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VIA ELECTRONIC SUBMISSION

November 22, 2006

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

**Re: Docket Number 2006D-0331: Conduct of Emergency Clinical Research:
Public Hearing [Federal Register: August 29, 2006 (Volume 71, Number 167,
Pages 51143-51146)]**

Dear Sir/Madam:

Northfield Laboratories Inc. would like to commend the FDA on its initiative to address conduct of emergency research in the absence of informed consent under 21 CFR 50.24 ("the Rule") and to determine whether the current regulatory framework is adequate to ensure that such clinical investigations are justified by the highest scientific and ethical principles and conducted with the appropriate safeguards for human subject protection.

In the decade since the issuance of the Rule, there have been approximately 20 clinical investigations of devices and pharmaceutical products conducted under this regulation. The recent experience of Northfield Laboratories Inc. in the conduct of our investigational study of PolyHeme[®] for the treatment of acute blood loss beginning at the scene of injury represents one such example. The PolyHeme[®] trial was conducted over a two and half year period (2004-2006), involving personnel at 32 sites in 18 states, with the participation of approximately 300 ground and air ambulances. Seven hundred and twenty patients were enrolled in this study. The experience we derived from the initiation and conduct of the trial has provided us with some unique perspectives on which to assess the Rule, and the supporting Guidance Document, and from which to propose enhancements to the process.

Emergency research is critical to the advancement of critical care medicine. It is imperative that the regulatory framework enable such research to continue. As

evidenced by the draft Guidance, this can only be accomplished through the shared responsibility of clinical investigators, their Institutional Review Boards (IRBs), the FDA and sponsors. Through our experience, it has been clear that the collaboration of all those cited is critical to the ability to ensure appropriate review and approval of each study in the interest of safeguarding human subjects. As outlined in the Guidance document, while there are numerous shared activities, each group also has its own specific roles and responsibilities to fulfill. In reviewing the list of questions cited in the Federal Register Notice of August 29, 2006 (Volume 71, Number 167; pages 51143-51146), for which FDA seeks input, and as a sponsor, Northfield believes it is best positioned to provide comment on those relating to Community Consultation and Public Disclosure.

Our responses to the individual questions related to Community Consultation and Public Disclosure follow.

Community Consultation

5. What are the costs, benefits and feasibility of community consultation as currently required under Sec. 21 CFR 50.24?[Federal Register Page 51145]

In our experience, the costs of conducting community consultation varied widely from site to site, depending upon the strategies employed to raise awareness of the study in the particular location and encourage community involvement, the size of the site's catchment area, and the demographics of the community. Larger communities, especially those which are ethnically diverse, required outreach to multiple groups, in multiple languages, with corresponding costs. Expenses that may be expected include the following:

- Personnel time (Investigators, Nurses, Paramedics, etc.)
- Travel expenses for personnel
- Food (catering, lunches, etc.)
- Rental fees for booths at public events
- Rental fees for conference rooms or auditoriums
- Audio/visual equipment rental
- Printing (pamphlets, postcards, surveys, etc.)
- Postage fees for mailings
- Mailroom expenses (personnel to prepare and send mailings)
- Phone survey/research company fees
- Paid media placements (radio, TV, print)
- Legal advertisement fees
- Video and print monitoring services
- Fees to create a video for meetings/public events
- Transcription fees
- Website design and administration fees
- Translation services

The benefits of community consultation are clear: the process allows investigators and IRBs to obtain community input about the planned research, and can therefore promote understanding and trust. Nonetheless, there are many practical challenges involved in conducting meaningful community consultation: defining the community and its appropriate representatives, identifying methods to actively engage the community, the lack of uniformity among IRBs in defining the required community consultation activities, and the lack of measures to evaluate the adequacy and appropriateness of community consultation. Perhaps the greatest challenge is in obtaining the active input of the community members. The process requires active participation by community members; however, it is not designed or intended to obtain formal community approval.

7. Are there elements of community consultation, both procedural and substantive, that should, at a minimum, be required (e.g., types of information presented, number and types of meetings or interactions, number of people reached)? [Federal Register Page 51145]

While final authority for conducting community consultation is rightly the purview of the local IRB, and the process must be tailored to the individual community, it is our view that for multicenter studies the FDA should encourage the sponsor to provide a model community consultation plan along with templates for various communications vehicles spanning a range of technological approaches. This would ensure a level of consistency of message across all communities involved in the research. The minimum should be an adequate representation of the proposed research in terms that can be clearly understood by the public.

