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The OHSRP Education Series: When IRB Approval Is Necessary and How to Complete the New *Investigator Attestation* for Tech Transfer Agreements

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The Protocol Navigation Training Program Seminar Series

March 18, 2019 12:30 – 2 p.m.

Outline

- Human Research Subject Protections Terminology
- Pathways for Review of Research at NIH
  - Decision Tree for Human Subjects Research Requiring IRB Approval or an *Exemption*
  - Review of Secondary Human Subjects Research
  - Review of *Exempt Human Subjects Research*
  - Change in Requirement for Review and Approval of “Not Human Subjects Research”
  - Submitting for Review and Determination of “NHSR” or an *Exemption*
- The *Investigator Attestation*
  - What is the *Investigator Attestation*?
  - The Three Scenarios
  - Investigator Responsibilities
  - Completing the *Attestation*
  - Determining When Sharing Biopecimens or Data from IRB-Approved Protocols is Allowed
  - When an Amendment to the Consent Form or Waiver of Consent is Required….

Human Research Subject Protections Terminology

- **The Common Rule**: refers to 45 CFR (Code of Federal Regulations) 46, Subpart A, the Basic HHS Policy for the Protection of Human Research Subjects.
  - It was published in 1991.
  - Applies to all research involving human subjects that is conducted or supported (e.g. funded) by DHHS (e.g. NIH)
  - Fifteen other federal agencies have included Subpart A in their chapter of the Code of Federal Regulations and adhere to it for the research they conduct or support

- **The Revised Common Rule (rCR):** a revised version of Subpart A, also referred to as the "2018 requirements" and "the Final Rule",
  - Had an effective compliance date of January 21, 2019 for all new research reviewed on and after that date

Terminology, cont.

- **FWA:** a Federalwide Assurance, an assurance of compliance that the institution will commit to follow the regulations for the protection of human subjects at 45 CFR 46.
  - When an institution is conducting DHHS-funded (e.g. from NIH) *human subjects research*, it is required to have an FWA.
  - As part of the FWA, the institution must designate the IRB(s) which will review its *human subjects research*.
- IRB review is typically conducted at the site that is conducting the *human subjects research*, unless the site contracts with a commercial IRB or executes a reliance agreement to rely on another IRB for oversight of its activities.

Terminology, cont.

- **Human Subject**: a living individual about whom an investigator (whether professional or student) conducting research:
  - (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  - (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. (45 CFR 46.102(e)(1))

This definition changed as part of the revised Common Rule (rCR).

- **Research**: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(l))

Terminology, cont.

- ***Human Subjects Research:*** Activities in which an individual, for research purposes:

1. Obtains information or biospecimens through intervention or interaction with an individual;

Or

2. Obtains, uses, studies, analyzes, or generates identifiable private information [data] or identifiable biospecimens.
   - This includes the use of coded and linked data or biospecimens (with access to the code key).

Terminology, cont.

- ***Exempt Human Subjects Research*:** Research activities that meet the definition of *human subjects research* but is excepted from needing to follow all of the requirements of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR part 46.
  - This is *human subjects research* which is considered so low risk by the regulators that it does not have to be reviewed by the IRB.

- **"Not Human Subjects Research" (NHSR):** Activities in which an individual, for research purposes:
  - Obtains, uses, studies, or analyzes de-identified biospecimens or data (with no access to a code key)

Pathways for Review of Research at NIH

Is the NIH Researcher Conducting Human Subjects Research Requiring IRB Approval or an Exemption?

An individual is considered to be conducting human subjects research *when for research purposes*, he or she, e.g.:

- Obtains consent from subjects;
- Interacts or intervenes with subjects; or
- Conducts activities with identifiable data or specimens. *Note: Coded data or specimens are considered identifiable, if the investigator or any member of the research team has access to the code key.*

YES

Activity is research involving human subjects; Submit a protocol to the IRB for review or consideration for an IRB exemption

NO

Activity is NOT research involving human subjects; No submission for human subjects protections review is required; Other NIH policies may apply

Review of Secondary Human Subjects Research

- When an investigator is conducting secondary research with coded and linked biospecimens or data and will generate results that he or she can link back to the identifiers of his or her research subjects, **this is considered human subjects research requiring prospective IRB review and approval**.

