

# FOOD AND DRUG ADMINISTRATION

## REQUEST FOR COMMENTS ON THE FOOD AND DRUG ADMINISTRATION'S CURRENT RULE ON CONDUCT OF EMERGENCY CLINICAL RESEARCH -- 21 CFR § 50.24 DOCKET No: 2006D-0331

Comments Submitted By: Ms. Shevon L. Scarafile  
Villanova University School of Law  
299 North Spring Mill Road  
Villanova, PA 19085  
sscarafile@law.villanova.edu

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Comments Submitted To: Terrie L. Crescenzi  
Office of the Commissioner (HF-18)  
Food and Drug Administration  
5600 Fishers Lane, Room 14B-45  
Rockville, MD 20857

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### I. INTRODUCTION

I would like to take this opportunity to thank the Food and Drug Administration (“FDA”) for seeking comment on the current rule entitled: “Exception from Informed Consent Requirements for Emergency Research.”<sup>1</sup> I am currently a third-year law student at Villanova University School of Law and I have a Master’s and Bachelor’s degree in psychology. I am particularly interested in this regulation because I have conducted research before with human subjects, as part of my Master’s thesis. Also, I have submitted and received Institutional Review Board (“IRB”) approval for several projects I worked on at The Catholic University of America, my alma mater. Although none of the studies I have conducted or have been involved in were with humans who had a life-threatening condition, I still understand the informed consent procedures and the medical, legal and ethical theories behind the importance of obtaining informed consent from participants in a clinical investigation. Please be advised that the opinions expressed in this comment are solely my own and do not reflect the opinions of Villanova University or Villanova University School of Law.

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<sup>1</sup> 21 C.F.R. § 50.24 (effective Oct. 2, 1996).

Overall, I think that the regulation promotes rigorous scientific research while adequately protecting human subjects. Even though the regulation is adequate in its current form, the FDA could make several improvements. First, several provisions of the regulation could be more adequately defined. Second, the FDA should add additional provisions to further protect children, subjects involved in placebo-controlled investigations, and subjects with life-threatening morbidity conditions. Third, the regulation should require that the following information be disclosed at the community consultation and public disclosure stages: the methodology of the study, the risks, the benefits, and the outcome of the study, whether positive or negative. Finally, the regulation should include opt-out mechanisms and a Central IRB to review all Section 50.24 requests as additional human subjects' protections.

Part II of this Comment discusses the background of 21 C.F.R. § 50.24, including its criteria and purpose. Part II also discusses the public's initial response to the proposed rule in 1995 and why the FDA, ten years later, is seeking further comment on the regulation. Part III of this Comment is divided into four sections: Scientific Aspects of Emergency Research and Human Subject Protection, Community Consultation, Public Disclosure and Additional Challenges and Thoughts. Within each section, I have listed several questions from the Federal Register Notice and my answers to those respective questions. Finally, Part IV concludes that even though the regulation adequately protects human subjects, the FDA could further revise and clarify several provisions.

## **II. BACKGROUND of RULE**

On October 2, 1996, the Food and Drug Administration issued 21 C.F.R. § 50.24. This regulation provides a narrow exception to the requirement for "obtaining and documenting informed consent from each human subject prior to initiation of a clinical investigation."<sup>2</sup> Normally, when a human subject participates in a clinical investigation, the researcher/investigator has to obtain and document each subject's informed consent. Under Section 50.24, the FDA grants the investigator a waiver or an exception from obtaining the informed consent of a human subject if the investigator complies with certain criteria. The criteria include the following:

- Human subject is in a life threatening situation and available treatments are unproven or unsatisfactory;<sup>3</sup>
- Obtaining informed consent is not feasible;<sup>4</sup>
- Participation in the research will directly benefit the human subject;<sup>5</sup>

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<sup>2</sup> 71 F.R. 51143, 51143 (Aug. 29, 2006).

