Yale *Human Research Protection Program*

IRB Essentials

Sample Protocol Review: What is the IRB Looking for During Review?

Stacey Scirocco, BA, CIP & Jennifer Reese, MS, CIP

June 29, 2026

Yale *Human Research Protection Program*

Learning Objectives

- Learn what IRB reviewers agree is important for swift, seamless, review of an initial protocol submission.
- Identify common pitfalls and what stops the review process.
- Learn to review your product before submission.

Training Agenda

Topic	Slide #
Survey: What are IRB reviewers looking for?	
Detail – *Methodology, Risk and Inconveniences, and Inclusion/exclusion criteria.* *How the IRB reviews an initial submission*	
What to do for an efficient review Common delay drivers / inconsistency issues	
Pain Points	

IRB Review

- The primary responsibility of an IRB is to protect the rights, safety and welfare of human subjects participating in research.

- One way that IRBs fulfill this responsibility is by reviewing research applications to ensure that core criteria for approval are met. A research protocol is part of the group of documents that conveys all the necessary information about research with human subjects to IRB reviewers.

- Investigators may choose to use one of several protocol templates offered by Yale IRB to draft and develop a new protocol. These templates can be found in the IRES IRB Library.

Yale *Human Research Protection Program*

What is the IRB looking for during initial review?

Yale *Human Research Protection Program*

And the "Survey" said….

We conducted an informal survey of staff IRB-member reviewers and Chairs, to ask:

- What is important for a swift, seamless, review?
- What stops the review process?
- What is often missing?

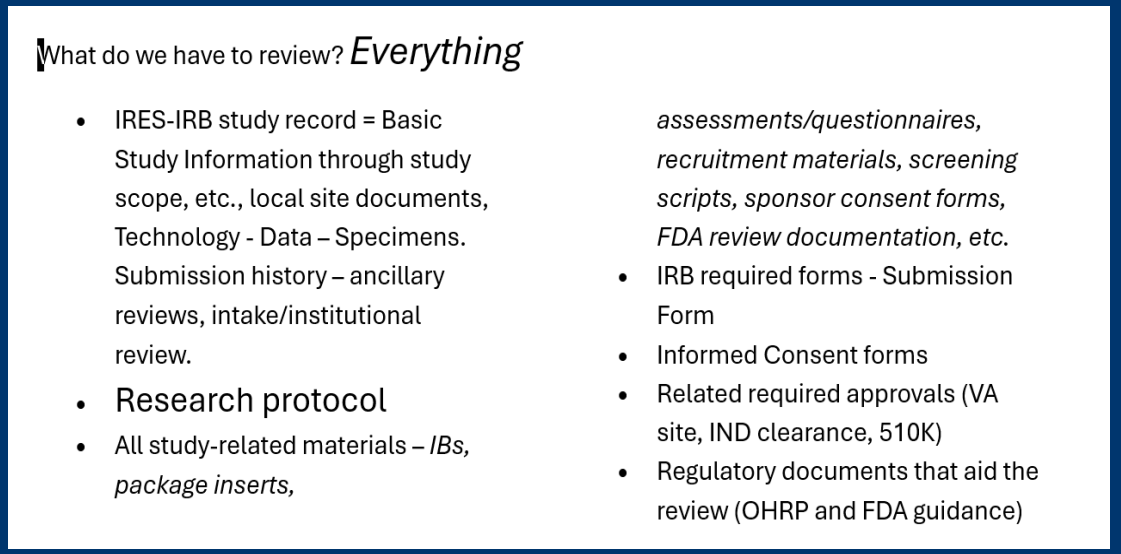
We were able to categorize answers under two main themes.


"What is- appropriate DETAIL and
CONSISTENCY, Alex?!"

Disclosures…

The amount of detail the IRB needs makes inconsistency a natural hazzard.

- We understand!
- *We have suggestions…*
- *We accept them too!*



What do we have to review? *Everything*

- IRES-IRB study record = Basic Study Information through study scope, etc., local site documents, Technology - Data – Specimens. Submission history – ancillary reviews, intake/institutional review.
- Research protocol
- All study-related materials – *IBs, package inserts, assessments/questionnaires, recruitment materials, screening scripts, sponsor consent forms, FDA review documentation, etc.*
- IRB required forms - Submission Form
- Informed Consent forms
- Related required approvals (VA site, IND clearance, 510K)
- Regulatory documents that aid the review (OHRP and FDA guidance)

"The opinions expressed in this presentation are not necessarily representative of the entire IRB (or HRPP)."

