to consumers, but may also reflect on a very low public health need for the data bank

Summary:

Clearly, the American public has the right to know of the existence of clinical trials funded with their tax dollars. Thus, there is a legitimate obligation for the National Institutes for Health to disclose such information. Likewise, public held device companies are obligated to disclose, through the Securities and Exchange Commission, some of their product development activities that have a direct bearing on investors. It is a totally different, and far more serious, matter for the federal government to decide to obligate sponsors of device trials to publicly disclose their activities for a potential benefit to a select few. If the outcome of device trials is of critical public health importance, as I am sure we agree it is, we should leave the completion of the trials to the individuals responsible for their conduct without additional pressures created through federal disclosure.

Thank your for the opportunity to comment on this fascinating and intriguing topic.



Steven Rohr

cc: Robert Gatling, Center for Devices and Radiological Health

Steven Peckman/3314 Rowena Avenue #4/Los Angeles/California/90027

via facsimile and mail

August 20, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: Docket No. 99N-1737/Request for Comments on Public Availability of
Information on Clinical Trials for Investigational Devices Intended to Treat
Serious or Life-Threatening Conditions

To whom it may concern,

Please accept this letter as a response to the request for public comment on the Food and Drug Administration (FDA) proposal to publicly post information on clinical trials for investigational devices. My comments will address three themes: (1) therapeutic misconception, (2) the role of federal agencies in ensuring the protection of the rights and welfare of human research subjects, and (3) FDA resources.

Research is an important tool for ensuring the health and welfare of the community. Without biomedical research we are lost in assumptions regarding the best treatment for any particular disorder. Biomedical research has resulted in tremendous advances for the welfare of the citizens of the USA and the world. The advances, however, come with related costs that have greatly impacted the rights and welfare of human research subjects, such as, the thalidomide scandal, the Center for Disease Control/Kaiser Permanente measles collaboration, Orange County Children's Hospital cancer research, and the Manhattan Ear, Eye, and Throat Hospital plastic surgery scandal.

We should not, however, confuse advertising clinical trials with the societal importance of biomedical research. The June 22, 1999, federal register asked for public comment regarding FDA's responsibility in advertising clinical trials and posed the question: Is there a public health need for publicly posting device trials? My response: the public, the public health and the public trust in FDA is not well served when the Agency takes responsibility for posting clinical research for a purpose other than alerting the public of experiments or researchers that should be avoided.

THERAPEUTIC MISCONCEPTION

The practice of medicine is based on trust, i.e., trust shared by the physician and the patient. The bond of trust was initially created over 2300 years ago when Hippocrates suggested that the

Steven Peckman Comment
Docket No. 99N-1737

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physician first and foremost do no harm to the patient. This means that the physician should always do what is in the best interest of the patient. The public health is best served by maintaining the shared trust of physician and patient, for without that trust, physicians receive incomplete, inaccurate information and we endanger the individual and society.

The Belmont Report serves to guide us in the protection of human research subjects from undue harm. The meaning of *Belmont*, specifically the ethical principles of beneficence and justice, has recently been manipulated from the traditional focus on protecting human subjects from undue harm to protecting human subjects from being excluded from research. The AIDS crisis created a profound paradigm shift in the public perception of clinical trials. AIDS healthcare advocates rightfully noted that there were no treatments for this new deadly disease and unproven drugs held out the only hope. The scenario resulted in a newly accepted definition: research equals treatment. For AIDS patients this was absolutely true. The AIDS example is the exception and not the rule. For most disease groups, equating research with treatment is a fallacy that is both scientifically and ethically indefensible. Yet many healthcare groups and companies attempt to capitalize on the concept of research equaling treatment and the societal cult of the "new" in order to maximize enrollment in clinical trials.

We should recognize that, "Research itself is not therapeutic; for ill patients, research interventions may or may not be beneficial. Indeed the purpose of evaluative research is to determine whether the test intervention is in fact therapeutic."¹ Biomedical human research, requires that both the physician and the patient suspend the trust built through practice of the Hippocratic Oath, at least temporarily, in order to gather information regarding the safety and effectiveness of healthcare strategies. For example, a patient and a physician, suspend the concept of "do no harm" when enrolling in and conducting randomized trials. Though the trial may include extensive safety mechanisms, there is little debate that the scientific design of the research and the comparison of groups requires that the interest of the patient becomes secondary to the interest of science.