- The same is true of collaborations with external researchers in which the NIH investigator shares coded and linked biospecimens or data and receives coded and linked results back (when he or she has access to the code key).

Review of *Exempt Human Subjects Research*

- Per NIH policy, investigators must submit a request for consideration for an exemption and receive a determination before commencing any research activities.
- The revised Common Rule (rCR) contains some new exemption categories as well as some new criteria under the existing categories.
- Presentation focused on the exemption categories will take place on June 13 from 1 – 2 p.m. in the Lipsett Amphitheater
- There are now eight categories of *exempt human subject research*
  - Only 6 of these are currently allowable for research being conducted by NIH staff
  - Only about 3 of these will likely be relevant to NIH research on a regular basis

Highlights about *Exemption* Categories

- Most common exemption category at the NIH: Exemption Category 2
  - Research involving educational tests, surveys, interviews or observation of public behavior
  - Some restrictions in the use of this category with research with children

- New category: Exemption Category 3
  - Research involving "**benign behavioral interventions"**
  - Data collection must be limited to verbal or written responses, including data entry or audiovisual recordings
  - Restricted to research with adults

- Exemption Category 4: Secondary research of identifiable data or biospecimens when data is recorded by the investigator in a de-identified manner, i.e. no identifiers are accessible to the researcher once the analysis begins
  - For example, a retrospective medical chart review in which the investigator records the necessary data in a data sheet for future analysis without any personal identifiers nor a code allowing linking back by the investigator.

Not Sure Whether Your Research is Human Subjects Research or Might Qualify for An *Exemption*

- For more information about human subjects research, “not human subjects research” and *exempt human subjects research*, review “Does Your Project Require Submission for a Determination of NHSR or IRB Exemption?” and related presentations which can be found here: https://irbo.nih.gov/confluence/display/IRBO/Templates+Forms+and+Guidelines#TemplatesFormsandGuidelines-Guidance

- For information about whether your project might qualify for an exemption, contact julie.eiserman@nih.gov to request a consult

Change in Requirement for Review and Approval of “Not Human Subjects Research”

- Historically at NIH, investigators were required to submit for determinations of “not human subjects research” to OHSRP, prior to initiating any research activity, even if it was clear that the activity did not require IRB approval.

- **As of January 1, 2019, there is no longer a requirement for investigators to submit for a determination when they are conducting research activities with only de-identified data or biospecimens and have no access to identifiers or the code key.**

- One is still able to submit for and receive a determination for “Not Human Subjects Research” if desired.

Submitting for Review and Determination of "NHSR" or an *Exemption*

- As of January 21, 2019, all requests for determinations of "Not Human Subjects Research"(NHSR) or Exemptions must be submitted through the electronic IRB submission system, iRIS (https://irb.nih.gov/).

- Instructions for submitting for a determination of "NHSR" or an Exemption in iRIS are now available under *Guidance on Exemptions and "Not Human Subjects Research (NHSR)"* here: https://irbo.nih.gov/confluence/display/IRBO/NIH+iRIS (see instructions sheets)

- If you need training on how to submit for a determination of "NHSR" or an Exemption in iRIS, please contact the iRIS team: iris_training@od.nih.gov

Submitting for an *Exemption*, cont.

- Requests for exemptions now require submission of either a protocol for *Prospective Data Collection* or a protocol for *Secondary Research with Biospecimens or Data*

  - Templates for these two types of protocols are available here: https://irbo.nih.gov/confluence/display/IRBO/Templates+Forms+and+Guidelines#TemplatesFormsandGuidelines-Templates

The Investigator Attestation

What is the *Investigator Attestation*?