"This was not research subject to IRB review because it was not systematic and is not generalizable."

Survey- Reviewers Agree Detail is Key!

- Reviewers at all levels,
- Without any prior knowledge or expertise,
- Need to understand from the documentation, the

Who, What, When, Where, Why, and How?,

of the research ***or is it...***

What, Why, Who (by), How, to Whom, Where, and at What cost (if any)**?**

WHY? to assure CFR criteria for approval of research, (+) are met.

Criteria for approval (partial)

Risks to subjects **are minimized**: using procedures that are consistent with **sound research design** and that do not unnecessarily expose subjects to risk, and whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes.

Risks to subjects are **reasonable in relation** to anticipated **benefits**, if any, to subjects, and the **importance of the knowledge** that may reasonably be expected to result.

Selection of subjects is equitable. In making this assessment the IRB should take into account the **purposes of the research** and **the setting** in which the research will be conducted.

Link to full criteria: 45 CFR 46.111

Specificity is Important! – In all project types

Vagueness and overgeneralization

lead to questions and delay

("no secrets!" -anon)

- Exactly what data? "*What do YOU mean by "de-identified?*"
- *which* platform? What local research organization?

➢Three sections to explore: Methodology, Risk and Inconveniences, and Inclusion/exclusion criteria.

Methodology

- Specific aims, population, procedures, and endpoints must be detailed *and aligned*.
- We must understand what is being done and whether the study design will enable answering the study questions.
  - How will they do that?
  - How will they determine that?
- Background and References
  - Support why the research should be done.
  - Identify what previous and existing research has found.
  - Support the potential scientific impact of the research and/or justify risks.
  - Potentially justify the methodology used.

Risks and inconveniences – Consider

- Includes Medical, physical, social, financial, privacy, employability, legal, psychological …
- Remember Investigator brochures, package inserts, investigational device brochures, and product brochures for applicable risks.

  Tip: Cross check these with the protocol and consent form
- Consider how to minimize risk to increase safety to participants
  - Inclusion/exclusion criteria
  - How you will respond to expected and unexpected events.

Managing and minimizing risk to participants

Consider your inclusion and exclusion criteria, tapping existing procedures performed for a different purpose, and a plan for responding to adverse events, to minimize risk to participants.

Please Detail:

- How you will respond to adverse events (all)
  - Signs and symptoms you will monitor for
  - Your plan of action
- Participant and study stopping rules.

Leveraging existing Procedures: Standard of Care'

- Distinguish between often 'done clinically' and part of the standard of everyday care (approved and part of an accepted standard locally / nationally). Be specific.

- Not everything is standard of care (SOC) for everyone. SOC may carry risks for alternate populations, controls.

- Consider how randomizing impacts risk.

Tips for Inclusion and exclusion criteria

Always address the following questions to- 1st identify what is required to participate and then identify what would exclude those potential participants.

- *"In order to be eligible to participate in this study, an individual must meet all of the following criteria:"*
- *"An individual who meets any of the following criteria will be excluded from participation in this study:"*

Tips for Inclusion and exclusion criteria

No *Ifs, ands, or buts*," in these criteria –

Excludes those:

1. Currently taking an antidepressant medication …. If a subject meets all other study criteria, he/she may consider discontinuation …patient's clinician."

➢This is not an exclusion criterion.

Tips for Inclusion and exclusion criteria

No *Ifs, ands, or buts*," in these criteria -

Inclusions-

1. Engaged in treatment for depression […]
2. Those not engaged in treatment at the time of screening will be required to engage in treatment as a condition of study participation.

➢That is not an inclusion criterion

Often missed and very important: Be specific about how each criteria will be assured (medical record review, assessments, physical exam, self-report).

