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

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RE: Guidance for industry: Information Program on Clinical Trials for serious of life-threatening diseases: Establishment of a Data Bank. Docket no 98D-0293, section 113, is stated in the this draft under section IIIA. It is not clear whether this is also the docket number of the draft guidance.

This letter intends to comment on the draft guidance released on 03/29/00.

Although this guidance document only addresses the statutory requirements for submission of protocol information to the Clinical Trials Data Bank, some procedural issues will be addressed in this letter, to support the comments on the statutory requirements.

The Clinical Trials Data Bank intends to be a central resource providing current information on clinical trials testing effectiveness in individuals with serious or life-threatening diseases and is as such a marketing tool for sponsors of the clinical studies to patients, other members of the public, health care providers and researchers.

When the Government exposes patients, public, health care providers and researchers to a Data Bank listing trials intended to evaluate treatment strategies for serious or life-threatening diseases, it may be a responsibility to guarantee as much quality assurance and control as possible on the information provided. The current information trial sponsors are required to submit and the information made available to the public does not guarantee quality. The Trials Data Bank seems therefore a marketing tool for sponsors rather than a real benefit to patient care.

(Van Hoef/Draft Guidance for establishment of a Trials Data Bank)

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There are currently a large number of treatment strategy- or product development-related studies designed to test effectiveness that may not warrant patient enrollment for a variety of reasons. In particular the Fast Track Approval procedure which supports industry to obtain approval for serious and life-threatening indications without the need of confirmation of efficacy before market clearance invites to design studies that serve business purposes rather than patient care. The Orphan Product Procedure, in itself an excellent regulation, and Off-Label prescription add opportunities that increase this challenge.

A Trials Database obligating sponsors to register all trials testing effectiveness of biopharmaceutical products and devices for serious and life-threatening diseases, as well as all trials conducted to test effectiveness according to the Fast Track or Orphan Product Procedure could be developed as a tool that primarily supports FDA in the efforts to improve patient care rather than industry in its business goals.

Quality assurance and control can be achieved by increased statutory requirements and development of procedures for trial registration that support the latter purposes:

Statutory requirements for submission of information to the Trials Data Base:

- Full protocol
- Protocol summary listing:
 - Study title
 - Study rationale and purpose
 - Study objectives/endpoints
 - Study design/methodology
 - Eligibility criteria
 - Response or evaluation criteria
 - All published literature (abstracts, articles, other promotional materials) related to the treatment strategy or the product to be tested.
- Regulatory context in which the study is being conducted (e.g. IND, IDE, Fast Track, Orphan Drug Designation)
- Study status
- Summary of available safety/efficacy/outcome information
- Contact and administrative data

Brief description of procedures:

The submitted information should be reviewed by specialized people in a certain therapeutic area to support quality assurance and control before the study is listed in the Trial Data Bank. It might be advisable that literature review be pursued by the reviewer to support the recommendation to list the trial. Criteria for evaluation could be developed. If the criteria are not met, the reviewer may recommend not to list the trial as such with brief recommendations for adjustment if warranted. The sponsor and FDA may be informed about such recommendation.

To support enhancement of quality it might also be worth to increase the information to the public. In addition to provision of:

(Van Hoef/Draft Guidance for establishment of a Trials Data Bank)

- Descriptive information
- Recruitment information
- Location and contact information
- Administrative data

Quality assurance and control information may be added. This information might include:

- 1) Evaluation or response criteria
- 2) Available safety and efficacy data
- 3) Referral to published literature

It occurs that studies are designed to evaluate a compound that will predictably not induce effectiveness, for example because the malignancy for which the study is designed does not express the receptors through which the compound can induce efficacy, or, the response criteria do not relate to study objectives or outcome information, or, the published response is a site effect, toxic or not, of the compound, rather than the desired effect stated in the protocol, and so on. This type of trials may better not be promoted through the Data Bank because promotion of studies to support products that may potentially be harmful rather than effective or that may predictably not induce quality in patient care might induce legal consequences.

In section IIIB of the guidance is stated that "FDA does not specifically approve an IND protocol". FDA may consider the Trials Data Bank statutory requirements and QA/QC procedures a support mechanism to induce quality in clinical research and product development.

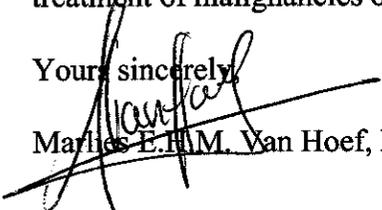
Section IIIE states that "studies that do not test effectiveness or support indications other than serious or life-threatening diseases may be included in the Data Bank". It may be recommendable to develop a separate section in the Data Bank for this type of studies and develop separate procedures for evaluation of the value of this type of studies for patient care.

Section V states that "the Trials Data Bank does not reflect any judgement on the adequacy of the conduct". Conduct can refer to content (see above) or procedure. The above comments refer to the content. If the sentence in this section refers to the procedure an adjustment of phrasing may enhance clarity.

Section VI first paragraph: A definition of "group C protocols" may clarify this statement.

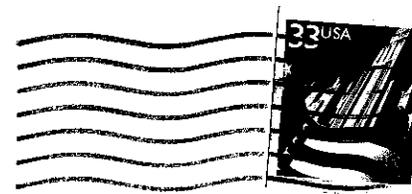
Finally, I have given the value of Trials Data Banks considerable consideration in the past and would be delighted to work with the authorities on development of a procedure to evaluate protocols. Furthermore, I would be delighted to review protocols according to such procedure designed to test drugs, biologics, any type of cell and gene therapy, vaccines and devices for treatment of malignancies or transplantable non-malignant diseases.

Your sincerely,


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