Biosafety Protocol Management System Guide

Please Read This Notice

Research with biological materials, such as recombinant DNA and/or biological pathogens, is required to be approved through an Institutional Biosafety Committee (IBC). A biosafety protocol is generated by a Principal Investigator to describe such research to provide the IBC with information to:

1. **accurately assess risks associated with the research**
2. **recommend an appropriate biosafety level for conducting the research**
3. **approve the protocol to allow research to continue**

Please be aware that all grants must be congruent with the biosafety protocol. If there is proposed work in a grant that is not in the biosafety protocol (but is required to be), the grant will be held.

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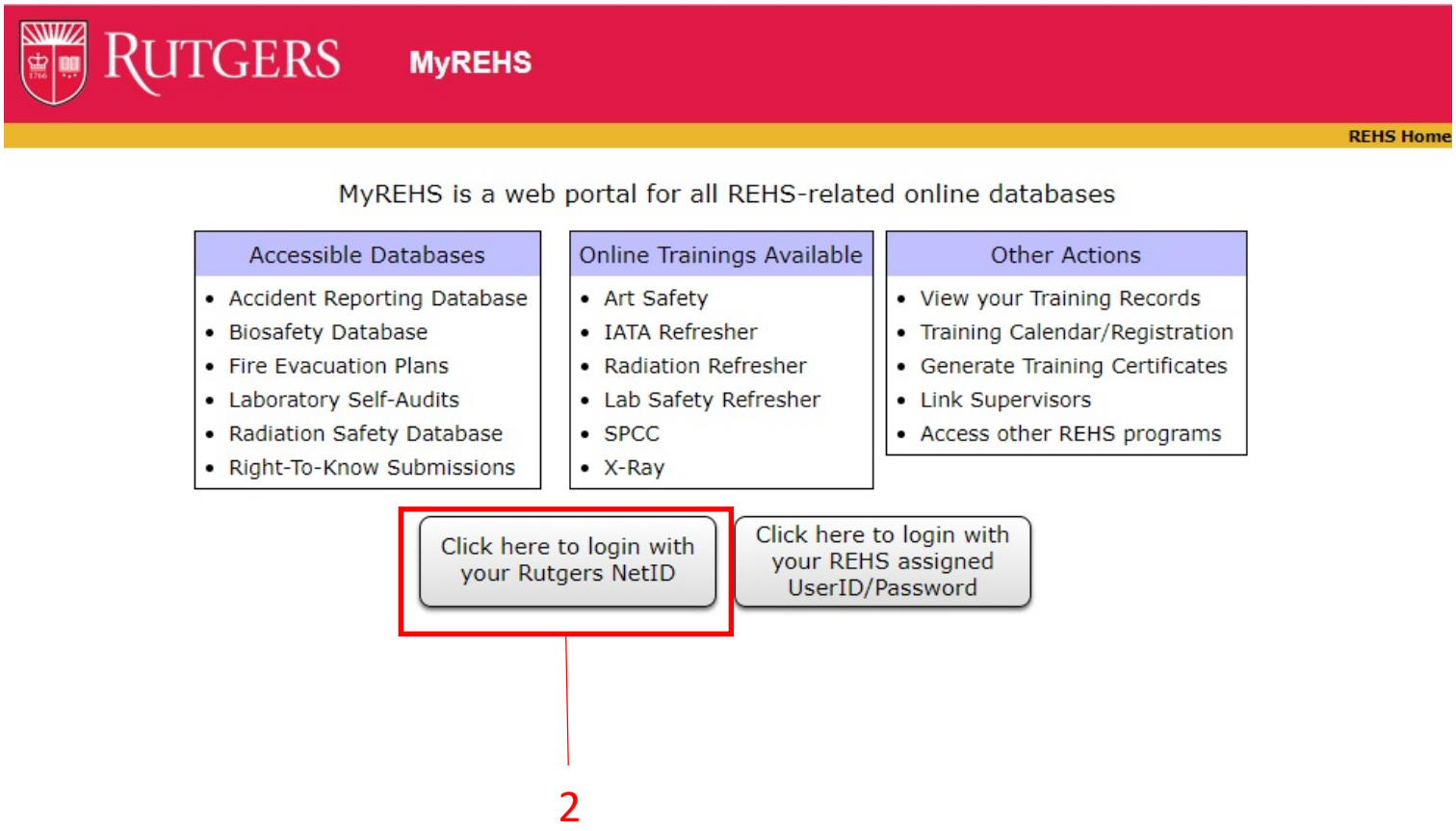
Create a New Protocol

1. To create a new registration:

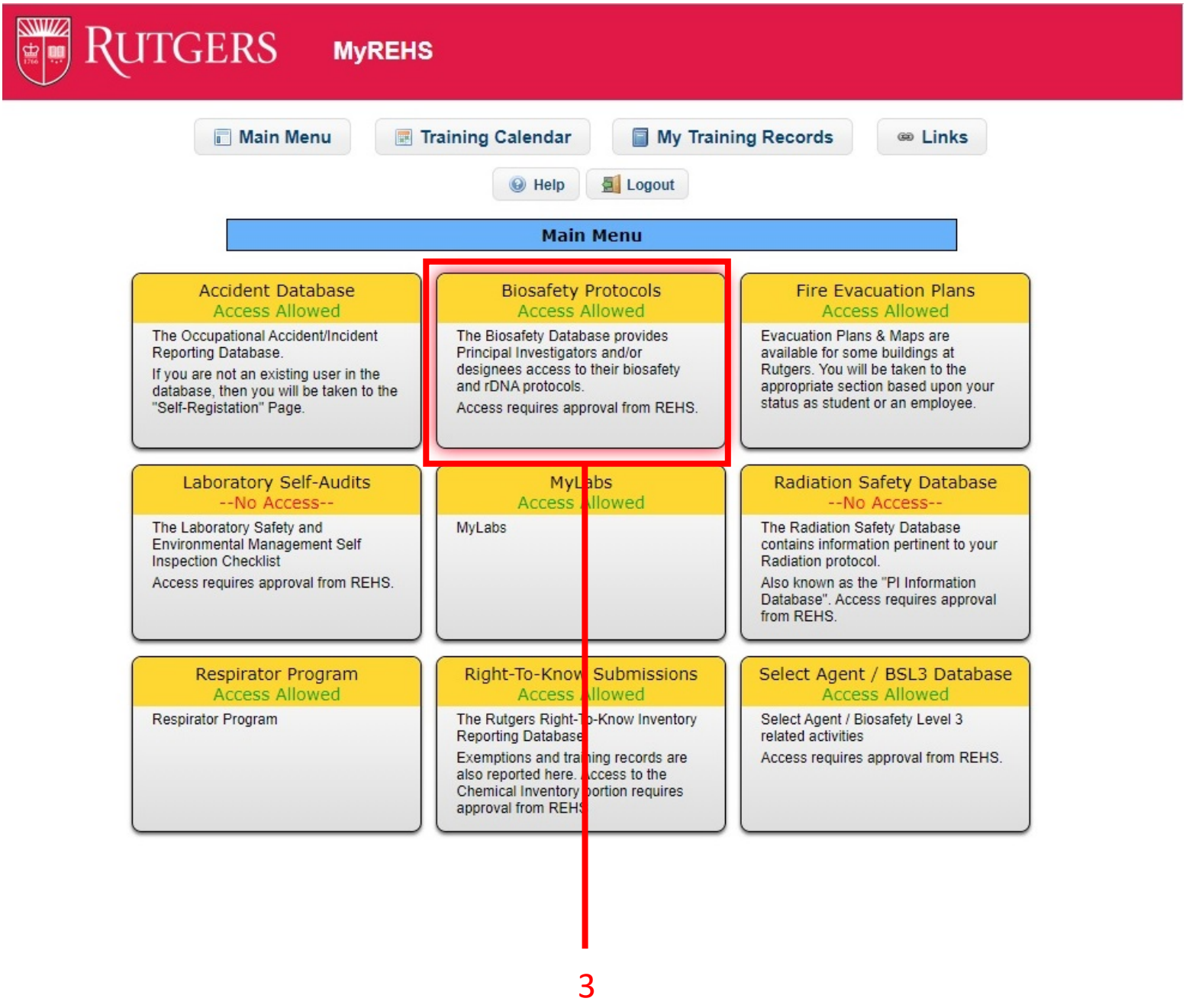
1. Go to https://myrehs.rutgers.edu/
2. Click on "**Click Here to login with your Rutgers NetID**". You will then need to login with your NetID and password



Create a New Protocol

1. To create a new registration:

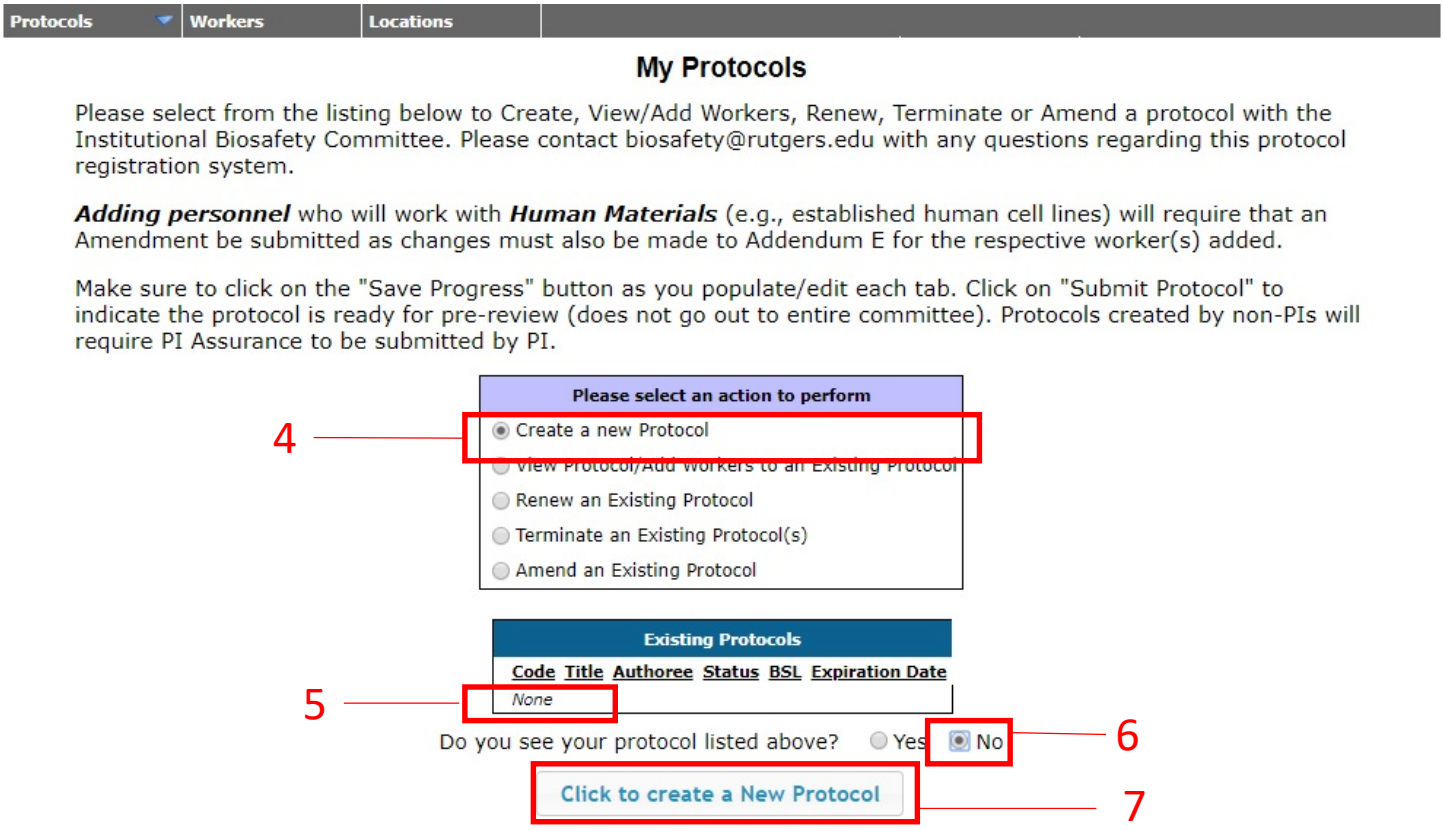
3. Once logged in, you will be able to click on **Biosafety Protocols** to access the BPMS



Create a New Protocol

1. To create a new registration:

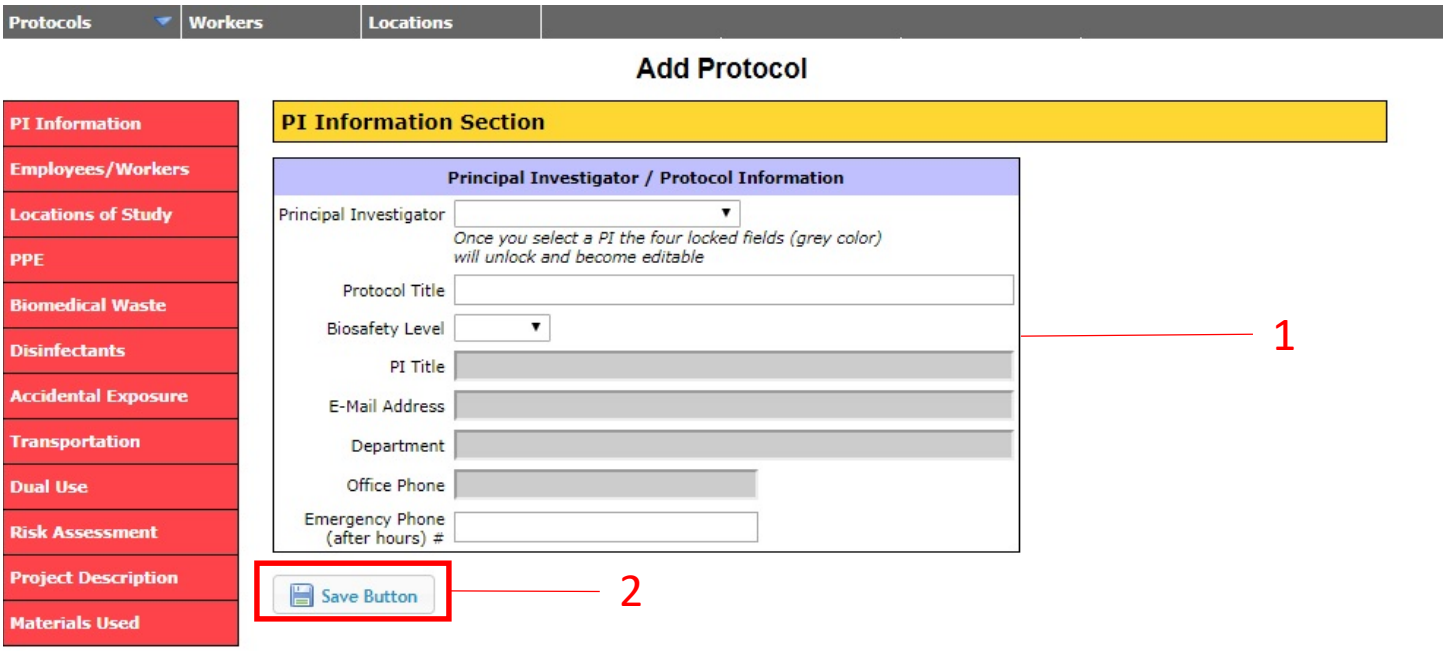
4. In “My Protocols”, click on “Create a new Protocol”
5. Verify that a similar protocol does not already exist in the “Existing Protocols” panel
6. Click “no” if there is no similar existing protocols
7. Click on “**Click to create a New Protocol**” button