Inclusion and exclusion criteria, *avoiding pitfalls*

- Keep it simple yet specific
  - Recent history of meeting criteria for alcohol or substance use disorder
  - ➢Meets criteria for alcohol or substance use disorder (documented within the last 6 months)

Exclusion criteria for healthy controls:

1. No current DSM-V psychiatric disorder, excluding nicotine and caffeine use disorder;
2. No lifetime use of psychiatric medication >3 months (proxy for psychiatric disorders).
3. No family history of serious mental illness (e.g., schizophrenia, bipolar disorder)

- Rarely is the reverse of a criterion needed -

Inclusion:

- Non-pregnant females

Exclusion:

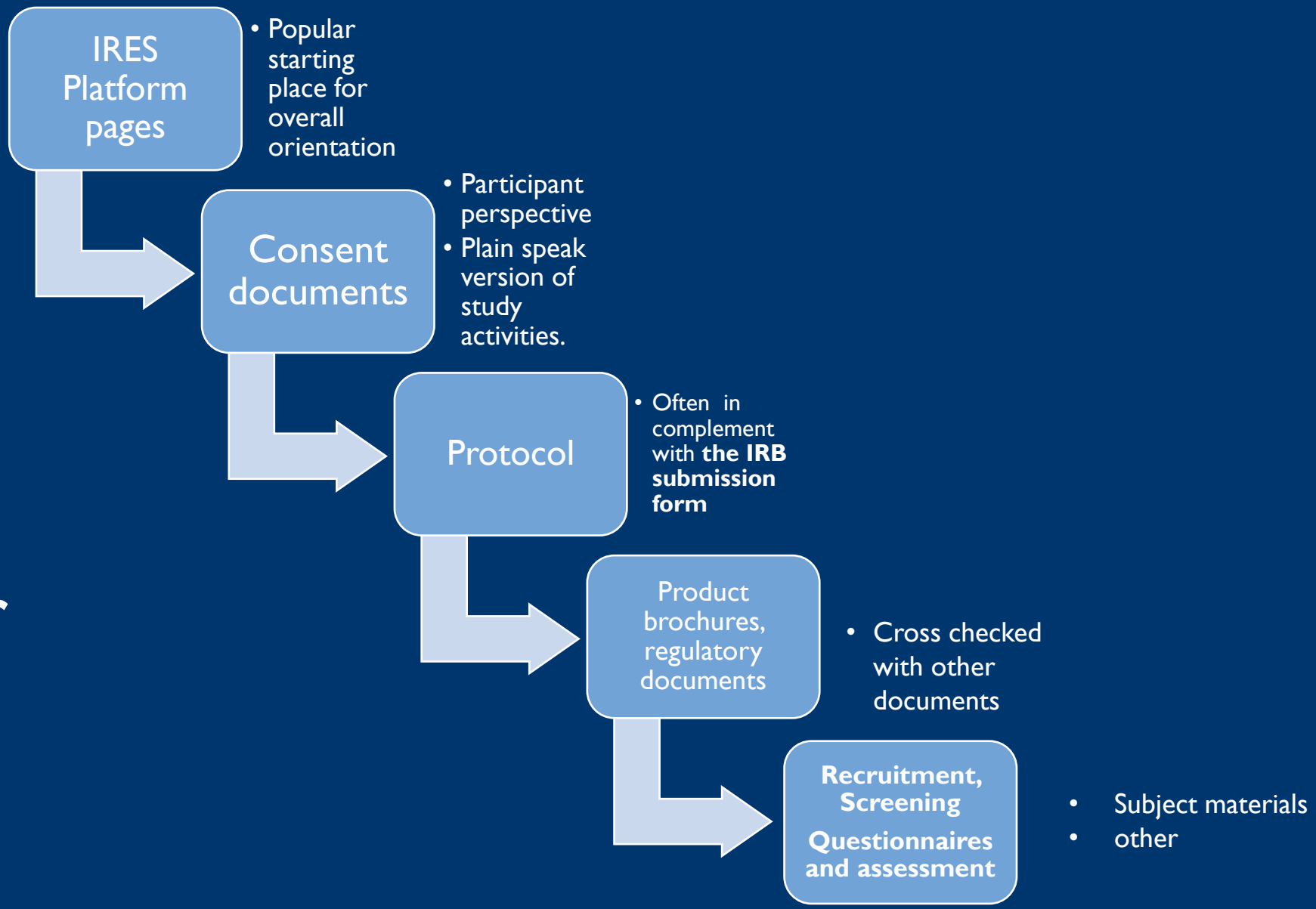
- Pregnant
- male

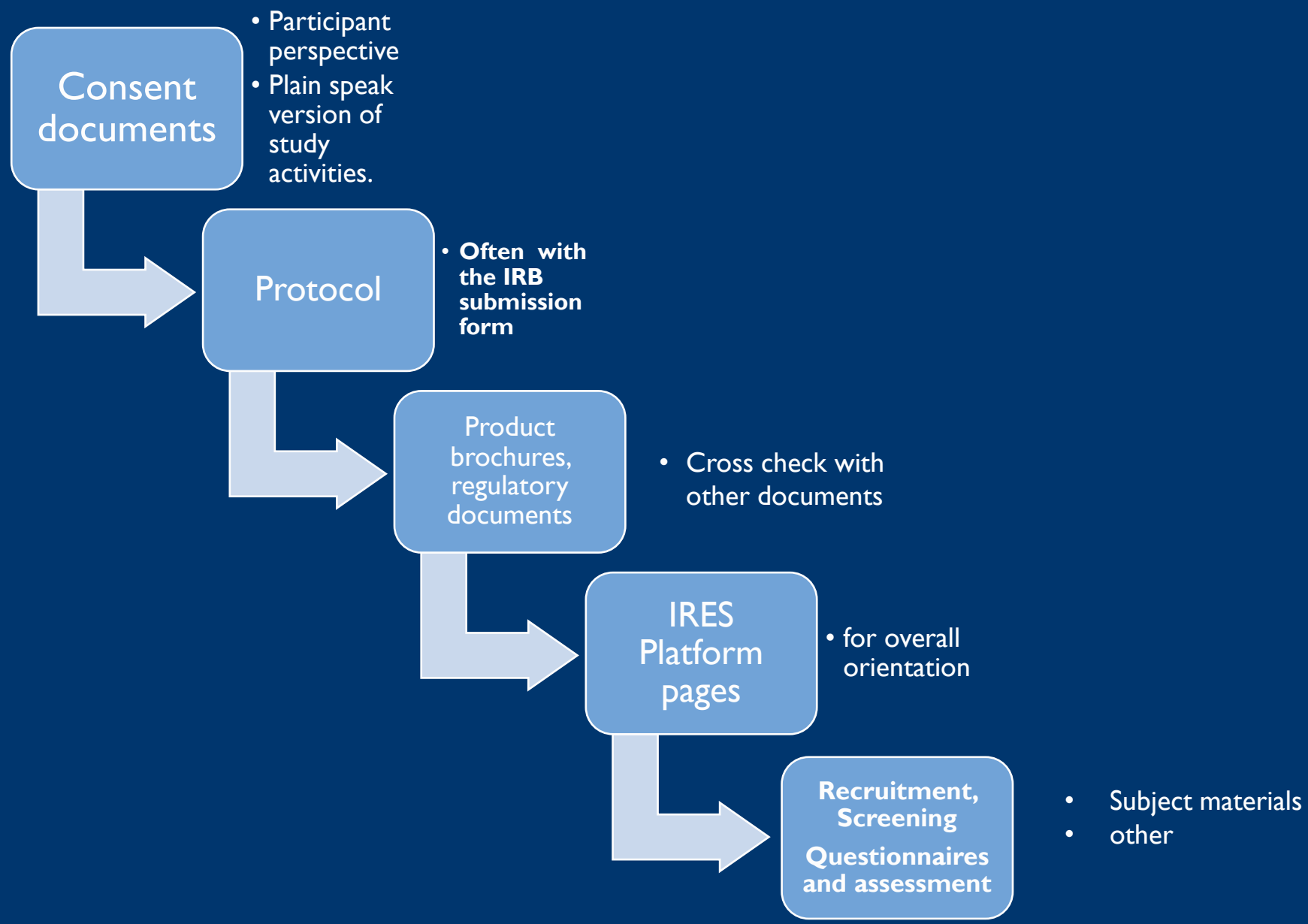
Yale *Human Research Protection Program*

Sample Protocol Review
How Does the IRB review an initial submission?

Yale *Human Research Protection Program*

Whether


IRES Platform pages
• Popular starting place for overall orientation
Consent documents
• Participant perspective
• Plain speak version of study activities.
Protocol
• Often in complement with **the IRB submission form**
Product brochures, regulatory documents
• Cross checked with other documents
Recruitment, Screening
Questionnaires and assessment
• Subject materials
• other

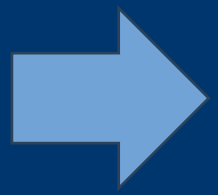

Consent documents
• Participant perspective
• Plain speak version of study activities.
Protocol
• Often with the IRB submission form
Product brochures, regulatory documents
• Cross check with other documents
IRES Platform pages
• for overall orientation
Recruitment, Screening
Questionnaires and assessment
• Subject materials
• other

Or

No two ways were alike!

