

This presentation discusses changes that the IRB made to processes and forms. I will explain what problems we've encountered and how we addressed the problems. At the end of the presentation, I'll share how you could be part of our continued improvement.



What you asked for

- Clear questions and instructions
- Efficient, consistent processes
- Integration of HIPAA into all reviews
- Flexibility in considering investigator proposals for alternate wording or solutions
- Help with ongoing compliance

In general, investigators and coordinators asked for:

- Clear questions and instructions
- Efficient, consistent processes
- Integration of HIPAA into all reviews
- Flexibility in considering investigator proposals for alternate wording or solutions
- Help with ongoing compliance

The first four points serve as a basis for all of the changes to processes and forms.

With regard to the last point, I'm pleased to tell you what we can offer on a more immediate and tangible basis. [See next slide.]



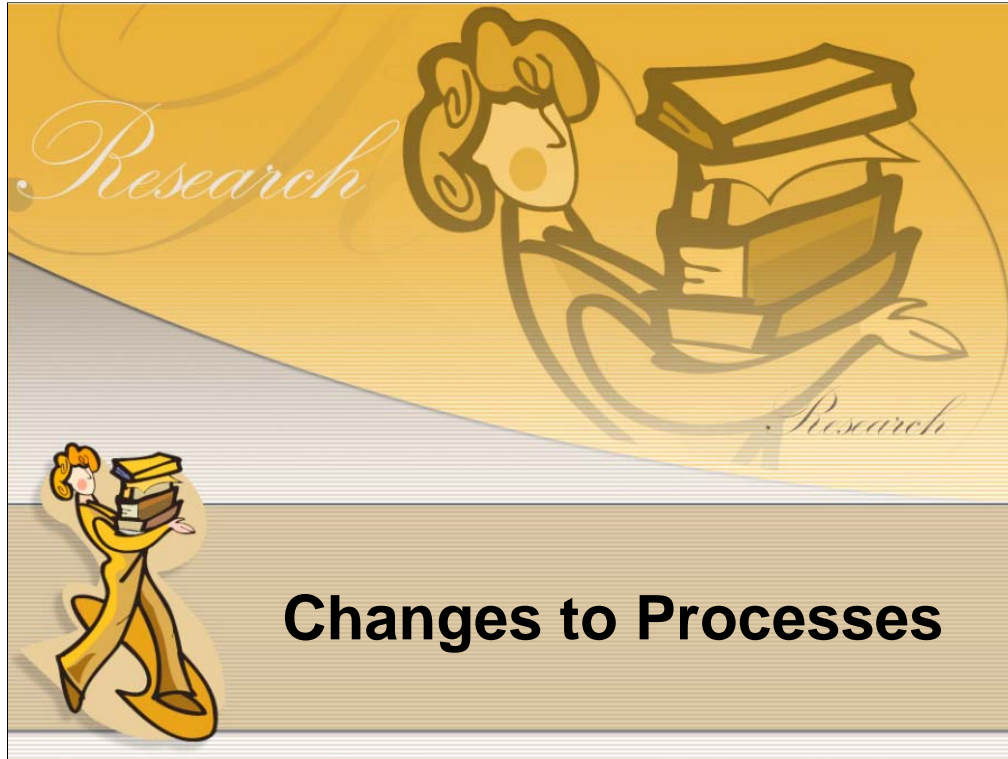
Audit program

- Department of Research Regulatory Affairs hired a new Clinical Research Quality Assurance Analyst: Sherri Gabbert, Ph.D.
- Auditor will not be a member of IRB staff (and will not be limited by IRB scope). She could:
 - Serve as a resource to investigators regarding study development without a potential conflict of interest.
 - Advise research teams about best practices
 - Examine data quality and advise on better data collection methods.

The Department of Research Regulatory Affairs hired a new Clinical Research Quality Assurance Analyst: Sherri Gabbert. Sherri will not be a member of IRB staff. Therefore, she will not be limited by potential scope of the IRB. Because Sherri is not limited, Sherri could serve as a valuable resource to investigators regarding study development without a potential conflict of interest.

- During an audit, she could advise research teams about best practices without the appearance of IRB “mission creep.”
- She could examine data quality and advise on better data collection methods.

Sherri has already started fielding questions about best practices. Feel free to contact her as a resource.



The following slides pertain to changes to IRB processes.