- The *Investigator Attestation* was created to provide documentation to the Tech Transfer Office that it is permissible for the NIH investigator to share or receive human biospecimens or data for research purposes under a **Material Transfer Agreement (MTA)**, **Data Transfer Agreement (DTA), Data Use Agreement (DUA)**, or **Research Collaboration Agreements (RCA).**
- Applies to new and modified agreements that are executed by NIH Tech Transfer Offices beginning **February 6, 2019**

What is the *Investigator Attestation*?, cont.

- A copy of the fillable *Investigator Attestation* is available here: https://irbo.nih.gov/confluence/display/IRBO/Templates+Forms+and+Guidelines#TemplatesFormsandGuidelines-Forms
  - Use the version dated 3-19-19 which includes instructions

- The lead investigator who will be sharing or receiving the biospecimens or data must complete the *Attestation,* sign and date it and provide it to their Tech Transfer contact.

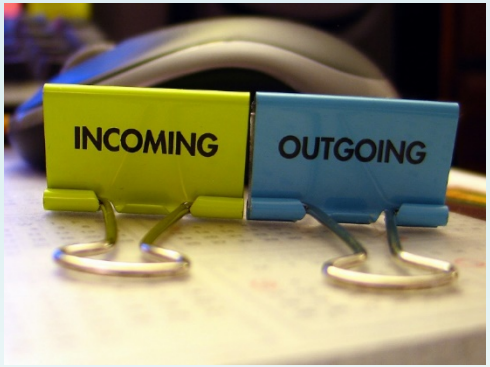
The Three Scenarios

The *Attestation* includes **three** possible scenarios related to the transfer of biospecimens or data:

1. Outgoing Human Biospecimens and/or Human Data Collected as Part of an IRB-approved Protocol Involving NIH Investigators (who will be doing the sharing)
   - This includes an IRB-approved protocol, in which an NIH staff person was listed as an investigator, but the reviewing IRB is external to the NIH.
   - This includes protocols that are still currently open or **closed** with an IRB.

The Three Scenarios, cont.

2. Outgoing Human Biospecimens and/or Human Data from All **Other** Sources
   - Applies to scenarios in which the materials were not collected nor ever maintained under an IRB-approved protocol involving the NIH investigators **who will be doing the sharing**
     - Biospecimens, originally collected at NIH for purely clinical purposes and not used as part of a research protocol, e.g. blood samples collected for testing in Laboratory Medicine because a research subject became ill
     - Biospecimens or data which were previously transferred to this research team from another NIH IC or an external institution



The Three Scenarios, cont.

3. Incoming Human Biospecimens and/or Human Data (to be received by NIH investigators)
    - Some examples include:
        - Biospecimens or data collected under an IRB-approved research protocol outside of the receiving NIH IC
        - Biospecimens or data originally collected for clinical purposes outside of the receiving NIH IC
        - Biospecimens or data originally collected for other purposes outside of the receiving NIH IC

Investigator Responsibilities

- Review the entire *Attestation*
- Determine which scenario matches the planned transfer of materials (one of three); place checkmarks in the appropriate boxes; and sign
  - Only complete the form, if you can attest to the veracity of the statements exactly as written and check all the required boxes under a given section
- For additional guidance about interpreting consent form language and making determinations about the ability to share specimens or data, please review slides 30-33.
- When able to attest to the veracity of the statements, no further IRB review nor IRB signature is required.
- After signing the form as the investigator, email the form to your Tech Transfer contact.

Investigator Responsibilities, cont.

- When unable to attest to the veracity of the statements or unsure if sharing is allowed per the consent form(s) and the materials are being shared from NIH IRB-approved protocols, contact the reviewing NIH IRB Chair or office (via telephone or email) to discuss the circumstances.
  - Be sure to provide copies of all versions of the consent form for review (highlight any language about sharing of specimens or data for research).

- If the IRB Chair or representative decides that sharing is permissible, he or she should sign the *Attestation* (rather than the PI).
  - After obtaining a signature from the IRB Chair or representative, email it to your Tech Transfer contact.