Create a New Protocol

2. Initial PI Information:

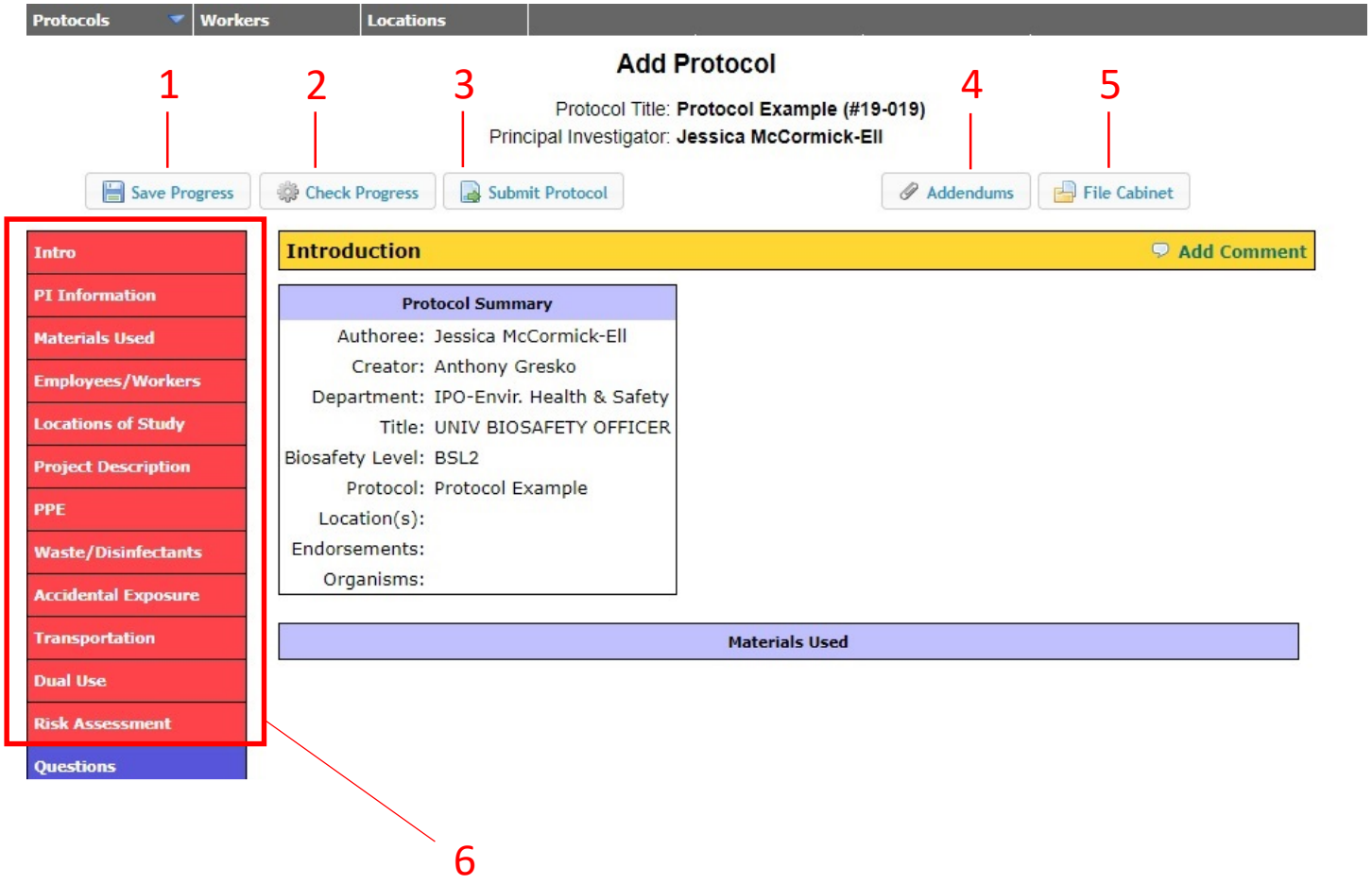
1. Fill out Principal Investigator Information
   - *i. Information should be up-to-date*
   - *ii. Biosafety Level is the projected biosafety level of the laboratory for this protocol*
2. Click “Save Button”



Create a New Protocol

3. Home Screen:

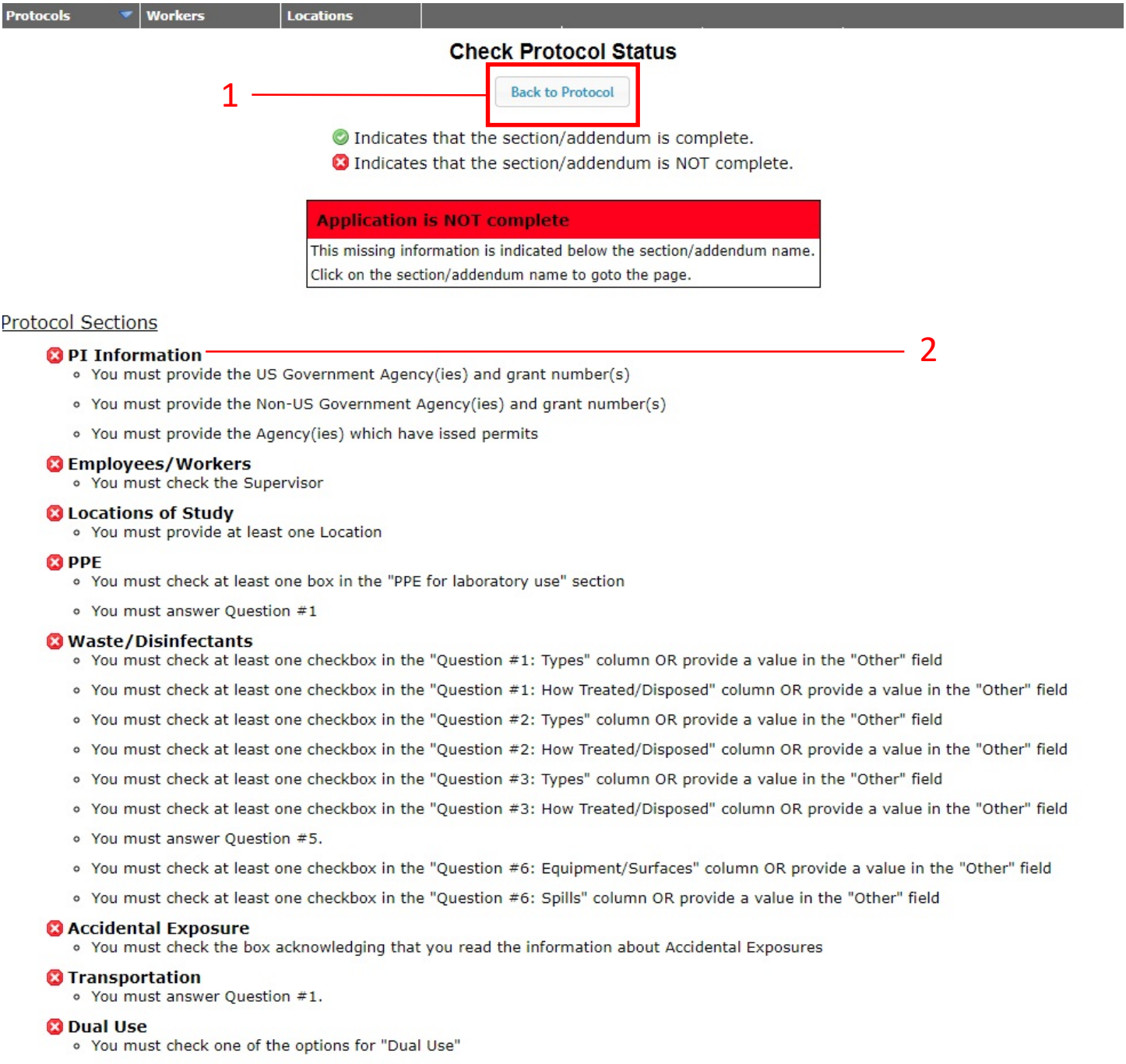
1. "Save Progress" button – *allows progress to be saved.* ***This should be clicked often to continually save your progress.***
2. "Check Progress" button – *provides indications of sections yet to be completed*
3. "Submit Protocol" button – *will submit protocol upon completion of ALL sections*
4. Addendums – *Additional sections of the protocol to describe materials used. Each addendum will be created only after you complete the "Materials Used" section of the Protocol*
5. File Cabinet – *allows uploads of additional documents (i.e. laboratory SOPs, plasmid/vector maps, permits, etc.)*
6. Protocol Sections – *must be completed (see next pages of this guide)*



Create a New Protocol

4. Check Protocol Status:
This section provides notifications of sections that are incomplete and must be completed prior to submission of protocol.

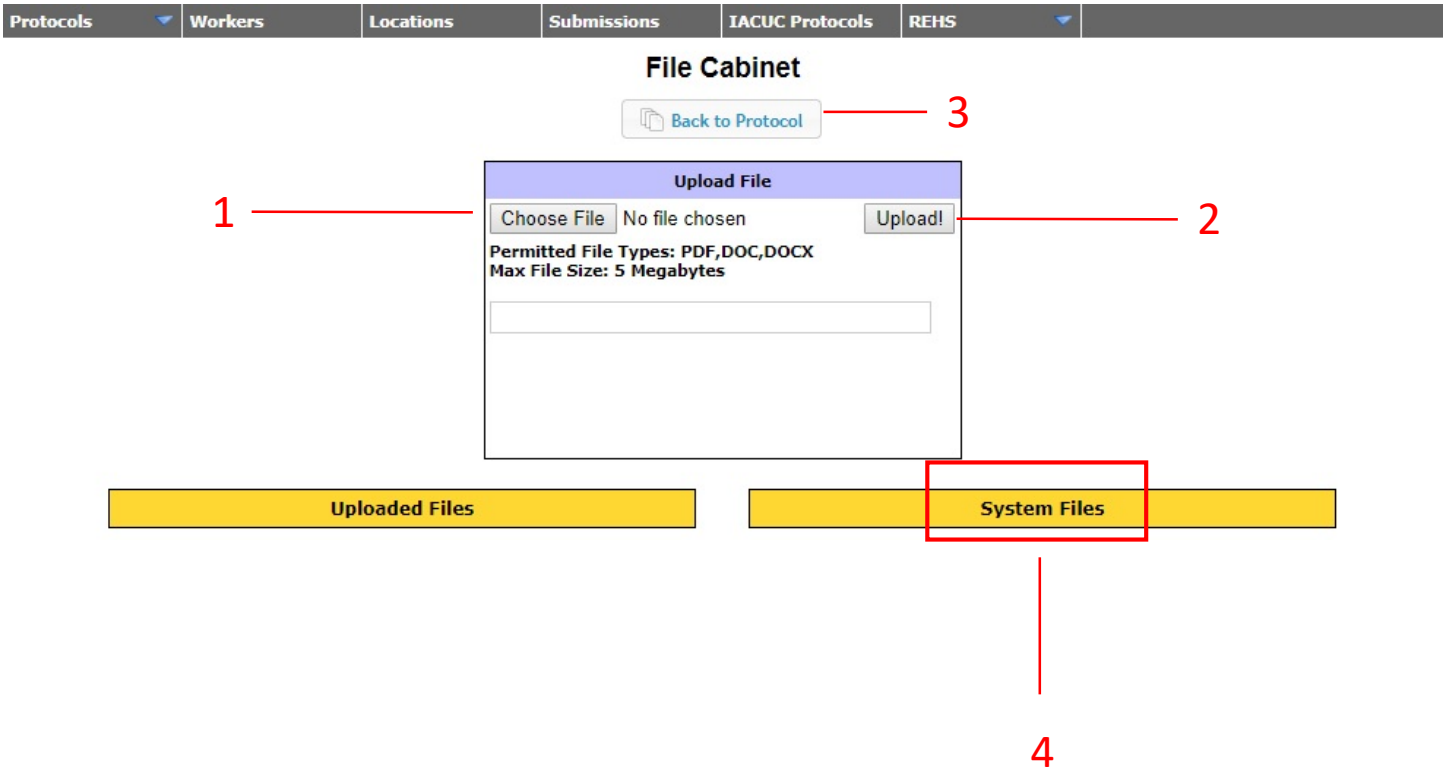
1. "**Back to Protocol**" – allows return to home page of protocol
2. Clicking on the Bold Section Header will bring you to that section to edit/view it



Create a New Protocol

5. File Cabinet:
This section allows uploads of additional documents (i.e. laboratory SOPs, plasmid/vector maps, permits, etc.)

1. Click "**Choose File**" to choose a file from computer
2. Once file displays next to "**Choose File**" button, click "**Upload!**" button
3. Click "Back to Protocol" to return to protocol
4. System files will show approval letters and PDFs once submitted/approved.

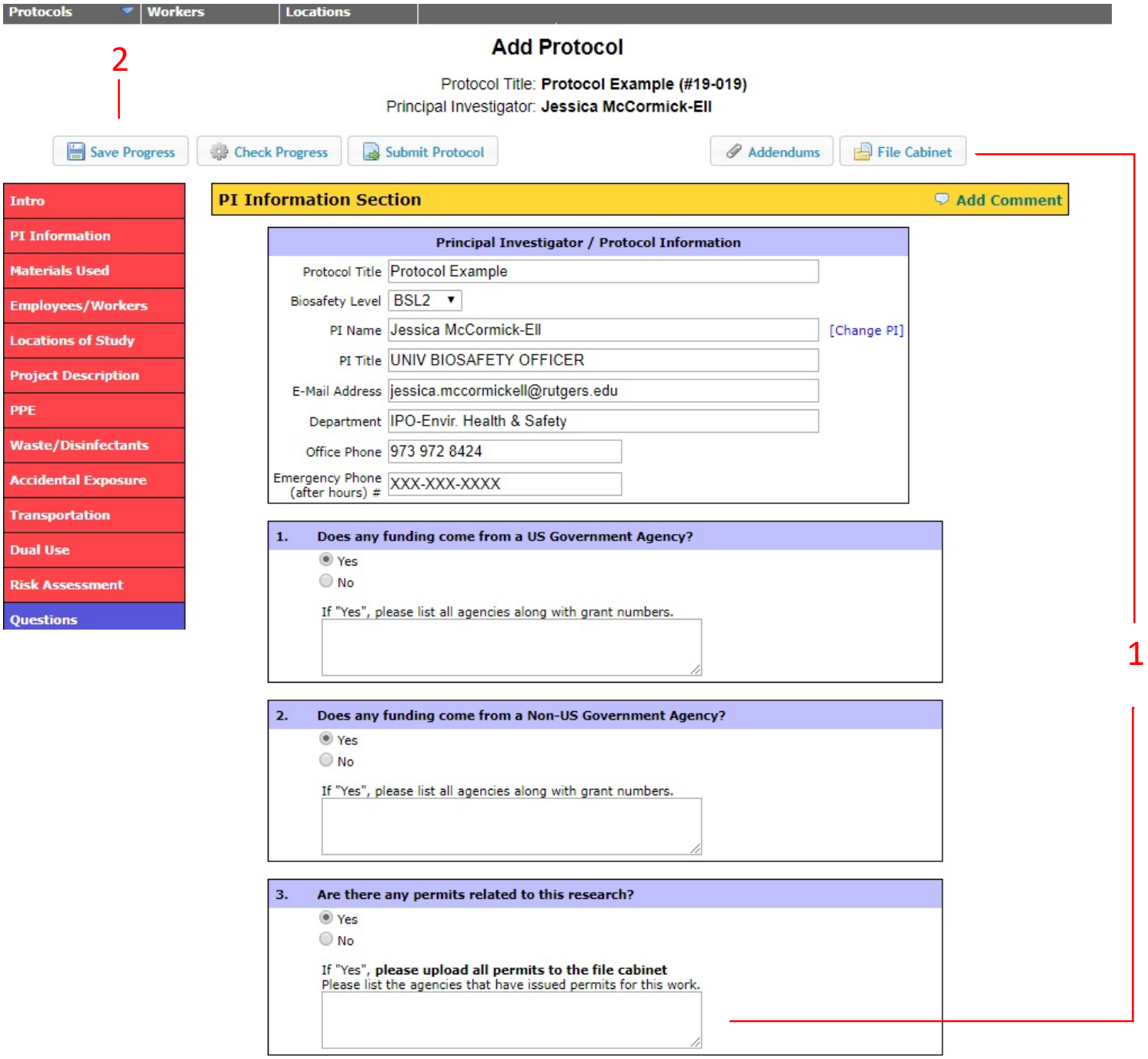


Create a New Protocol

6. PI Information Tab:

This section requires information surrounding funding sources and permits related to the research. Each question must be answered. If "yes" is answered, additional information is required to be input into the text box.