8. Would opt-out mechanisms (e.g., advanced directives, jewelry similar to medical alert bracelet/necklace, and driver's license indicators) to identify individuals who do not wish to be included as subjects in particular emergency research studies provide a necessary protection for human subjects? If so, are they feasible? [Federal Register Page 51145]

Just as members of the community where emergency research is conducted are not asked for their individual approval or consent of the protocol, it is impractical and unrealistic to expect to find a feasible way to allow individuals to opt-out of participating in a research study under the Rule. The practical reality of keeping track of individuals and their preferences represents an overwhelming and impractical burden for sponsors and sites. Opt-out mechanisms such as bracelets lose value as people discard them over time. Maintaining a database of such individuals, in addition to raising serious privacy concerns, would be of limited value, since the very nature of emergency research under the Rule does not allow emergency personnel enough time prior to making the necessary intervention to search a database (in addition to the fact that most ambulances are not equipped with on-board computers

with internet access). The whole point of the Rule is that individual consent cannot be obtained in a timely manner; likewise, individual exclusions do not seem feasible.

11. The community consultation process typically includes meetings and discussions about the study with the community. [Federal Register Page 51145]

(a) Should the regulation require documentation of meeting activities and discussion in sufficient detail to show the information that was disclosed and the community reaction to the clinical investigation? If so, who should be responsible for documentation (e.g., clinical investigator, sponsor)?

The regulation should require documentation of the date and time of the meeting(s), the number of attendees, and copies of the materials presented to the community. This should be the responsibility of the investigator or IRB member who conducts the meeting. The materials should be housed on the clinical investigation site's website so that community members who wish to review the materials may do so even if they do not attend the meeting(s). It would also be useful to provide a feedback mechanism for community members to complete once they have reviewed the materials.

It is important to note, however, that in our experience, community meetings are in general not particularly well-attended and should not be relied upon as the sole basis for community consultation or dialogue. Other activities, such as phone surveys, booths at community events such as sporting events or in shopping areas may provide better means of "meeting the community where it is" rather than demanding that the community come to the investigator to be informed.

(b) The regulations (see 21 CFR 312.54(a) and 812.47(a)) currently require the sponsor to submit the information publicly disclosed prior to study initiation and after completion to FDA Document Number 1995S-0158 (formerly 95S-0158). Should the regulation also require that documentation of community consultation activities be submitted to FDA, for example, by being placed in the public docket? If so, who should be responsible for doing this?

The regulation should require that the sponsor submit documentation of the publicly disclosed community consultation materials to the docket as soon as it is available from the site or at the latest at first drug shipment to that site. The docket needs to be easily searchable by 1) sponsor name, 2) study title/number, 3) product name and 4) site/hospital participating. It is currently very difficult to search the docket for such materials even though they may have been submitted by the sponsor. Some links do not work and some materials are not appropriately indexed. The FDA website must be upgraded to make it easily searchable by the public. The sponsor should be required to simultaneously submit the information to the IND as well.

(c) Should this information be available elsewhere such as on clinicaltrials.gov?

Materials would be more easily available to the public if there were a link to community consultation materials by site from the clinicaltrials.gov site to the docket.

Public Disclosure Prior to Initiation

12. Are there certain types of information (e.g., adverse event reports, study protocol, informed consent document) that should, at a minimum, be publicly disclosed to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn? [Federal Register Page 51145]

Certain types of information should be publicly disclosed to the community. For example:

- Summary of the protocol with treatment groups, endpoints, and evaluations;
- Summary of all previous clinical data (efficacy and safety) with the product in the relevant clinical setting;
- Summary of benefits/risks to participating in the particular study.

The difficulty that may be encountered is translating complex scientific and clinical information into language that the average community member can comprehend. Nonetheless, this should be attempted. If the sponsor were to be encouraged to provide templates of information, the information provided would at minimum be consistent from site to site. This information could be published on a site-specific, study-specific website.

It is important that sponsors and investigators not rely upon the news media to accurately inform the public. Local media, even “health” reporters, may not be equipped to explain the nuances of complex emergency research. In order to avoid confusing the public with inaccurate or incomplete information, each study site should be required to maintain a study website where the public can seek more medically complete information about the study and also provide feedback.