In 1998 the Department of Health and Human Services, Office of Inspector General (OIG) reported that, "the line between research and therapy has become increasingly blurred."² The concept of research equaling treatment has been called the "therapeutic misconception" by George Annas, Alexander Capron, and Evan DeRenzo.³ The therapeutic misconception

¹ Office for Protection from Research Risks, Protecting Human Research Subjects: Institutional Review Board Guidebook; Washington D.C., (1993) 1-2.

² June Gibbs Brown, Institutional Review Boards: A Time for Reform, Department of Health and Human Services-Office of Inspector General; Washington, D.C: (June 1998) A-1.

³ George Annas, Questing for Grails: Duplicity, Betrayal and Self-Deception in Postmodern Medical Research. Journal of Contemporary Health Law and Policy, Vol. 12:100 (1996).

- Alexander Capron, Statement of Commissioner Alexander M. Capron, LLB, in National Bioethics Advisory Commission, Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity, Volume 1; www.bioethics.gov/capacity/TOC.html (1998).

- Evan G. DeRenzo, The Ethics of Involving Psychiatrically Impaired Persons in Research, IRB, Vol. 16, No.6; (November-December 1994).

Steven Peckman Comment
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construes "research interventions as beneficial to subjects (especially those for whom no other effective medical interventions are available) even when the prospect of benefit is nonexistent or extremely remote."⁴ The therapeutic misconception seeks to abolish the distinction between research and therapy, researcher and physician, and patient and subject. It capitalizes on the blind trust of patients nurtured through the Hippocratic Oath and serves to obscure the risks of participation in research.

In the discussion of advertising clinical trials, it is important to acknowledge that our contemporary society places great value on what is perceived as "new" regardless of its proven worth. We see this in the advertisements for products and clinical trials. Newness itself, in the public mind, makes one product superior to another. For unproven biomedical interventions this is surely misleading and may ultimately be dangerous. The Advisory Committee on Human Radiation Experiments observed, "there is reason to worry that participants in research may have unrealistic expectations about the possibility that they will personally benefit from participation [in research]..."⁵ We recognize in the scientific community that the new unproven product is not necessarily the best treatment for an ailment. The history of biomedical research is the story of one new product after another whose safety, efficacy, or superiority is never proven and never approved by the FDA. The FDA posting of clinical trials is the equivalent of the government advertising for unproven therapies and ultimately is counter productive to protecting the safety of society.

THE ROLE OF THE FDA

The public looks to the FDA as its protector. The FDA was created in order to ensure the welfare of the public through federal oversight and regulation of food, drugs, biologics, and medical devices. The creation of a publicly available FDA database of clinical trials will serve as Agency endorsement, advertising, and promotion of unapproved products with no proven worth, value, or safety. The public FDA database will exacerbate the therapeutic misconception of both patients and researchers and lead patients to believe that an experimental device is proven better than the standard therapy. In other words, I fear the database will be confused with FDA approval and endorsement of experimental devices over standard therapies. Ultimately, since the products are unproven, the database can only serve as a promotional arm for industry advertising of clinical trials. Additionally, the database may create a conflict of interest, that is, it will give the appearance that FDA is not the watchdog of research but rather promotor and advertiser of clinical trials.

My passing familiarity with Investigational New Drug (IND) exemption and Investigational Device Exemptions (IDEs) has highlighted that oftentimes sponsors and investigators confuse the issuance of the exemption with an FDA approval of the product. It is my understanding that IND or IDE status is not an FDA approval of the product but rather acknowledgment and

⁴ Annas, p. 106

⁵ Advisory Committee on Human Radiation Experiments, Final Report, Washington D.C. (1995) Chapter 18, Section 2.

Steven Peckman Comment
Docket No. 99N-1737

page 4

permission from the Agency for a sponsor and/or investigator to conduct a specified experiment under strict guidelines and protocol. This fine semantic point, I am afraid, will be lost on the general public, not versed in regulatory affairs, searching a database seeking treatments for disease.