1. Question 3 requires PDF versions of permits to be uploaded to the File Cabinet tab.
2. Another reminder, it is good practice to click the "**Save Progress**" button as you complete each tab.

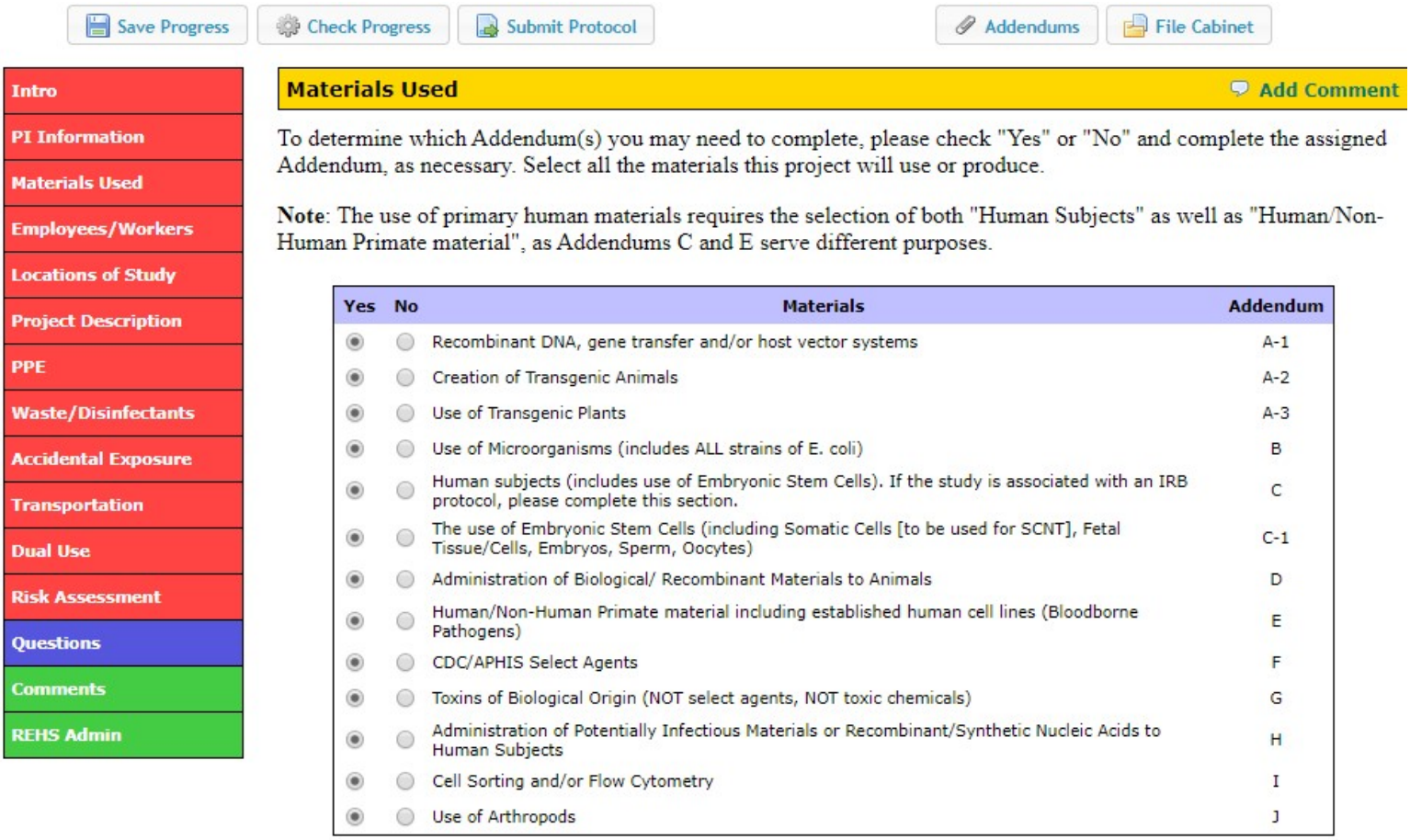


Create a New Protocol

7. Materials Used:

Each question must be answered with either “Yes” or “No”. Each time a “Yes” is checked, another Addendum tab (named A-1, A-2, A-3, B, C, etc.) is added in the Addendum section.

1. Once all questions in this section have been answered, Addendum tabs will be created in the Addendum section, which is described later in this guide.



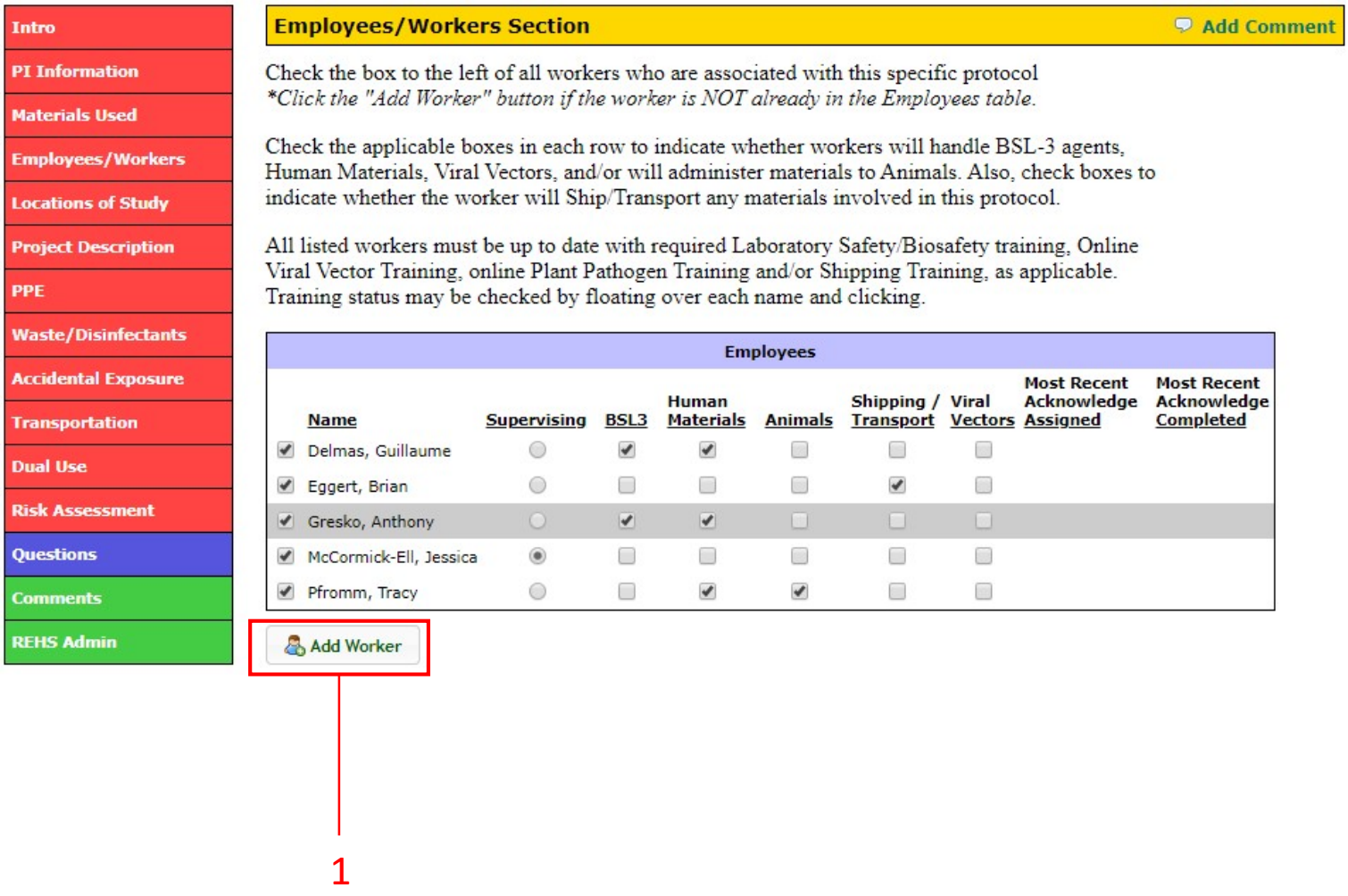
Create a New Protocol

8. Employees/Workers:

1. Follow the directions displayed to Add Workers to the protocol. Start by clicking the "**Add Worker**" button.

** Adding new workers to an existing protocol can be done at this page and does NOT need to be submitted in an amendment.

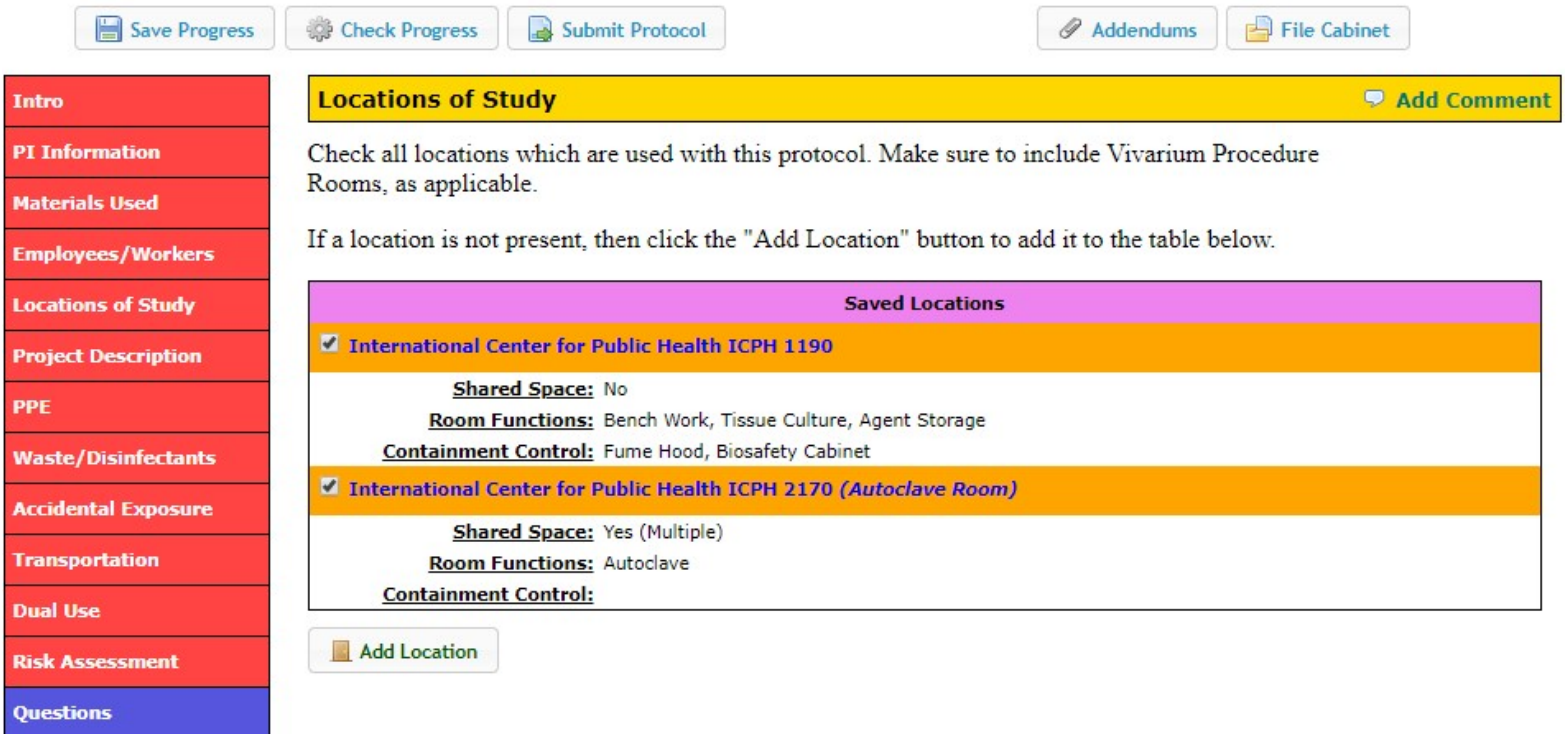
- You must mark what role the worker has in the laboratory. Working with human cell lines (established cell lines) is working with Human materials
- Shipping/Transport should only be marked if someone is transporting materials on a road or by air (not hand carrying)



Create a New Protocol

9. Locations of Study:

Add each room that workers will be utilizing for any work involved in this protocol, **including autoclave rooms**. Describe the function and containment controls utilized in each room.

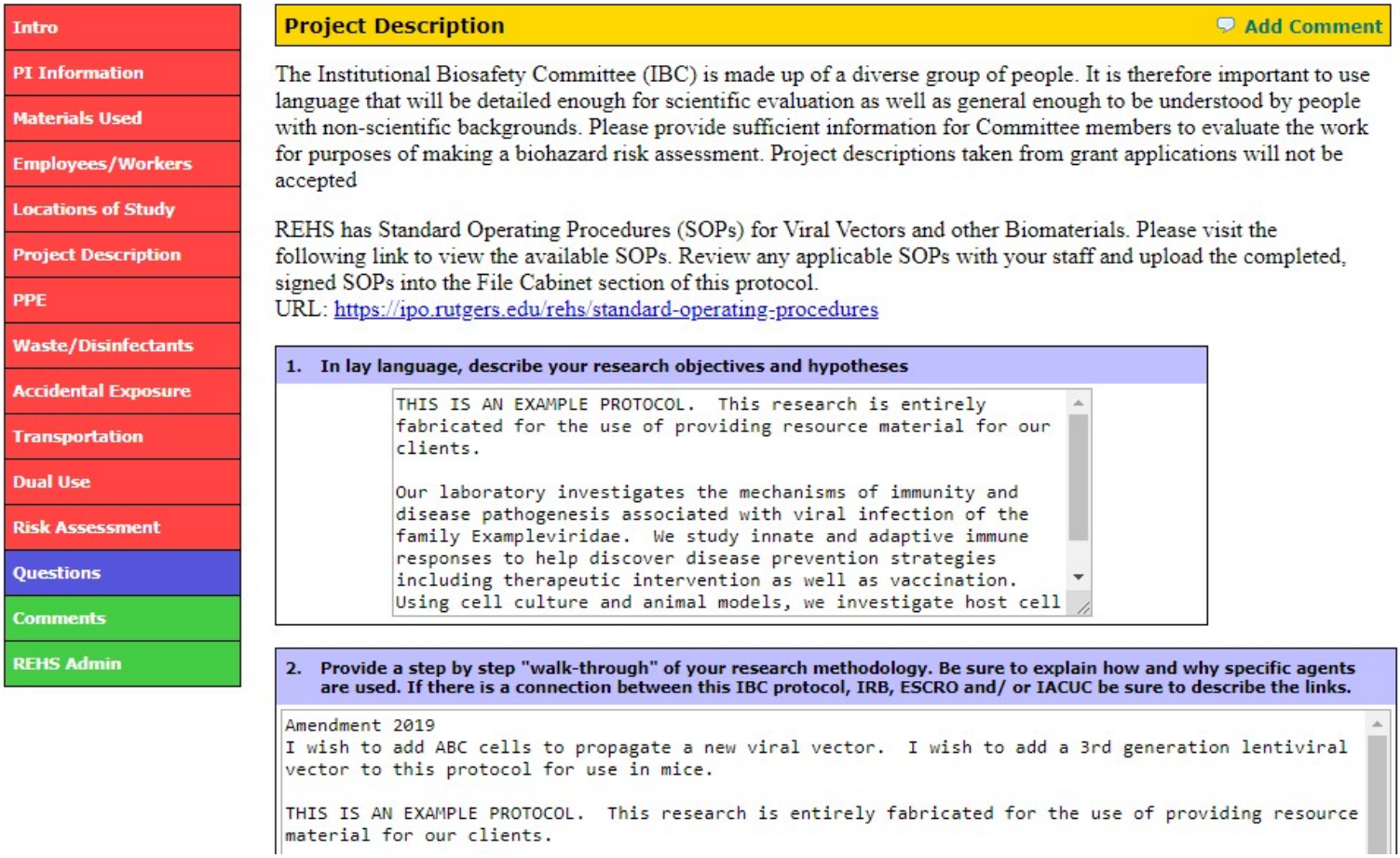


Create a New Protocol

10. Project Description:

1. Please describe your research in terms that a lay person can understand. Do NOT copy and paste from a grant what the specific aims are.
2. This question asks to describe experiments that you will be performing and why specific biological material is needed for those experiments. For each experiment, describe what precautions will be used to minimize risk (engineering controls, work practices, etc.). This is NOT a recreation of your grant but instead is a section to describe how you will perform each of your experiments safely. Please include work with animals, human subjects, and analysis of infected tissues.