<sup>3</sup> 21 C.F.R. § 50.24(a)(1).

<sup>4</sup> *Id.* § 50.24(a)(2).

<sup>5</sup> *Id.* § 50.24(a)(3).

- Clinical investigation cannot be carried out without the exception from informed consent;<sup>6</sup>
- Proposed investigational plan defines the length of the therapy and the investigator intends to continue seeking informed consent from a legally authorized representative of the human subject;<sup>7</sup> and
- IRB has reviewed and approved consent procedures and forms to be used with the legally authorized representative, if one exists.<sup>8</sup>

Section 50.24 also requires additional human subject protections, such as community consultation before the clinical investigation is conducted; public disclosure to the community prior to the initiation of the investigation; public disclosure after the completion of the investigation; and establishing an “independent data monitoring committee” to exercise oversight.<sup>9</sup>

The FDA’s primary purposes for enacting this regulation were to (1) “permit harmonization of Federal policies on emergency research;” (2) “reduce confusion as to when research can proceed without informed consent;” and (3) “respond to growing concerns that current rules make high quality acute case research difficult or impossible to commence.”<sup>10</sup> The exception applies to a limited pool of research activities in which the human subjects cannot legally consent because of their life-threatening condition. Because of their need for emergency medical intervention and the lack of a legally authorized representative to consent on their behalf, this rule permits human subjects’ enrollment in a clinical investigation.

When the FDA first proposed the rule in 1995, the FDA received approximately ninety comments regarding the proposed rule. Organizations and associations submitted the majority of the comments. These organizations, for the most part, supported the proposal and in their comments sought clarification of certain terms and requirements. On the other hand, the FDA received sixteen comments from individuals who were adamantly opposed to the proposal and who argued that informed consent should not be waived under any circumstances. In addition to the proposed rule, in March of 2000, the FDA released its draft guidance entitled “Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent Requirements for Emergency Research” to supplement the proposed rule and help explain its provisions. The draft guidance provides definitions, input on how to conduct community consultation

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<sup>6</sup> *Id.* § 50.24(a)(4).

<sup>7</sup> *Id.* § 50.24(a)(5).

<sup>8</sup> *Id.* § 50.24(a)(6).

<sup>9</sup> *Id.* § 50.24(a)(7).

<sup>10</sup> 60 F.R. 49086, 49086 (Sept. 21, 1995).

and public disclosure, and important contacts if the investigator has questions. The FDA is currently amending the draft guidance and seeking comment on that as well.

Ten years later, the FDA is seeking comment on this rule for several reasons. First, the FDA announced the Human Subject Protection and Bioresearch Monitoring Initiative which has the goal of extensively reviewing rules concerning human subjects to assess if the rules adequately protect human subjects involved in medical investigations. Second, the FDA has received informal comments from individuals that both support and oppose Section 50.24. Some argue that Section 50.24 is insufficient and too poorly defined, while others argue that it does not provide enough protection for human subjects. Finally, the FDA wants to determine whether the current framework is adequate for the ethical conduct of emergency research or whether it needs modification.

### **III. DISCUSSION**

#### **A. Scientific Aspects of Emergency Research and Human Subject Protection**

*Q1: Are the criteria for allowing studies conducted under § 50.24 adequate to protect human subjects?*

The criteria for allowing studies conducted under Section 50.24 are adequate to protect human subjects for several reasons. First, the clinical investigator has to attempt to contact the human subject's legally authorized representative before the investigator administers the treatment. Second, during the course of the clinical investigation, the clinical investigator has the continuing duty to try and contact the human subject's legally authorized representative to obtain consent. Third, the clinical investigator is required to establish a data monitoring committee to oversee the data collection and investigation to ensure that the investigator complies with Section 50.24. Finally, the clinical investigator has to submit his/her research proposal to the IRB. The IRB rigorously reviews the proposal to ensure that the proposal complies with Section 50.24. All of these requirements function to protect the human subject because it makes the clinical researcher accountable to both the human subject's legally authorized representative and the IRB.