Fee Schedule

- Effective date: April 1, 2009. Old fee schedule was honored for studies in development until July 1.
 - Initial review: \$1750 (\$250 increase)
 - Continuing review: \$1200 (unchanged)
 - Amendments (new fees):
 - Diaries, questionnaires: \$100
 - Protocols, consent forms, investigator brochures or any combination (including diaries & questionnaires) submitted at one time: \$250

The new IRB Fee Schedule took effect for new submissions after April 1, 2009. The fees apply to studies not eligible for a fee waiver. A 90-day grace period was implemented for studies in development. However, studies submitted after July 1 will be assessed the new fees.

The new fees are lower for initial review than our local competitors, but we will start charging for some ongoing reviews. Note the new fees for amendments:

- The charge is \$100 for review of diaries and questionnaires.
- The charge is \$250 for review of protocols, consent forms, investigator brochures or any combination of these forms including diaries and questionnaires, so long as they are submitted together in a single batch.

The fee schedule is posted on the IRB website at the top of the Submissions page.



Education Certification

- Education deadline is approaching: 08/03/2009
- Certifications accepted:
 - CITI NJH
 - CITI COMIRB
 - NIH Human Subjects Tutorial
 - NJH IRB CD training (will be phased out)
 - Other institution's HSP education considered on case-to-case basis
- Education must be renewed every three years.
- IRB will not provide initial approval or renewals unless all certifications are verified as current.
- IRB will provide reminders within 60 days of expiration and at continuing review.

Last year, the IRB implemented a requirement that all research personnel demonstrate current certification. This requirement applied to all initial reviews, but was phased in for continuing reviews. The IRB created a deadline of 08/03/2009 by which all research staff must have evidence of current certification.

The IRB accepts the following evidence of certification. [Review list in slide.]

Be advised that:

- Education must be renewed every three years
- The IRB will not provide initial approvals or renewals unless all certifications are verified as current
- The IRB will provide reminders within 60 days of expiration and at continuing review.



Curricula Vitae

- Current (within 3 years) CVs must be on file for each investigator.
- IRB will provide expiration reminders at continuing review.

As part of our due diligence, the IRB is now collecting CVs. CVs must be updated every three years. The IRB will maintain the CVs on file (so they need not be provided with study documentation) and the IRB will provide reminders of expiration.



HIPAA Review

- NJH IRB serves as the institutional privacy board
- HIPAA compliance is now evaluated in all IRB reviews

The NJH IRB serves as the institutional privacy board and collaborates with the institutional Privacy Officer.

HIPAA compliance is now evaluated in all IRB reviews.



COMIRB Reciprocity

- The institutional cooperative agreement allows each IRB to cede review responsibilities to the other.
- Problems arose from incomplete ceding.
- New process involves complete reciprocity.
 - The secondary IRB performs only facilitated review.
 - Investigators report to only one IRB for all continuing review and reportable issues.
 - New SOP to educate IRBs and investigators.

Research

Many of you conduct research at both National Jewish and UC Denver, so you may be familiar with both the National Jewish Health IRB and COMIRB. The institutional cooperative agreement allows either COMIRB or the NJH IRB to serve as the IRB of Record for research at the other institution.

Problems arose from incomplete ceding. Each IRB had its own process for tracking ongoing research. At NJH, we conducted continuing review even if COMIRB had just done so. This inefficient process didn't afford any additional protections.

The new process involves complete reciprocity. When COMIRB serves as the IRB of Record for research conducted at NJH, the investigator must still submit for NJH IRB initial review, but we will perform only a facilitated review and no ongoing reviews. For those of you unfamiliar with a facilitated review, the review involves:

- Verification that the primary IRB had performed the correct review and addressed the most important issues for human subjects protection
- Consideration of local context issues involving human subjects protections at NJH
- With an institutional consideration, we ask "Is this study appropriate for National Jewish Health?"

You will notice immediate benefit from this change. You'll submit continuing review and report problems to only one IRB for the life of the study.

We are finalizing our Standard Operating Procedure with COMIRB. Once finalized, we will make the policy available to you and we'll apply it to current studies using COMIRB as the primary IRB.



IRB Jurisdiction

- Determination of IRB jurisdiction is not exclusive to funding and majority of research. These are guidelines, not rules.
- Institutional liability is now a consideration for IRB jurisdiction.
- Funding is not tied to the institution providing IRB review.
- Communication with IRBs is critical. The IRB Directors will confer and come to consensus.