SEE NEXT PAGE FOR VERY HELPFUL HINTS



Creating a New Protocol

10. Project Description

HELPFUL HINT 1: This section is NOT a copy/paste from the specific aims section of a grant. If the grant is selling how impactful the research will be, the project description is selling how safe the research will be.

- **Grant Example**: “Performing our vaccine challenge into mice will determine the efficacy of the vaccine in inducing both cellular and humoral immunity against infection which will determine possibility of a platform to prevent human disease”
- **Project Description Example**: “Performing our vaccine challenge into mice will be done inside a Class II biosafety cabinet to protect against potential aerosols. Injection will be performed with safe sharps to reduce the chance of needle stick exposure.

This is going to a Biosafety Officer and IBC reviewer, not a funding committee. They are not checking for the validity and/or reasoning for doing your science, but instead are reviewing for the safety of your science.

HELPFUL HINT 2: The **Project Description** section should describe how each experiment is done TO A CERTAIN EXTENT. This means that each experiment should be described as to what they are doing and how, but specific SOPs are not to be written here. Example below.

Good: Cells will be transfected with RNAi molecules against XYZ gene and are then infected with example virus in a biosafety cabinet. Cell monolayer is harvested for total nucleic acid or protein purification to determine gene expression using SOP 1(uploaded to file cabinet)

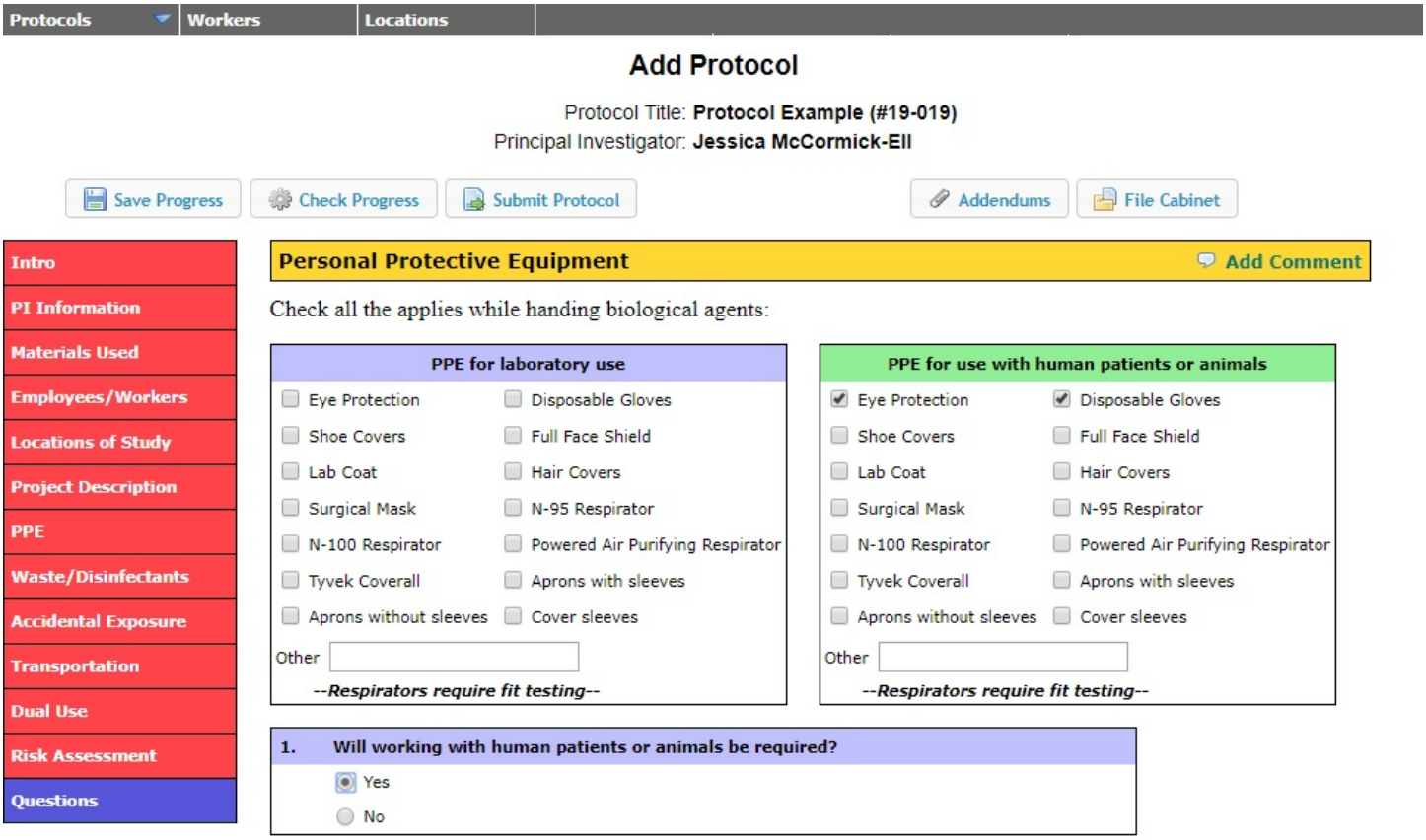
Bad: 1. Open flask. 2. Remove media. 3. Wash with PBS. 4. Transfect cells with 50 nanograms/1 million cells of siRNA targeting XYZ gene. (And continuing like this)

The bad example above is in SOP format. SOPs can be mentioned but should not be written out in the **Project Description**. They should be uploaded into the **File Cabinet**, which is a section to store all external files (SOPs, plasmid maps, permits, publications showing data).

Create a New Protocol

11. PPE:

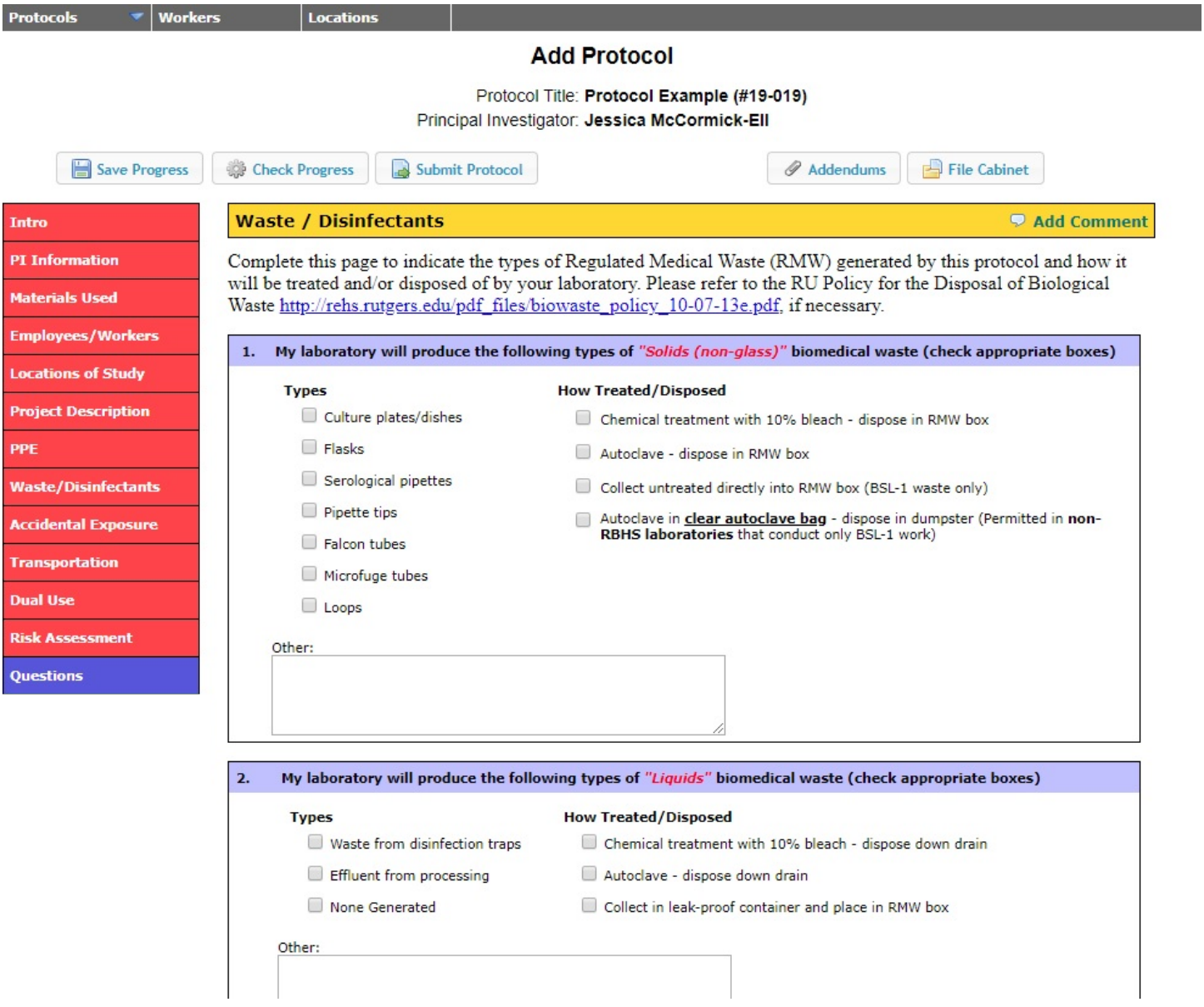
Check all boxes that would apply to PPE that would be required to work with the biological hazards in your laboratory.



Create a New Protocol

12. Waste/Disinfectants:

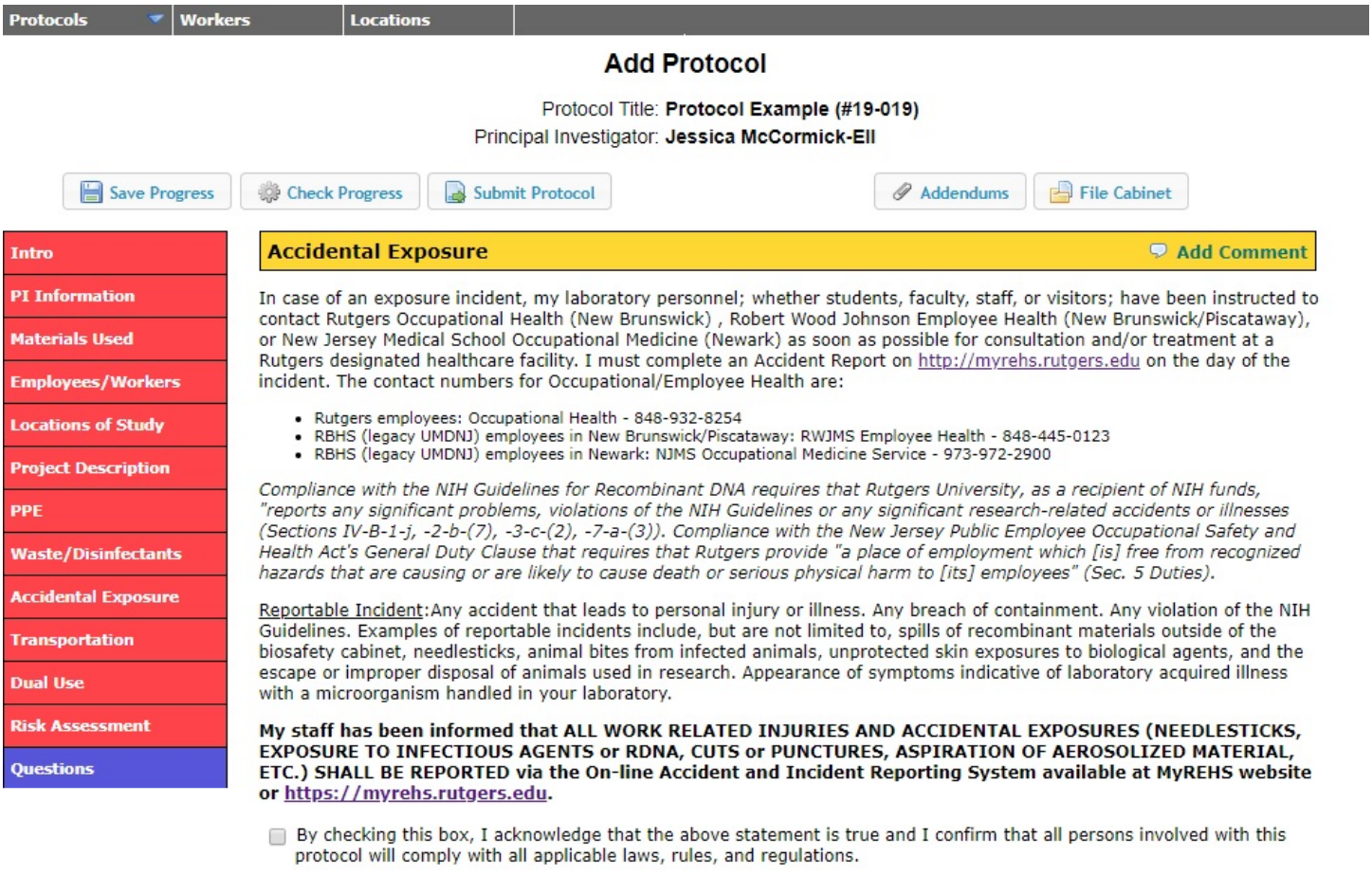
Describe how all types of waste will be treated. If you need more information, please refer to the RU bioguide for more information (see link below).
https://ipo.rutgers.edu/sites/default/files/RU%20Biosafety%20Guide.pdf
- 70% ethanol is never acceptable as a primary disinfectant