- If the IRB Chair or representative, determines sharing is not permissible in the specific circumstances, the specimens or data cannot be shared.

Investigator Responsibilities, cont.

- In cases that the planned sharing or research would require new IRB approval (i.e. new human subjects research is being conducted using the specimens or data), amend the protocol and/or consent form (or submit a new protocol or consent form to the IRB).
  - For more information, review “Best Practices for the Approval and Conduct of Secondary Research, including Repositories” under https://irbo.nih.gov/confluence/display/IRBO/Training+and+Education#TrainingandEducation-EducationalSeminars

- For general questions about how to complete the form or about sharing or receiving of de-identified materials from sources other than NIH IRB-approved protocols, contact Julie Eiserman (julie.eiserman@nih.gov)

Completing the *Attestation*

For Outgoing Human Biospecimens and/or Human Data Collected as Part of an IRB Approved Protocol Involving NIH Investigators

Check the following, if true (If you are unsure, consult with the IRB):

____ There is sharing language in the original consent form, **AND** that language is consistent with the proposed research and sharing plan.

Also check one of the following:

____ The human biospecimens and/or human data are linked to identifiers; **the NIH research team will receive research results that they can link to identifiers** as part of a research collaboration; and I have or will seek IRB review and approval prior to initiating the planned research.

____ **The NIH research team will not receive research results that they can link to identifiers** as part of a research collaboration.

Completing the *Attestation*, cont.

For Outgoing Human Biospecimens and/or Human Data from All Other Sources

Only check one of the following:

____ **No one at NIH has access to identifiers** linked to the human biospecimens and/or human data.

____ The human biospecimens and/or human data are linked to identifiers, but **the NIH research team will not receive research results that they can link to identifiers** as part of a research collaboration.

____ The human biospecimens and/or human data are linked to identifiers, **the NIH research team will receive research results that they can link to identifiers**, and I have or will seek IRB review and approval prior to initiating the planned research.

Completing the *Attestation*, cont.

For Incoming Human Biospecimens and/or Human Data

Only check one of the following:

____ The human biospecimens and/or human data that will be received **will not be identifiable to the NIH research team**.

____ The human biospecimens and/or human data **will be identifiable to the NIH research team**, and I have or will seek IRB review and approval prior to initiating the planned research.

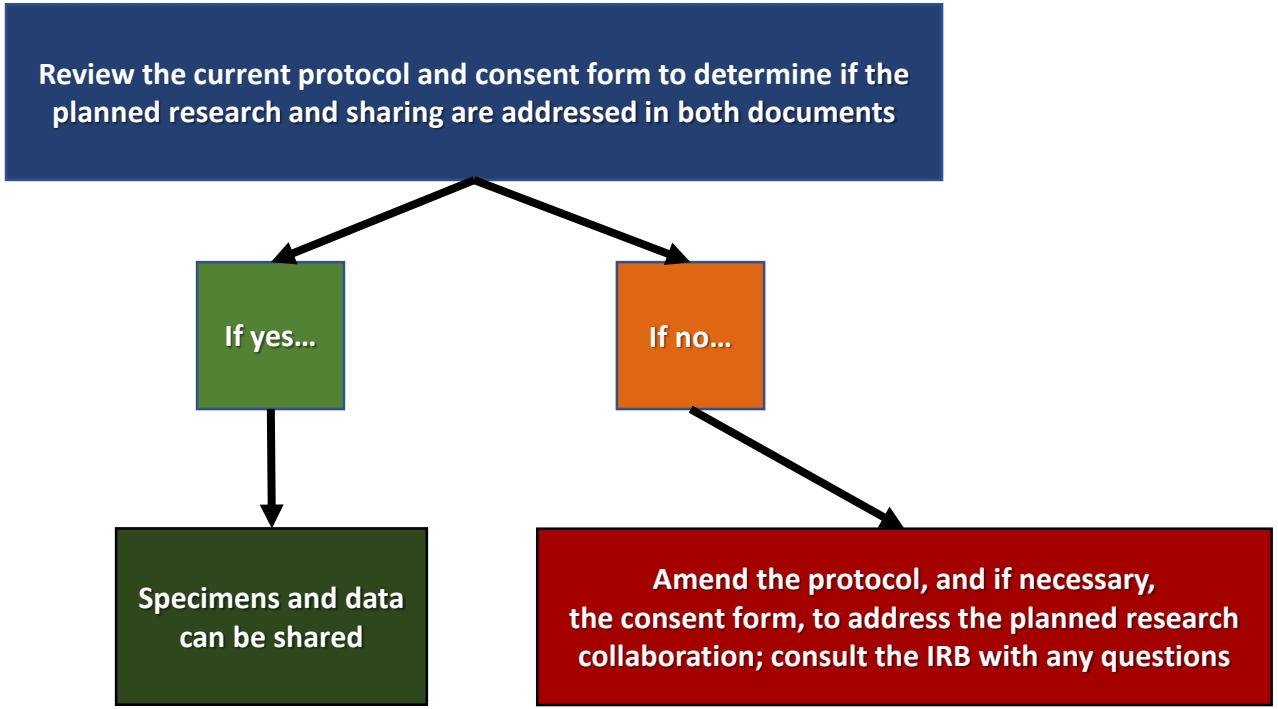
Completing the *Attestation*, cont.