Top responses:

- *IRES-IRB platform pages first*
- Protocol supplemented by the IRB submission form
  - Some cross review with the IB / product information simultaneously.
- Consent form for participant perspective and plain speak version of study activities.



Consistency and accuracy are key!

How the IRB Reviews an Initial Submission:

- Take a look at the IRES record / submission summary
- Identify submission type/level of review, what the team is asking IRB to approve, **what changed (if applicable),** and whether all required documents are present.
- Form a "mental model" of the study
- Do a quick read to answer: *Can I clearly picture what participants will be asked to do?*

How the IRB Reviews an Initial Submission:

- Read the "source of truth" (Protocol)
- Confirm study design, objectives, population/eligibility, recruitment approach, procedures/visit schedule, endpoints, and data/privacy plan.
- Annotate with tracked changes/comments as needed.
- Read from the participant perspective (Consent/ICF)
  - Verify the ICF matches the protocol

How the IRB Reviews an Initial Submission:

- Review supporting materials
  - Recruitment materials (ads, scripts, screening language/tools): match the described recruitment process; don't overstate benefits; align with eligibility and procedures.
  - Study-related attachments (IBs, package inserts, questionnaires/assessments, data collection forms)

- Confirm readability and clear version control (dates/versions).

- Cross-document alignment check (final pass)
  - Reconcile key facts across IRES record + protocol + IRB submission form + consent + other attachments

Yale *Human Research Protection Program*

Tips for Efficient Review

Yale *Human Research Protection Program*

What to do (for efficient review)

- Add a brief protocol summary in IRES IRB.
- Keep one source of truth: avoid duplicating the same info in multiple sections/documents.
- Ensure alignment across all materials (protocol, application, consent, recruitment, instruments): aims, population, procedures, endpoints.
- Include a plain-language schedule that describes "what happens to a participant" (timing, duration, setting, and who does what).

What to do (for efficient review)

- Include **complete attachments** (final surveys/scripts/ads/forms; provider permission/registry language; references).

- If applicable, document plans for **vulnerable population** (justification, protections, assent/permission, capacity, language access, accommodations).

What to do (for efficient review)

- Do an internal cross-document quality control; make sure the PI reviews the final draft.
- Avoid copy-paste "amalgamation" drafts that create contradictions.
- Use **version control** (consistent dates/version numbers everywhere); once a protocol number is issued, add it to documents.

Yale *Human Research Protection Program*

Common Delay Drivers, Inconsistency Issues

Yale *Human Research Protection Program*

Common delay drivers / inconsistency issues

- Study described incompletely (IRB reviewers must tease out key info/risks).
  - Incorrect or incomplete risk information (e.g., mixing clinical vs research risks; missing drug/device details).

- Protocol, submission form, and consent don't match (procedures, risks, benefits, compensation/costs, injury/withdrawal language, data use/future use).

- Procedure details don't reconcile (e.g., blood draw totals don't add up).

Common delay drivers / inconsistency issues

- Monitoring/stopping rules missing when needed.
- Instruments referenced in protocol not uploaded in the record.
- Missing documents, wrong upload location, or unclear file names.
- On that note, don't embed consent forms or other documents inside the protocol.

Pain Points

- Essential information/documents are missing
- Information is presented in an inconsistent manner across documents
- Information is presented at a highly technical level
- Study team completed the wrong protocol template (e.g., exempt vs expedited)
- Forms are uploaded to the wrong location in IRES IRB
- Required documents/attachments missing.
- Revised documents uploaded incorrectly (should be **new versions layered onto** previously approved files, not standalone/misfiled).
- Typos and avoidable errors (proofread).

Resources

- HRPP Policy and Procedure Manual
- HRPP Investigator Manual
- IRES IRB
- IRES IRB Library (all templates here)

- IRB Questions: hrpp@yale.edu

New Protocol Templates

- The HRPP and IRB are currently updating the protocol templates available in the IRES IRB library.
- Our goal is to simplify the templates (including the instructions) to promote high-quality, complete submissions that are more easily completed by the research community and reviewed by IRB staff and members.

Questions?

Questions? Contact HRPP@yale.edu
Yale HRPP Website

Yale *Human Research Protection Program*