Create a New Protocol

13. Accidental Exposure:

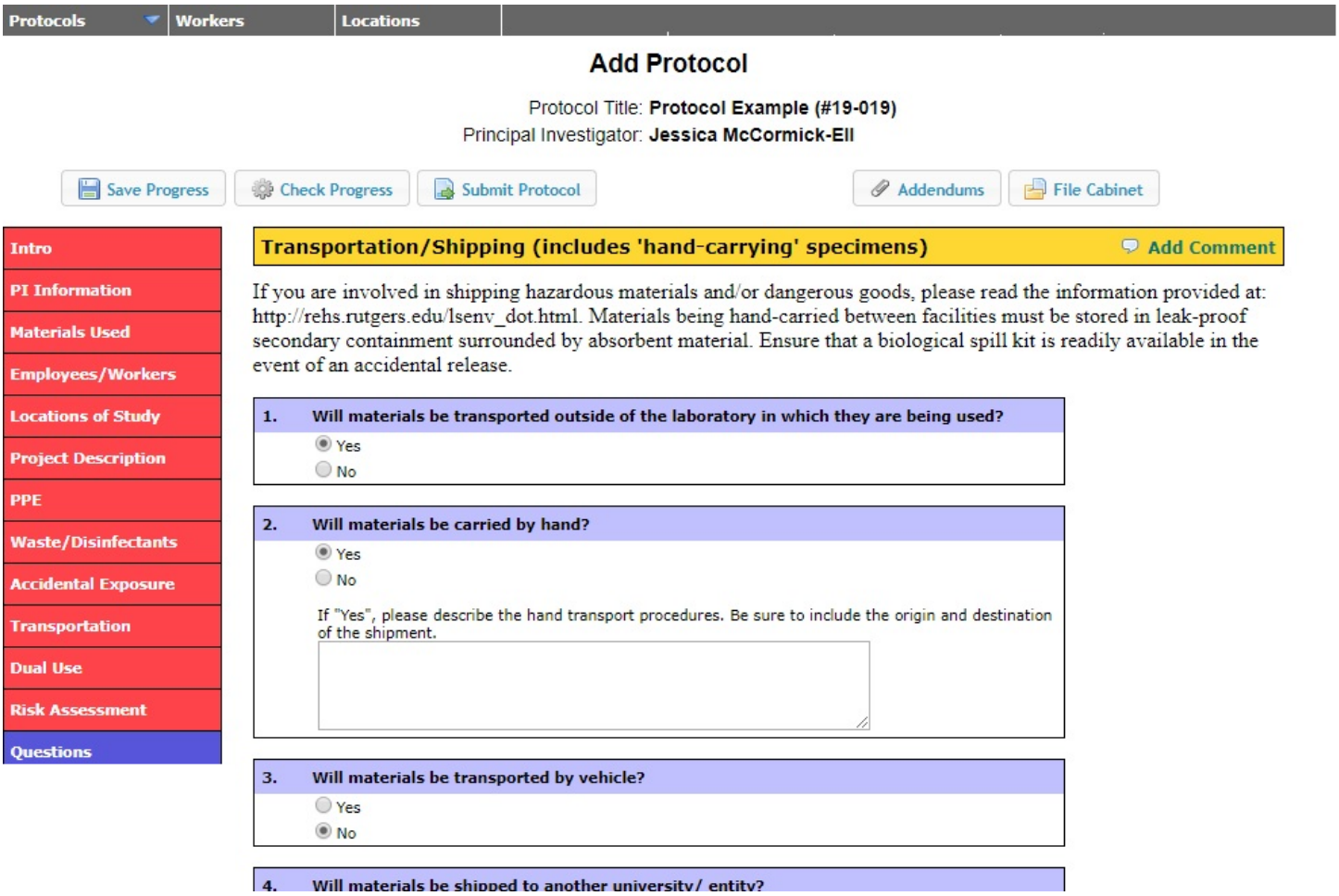
Read and acknowledge this disclaimer.



Create a New Protocol

14. Transportation:

Describe how you will be transporting biological material. .

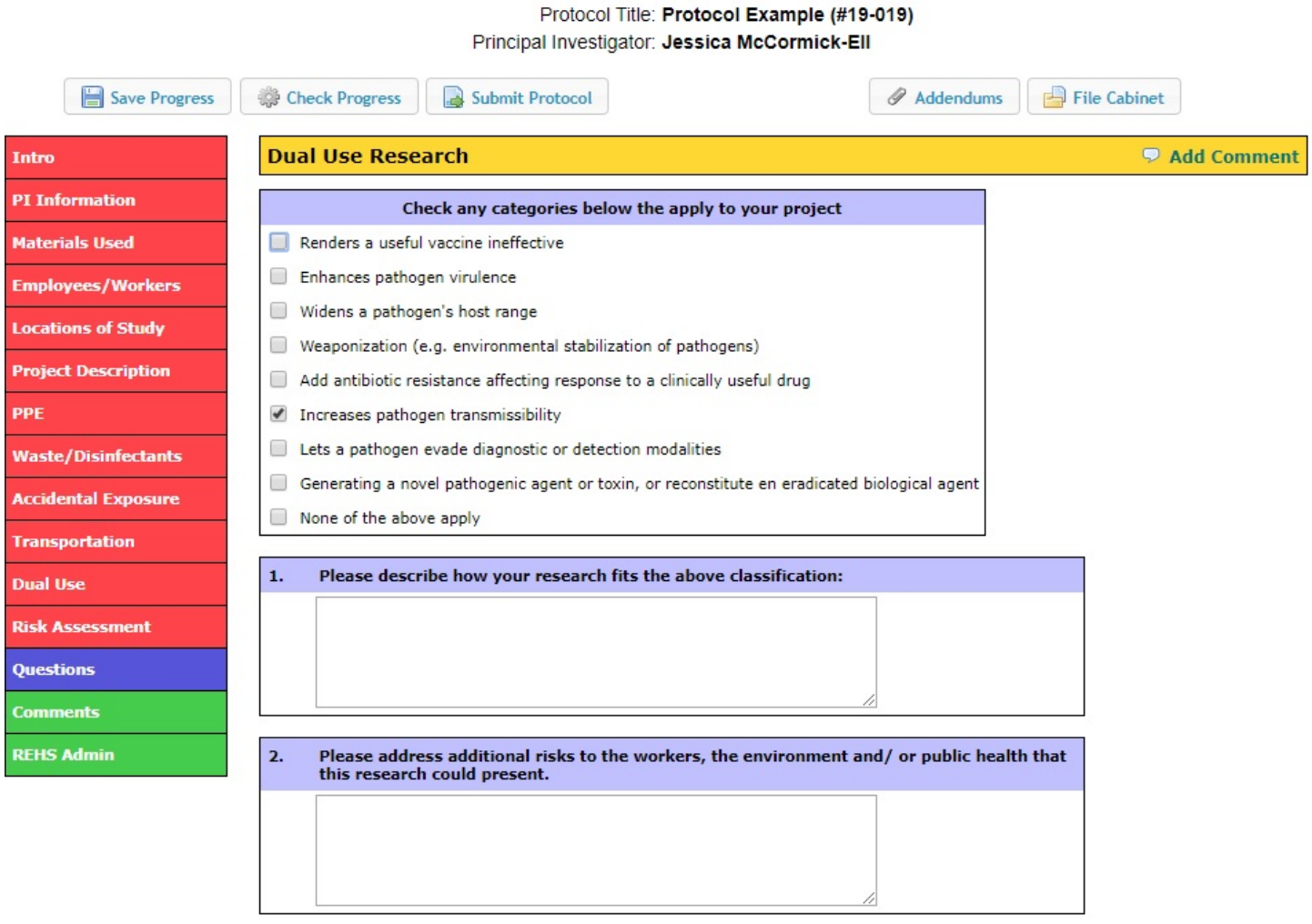


Reviewing a Protocol

15. Dual Use

Taken directly from the NIH website...
"Dual Use Research of Concern (DURC) is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, material, or national security." https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/dual-use-research

It is the responsibility of the PI to assess their research for its DURC potential and the questions in the BPMS help do this. If any question is checked, then the research will need to be further assessed by the IBC working with the PI to conduct an ongoing assessment. If the research is DURC, the IBC must work with the PI to develop and implement a risk management plan, to which the research findings must adhere to.



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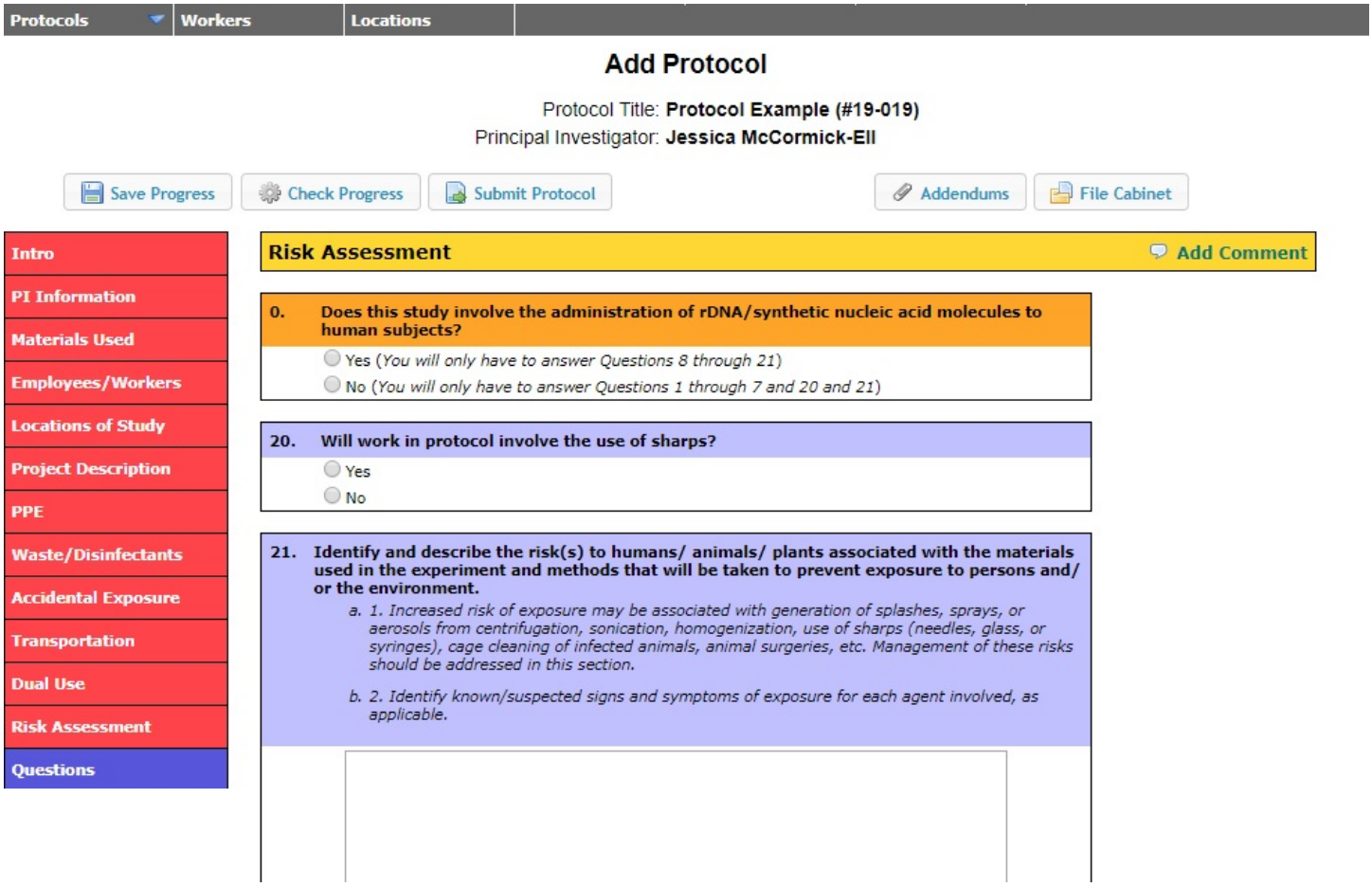
16. Risk Assessment:

Please describe in detail the hazards associated with the biological materials you will be working with.

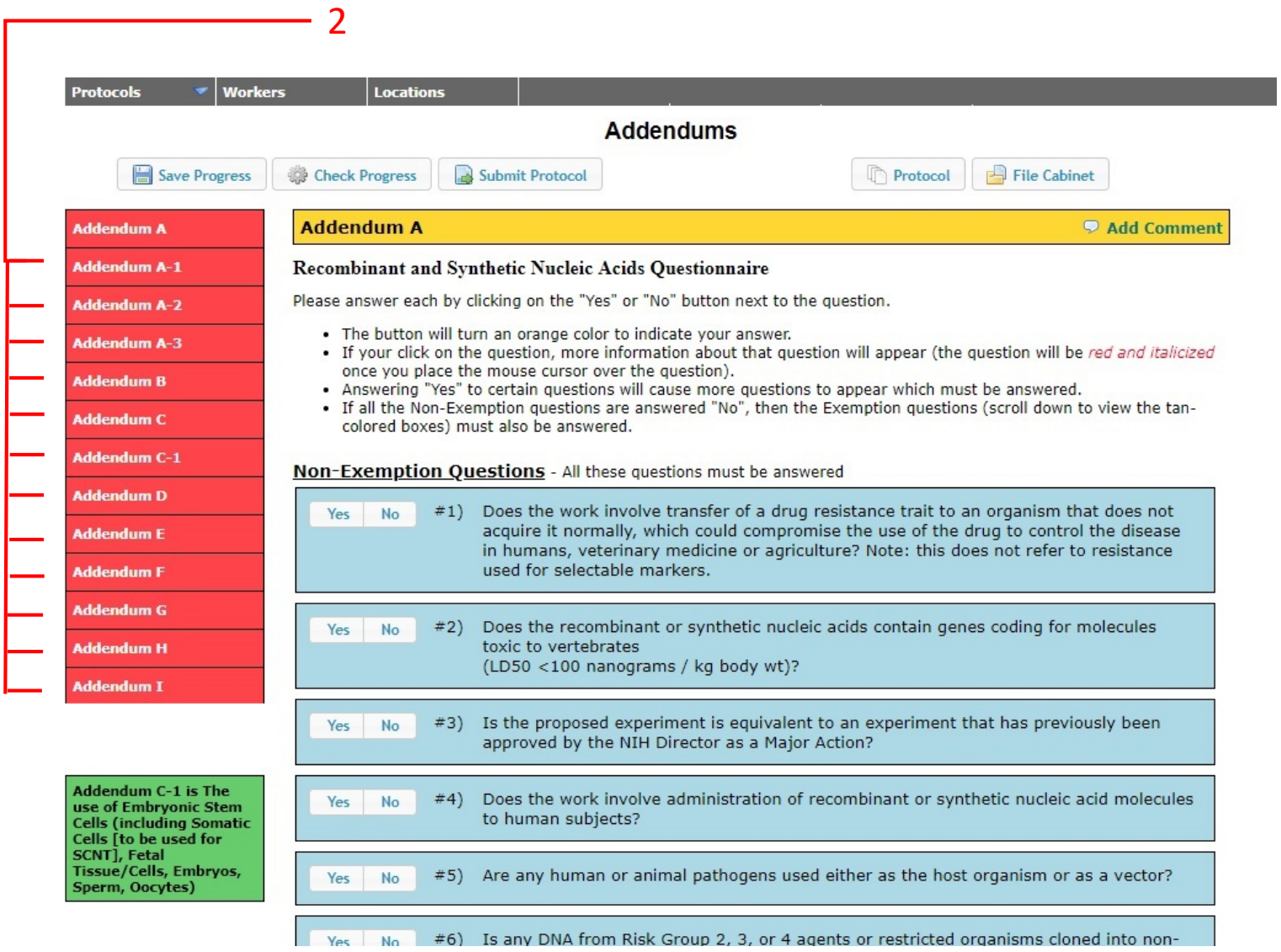
- Please do not write “no risk” when working with human cells. Human cell lines always have a risk of blood borne pathogens (even established cell lines).
- Acknowledge the risk of gene expression in a lab worker that would be accidentally exposed to recombinant/gene editing technologies (viral vectors, CRISPR, etc)
- If you are working with Sharps, as would be mentioned in the Waste section, please describe the risks associated with Sharps in this section as well.