13. Should the full protocol, or other information such as the investigator’s brochure, for emergency research be available (through the FDA’s public docket, or clinicaltrials.gov) to the general public before initiation of the clinical investigation? If so, should protocols or other information be available for all emergency research or only for certain emergency research? [Federal Register Page 51145]

The full protocol and Investigator’s Brochure (IB) are made available to investigators, IRBs, study personnel and FDA who are sufficiently knowledgeable to understand all

the scientific and medical information. They contain details that are generally outside the scope of understanding of the general population and therefore may confound the lay person's understanding of the study.

From a competitive perspective, the protocol and the IB may include statistical, product, study design and other proprietary information that places the sponsor at a disadvantage if revealed to competitors. Further, such information routinely constitutes confidential commercial information not releasable to the public under FDA's Freedom of Information Act policies and regulations.

For marketed products, the package insert is intended for the practitioner and pharmacist. For many prescription products, a separate "information to patient" leaflet written in lay language is provided to the patient. If one follows this model, the full protocol/IB should not be provided as it obscures the relevant information for the prospective patient.

Public Disclosure Following Completion

14. Is there information regarding the study results that, at a minimum, should always be disclosed after the clinical investigation is completed? If so, what is this information? [Federal Register Page 51145]

Upon enrollment of the last patient, the sponsor should inform the study sites that enrollment is complete. Sites should then initiate activities to disclose the completion of enrollment to the community.

A study is not complete until the data have been collected and analyzed.

The overall results of the study should be made available to the public after the data have been collected and analyzed, e.g., did the study meet its endpoints, and key safety and efficacy information gained from the study are understood. It may be worthwhile to indicate the number of patients enrolled at a particular site.

The sponsor should make this information publicly available via press release and website postings and should also provide the principal investigators with sufficient information to initiate disclosure activities at each site. It is important that neither sponsors nor sites rely exclusively upon the news media to transmit the information; the information should be made available on the sponsor's and the site's website. In addition, this information should be made available on clinicaltrials.gov.

Communication of trial results should be done in a non-promotional manner consistent with 21 CFR 312.7 and FDA should provide clear guidance to companies as to how the agency expects this to be done.

15. How can this disclosure best be accomplished? Who should be responsible for this disclosure? [Federal Register Page 51145]

Disclosure should be the joint responsibility of the sponsor and the investigator at each site.

The sponsor should issue a press release and provide it on its corporate website. Clinicaltrials.gov should be modified to provide fields for 1) a data summary and 2) site-specific enrollment information.

The investigator should place the press release on the study site website and should also be encouraged to conduct appropriate outreach to local news media.

16. When should a clinical investigation be considered "completed"? How soon after a clinical investigation is completed should the results be disclosed? [Federal Register Page 51146]

The study should be considered complete for the purposes of this disclosure once enrollment and follow-up are completed, the data have been collected and fully analyzed, and study results are known. Normally, the timing for disclosure should not exceed 6 months following the time that study results (upon full data analysis) are known.

17. How can we assure timely disclosure of study results after completion of a study? [Federal Register Page 51146]

The sponsor should be required to submit a high level data summary to clinicaltrials.gov.

Public Discussion of Emergency Research

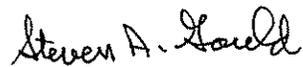
Currently, all emergency research protocols are subject to IRB review and community consultation. FDA has received some suggestions that it may be important, at least in some cases, to have additional public discussion, such as during an open meeting or an advisory committee or other expert panel. We invite comment on the following questions: Is there a need for such additional review and public discussion? If so, what criteria would be used to determine which protocols should be subject to this additional review and discussion? [Federal Register Page 51146]

Northfield does not believe that there is a need for additional review and public discussion of emergency research protocols under the Rule. Given that each community and each investigation is different, the process of community discussion should rightly be the purview of the IRB responsible for safeguarding patient rights in

a given community. To hold special advisory panel or other expert meetings in Washington or some other non-local venue is to strip the community of its uniqueness and invite the comment of individuals and groups who have no direct stake in the research and whose agendas may not be the same as the community where the research will be conducted and from which the research subjects will be drawn.

Northfield appreciates the opportunity to comment on this important subject.

Sincerely,

A handwritten signature in cursive script that reads "Steven A. Gould".

Steven A. Gould, M.D.
Chairman and CEO
Northfield Laboratories Inc.