If the device and drug manufacturers perceive a need for a public database of clinical trials, they should pool their resources and develop such an entity under the guidance and oversight of the FDA. The federal agency should not serve as a promotional arm of industry.

FDA RESOURCES

It is well-known that federal agencies have decreasing budgets in which to manage their workload. The clinical trials database will result in the squandering of precious federal resources that, as explained above, will not address the public health of the citizens of this country. FDA should consider allocating these precious resources to promote the health and welfare of the public that is participating and will consider participation in clinical trials. Specifically, it is well known that adverse event reporting for clinical trials is sorely in need of overhaul and possibly centralization. Sponsors, investigators, and Institutional Review Boards (IRBs) are in need of a central reporting and review body for timely monitoring of adverse events. The current decentralized system for adverse event reporting does not serve to protect subjects participating in multi-center clinical trials.

The current system relies on sponsors reporting to the FDA and local investigators all adverse events related to a study product in a multi-center trial. The IRBs receive the reports from centers all over the world with little information applicable to the local site or analysis of trends that may affect the welfare of the subjects. Limited IRB time and resources is spent reviewing undifferentiated reports without the ability to statistically identify trends on a national or international level and make relevant local decisions. I strongly recommend that the resources earmarked for the clinical trials database be reassigned to the creation of an FDA centralized adverse event reporting system that collects data, conducts statistical analysis, and reports trends to IRBs for local deliberation and action. The designation of resources to a centralized adverse event collection and reporting group will serve to protect and ensure the public health in a much more profound fashion than a clinical trials database.

Thank you for consideration of my comments. Please do not hesitate to contact me at 310.825.5344 if you have any questions.

Sincerely,



Steven Peckman

Appendix 2

Summary Minutes
Public Meeting
July 8, 1999

Summary Minutes
Food and Drug Administration Modernization Act
Section 113(b) – Device Clinical Trials Database
Public Meeting
July 8, 1999
1:30 PM – 4:00 PM
Room 20B
9200 Corporate Blvd.
Rockville, Maryland

Attendees:

Bob Gatling, FDA/CDRH	Patsy Trisler, Paragon Biomed.
Terry Toigo, FDA/OSHI	Doug McNair, Abiomed, Inc.
Alexa McCray, NIH/NLM	Susan Alpert, FDA/CDRH
Debbie Katz, NIH	Kimber Richter, FDA/CDRH
Marlene Tandy, HIMA	Joanne Less, FDA/CDRH
Stephen Northrup, MDMA	Nancy Pluhowski, FDA/CDRH
Kristine Rapp, Baxter International, Inc.	Ron Jans, FDA/CDRH
Patricia Garvey, Baxter Healthcare Corp.	Al Thomas, FDA/CDRH
Mark Gosnell, Boston Scientific Corp.	Greg Cambell, FDA/CDRH
Kathy Stover, Thompson Publishing	Diane Perticone, FDA/CDRH
Jon Hargreaves, FDC Reports	Brandi Stuart, FDA/CDRH
Chad Gorski, NNN	Jessica Auerbach, FDA/CDRH
Tim Kraesdoph, TCI	Richard Galgon, FDA/CDRH

Background

The Food and Drug Administration Modernization Act of 1997 (FDAMA) (P.L. 105-115) was enacted on November 21, 1997. Section 113 of FDAMA amends section 402 of the Public Health Service (PHS) Act (42 U.S.C. 282). Section 113(a) directs the Secretary of Health and Human Services (the Secretary), acting through the Director of the National Institutes of Health (NIH), to establish, maintain, and operate a data base of information on clinical trials for drugs for serious or life-threatening diseases and conditions.

Section 113(b) (Collaboration and Report) of FDAMA, directs the Secretary, the Director of NIH, and the Commissioner of Food and Drugs to collaborate to determine the feasibility on including device investigations within the scope of the data bank under section 402(j) of the PHS Act. In addition, FDAMA directs the Secretary to prepare and

submit to the Committee on Labor and Human Resources of the Senate and the Committee on Commerce of the House of Representatives a report on the following:

- A. the public health need, if any, for inclusion of device investigations within the scope of the data bank under section 402(j) of the Public Health Service Act;
- B. the adverse impact, if any, on device innovation and research in the United States if important information relating to such device investigations is required to be publicly disclosed; and,
- C. such other issues relating to section 402(j) as the Secretary determines to be appropriate.