Research

This slide discusses changes to jurisdiction between COMIRB and the NJH IRB. I'd like to start out by providing a little background.

IRB review jurisdiction is based on a few considerations. IRB review is generally provided at the institution receiving the funding and performing the majority of procedures. Why?

1) IRB review is expensive. It actually costs the institution a lot more than what the IRB charges. Therefore, IRB review is generally performed at the institution that receives the funding.

2) As another consideration, the institution that bears the liability wants to have the oversight.

However, not all research studies have clear delineations of institutional funding and/or liability. While there still are guidelines to help an investigator make a jurisdictional assessment, these should be considered as guidelines, not rules because the institutions through their IRBs also have a role in making the determination.

With regard to liability, be advised that both IRBs are looking more carefully at potential liability issues of their respective institutions. Therefore, there will be circumstances when the institutions will override the investigator's jurisdictional assessment.

When an institution overrides the general guidelines for jurisdiction, I want it to be clear that funding does not have to be tied to the institution that provided IRB review. Study conduct and funding should remain the same regardless of which IRB provides review.

Because this flexible jurisdiction could be confusing at times, investigators are encouraged to contact the IRBs directly. Facility utilization liaisons do not have the authority to make these decisions. When there is question, the COMIRB director and I will come to consensus about jurisdiction.



IRB Website

- Need for changes
- Change already implemented:
 - IRB now maintains its own website and all content.
 - Can provide real-time guidance and updates to investigators.
 - Forms can be fixed and uploaded in a matter of moments.
- Process change:
 - Investigators must obtain all forms from the website to ensure use of the most current form. Obsolete forms will not be accepted.
 - Requirement will be phased in during July, 2009.

Before December, 2008 (when the IRB website went live), we faced the problem that investigators had no easy access to forms. So once they obtained a form, they used it for every study and recycled forms. The IRB couldn't realistically reject obsolete forms when investigators couldn't obtain updated forms.

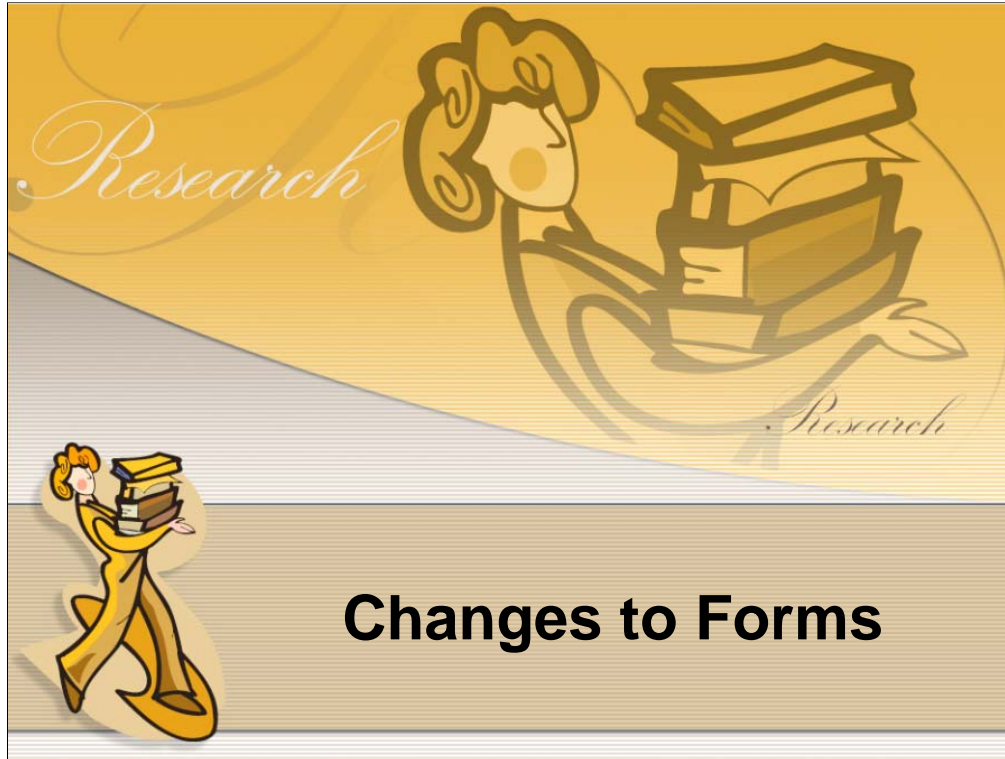
Now IRB staff not only have a website, but we have full control over content and can make changes ourselves, whenever we want, at no cost. We are pleased that:

- The IRB can now provide real-time guidance and updates to investigators.
- Forms can be fixed and uploaded in a matter of moments.

