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IRB Reduces Approval Times for Expedited Actions

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Approval times for expedited amendments and expedited continuing reviews are influenced by the complexity of submissions, the timeliness of researchers to respond to questions, availability of a physician or pharmacist reviewer, and IRB office document processing.

With the goal of reducing the time between submission and approval, the IRB office staff targeted internal workflow strategies. Specifically, IRB staff worked to improve efficiency for IRB office document processing and review.

As part of our efforts, you may have noticed that:

1. Michele Gaffigan pre-screens incoming submissions. This improved screening process allows the IRB to immediately alert researchers of missing documents or expired education. Researchers can then rectify some types of problems before the IRB member performs review.
2. IRB staff members rearranged the workflow to better engage a (newer) IRB reviewer, Diana Pruitt, hired January, 2011. Diana reviews many, if not most, expedited amendments now.
3. IRB reviewers telephone researchers, whenever possible, to receive immediate information about unclear items, enabling reviewers to provide focused stipulations and guidance.

Results:

1. *Expedited amendments:* From July to December, 2011, approval times were reduced from 15.5 days to 5.5 days. Within the past three months, half of expedited amendments were approved in 4 days.
2. *Expedited continuing reviews:* Between months July and December for years 2009 – 2011, approval times decreased by almost 4 days.

As noted above, approval time is influenced by many factors outside the IRB's control, including investigator response time. The IRB office will continue to track approval times with a goal of further improving efficiency.

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Understanding Subject Screening and Enrollment Numbers

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The IRB requests information about proposed subject screening and enrollment numbers to gauge how many persons could be placed at risk from study participation. In this article, we'll attempt to show you how to fill out Section 3.1.1 in the New Protocol Application and how to make revisions to these estimates over the course of the study.

To augment the explanations, we provided screening and enrollment estimates for an imaginary multiple-visit study. We used these estimates to complete Section 3.1.1 on the next page.

How do I complete Section 3.1.1 for initial submission?

First refer to the protocol or contract for the number of subjects needed for enrollment at National Jewish Health. We then recommend answering the questions in Section 3.1.1 in the following order:

1. Will you replace enrolled subjects who withdraw or must be discontinued? If you plan to replace subjects who do not complete the study, be aware that you will need to screen and enroll more subjects.

For this example, 20 subjects must complete the study to have enough statistical power. Any subject that does not complete the study must be replaced. It is estimated that 4 subjects will not complete the multiple-visit study and will need to be replaced.

2. How many subjects will be enrolled (meet all screening criteria and have provided informed consent)? This question asks how many subjects will pass the screening process and will start proceeding with protocol-specified procedures. This is an important estimate because these subjects could receive all of the procedures (and risks) described in the protocol. If subjects will be replaced, the replacement subjects should be included in the enrollment estimate.

As noted above, we estimate that 4 subjects will be replaced so that 20 subjects will complete the study. To meet this goal, we will enroll 24 subjects. (NOTE: You may complete this answer as "24 subjects" or "20 completions + 4 replacements.")

3. What is the anticipated screen failure rate? A "screen failure" is a person who does not meet all eligibility criteria for the study. These persons provide informed consent and complete some or all of the screening process, but do not meet the protocol's eligibility criteria to continue further in the study. The screen failure rate is often based on historical experience or the literature.

For this example, we anticipate a 40% screen failure rate based on historical experience with this subject population.

4. Considering the screen failure rate, how many subjects will you need to consent and screen in order to enroll the desired number of subjects? This number will need to take into account enrolled subjects and screen failures.

To calculate this number correctly, start out with the planned number of enrolled subjects. Then DIVIDE by (1 - the screen failure rate) to achieve the total number of persons who should provide consent and go through the screening process.

For this example, recall that we plan to enroll 24 subjects. We will then divide 24 by (1 - 0.4 [the screen failure rate] = 0.6) to achieve the total number of persons who should provide consent and go through the screening process. [24 / 0.6 = 40]. If screening 40 persons, we expect that 40% (16 persons) will screen fail, and 24 persons will enroll in the study.