To solicit input on this issue, the Food and Drug Administration (FDA) announced in the Federal Register of June 22, 1999, that a public meeting was to be held on July 8, 1999.

Meeting Minutes

There were six speakers at the July 8 meeting. Terry Toigo (FDA/Office of Special Health Issues) and Alexa McCray (NIH/National Library of Medicine (NLM)) gave an update on activities related to 113(a). Bob Gatling (FDA/Center for Devices and Radiological Health (CDRH)) discussed 113(b) and went over the list of eight questions that were included in the Federal Register notice requesting comments on this FDAMA provision that were to aid in the preparation of the report to Congress. Marlene Tandy spoke for the Health Industry Manufacturers Association (HIMA). Stephen Northrup spoke for Medical Device Manufacturers Association (MDMA). Kristine Rapp (Baxter International) made brief remarks, both from her perspective as a member of regulated industry as well as a member of an Institutional Review Board (IRB) on which she serves. Bob Gatling also read a statement from Public Responsibility in Medicine and Research (PRIM&R) into the record.

Terry Toigo presented information on the current AIDS clinical trial database that has been jointly administered by FDA and NIH since 1988. She mentioned other clinical trial databases on the web. She mentioned the current status of the data bank being established with NIH and NLM for pharmaceutical products under FDAMA section 113(a). This data bank will be accessed by the public and will be in lay language. She also presented issues for FDA to consider as part of the data bank. These issues include the definition of serious or life-threatening condition, what type of trial and what information should be included, the role of the IRB in deciding what information to be posted in the data bank, and the timing of the submission of the information to the data bank.

Alexa McCray presented information on the role that NIH and NLM have had in implementing the AIDS clinical trial database and the current status of the FDAMA section 113(a) data bank. She indicated that NIH will phase in the data bank with the

first phase being NIH sponsored clinical trials. The second phase will include clinical trials sponsored by other government agencies and industry.

Bob Gatling presented the requirements of the information to be included in the report to Congress for FDAMA section 113(b). The report is due to Congress by November 21, 1999, the two year anniversary of FDAMA. He also presented a list of eight questions that were included in the Federal Register notice requesting comments on this FDAMA provision.

Marlene Tandy of HIMA indicated that HIMA is still in consultation with their member companies and that HIMA plans to submit comments to open docket. She indicated that the idea of having a information accessible to the public on clinical trials for serious or life-threatening diseases is a positive concept. She indicated that industry does have concerns about confidentiality; effect of disclosure on innovation; the exact information to be disclosed; the timing of disclosure; the definition for serious or life-threatening illnesses; and implications for IRBs. She also indicated that there should be a 2-year pilot with the pharmaceutical data bank before consideration of adding devices to the data bank.

Stephen Northrup of MDMA indicated that making information on device clinical trials might hurt innovation. There needs to be a balance between the needs of the public for information and the need of industry for confidentiality. He also indicated that there may be possible adverse effect on reimbursement for device trials.

Kristine Rapp of Baxter International indicated that there are resource implications for the government in establishing and maintaining the data bank and in assuring the accuracy of the data. She also mentioned that investors in clinical research might be concerned about device clinical trial support if the information about the trials is made public. She indicated the additional cost to companies of a public disclosure requirement for clinical trials might drive those trials to foreign sites.

Bob Gatling read a statement from PRIM&R into the record. PRIM&R strongly supports the concept of a publicly available data bank and any other FDA efforts to promote openness and improved access to relevant information. PRIM&R especially wants outcome results from clinical trials to also be made public.

There was a general discussion by those in attendance. Industry and consumers are interested in this issue. The discussion indicated that there are concerns about the benefit of this access to patients, the ability of patients to understand the information placed in a data bank, the quality and type of information that would be provided to the data bank, the potential impact on small companies regarding their funding from the private sector where multiple companies are known to be developing similar devices and technologies, and the impact of a data bank on FDA resources.

Many of the attendees indicated that they would speak to their constituencies and send comments to the docket.