Now that current forms are easily accessible to anyone with an internet connection, we'd like to address the problem that investigators are using obsolete forms. Investigators are recycling forms that are up to five years old. We now have the reason and ability to update submission forms and we'd like investigators to use the updated forms.

The IRB is implementing a change to forms submission. We'll require that investigators go to the website any time they need a form to ensure that they have the most current version. Also, the IRB has the authority to reject any submission on an obsolete form, but we will use some common sense.

This change will take effect immediately, but we will implement a grace period of 30 days. We will accept any obsolete forms that you are currently working on. But effective August 1, 2009, we will require you to use the new forms. Once you see the new forms, you'll be eager to use them.



The IRB made changes to nearly all of the forms. Minor changes for presentation or clarity will not be discussed today. However, we are implementing major changes to certain forms. We will not discuss the forms themselves today, but they are all available on the IRB website.



New Protocol Application

- Need for changes
- Changes:
 - Improved instructions and questions
 - Sections may be skipped if references to are made to particular pages in the protocol or investigator's brochure.
 - More detail is requested about:
 - Research staff contact info
 - Research locations. (Instructions provided about research in facilities under cooperative agreements.)
 - Protections for vulnerable populations (separate form)
 - Screening process
 - Strategies for paying subjects

The New Protocol Application (NPA) is the most complex submission form and therefore has the most problems. We noted which sections seemed to have the most stipulations. We learned that we were not asking good questions.

Along those lines, we noted that investigators were not using the separate instructions document, so we put the most critical directions into the application form itself so that all of our investigators would see them. We broke apart multipart questions so that there are separate fields for each question. For difficult questions, we provided examples of the types of answers we are looking for.

As another problem with the old NPA, it was rife with redundancy. Any redundancy creates error. In the new form, we are reducing redundancy by allowing investigators who have a separate protocol to reference the protocol instead of copying the protocol (and sometimes editing one or the other inconsistently). In the NPA, we ask you to cite specific page numbers and paragraphs in the protocol or IB.



New Application for Research on Existing Data or Specimens

- Need for changes
- New application:
 - Streamlined application designed for retrospective research
 - A single application can accommodate non-human subject determinations, exempt review, expedited review, or full committee
 - Addresses all HIPAA considerations
 - IRB will facilitate communication with certain repositories

Today, I am officially unveiling a new application form I created exclusively for retrospective research.

Previously, there was no appropriate approach to these types of studies. None of the application forms was suitable for the unique and challenging issues that arise in retrospective research. Also, many investigators incorrectly filled out the exempt research form and had to start over with the New Protocol Application.

Some immediate benefits of the new application form are:

- From an investigator standpoint, the application process is a streamlined approach. It guides the investigator to complete or skip certain sections depending on their access to identifiable data.
- A single form asks enough questions for the IRB to find the right review determination: non-human subjects, exempt, expedited, or full committee review.
- The form addresses the complex HIPAA considerations (including Waivers of authorization and limited data sets).
- This form also combines applications from the National Jewish Research Database, biobank, and ILD repositories. After IRB approval, the IRB will facilitate communication with these repositories. The IRB can approve the research, but these groups must approve access to their own data or specimens. We hope that IRB communication with these departments increases speed of secondary review.



Continuing Review

- Need for changes
- Changes:
 - Federally- and non-federally funded continuing review forms are combined into one form. User will opt out of questions specific to particular funding source.
 - Basic instructions are included throughout the form

Before today, there were two, nearly identical continuing review forms: one for federally-funded research, and one for non-federally funded research. There were a few additional questions for federally-funded research. The problem with this approach is that some people didn't know which form to complete.

To reduce the likelihood of this error, we combined the applications into one form. The form contains directions on which questions could be skipped based on funding sources.

The separate instruction form was eliminated because we placed the critical directions directly into the application.