*Q2: Are the following criteria easily understood, and, if not, how can they be clarified?*  
*(a) "Available treatments are unsatisfactory or unproven;" (b) "Prospect of direct benefit;" (c) "Practicably."*

The criteria "available treatments are unsatisfactory or unproven," "prospect of direct benefit," and "practicably" are not easily understood. The FDA has not clarified these terms either in the definitions section of the regulation or in the draft guidance. The definitions of these terms should at least be included in the new proposed draft guidance because the criteria can be interpreted differently by researchers and IRBs.

First, the FDA should define unproven as “a treatment that through clinical and/or animal studies has not demonstrated its effectiveness at all.” This is the most common definition used in the scientific literature. In addition, several of the speakers at the public hearing proposed this as an adequate definition. Even though “unproven” is easily defined, “unsatisfactory” is not. Currently, several investigators interpret the term differently when conducting their clinical investigations. For instance, Dr. Ronald Maio of the Pediatric Emergency Care Applied Research Network (“PECARN”) advocated that the “threshold test” for allowing a study under Section 50.24 should be clinical equipoise; that is “the preponderance of evidence to date suggests that the two treatments are equal but there is a suggestion that a new treatment may be better.” He cited the example that if current therapy for near-fatal asthma has a 70% survival rate and animal studies of a new medication suggest an 80% survival rate, that the 70% survival rate treatment be considered an “available treatment that is unsatisfactory.” On the other hand, Dr. Robert Nelson from The Children’s Hospital of Philadelphia argued that the criterion should be “stricter than the ethical requirement for equipoise.” He suggested that the criterion “unsatisfactory” should mean that the “available treatment fails to prevent a significant proportion of deaths or permanent disabilities.”

I believe that Dr. Nelson’s definition of “unsatisfactory” conforms better to the goals and purposes of Section 50.24. Section 50.24’s main purpose is to protect human subjects who cannot legally consent for themselves and who do not have legally authorized representatives to consent on their behalf. By adopting Dr. Nelson’s definition, the FDA ensures that the treatment administered to the human subject is significantly effective because it has prevented a significant proportion of deaths or permanent disabilities. If the FDA adopts Dr. Maio’s suggested definition, researchers can conduct studies on human subjects when there might only be a minute--but not detectable or even positive-- difference between the available treatment and the investigatory treatment. Dr. Nelson’s definition is a stringent requirement but it comports most with the human protection aspect of Section 50.24. Therefore, the definition of “available treatment is unsatisfactory” should be that the “available treatment fails to prevent a significant proportion of deaths or permanent disabilities.”

Second, the criteria “direct benefit” is also not adequately defined in the regulation, the regulation’s definition section, or the draft guidance. “Direct benefit” should be defined utilizing mortality and morbidity end-points. For instance, for patients suffering from a fatal condition, direct benefit could mean that the proposed investigatory treatment will increase the subject’s rate of survival by 2%. For patients suffering from a severely morbid condition, direct benefit could mean that the proposed investigatory treatment increases the likelihood of better vision in those suffering from severe blindness or diseases of the eye. On the other hand, the FDA should not define direct benefit as the investigatory treatment being less risky than the available treatment.

Finally, the criteria “practicably,” while not defined in the regulation, is defined in the draft guidance. By practicably, the FDA means that (1) “results obtained in consenting subjects would be expected to apply to subjects who are unable to provide consent or (2) that the research would not be unduly delayed by restricting it to consenting

adults.”<sup>11</sup> Neither of these definitions adequately defines “practicably.” The FDA could supplement the current definition with a further definition and define practicably to mean “logistically feasible and scientifically appropriate.” For instance, if a human subject has suffered a massive stroke and is unable to consent, enrolling the human subject in a clinical investigation that provides a direct benefit is both logistically feasible and scientifically appropriate. It is logistically feasible because the human subject cannot consent themselves and might not have a legally authorized representative to consent on his/her behalf when the treatment needs to be done. It is also scientifically appropriate because if the investigatory treatment holds out the prospect of a direct benefit, then it is the investigator’s ethical and moral duty to administer the investigatory treatment. If the FDA defines “practicably” this way, clinical researchers and investigators will be able to easily understand it and apply it.