Create a New Protocol

17. Addendums:

1. Follow the directions and answer each Yes/No question by clicking on either "Yes" or "No".
2. Once all questions for Addendum A have been answered, proceed to Addendum "A-1" by clicking on the red tab to the left of the screen entitled "Addendum A-1". Complete ALL Addendums that are present. Keep in mind, you only have Addendum tabs to which you checked "yes" to in the "Materials Used" tab from the Protocol.
3. For a sample response to these questions, please see the attached document "Biosafety Protocol Template"



Create a New Protocol

17. Addendum A and A-1 Helpful Hints:

Addendums A and A-1 are often a source of difficulty when creating a protocol. Here are some hints to think about when/if you are required to complete these addendums. Also, the IBC Protocol Example is a great resource to show you an example of responses to the questions in these addendums.

Addendum A

This section is to determine how rDNA will be used.

1. Where does the research fall under the NIH guidelines?
2. What/how rDNA is being used?
3. What/how viral vectors are being used?
4. Do genes of interest (rDNA) pose an increased risk? (oncogenic, immunosuppressive)
5. What are the viral vector concerns?
    a) Competent vs Incompetent
    b) Recombination potential
    c) Residual viral gene expression
    d) Method of vector construction/propagation
    e) Integration potential

If the research includes CRISPR or viral vectors, make sure you read/sign the CRISPR guidesheet or viral vector factsheets and upload to the **File Cabinet**.

Addendum A-1

This section is to further determine the risk of rDNA and vectors.

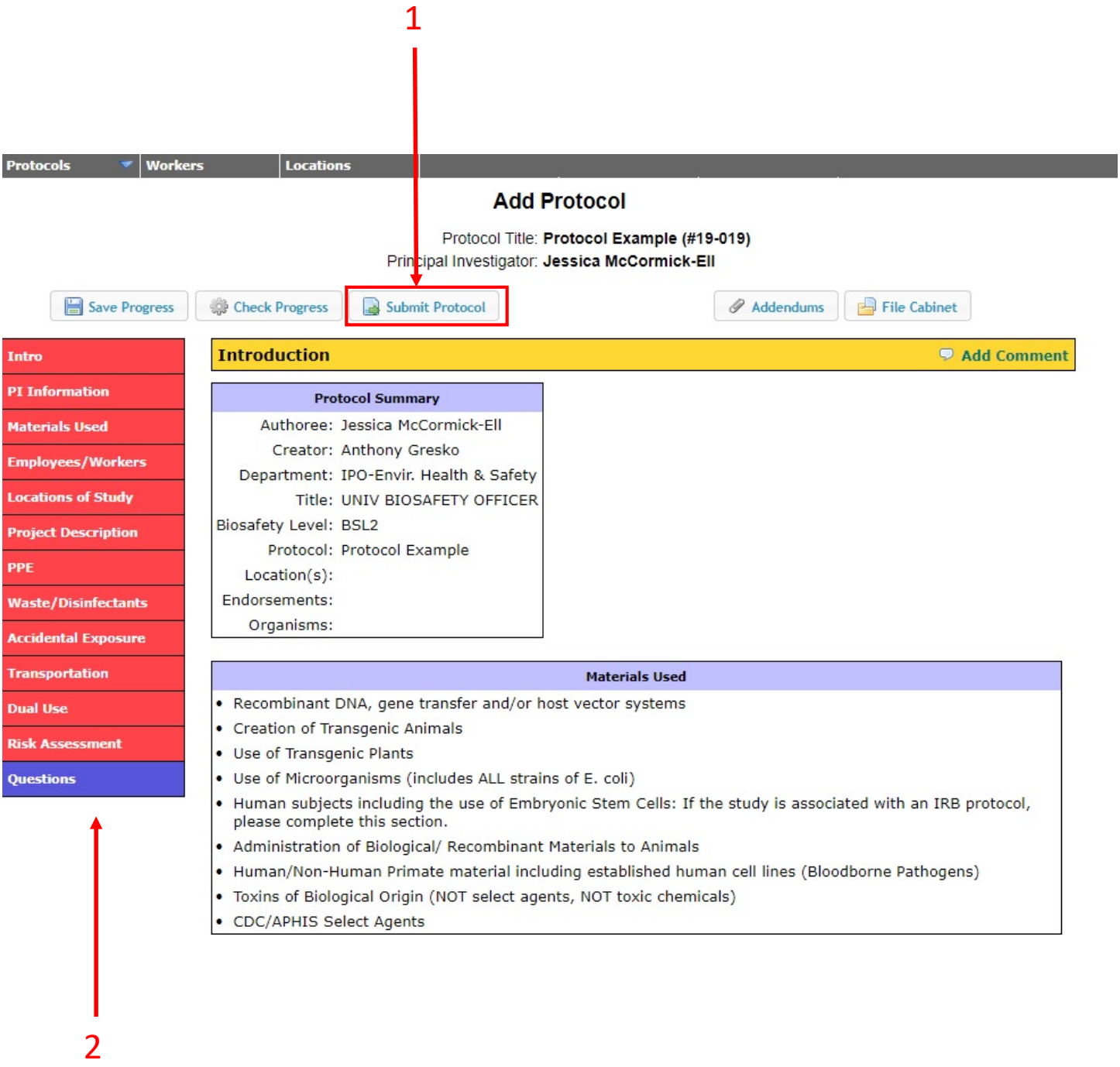
1. Do the vectors/strains/gene targets present any hazards?
    a) Are the gene targets oncogenic?
    b) Does putting the vector into the host present additional risks?
2. Is the viral vector contaminated with replication competent virus?

E.coli must be mentioned here. You also need to ensure all plasmids are listed, including the transfer **AND** packaging plasmids. Plasmid maps should be uploaded into the **File Cabinet**, and should relate to the vectors in the chart here.

Create a New Protocol

18. Submit Protocol:

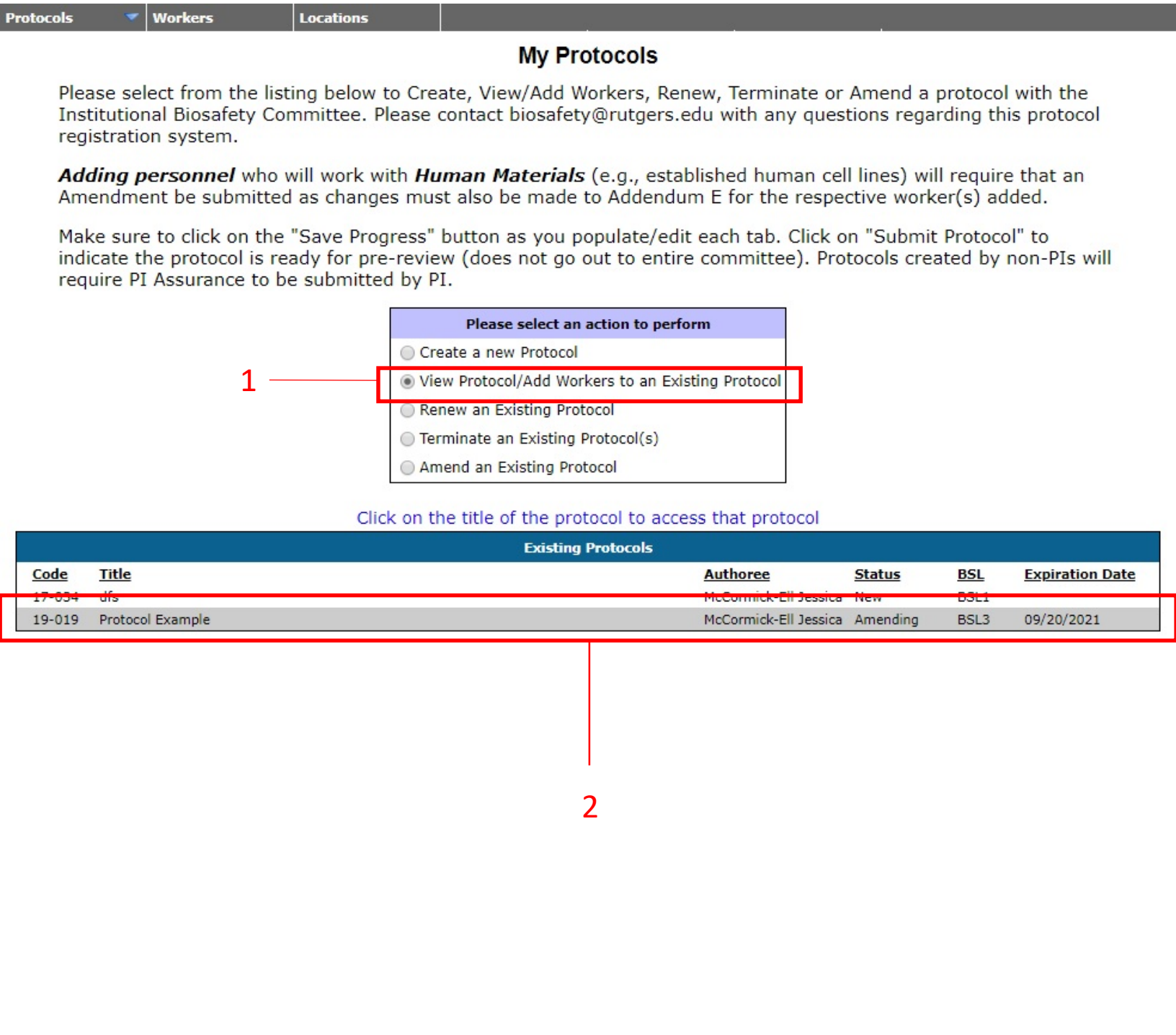
1. Click on the “Submit Protocol” button to submit a finished protocol.
2. When the protocol is being reviewed by Biosafety, the PI will need to answer questions in the questions tab. When reviewers ask for more information through a question, please provide the information **in the requested sections of the protocol.**



Adding a Worker

To add a worker to a protocol:

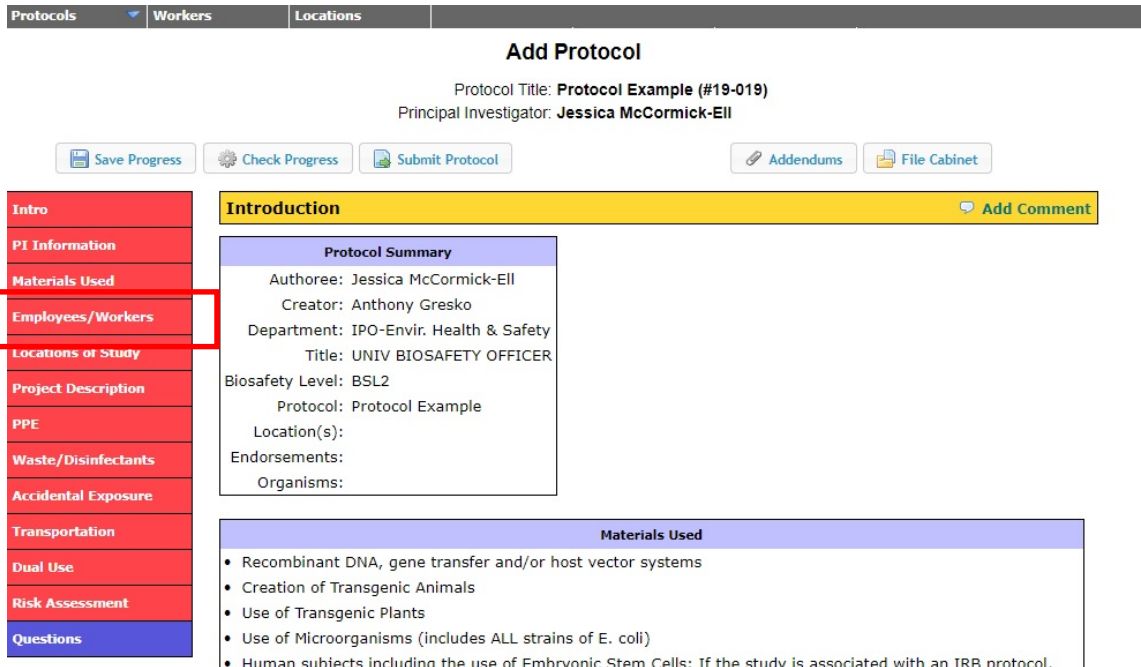
1. In "**My Protocols**", click on "**View Protocol/Add Workers to an existing Protocol**"
2. Click on the protocol you wish to add a worker to.



Adding a Worker

To add a worker to a Protocol:

3. Click on "**Employees/Workers**" tab
4. Click on "**Add Worker**" button



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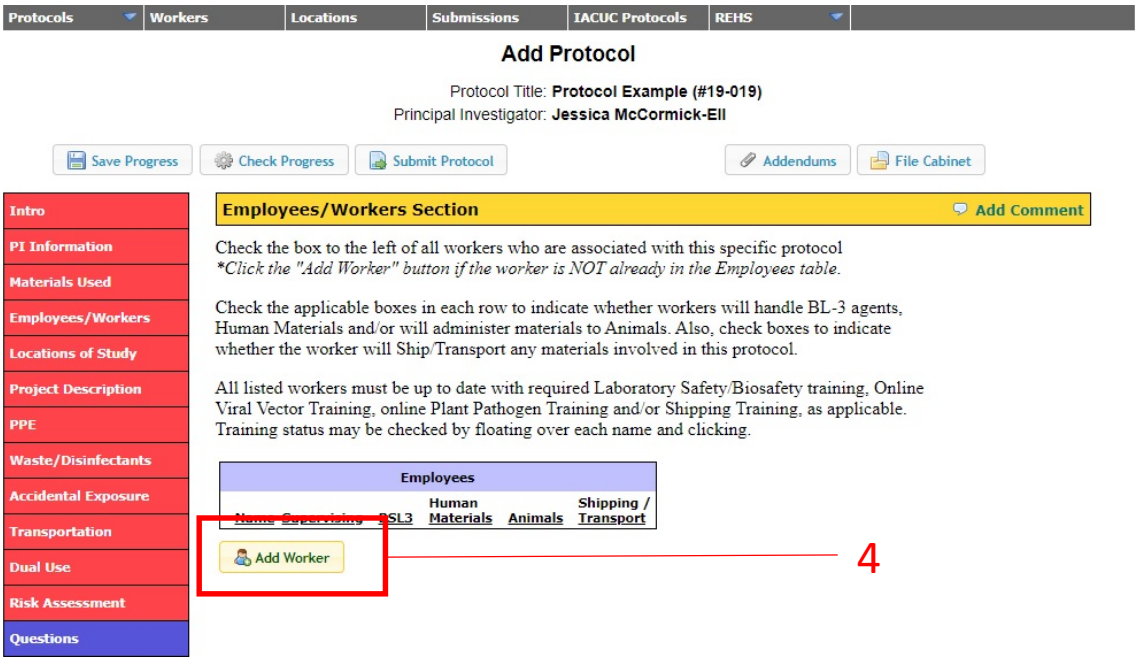