- All applicable boxes under each scenario must be checked before Tech Transfer will accept the form
- There is one exception associated with outgoing materials from IRB-approved protocols
  - If the consent form is silent on the topic of sharing, the investigator will never be able to check this box below:

    ____ There is sharing language in the original consent form, **AND** that language is consistent with the proposed research and sharing plan.
- After review, the IRB *may* still allow sharing and sign the *Attestation* on behalf of the Investigator
- In this case, the check box associated with this condition should be left blank

Determining When Sharing Biospecimens or Data from IRB-Approved Protocols is Allowed

Can I Share Specimens or Data from My IRB-Approved Protocol for Primary Research*?



***Primary research:** research use of biospecimens or data for the original purpose(s) for which the biospecimens or data were initially collected through interaction or intervention with living individuals

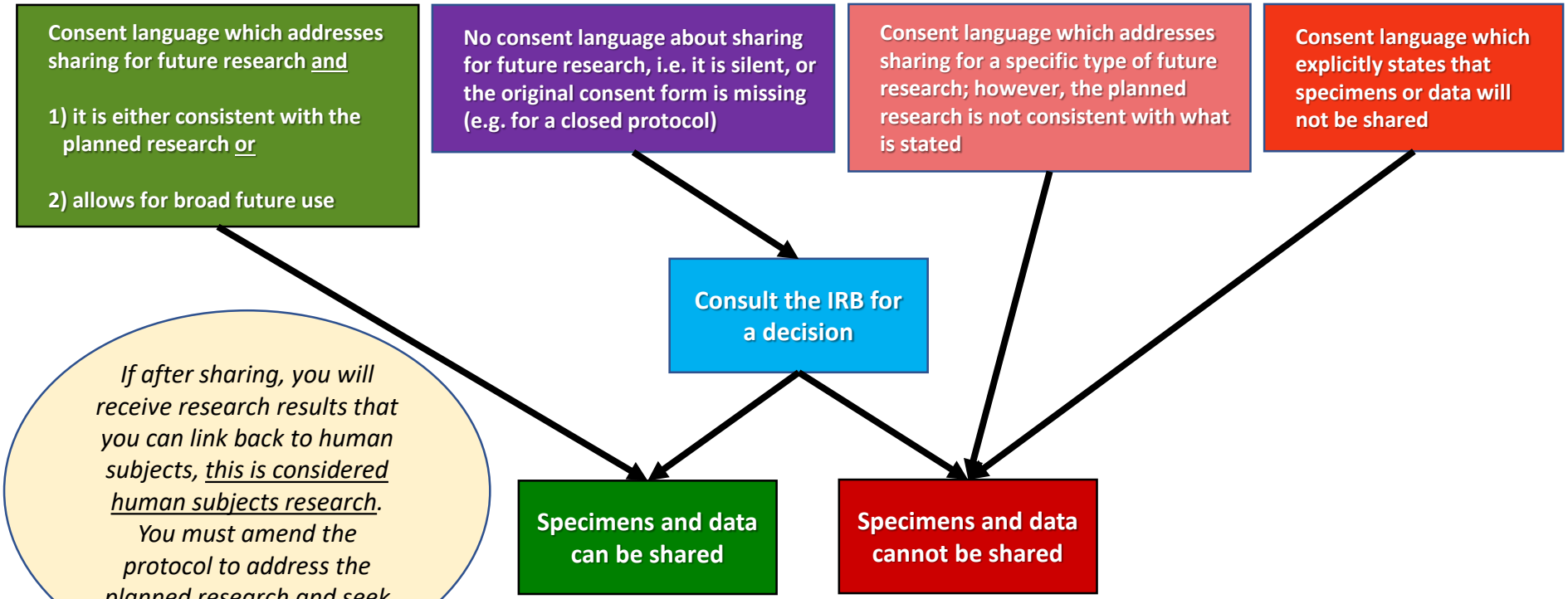
When an Amendment to the Consent Form or Waiver of Consent is Required….