*Q3: Are there other criteria in the regulation, besides those identified in criterion (2)(a) through (c) that need to be clarified?*

Besides the criteria mentioned in Question 2 above, the FDA does not need to clarify other criteria in the regulation. However, the FDA should expand “life-threatening condition” in Section 50.24(a)<sup>12</sup> to not only include life-threatening conditions but also conditions of significant morbidity, such as loss of limb, vision or hearing.<sup>13</sup> There is little opportunity in emergency settings to study conditions with high potential for serious long-term morbidity. Moreover, conditions of significant morbidity could have detrimental, long-term physical and psychological effects on human subjects. If the definition of “life threatening condition” included conditions of significant morbidity, this would help facilitate research in this area. All the same criteria that are applicable to life-threatening conditions could be applicable to serious long-term morbidity conditions.

*Q4: Are there challenges that have not been explicitly addressed in the regulation in designing scientifically rigorous and ethically sound emergency research protocols?*

The FDA has not addressed two specific challenges in the regulation in designing scientifically rigorous and ethically sound emergency research protocols. The first challenge is pediatric research. The second challenge is placebo-controlled randomized investigations.

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<sup>11</sup> Food and Drug Administration, *Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research* 4 (Draft Ed. 2006).

<sup>12</sup> Section 50.24(a)(1) requires that a human subject suffer from a life-threatening condition before the IRB approves an exception to informed consent. As defined by the draft guidance, life-threatening condition means “[d]iseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted.” Food and Drug Administration, *Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research* 25 (Draft Ed. 2006). The draft guidance also explicitly states that the exception to informed consent ONLY applies to life-threatening conditions.

<sup>13</sup> Dr. Maio of PECARN supports this expansion, concluding that an investigator should be able to research treatments for conditions of significant morbidity, which could be as debilitating, as well as treatments for life-threatening conditions.

## 1. Pediatric Research

As for pediatric research, the FDA should develop a separate set of guidelines for an exception from informed consent when children are the human subjects involved in the clinical investigation. Even though it is not feasible for there to be separate guidelines for every type of condition and population, children are a different research group from adults.

First, the prospect of direct benefits from an available treatment for children could be significantly different from the direct benefits of the same treatment for adults. Therefore, “direct benefit” for children should be defined differently from adults. It could include morbidity and mortality endpoints but to a significantly different degree than for adults.

Second, a child who presents with a life-threatening condition will not necessarily have a parent or guardian present who can decide on research participation. For these situations, the investigator should try and contact the child’s family before enrolling the child in the clinical investigation. However, given the fact that children are still developing and growing and that they could respond better to certain treatments than adults, the FDA should permit the investigator to enroll the child immediately in the clinical investigation. Similar to the current rule, though, the investigator should still have the continuing duty to contact a parent or legally authorized representative throughout the clinical investigation. When the investigator contacts the parent or legally authorized representative, the regulation should indicate that the parent has the ability to withdraw the child from the clinical investigation immediately or at any point in the future.

Finally, even when parents or other family members are present, “the emotional distress experienced during a medical crisis precludes meaningful discussions about informed consent during the therapeutic window.” As Dr. Maio reasons, a narrow therapeutic window “may not provide sufficient time for a parent to make an informed and voluntary choice to permit a child’s enrollment in emergency research.” Therefore, for children with family members present, the therapeutic window for seeking informed consent should be longer than the therapeutic window for seeking consent from adults.