Conflict of Interest

- Need for changes
- Changes:
 - Each investigator must complete separate form whenever he/she is added to the study
 - Form requests category of conflict and basic detail
 - Provides instructions on how to start institutional COI management plan

The old conflict of interest form had been non-compliant on a few levels. But the most important consideration was that the form was only completed at initial review. If an investigator was added to the study after approval, there was no conflict of interest assessment.

To ensure we are performing our due diligence, the IRB modified the form so that each investigator signs a separate (shortened) form whenever he/she is added to the study.

For changes to content, the form requests the category of conflict and asks for basic detail with no monetary disclosures. If an investigator indicates a conflict of interest, the form provide directions on how to start the institutional COI submission and review process.



Unanticipated Problems

- Need for changes
- FDA and OHRP minimum reporting requirements
- Process is used by COMIRB, Quorum, & WIRB
- Unanticipated Problems must involve all three of the following criteria:
 1. Unanticipated,
 2. Related to study participation, and
 3. Could place subjects at increased risk than previously known or recognized

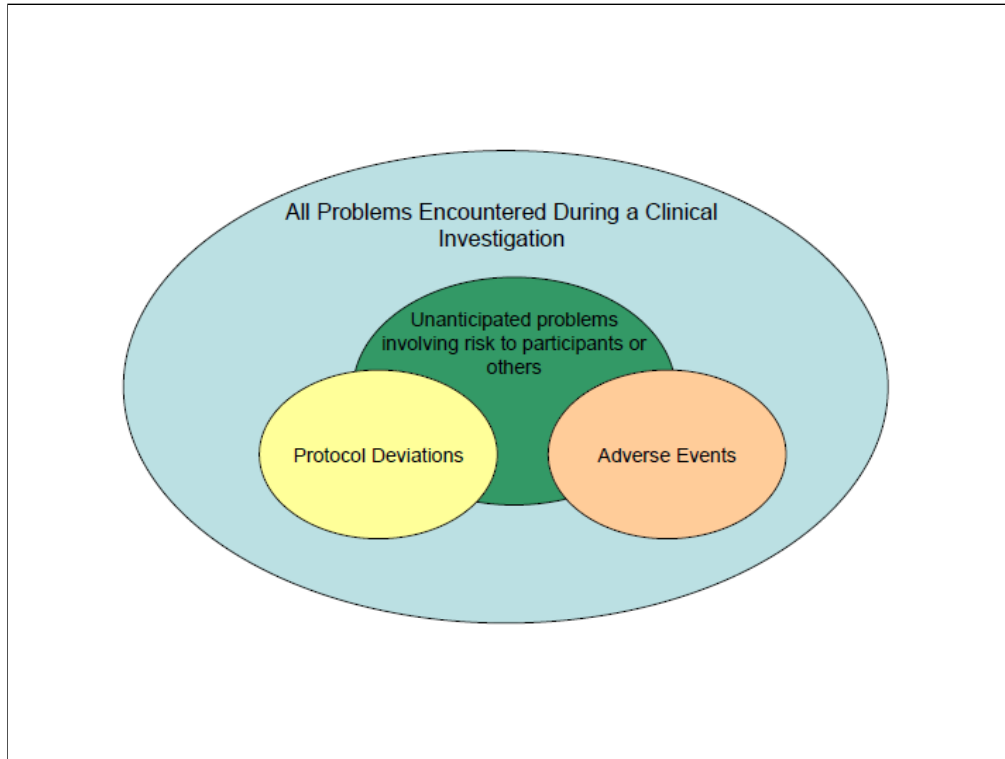
Before today, the IRB requested reports of ongoing problems to research in External AE report forms (typically IND safety reports), Internal AE report forms, Protocol Deviation reports, and summaries provided at continuing review. By having separate reports for all minutiae, we were exceeding the federal reporting requirement, but we were also reducing our ability to perform effective review.

FDA and OHRP don't specify which types of events must be submitted except that IRBs must have a reporting mechanism in place for unanticipated problems – the minimum standard.

COMIRB, Quorum and WIRB—the only other IRBs that can approve research at NJH--had all adopted the Unanticipated Problems reporting standard. Therefore, the NJH IRB was the only IRB that hasn't adopted the modern reporting interpretation for research taking place here. We are finally coming in line.

