

The Eastern Association for the Surgery of Trauma (EAST) is an academic professional organization with a national membership of nearly one thousand academic trauma surgeons and other health care professionals involved in the emergency care of the injured. Obviously, the organization has a vested interest in the conduct of emergency research. The issue of informed consent, among others (see attached EAST membership survey results), has seriously hampered our ability as clinicians, academicians, and researchers to provide the best care possible to our patients through the advancements and knowledge that such efforts garner. One overarching concern is the institution of onerous rules, regulations, and processes which often times serve only as time consuming and costly constraints on the investigator and that do not automatically translate into benefit or protection of the subject. Any efforts to reduce or mitigate these in existing or new policies would be welcomed by potential researchers in this arena.

As chairman of the EAST Task Force on Research Related Issues, the organization has asked me to comment on its behalf with regard to the specific questions on aspects of emergency research and additional human subject protections, as well as on the draft guidance entitled "Guidance for Institutional Review Boards, Clinical Investigator, and Sponsors: Exception from informed consent requirements for emergency research". The following are my comments and answers to those specific questions.

Section IV (1): This section states that "The human subjects are in a life threatening situation, available treatments are unproven or unsatisfactory..." this statement should additionally reflect that while some available treatments are unproven or unsatisfactory, other available treatments may, in fact, have been previously thought to be satisfactory but there may be other new interventions which are thought to potentially be more satisfactory or efficacious and therefore deserving of comparison to the standard and accepted practice or intervention.

Section V A (1): In general, the criteria for allowing studies conducted under 50.24 are adequate to protect human subjects and promote scientifically rigorous research. The process and data requirements for proving potential benefits of the interventions to be tested should not be overly rigorous and burdensome to the investigators.

(2)(a): Once again, even if available treatments are satisfactory and proven, this should not necessarily preclude further testing or comparison to other treatments and interventions.

(b): Further definition of this term would be helpful. Particular reference to: mortality; morbidity; length of hospital stay; financial benefit to patients, hospitals, health systems, society, etc. might be some specific examples.

(4): One issue that comes to mind here is that of advance directives in the chronically ill or elderly. Conceivably, these patients who do not wish extraordinary care or participation in experimental treatments (if expressed) should be excluded from enrollment in studies.

Section V B (5): While community consultation is for the most part feasible, the costs may well outweigh the benefits. Perhaps a guideline, or cap, on total budget expenditures allocated for this aspect of the project should be proposed by the FDA (e.g. 5-10%). The investigators should be allowed to choose the most cost effective method of community consultation taking into account the variable sociodemographic compositions of their local communities and variability of media markets.

(6): It would seem, as alluded to in the previous response, that there is no uniformly effective mechanism to inform the community and enhance human subject protection. Strategies could potentially include, but not be limited to, town meetings, mass mailings, local print and electronic media, billboards, flyers, etc. Once again, it would seem logical that the investigators should be given the opportunity to determine which single or combined strategy would be most cost effective in their local communities.

(7): A general outline of the information to be provided to the public should be included in the research proposal as should the strategy(ies) proposed to promulgate it. Estimates of the number of the community members reached (e.g. circulation of the newspaper in which a full page ad has been placed with the assumption of a 50% penetration) should be provided. Ultimately, the investigators should seek at least 50% community knowledge of the proposed research project. One method to establish proof of this might be small, random telephone or mail surveys of the community seeking to confirm their knowledge that the study will be conducted in their community.

(8): The “opt out” mechanisms outlined would seem feasible and capable of providing necessary protection for human subjects.

(9): The information obtained from the community consultation process should be used by the investigators, the IRB, and public officials to assess community support for the project and feasibility of initiating the study, or determining roadblocks to the conduct of the study and strategies to overcome them. The regulation should specifically address this point.

(10): Others who should play a role in determining the adequacy of the plan for community consultation and the material to be publicly disclosed should include, but not be limited to, : legal counsel representing the municipalities and, perhaps, those representing the investigators or their institution; elected government officials; key community leaders and media consultants.

(11): (a) Such documentation should be provided and it should be the responsibility of the investigators to do so.

(b) The regulations should not also require that documentation of community consultation activity be submitted to the FDA by being placed in the public docket. If this additional requirement does come to fruition, it should be the responsibility of the FDA.

(c) It may be of benefit to have this information be available elsewhere however, again, this should be the responsibility of the FDA and not the investigators.

(12): Public disclosure, at minimum, should include a brief synopsis of the study proposal including rationale, reasons for seeking exemption from informed consent, the study protocol and the risks and benefits of conducting the study in that particular community. This should be brief, and in layman's terms. Obviously, this should be provided in appropriate languages and in a culturally sensitive format in those communities that are multilingual.

(13): Only pertinent information regarding the study protocol which can be easily understood, and not misinterpreted by the lay public, should be made available. This disclosure should only be required for certain types of emergency research. These selective criteria for disclosure should be decided upon by the FDA in consultation with an expert panel of emergency care providers and researchers.

(14): Minimum information that should always be disclosed after the clinical investigation is completed should include the number and nature of any adverse events, and, in those cases where the study was terminated before completion, the reason(s) for that decision.

(15): It would seem disclosure would be best accomplished through posting on the public docket. It would be the responsibility of the investigators to provide appropriate information to the FDA and then it would be the responsibility of the FDA to do the actual posting. Of course the standard method of disseminating this information to the academic and research community would continue to be through presentation at scientific meetings and publication in peer review scientific journals.

(16): Typically the study is considered closed to accrual of subjects when the appropriate number of patients are enrolled, or the study is terminated prior to that for other reasons. The time to analyze results is variable depending on a number of different factors. The normal course of the dissemination of results involves submission of the work for peer scrutiny in the form of presentation at scientific meetings and publication in scientific journals. Study methods, results, analyses and conclusions are

generally not considered valid or accepted until completion of this process. This should generally take not longer than one year.

(17): It should be the responsibility of the investigators to provide at least preliminary results and conclusions to the FDA within six months of the study's closure to enrollment of subjects. Preliminary results in the form of abstracts and/or manuscripts to be submitted for peer review, presentation and/or publication, should be accepted. The investigators should also include the intended venue of presentation or publication (i.e. a dissemination plan). Time lines for this disclosure of preliminary or published results should be included in the guidance documents.

(18.), (19.): The additional review alluded to in these questions would seem to be redundant and superfluous, and would appear to only serve to prolong and confound the process of conducting the proposed research project in a timely and efficient fashion. This additional tier of review should only be considered under the narrowest of circumstances.

(20.), (21.): Further issues to be considered relate to: confidentiality; linkage of pre-hospital, hospital and post-hospital discharge data; documented verification of legitimate attempts to contact a consenting party; potential sanctions for violation of disclosure policies and falsified documentation of attempts to obtain consent should be considered for inclusion in the guidance document.

The Eastern Association for the Surgery of Trauma thanks the department of Health and Human Services, Food and Drug Administration for the opportunity to comment on this important process and guidance document. If EAST can be of any further assistance, or if there are any questions or need for further clarification regarding these comments, please do not hesitate to contact me.

Respectfully,

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