## 2. Placebo-Controlled Randomized Investigations

In addition to pediatric research, another concern that the regulation and draft guidelines minimally address is placebo-controlled randomized investigations. The draft guidelines state that “when a placebo is used, standard care would be given to all subjects, with subjects randomized additionally to receive either a test treatment or a placebo.”<sup>14</sup> In order to determine a treatment or drug’s efficiency and effectiveness, a clinical investigator tests the treatment or drug against a placebo. In animal studies, this is

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<sup>14</sup> Food and Drug Administration, *Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research* 5 (Draft Ed. 2006).

completely acceptable and ethical. However, when human subjects receive a placebo or standard care, the investigator is depriving them of a treatment or drug that could provide a direct benefit. This is neither acceptable nor should it be considered ethical because a clinical investigator is depriving a human being of a treatment with possible direct benefit to decide if the treatment works or not.

Because it is currently acceptable and ethical, the FDA should include more requirements in the current regulation. The requirements should include how the placebo is administered, the length of a placebo study (preferably short), certain situations where placebos should not be utilized at all (such as in extreme life-threatening situations), certain populations that should not be administered placebos (the elderly and children) and how a placebo study should be presented to the human subject's legally authorized representative. Furthermore, and most importantly, the guidelines should definitively state that those who do receive the placebo or standard care treatment should be able to receive the investigatory treatment after the clinical study has concluded, provided the treatment is effective.

## B. Community Consultation

*Q5: What are the costs, benefits, and feasibility of community consultation as currently required under § 50.24?*

The benefits of community consultation most likely outweigh the costs as currently required under Section 50.24. Under Section 50.24, community consultation requires “[c]onsultation with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.”<sup>15</sup> The draft guidance states that the community includes people from the geographic area where the clinical investigation will take place who share a particular characteristic as the subjects of the emergency research. The benefit of community consultation is that the researcher can elicit information from people who have suffered from the condition being studied, received treatment for the condition being studied, or know people who have suffered from the condition being studied. This provides the investigator with a wealth of knowledge not otherwise readily available. In addition, community consultation will help the researcher make minute and subtle changes to the clinical investigation based on the community's suggestions and concerns. Also, community consultation gives the human subjects who are not able to consent a voice and reminds the researcher that these are humans and not just subjects in a study. On the other hand, the costs of such consultation include the administrative fees that are necessary to advertise and conduct such a meeting and the costs associated with obtaining researchers who will present the research to the community.

While the benefits may outweigh the costs, the feasibility of gathering a significant number of individuals with similar characteristics as the research subjects is probably slim

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<sup>15</sup> 21 C.F.R. § 50.24(a)(7)(a).

to none. I would assume that in the case of pediatrics especially, it would be difficult to convince parents to attend this community consultation unless their child was involved in the research study directly. In fact, several researchers from the Part 15 FDA public hearing indicated that the community consultations are not very well-attended and do not result in large amounts of input from the community.

To solve this problem of under-attended meetings, the clinical investigator has several options. First, rather than holding a general public meeting for people to attend voluntarily, researchers should engage in targeted outreach with community leaders and support groups that have similar characteristics and medical problems as the research subjects. Second, the researcher should elicit comments via the internet through a website that provides information about the clinical investigation and provides the public the opportunity to comment through a virtual discussion board.

*Q7: Are there elements of community consultation, both procedural and substantive, that should, at a minimum, be required?*

The FDA should require, at a minimum, certain procedural and substantive elements of community consultation. First, the regulation should describe what type of information the clinical investigator is required to disclose at the community consultation. For instance, at the community consultation, the clinical investigator should have to describe the methodology of the study, the type of treatment that is administered, the demographics of potential research subjects, the expected benefits, and a brief proposal of the expected results. The draft guidance recommends that the clinical investigator present this information at the community consultation, but the regulation itself should require that the investigator disseminate the information. Second, the FDA should amend the regulations and adopt Dr. Henry Halperin's recommendation regarding community consultation. He suggests, and I agree, that the degree of community consultation should be in proportion to the investigation's risk. Thus, the higher risk the investigative treatment, the more community consultation that should occur and the less risky the investigative treatment, the less community consultation that should occur. Third, the regulation should not require that a minimum amount of people attend for the community consultation to be valid. It is not necessarily the amount of people that attend that is important, but rather the quality of information that the investigator obtains from the people who do attend.