To qualify as a reportable unanticipated problem, the event (or collection of events) must be:

- 1) Unanticipated (in terms of nature, severity or frequency) given the nature of the research procedures described in protocol-related documents and the characteristics of the subject population being studied,
- 2) Related or possibly related to study participation, and
- 3) Could place subjects or others at a greater risk of physical, psychological, economic, or social harm than was previously known or recognized.



Here is a Venn diagram that shows how Unanticipated Problems overlap with other types of problems that arise in a clinical trial.

When reporting only unanticipated problems, we are capturing some adverse events, some protocol deviations, and collections of other nebulous problems. The main difference is that Unanticipated Problems increase risk to subjects or others.



Unanticipated Problems (2)

- Changes:
 - New form to replace Internal & External AE reports and Protocol Deviation forms
 - Process reduces paperwork for investigators and IRB without compromising regulatory compliance
- Potential for Sponsor Pushback:
 - Some industry sponsors are demanding
 - IRB staff will provide private guidance

The new Unanticipated Problems report form replaces Internal & External AE reports and Protocol Deviation forms.

An immediate benefit is that the process reduces paperwork for investigators and the IRB without compromising regulatory compliance.

It is possible—if not likely—that some of the industry sponsors will still demand that you submit events that don't qualify as unanticipated problems. Contact the IRB if you face resistance. We can offer suggestions for how to communicate the IRB policy and/or how we could help.



Consent and Assent Forms

- Need for changes
- Changes:
 - Allow consent templates to serve as a guideline not a rule. Investigators could propose own wording as long as required elements are included.
 - Can't change institutional injury statements

A few years ago, an IRB subcommittee created mandatory standard statements for informed consent and assent forms. The intent was to provide guidance on how to meet regulatory requirements and to promote consistency among consent forms.

There were a few problems with this approach. First, investigators were not permitted to deviate from this language even if the statements were inaccurate or inappropriate for the study. Further, the standard statements rarely fit the style or tone of the document, so the consent and assent forms read like a bad cut-and-paste job.

The IRB is now adopting the same position on standard statements as COMIRB: Allow the standard statements to be used as guidance for those who need it, but allow investigators discretion to modify the statements to fit the particular details of the study and the flow and style of information in the form.

This could be a huge time savings for those of you who receive a consent template from industry. You could retain more of the sponsor's suggested wording. The only exception to this flexibility would be the institutional injury statements.

In the future, the IRB and institution may also decide that more sections must remain mandatory. But until then, we'd like you to use some creativity to make your consent forms accurate for your study and readable for your subject population.



Assent Form

- Need for changes
- Changes:
 - Allow investigators more discretion to customize the communication style and content to be suitable for the age and maturity of the intended subject population.
 - Removed references to financial compensation
 - Removed requirement for parental notification of pregnancy

The assent document is one of the most challenging documents to write and review because of the difficulty in communicating complex concepts to children ranging in age, education, and maturity.

Previously, the IRB had tried to create one-size-fits-all standard statements that had not effectively or appropriately communicate concepts to the particular child population being studied.

Like with the consent forms, the IRB is now allowing more investigator discretion for communication style and content. Please write your assent forms to be suitable for the age and maturity of the intended subject population.

With regard to investigator discretion, the IRB full committee has already agreed to two changes to the assent form:

- 1) References to financial compensation must be removed from the assent form.
- 2) Based on an institutional edict, there is no longer a requirement for parental notification of pregnancy.



Comment Period

- 90-day comment period to evaluate forms
- We need your feedback to make the forms better
- Submit all comments by Oct 1, 2009

The IRB did its very best to enhance the forms and processes, but we ultimately won't know how well they work until they are used with real studies.

To allow continued consideration for improvement, the IRB created a 90-day comment period to collect feedback.

We are asking for your help. We are eager to hear your experiences and suggestions so that we could make the forms and processes better.

Please submit all comments by October 1, 2009.



Conclusion

- Overriding themes:
 - Efficiency and clarity
 - Allowance for more discretion with non-regulated issues
- Request patience with changes

In conclusion, the IRB made changes in forms that focus on efficiency and clarity, and changes in processes that allow for more IRB and investigator discretion with non-regulated issues.

It will take time to implement the changes until we are comfortable with the outcomes. If we are patient, we will all become more responsive to human subject protection.

Thank you.



Questions

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Research

Research