- The investigator can check the appropriate boxes and sign the *Attestation, once* IRB approval of the revised consent form is obtained.

- **The IRB Chair** should sign the *Attestation,* once IRB approval for waiver of consent is obtained.
  - The Investigator should still check one of the two boxes which addresses the return of research results, prior to the IRB signing.
  - The box which addresses consent form language should be left blank.

Can I Share Specimens or Data from My IRB-Approved Protocol for Secondary Research*?

Review the consent form associated with the protocol to determine which scenario below is true. There is….



***Secondary research:** research use of biospecimens or data for other than the original purpose(s) for which the biospecimens or data were initially collected through interaction or intervention with living individuals

Other FAQs

- **Q. What do I do if there are multiple versions of the consent form?**
  - A. You should review the signed versions of the consent form to ensure that the subjects, whose materials you intend to share, signed versions that allow for sharing. If the protocol is closed and all of the signed consent forms are no longer accessible, the investigator should review the various versions of the consent form to ensure that all versions contained the sharing language.

- **Q. Does the *Investigator Attestation* apply to the execution of Clinical Trial Agreements (CTAs) or Cooperative Research and Development Agreements (CRADAs)?**
  - A. No.

Other FAQs, cont.

- **Q. Is the *Investigator Attestation* required for agreements that are being implemented between NIH ICs?**
  - A. If an MTA or one of the other applicable Tech Transfer agreements is involved, then yes.

- **Q. In this case above, how should the *Investigator Attestation* be completed?**
  - A. The sharing investigator should complete and sign one form and the receiving investigator should complete and sign another form.

- **Q. Is the *Investigator Attestation* required for NIH staff who work in Extramural?**
  - A. The requirement to complete an *Attestation* would apply to an extramural employee **who conducts research** as part of his or her role at NIH and is receiving or sharing biospecimens or data for research purposes through the use of one of the applicable Tech Transfer agreements.

Other FAQs, cont.

- **Q. Whose responsibility is it to collect and retain the *Investigator Attestation*?**
  - A. The NIH Tech Transfer Office must collect and retain the *Attestation* as part of the process of developing and executing the MTA or another applicable Tech Transfer agreement. Other offices, e.g. the IC CD's office, can request copies from that office if they wish.

Additional Guidance

- We will be uploading a document with Frequently Asked Questions (FAQs) soon to assist in use of the *Attestation* here*:* http://irbo.nih.gov/confluence/display/IRBO/Templates+and+Forms

Accessing this Presentation

- This presentation is being videocast and should be available for future viewing here: https://videocast.nih.gov/PastEvents.asp

- To request a pdf of this presentation or ask questions about its content:
  - Please email: julie.eiserman@nih.gov

Questions