*Q8: Would opt-out mechanisms 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?*

Opt-out mechanisms to identify individuals who do not wish to be included as subjects in particular emergency research studies would absolutely provide a necessary protection for human subjects. For adults, an appropriate opt-out mechanism would involve their driver's licenses. On the back of the driver's license, next to the question about organ donation, there could be a question about participating in emergency research studies. An adult would be able to elect whether or not they want to participate in a clinical investigation when he/she obtains or renews his/her license. Upon admission to

the hospital, the hospital and the investigator would have a clear indication about whether the person should automatically be enrolled in the clinical investigation or not.

Even though an opt-out mechanism on driver's licenses is a feasible option, I recognize that several potential problems exist. First, a person's willingness to participate in a clinical investigation could vary depending upon the nature of the clinical investigation. Second, even though this plan would capture the widest number of people, important populations would be left out, including children, the homeless, the mentally ill, and the financially challenged. Third, a driver's license program would require the cooperation of the federal government, state government, and administrative agencies. Despite these drawbacks, a driver's license program would capture the widest range of adults and provide the clearest indication of a human subject's consent to an investigation.

For children, a feasible and more suitable opt-out mechanism is a medical alert bracelet. Currently, children wear medical alert bracelets to indicate whether they have food allergies or other medical problems. This program should be expanded to offer parents the opportunity to purchase medical alert bracelets for their children regarding emergency research. The medical alert bracelet could indicate the parent's consent or lack of consent to their child's enrollment in an emergency clinical investigation. For the child whose parent consents to emergency research, the medical alert bracelet enables the investigator to enroll the child immediately in the emergency clinical investigation without wasting valuable time trying to contact the parent or legally authorized representative to obtain informed consent. This window of time could mean the difference between life and death. When the parent is contacted, though, the investigator should obviously inform the parents about the scope of the investigative treatment to give the parent a final opportunity to opt-out of the treatment.

### C. Public Disclosure

*Q12: Are there certain types of information 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?*

Similar to community consultation, the FDA should require that certain types of information, at a minimum, be publicly disclosed. First, the investigator should disclose to the public the demographic characteristics and research methodology of the study. The research methodology should include a summary of the different treatments the investigator is administering and why the investigator chose those treatments. The investigator should ensure that he/she conveys this information in a way that the public is able to understand and with minimal use of unnecessary medical terminology. Second, the investigator should disclose the expected risks and benefits of the study. Third, and most importantly, the investigator should disclose that he/she is conducting the investigation without the informed consent of the subjects and that he/she has the on-going responsibility to contact a legally authorized representative of the human subject. Public disclosure is an excellent way of ensuring that the investigator is accountable to

someone, especially when the human subject is unable to give informed consent and might not have a legally authorized representative.

*Q14: Is there information regarding study results that, at a minimum, should always be disclosed after the clinical investigation is completed? If so, what is that information?*

In the regulation, the FDA should require that the investigator disclose certain information after the clinical investigation is completed. The clinical investigator should disclose the results of the study first and foremost. This includes the study's effectiveness, its internal and external validity, and its generalizability to the general population. The results should also include the investigative treatment's degree of effectiveness as compared to the placebo or standard care treatment. If the investigative treatment did not have a significant effect, the FDA should require the clinical investigator to disclose this also. It is common in peer-review publications and in the scientific field to not report and not disclose the results of a study that were not significant to a certain degree. The absence of significant results, especially in emergency investigative treatments, is just as important as the presence of significant results. The absence of significant results signifies that this treatment does not work and should neither be studied further in the future nor used in the future. The public, for its own safety, has a right to this information.