Researchers commonly perform this calculation incorrectly by multiplying the number of enrolled subjects (24) by the screen failure rate (0.4) [24 x 0.4 ≈ 10] and then adding the rounded product to the number of subjects planned for enrollment [24 + 10 = 34]. However, if we screened 34 subjects with a 40% screen failure rate, we would only be left with about 20 eligible subjects -- four short of the necessary number of eligible subjects (24). Again, make sure that you DIVIDE by (1 - the screen failure rate) to correctly estimate the number of subjects you should screen.

5. Explain how you determined these screening and enrollment estimates (e.g., power analysis). In this field, explain how you determined how many enrolled and completed subjects were necessary.

(Continued on next page)

This information is often gleaned from the protocol. The IRB prefers a power analysis, when possible, but will accept a historical or literature-based description for pilot or exploratory studies.

6. Provide any other pertinent considerations. In this field, explain if there is anything else that the IRB should know.

Sample section completion based on the example:

3.1.1 2 **How many subjects will be enrolled (meet all screening criteria) at NJH?**
20 completions + 4 replacements = 24 subjects

3 **What is the anticipated screen failure rate?** 40%

4 **Considering the screen failure rate, how many subjects will you need to consent and screen in order to enroll the desired number of subjects?** 40

5 **Explain how you determined these screening and enrollment estimates (e.g., power analysis):**
The enrollment estimate is based on a power analysis (See Data Analysis section). The screen failure estimate is based on historical experience with this subject population.

1 **Will you replace enrolled subjects who withdraw (or must be discontinued)?** YES↓
 If YES, how many? 4

6 **Provide any other pertinent considerations:** N/A

NOTE: Investigators must seek IRB approval to consent or enroll more subjects than are requested/approved.



How should I describe enrollment of families or couples?

To address this issue, we must be mindful of the definition of “human subject.” A human subject is “a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or (2) identifiable private information.”

Say you plan to enroll married couples in talk therapy to help husbands improve their health. If you plan to interact with the husband and wife, both are considered research subjects—even if the husband is the only person targeted for behavior modification. In this scenario, if you plan to enroll 10 couples, you will enroll 20 subjects.

Why must enrollment and screening numbers be updated if estimated incorrectly?

As noted in the introduction, the IRB needs to know how many subjects may face risk from participation. The risks of enrollment are often well-documented in submission paperwork, but risks from screening are underappreciated. The following are different types of risk and examples that could be encountered from screening:

- Physical risks: withdrawing clinically-indicated medication; receiving procedures to confirm eligibility
- Psychological risks: completing questionnaires about depression
- Social risks: documenting medical history involving a sexually transmitted disease
- Legal risks: answering questions about illicit drug use

In every study, there is a risk of loss of confidentiality that could lead to accidental disclosure of private information.

How should enrollment and screening numbers be updated?

Update the New Protocol Application, Section 3.1.1.

The New Protocol Application is the only initial application document where screening, enrollment, and replacement of drop outs are documented. If this section is amended, the dates on pages 1 & 2 should be revised. Also there is a box in the middle of page 1 to indicate that the NPA is amended. That box should be checked and the initial box should be unchecked.

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What should I do if I screened or enrolled too many subjects?

If you discover that you have over-enrolled or consented more subjects than you were approved to screen, the following steps must be taken:

1. Complete a protocol deviation report and submit it to the NJH IRB for review and acknowledgement.
2. Revise the NPA section 3.1.1 and submit to the NJH IRB for review and approval.
3. If your request to increase the number of subjects screened exceeds 10% of what was originally approved AND your study was reviewed by the full committee, your request must be reviewed by the full committee. In this case, you are also required to provide 17 copies of your submission for full committee review.

4. If you are requesting increased ENROLLMENT, you must also revise the study protocol and informed consent document to reflect the new total number of subjects to be enrolled. Sufficient numbers of review copies must also be submitted for IRB review and approval (17, if enrollment increase is >10% of what was last approved; 2 if the change can be reviewed via expedited process).

NOTE: You must stop screening subjects until you receive IRB approval to screen more subjects.

If you have any questions please contact the NJH IRB.

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Please Remember ...

CITI Training

October 1, 2011 marked the three year anniversary of National Jewish Health's affiliation with the CITI program for online human subject protection training.

Because human subjects protection education expires after three years, please remember that

many researchers will soon be required to renew their human subjects protection education.

A study cannot be approved/renewed if current (within three years) human subjects protection education is not on file for all members of the research team.