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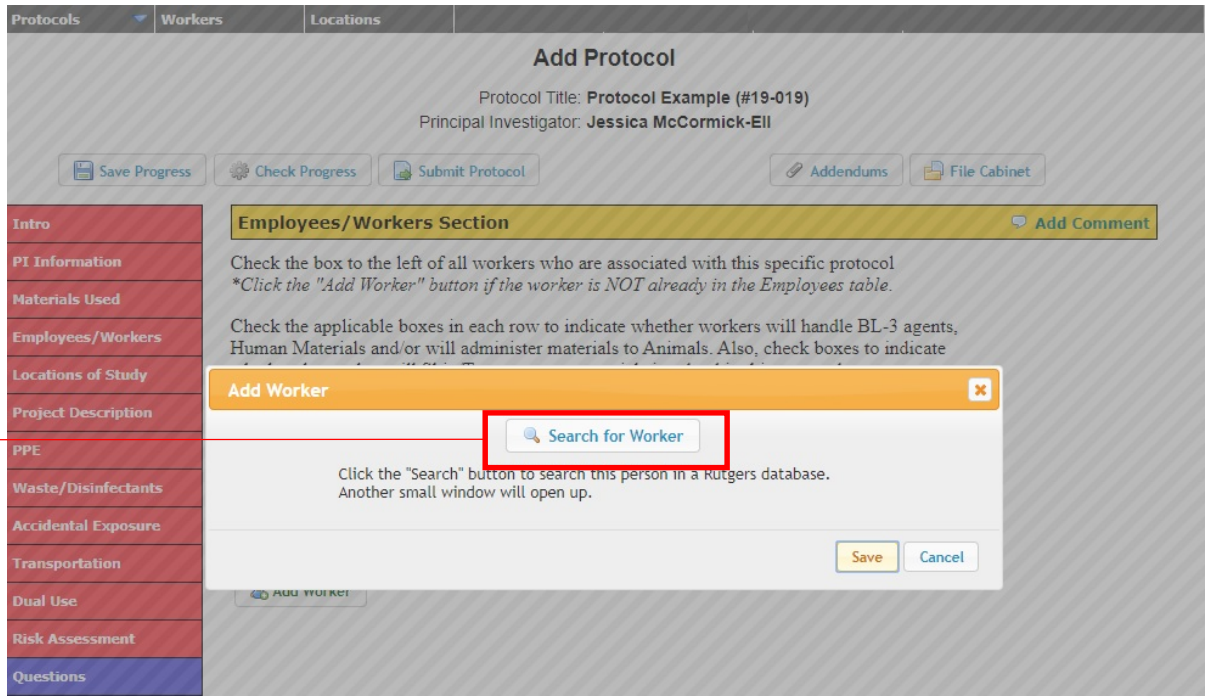
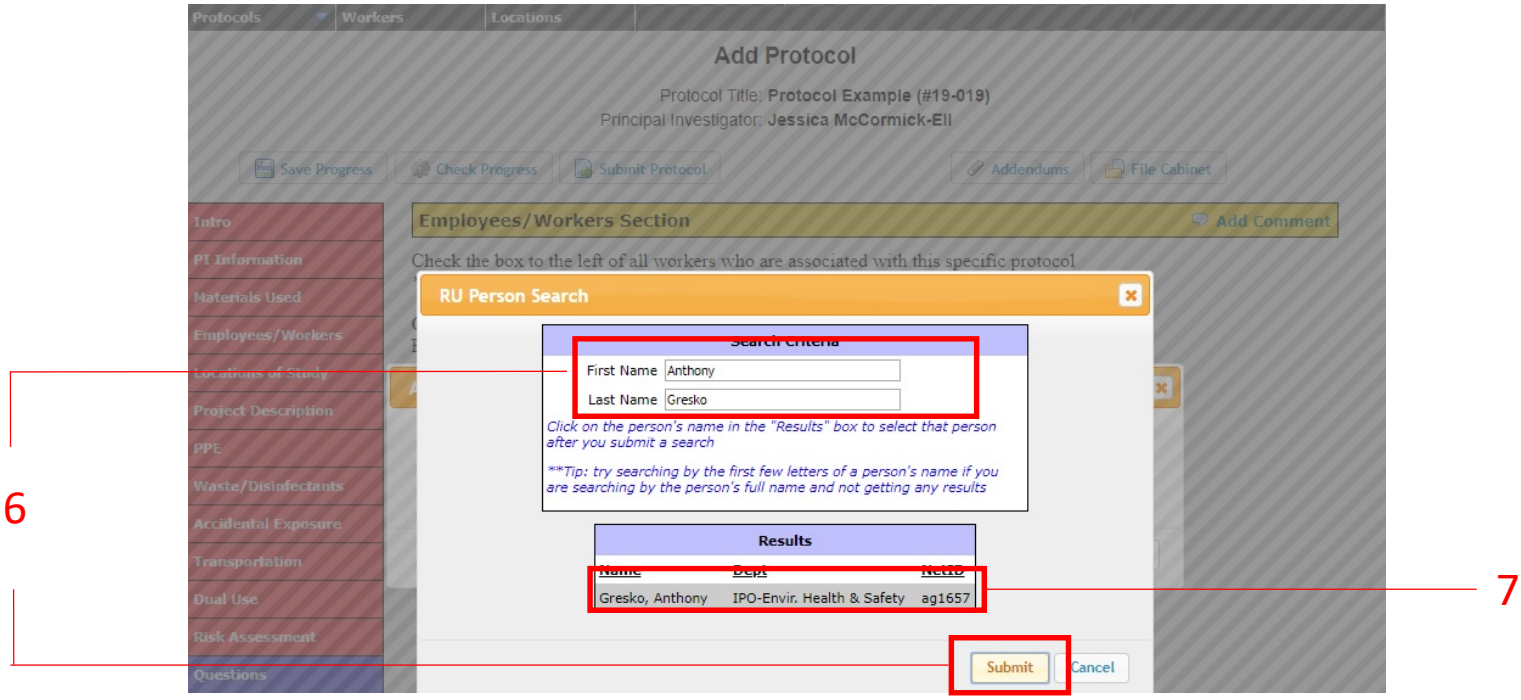
Adding a Worker

To add a worker to a Protocol:

5. Click on "**Search for Worker**" button
6. Type in the workers name and click "**Submit**" button
7. In the Results box, click on the name of the desired worker.

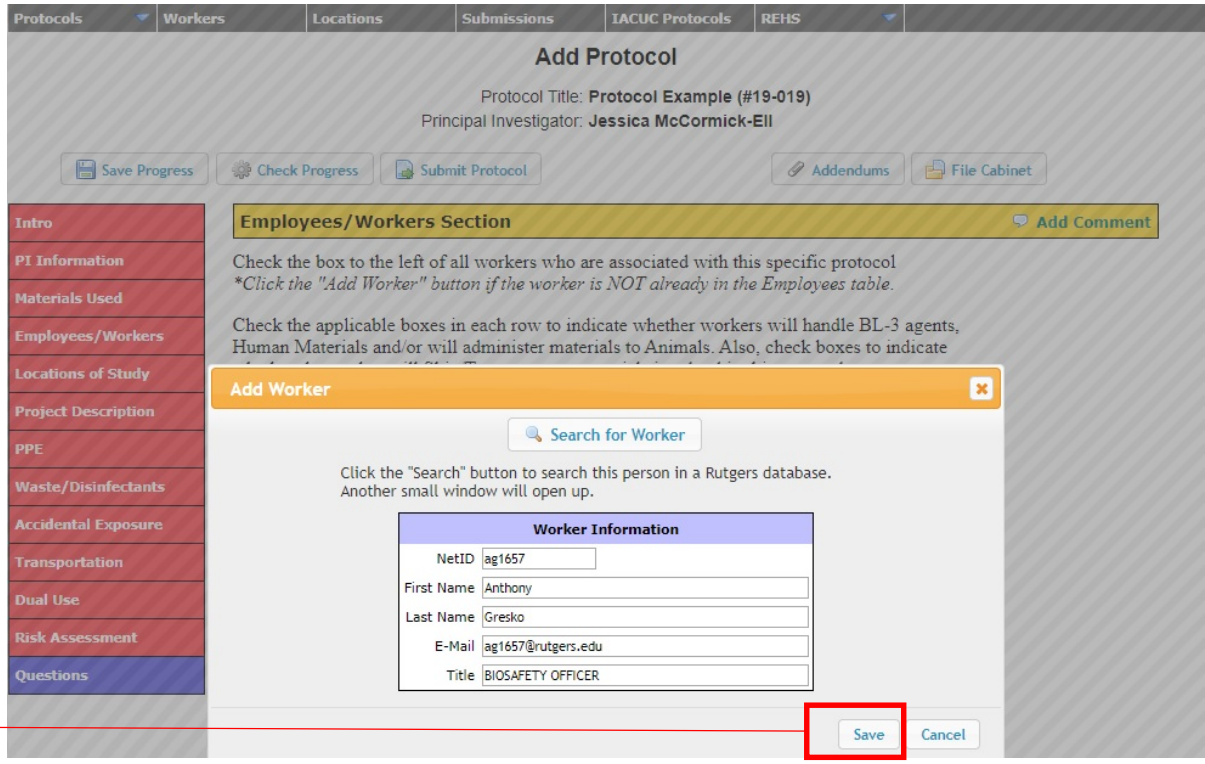




Adding a Worker

To add a worker to a Protocol:

8. Verify the worker information is correct and click "**Save**" button
9. Check on the role(s) that the worker will have in the laboratory. Note: Human Materials includes use of established cell lines (HEK, Vero, etc). Additional windows MAY appear, which must be completed.
10. Click "Save Progress" button



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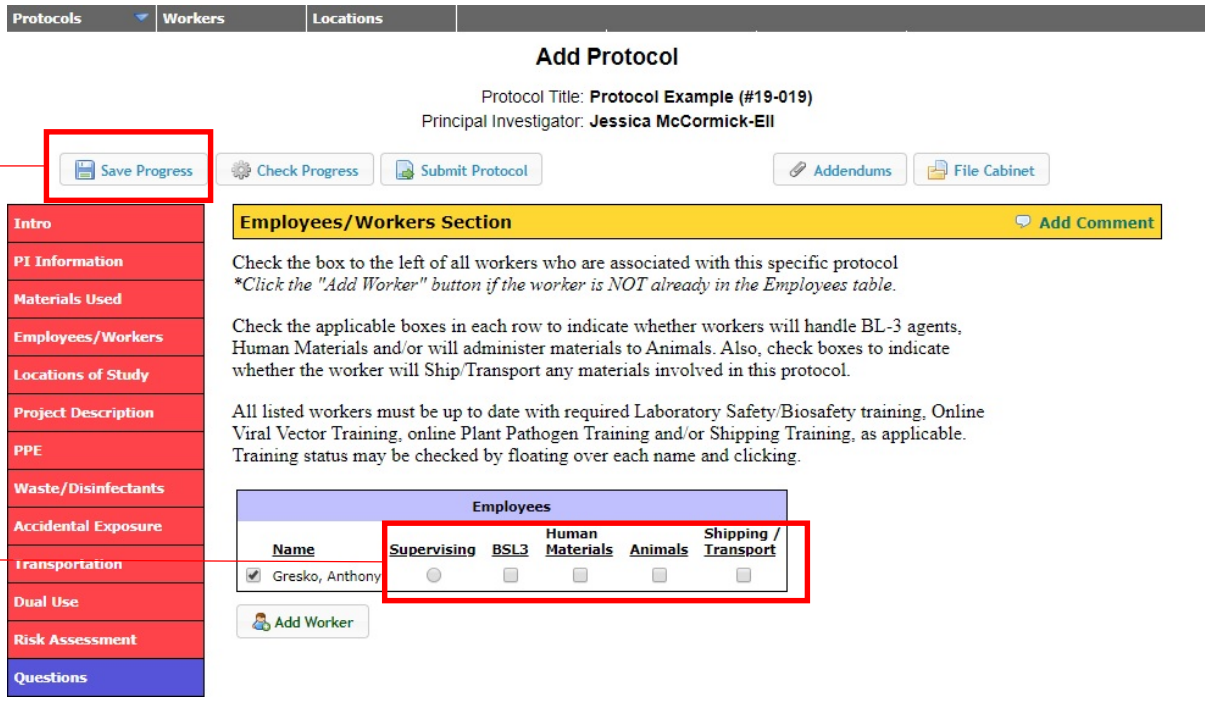

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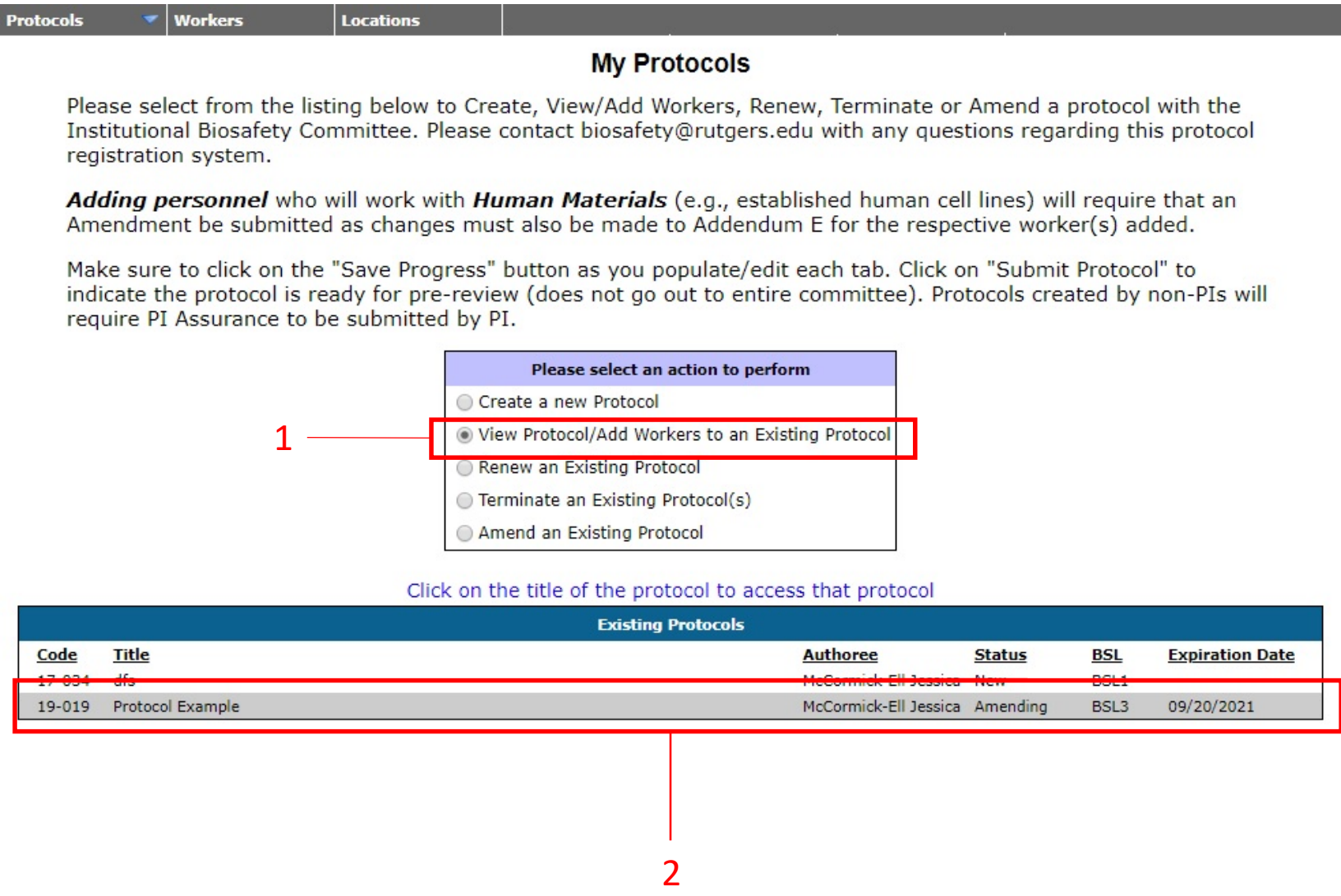
Removing a Worker

