

notifies the sponsor that an application is required for an investigation.

\* \* \* \* \*

(4)(i) A sponsor shall submit a separate IDE for any clinical investigation involving an exception from informed consent under § 50.24 of this chapter. Such a clinical investigation is not permitted to proceed without the prior written authorization of FDA. FDA shall provide such written authorization 30 days after FDA receives the IDE or earlier.

(ii) If the investigation involves an exception from informed consent under § 50.24 of this chapter, the sponsor shall prominently identify on the cover sheet that the investigation is subject to the requirements in § 50.24 of this chapter.

\* \* \* \* \*

20. Section 812.35 is amended by adding a new sentence to the end of paragraph (a) to read as follows:

**§ 812.35 Supplemental applications.**

(a) \* \* \* Whenever a sponsor intends to conduct a clinical investigation with an exception from informed consent for emergency research as set forth in § 50.24 of this chapter, the sponsor shall submit a separate IDE for such investigation.

\* \* \* \* \*

21. Section 812.38 is amended by adding a new paragraph (b)(4) to read as follows:

**§ 812.38 Confidentiality of data and information.**

\* \* \* \* \*

(b) \* \* \*

(4) Notwithstanding paragraph (b)(2) of this section, FDA will make available to the public, upon request, the information in the IDE that was required to be filed in Docket Number 95S-0158 in the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857, for investigations involving an exception from informed consent under § 50.24 of this chapter. Persons wishing to request this information shall submit a request under the Freedom of Information Act.

\* \* \* \* \*

22. New section 812.47 is added to subpart C to read as follows:

**§ 812.47 Emergency research under § 50.24 of this chapter.**

(a) The sponsor shall monitor the progress of all investigations involving an exception from informed consent under § 50.24 of this chapter. When the sponsor receives from the IRB information concerning the public disclosures under § 50.24(a)(7)(ii) and (a)(7)(iii) of this chapter, the sponsor

shall promptly submit to the IDE file and to Docket Number 95S-0158 in the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857, copies of the information that was disclosed, identified by the IDE number.

(b) The sponsor also shall monitor such investigations to determine when an IRB determines that it cannot approve the research because it does not meet the criteria in the exception in § 50.24(a) of this chapter or because of other relevant ethical concerns. The sponsor promptly shall provide this information in writing to FDA investigators who are asked to participate in this or a substantially equivalent clinical investigation and other IRB's that are asked to review this or a substantially equivalent investigation.

**PART 814—PREMARKET APPROVAL OF MEDICAL DEVICES**

23. The authority citation for 21 CFR part 814 is revised to read as follows:

Authority: Secs. 501, 502, 503, 510, 513-520, 701, 702, 703, 704, 705, 708, 721, 801 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351, 352, 353, 360, 360c-360j, 371, 372, 373, 374, 375, 379, 379e, 381).

24. Section 814.9 is amended by redesignating paragraph (d) as paragraph (d)(1) and by adding new paragraph (d)(2) to read as follows

**§ 814.9 Confidentiality of data and information in a premarket application (PMA) file.**

\* \* \* \* \*

(d)(1) \* \* \*

(2) Notwithstanding paragraph (d)(1) of this section, FDA will make available to the public upon request the information in the IDE that was required to be filed in Docket Number 95S-0158 in the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857, for investigations involving an exception from informed consent under § 50.24 of this chapter. Persons wishing to request this information shall submit a request under the Freedom of Information Act.

\* \* \* \* \*

Dated: July 17, 1996.  
David A. Kessler,  
*Commissioner of Food and Drugs.*

Donna E. Shalala,  
*Secretary of Health and Human Services.*  
[FR Doc. 96-24967 Filed 9-26-96; 8:59 am]  
BILLING CODE 4160-01-F

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**45 CFR Part 46**

**Waiver of Informed Consent Requirements in Certain Emergency Research**

**AGENCY:** National Institutes of Health, HHS.

**ACTION:** Waiver.

**SUMMARY:** The Department of Health and Human Services (HHS) is announcing the waiver of the applicability of the title 45 CFR part 46 (protection of human subjects) requirement for obtaining and documenting informed consent, for a strictly limited class of research involving activities which may be carried out in human subjects who are in need of emergency therapy and for whom, because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. However, because of special regulatory limitations relating to research involving prisoners (subpart C of 45 CFR part 46) and research involving fetuses, pregnant women, and human in vitro fertilization (subpart B of 45 CFR part 46), this waiver is inapplicable to these categories of research.

**EFFECTIVE DATE:** November 1, 1996.

**FOR FURTHER INFORMATION CONTACT:** F. William Dommel, Jr., J.D. Senior Policy Advisor, Office for Protection from Research Risks, 6100 Executive Boulevard, Suite 3B01J, National Institutes of Health, MSC 7507, Rockville, MD 20892-7507. Telephone (301) 496-7005, ext. 203 (not a toll-free number).