*Q16: When should a clinical investigation be considered "completed"? How soon after a clinical investigation is completed should the results be disclosed?*

A clinical investigation should be considered completed when the study is published in a peer-reviewed journal. When a study is published in a peer-reviewed journal, it has been reviewed and analyzed by several scientific researchers in the field. The researchers have reviewed the article to ensure the statistical analysis was completed correctly and that the effects are not being distorted or overemphasized. This ensures that the investigator is accurately reporting the true effects of the investigative treatments. In addition, the results of the study, whether they are positive or negative, should be reported in the peer-reviewed study. Even though this should be the accepted standard for when a clinical investigation should be considered complete, the peer review process takes a lengthy amount of time as a result of the revisions and rewrites that are necessary before the article is of publishable quality. The article and its results are not normally approved the first time the investigator submits them for review. Despite this, the peer review process is necessary to ensure that investigators are reporting results accurately.

One suggestion to expedite the process is to have the researcher post the article on an online publication exchange format, such as the Social Science Research Network ("SSRN"). As long as the researcher does not post the article before it is peer-reviewed, posting on an online publication exchange would enable the researcher to disseminate the information earlier. This option should not deter the researcher from publishing in the traditional paperback journals though.

## D. Additional Challenges & Thoughts

As a final thought, the FDA should establish a Central IRB whose primary responsibility is to review and approve or reject Section 50.24 requests. Currently, the criteria require that local IRBs review and approve investigations pursuant to the informed consent exception. The problem with local IRBs approving these studies, however, is the inconsistency with which the IRB enforces the regulation and the varying interpretations of several of the regulation's provisions. A Central IRB, composed of ethicists, researchers, and lawyers, who dealt only with Section 50.24 requests would provide uniformity and expertise that is lacking at the local level. In addition, with only one IRB approving or rejecting a Section 50.24 request, human subjects are more likely to be protected. Local IRBs are overworked and have several requests for a number of different studies on their agenda at any one time. The Central IRB could devote its attention to a research proposal to ensure that the researcher is implementing all human subject protections. Dr. Robert Silbergleit from the Neurological Emergencies Treatment Trials agrees and stated in his comment that “[c]entralized review of the key provisions of a proposed trial by a board capable of developing and maintaining expertise relevant to exception to informed consent would be more effective at improving review quality and decreasing variability.”<sup>16</sup>

One minor concern, however, with a Central IRB is that it would be inundated with requests and this would delay the implementation of emergency research. This would most likely not be the case though. Over the last ten years that the regulation has been in effect, approximately sixty requests for an exception pursuant to Section 50.24 have been made. This is approximately six requests per year, which is not an inordinate amount of requests. If it is the case that the Central IRB is inundated, then instead of having a Central IRB that decides all the Section 50.24 requests, the Central IRB could play an advisory role to the local IRBs to ensure uniformity and adequate human protections.

## **IV. CONCLUSION**

In conclusion, I would like to take this opportunity, once again, to thank the FDA for the opportunity to comment on the current rule, 21 C.F.R. § 50.24. This regulation is extremely important in the medical and scientific world because of the need to study and identify effective and non-effective treatments for life-threatening conditions. The FDA has done a tremendous job in crafting this rule and has had the difficult job of balancing two interests that should be aligned but that tend to be competing: promoting scientific advancements and adequately protecting human beings. Several additional provisions could be added and clarified, as discussed above, to further protect human subjects. Even though the rule in its current state might be onerous for clinical investigators, the FDA has demonstrated that its main priority is protecting those who cannot protect themselves.

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<sup>16</sup> NETT Investigators, Response to *Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors; Exception from Informed Consent Requirements for Emergency Research* 5 (2006).