**SUPPLEMENTARY INFORMATION:**

**Waiver**

Pursuant to Section 46.101(i) of title 45 of the Code of Federal Regulations, the Secretary of Health and Human Services (HHS) has waived the general requirements for informed consent at 45 CFR 46.116 (a) and (b), and at 46.408, to be referred to as the "Emergency Research Consent Waiver," for a class of research consisting of activities<sup>1</sup>, each of which have met the following strictly limited conditions detailed under either (a) or (b) below:

<sup>1</sup> Because of special regulatory limitations relating to research involving prisoners (subpart C of 45 CFR part 46), and research involving fetuses, pregnant women, and human in vitro fertilization (subpart B of 45 CFR part 46), this waiver is inapplicable to these categories of research.

(a) The Institutional Review Board (IRB) responsible for the review, approval, and continuing review of the research activity has approved both the activity and a waiver of informed consent and found and documented:

(1) that the research activity is subject to regulations codified by the Food and Drug Administration (FDA) at Title 21 CFR part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent, and

(2) that the requirements for exception from informed consent for emergency research detailed in title 21 CFR section 50.24 have been met relative to those protocols, or

(b) The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has found and documented that the research is not subject to regulations codified by the FDA at title 21 CFR part 50 and found and documented and reported to the Office for Protection from Research Risks, Department of Health and Human Services, that the following conditions have been met relative to the research:

(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

(2) Obtaining informed consent is not feasible because:

(i) The subjects will not be able to give their informed consent as a result of their medical condition;

(ii) The intervention involved in the research must be administered before consent from the subjects' legally authorized representatives is feasible; and

(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

(3) Participation in the research holds out the prospect of direct benefit to the subjects because:

(i) Subjects are facing a life-threatening situation that necessitates intervention;

(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence

support the potential for the intervention to provide a direct benefit to the individual subjects; and

(iii) The risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

(4) The research could not practicably be carried out without the waiver.

(5) The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document in accord with Sections 46.116 and 46.117 of title 45 of the Code of Federal Regulations. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research consistent with paragraph (b)(7)(v) of this waiver.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the research; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

In addition, the IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the research and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.

For the purposes of this waiver "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

#### Background

It had come to the attention of HHS that there are proposals to conduct certain research, including National Institutes of Health (NIH) funded research, which could not go forward in

the context of the current HHS regulations for the protection of human subjects (45 CFR part 46), unless certain informed consent requirements of those regulations were waived in accord with the waiver provisions provided at 45 CFR 46.101(i). HHS carefully reviewed the need for the exercise of the Section 46.101(i) waiver authority in these circumstances, and the requirements for informed consent were waived by the Secretary in the instance of only one specific multi-site study of head injuries which is currently underway (60 FR 38353).

The Secretary is now waiving the informed consent requirements for the class of research activities and no longer restricting the waiver to a single research project. This waiver provides clear instruction as to when research in emergency circumstances may proceed without obtaining an individual subject's informed consent. Elsewhere in this edition of the Federal Register, the FDA is publishing a final rule which amends FDA regulations to authorize a nearly identical waiver of informed consent in research which is regulated by FDA. The joint publication of these actions permit harmonization of the HHS and FDA regulations regarding

research in emergency circumstances. The HHS waiver, just as the FDA regulatory change, provides a narrow exception to the requirement for obtaining and documenting informed consent from each human subject or his or her legally authorized representative prior to initiation of research if the waiver of informed consent is approved by an IRB. The waiver authorization applies to a limited class of research activities involving human subjects who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have available a legally authorized person to represent them. The Secretary, HHS is authorizing this waiver in response to growing concerns that current regulations, absent this waiver, are making high quality research in emergency circumstances difficult or impossible to carry out at a time when the need for such research is increasingly recognized.

HHS notes testimonies to this effect delivered to (i) the Subcommittee on Regulation, Business Opportunities, and Technology, Committee on Small Business, U.S. House of Representatives (Washington DC, May 23, 1994); (ii) the

Coalition Conference of Acute Resuscitation Researchers (Washington DC, October 25, 1994); (iii) the meeting of Applied Research Ethics National Association (Boston MA, October 30, 1994); (iv) the meeting of Public Responsibility in Medicine & Research (Boston MA, November 1, 1994); and (v) the Food and Drug Administration/ National Institutes of Health Public Forum on Informed Consent in Clinical Research Conducted in Emergency Circumstances (Rockville MD, January 9-10, 1995).

#### Periodic Review

A periodic review of the implementation by IRBs of this Section 101(i) waiver will be conducted by the Office for Protection from Research Risks, National Institutes of Health, to determine the adequacy of the waiver in meeting its intended need or if adjustments to the waiver might be necessary and appropriate.

Dated: July 17, 1996.

Donna E. Shalala,  
*Secretary.*

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