To remove a worker to a protocol:

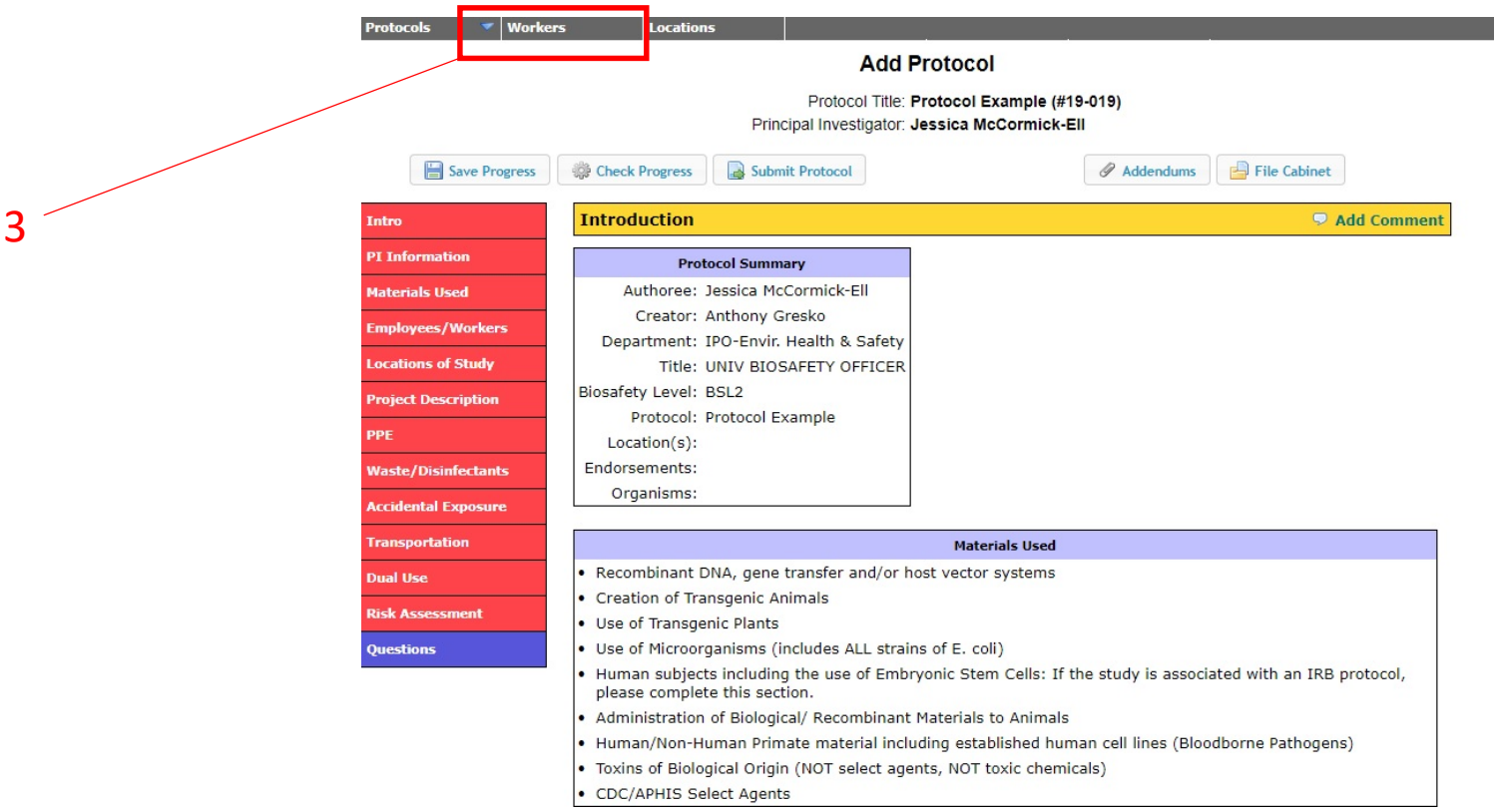
1. In "**My Protocols**", click on "**View Protocol/Add Workers to an existing Protocol**"
2. Click on the protocol you wish to remove a worker from.



Remove a Worker

To remove a worker to a Protocol:

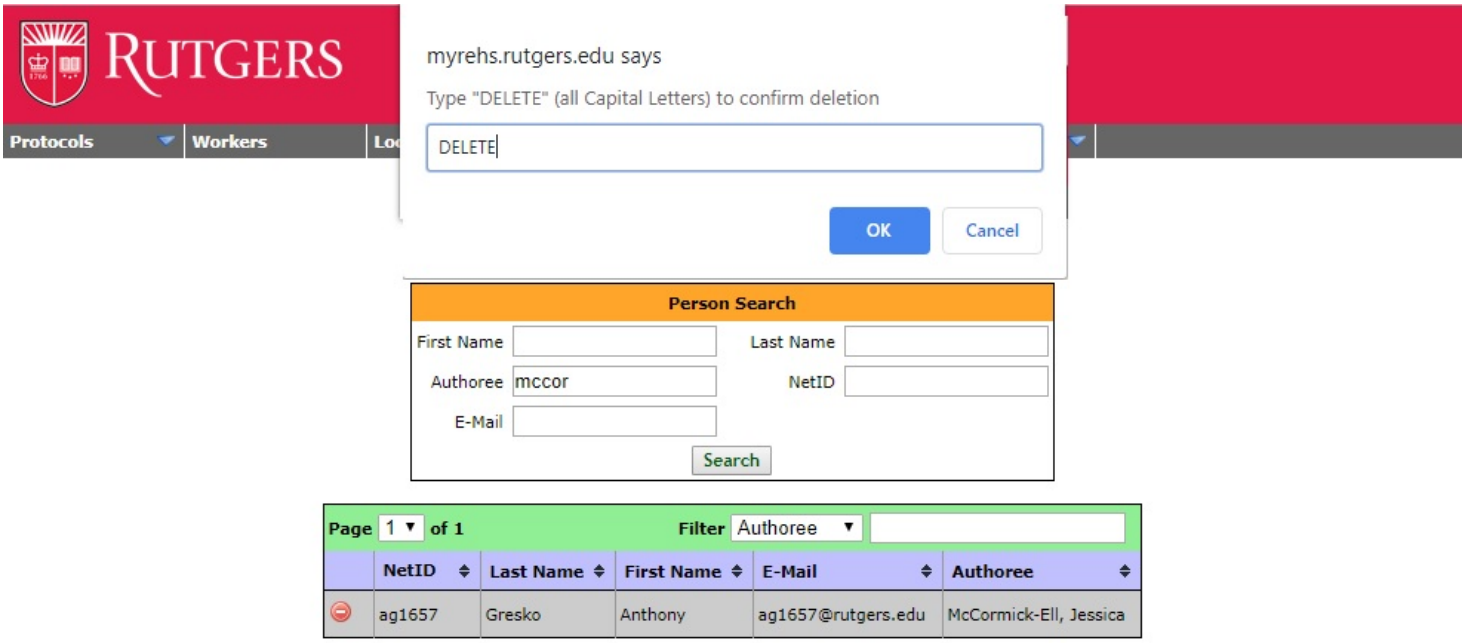
3. Click on "**Workers**" tab at the top in gray
4. Click on the red button next to the name of the worker you would like to remove from the protocol.



Remove a Worker

To remove a worker to a Protocol:

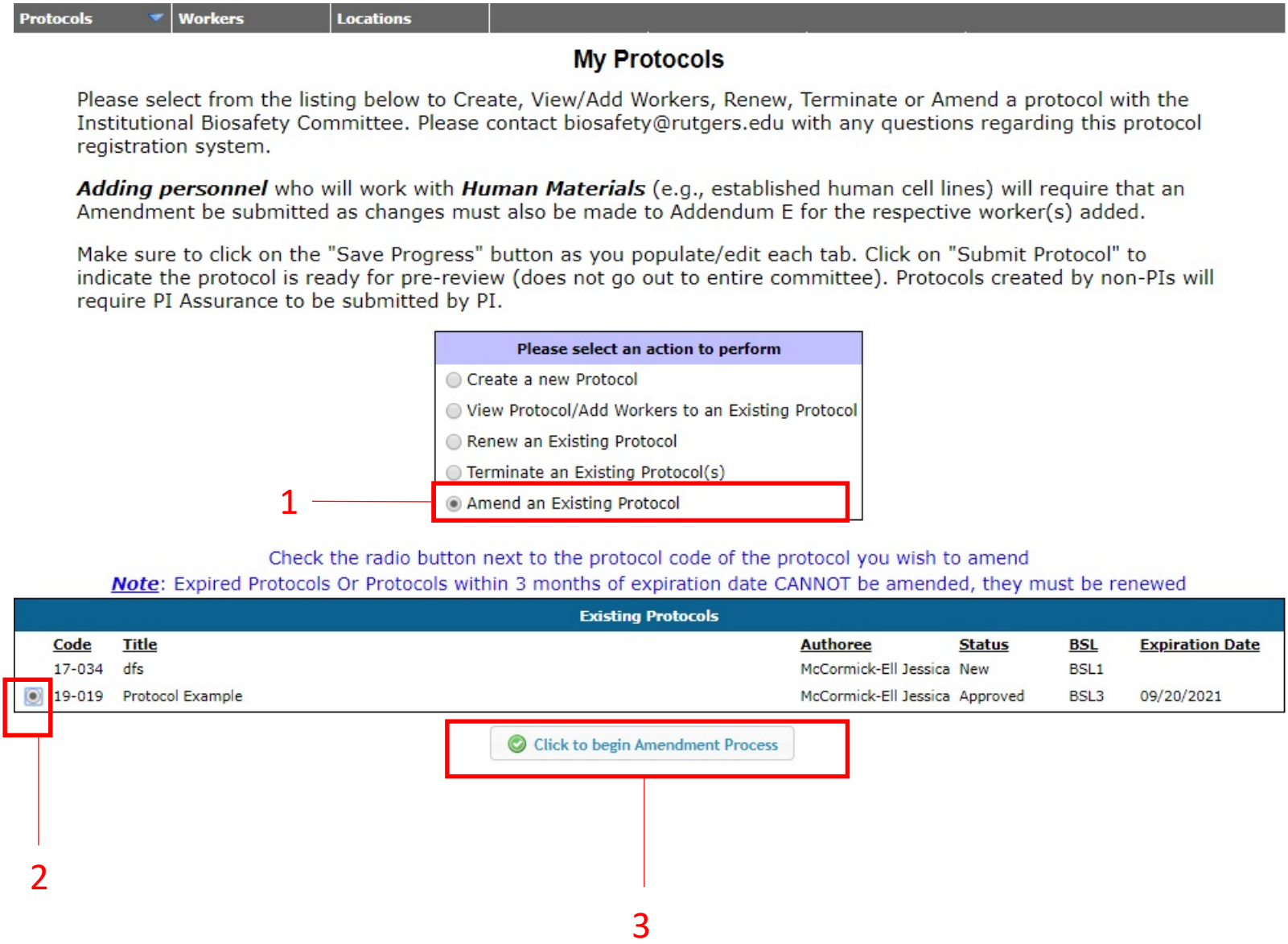
5. Type “DELETE” in all capital letters to confirm your intention to remove the worker from the protocol.



Adding a Location

To add a location to a protocol:

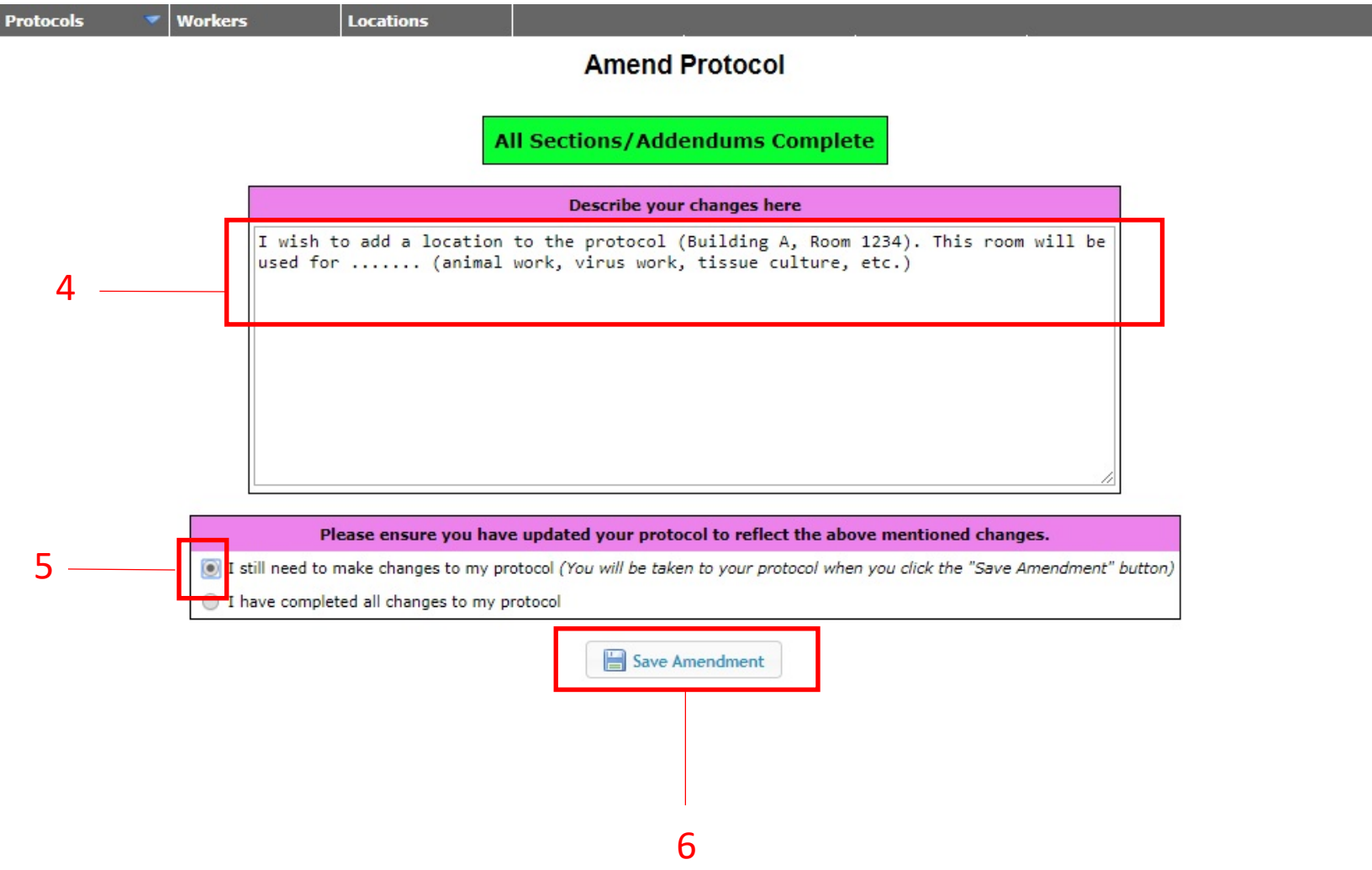
1. In "**My Protocols**", click on "**Amend an Existing Protocol"**
2. Click on the protocol that you wish to amend.
3. Click on the "**Click to being Amendment Process**" button



Adding a Location

To add a location to a protocol:

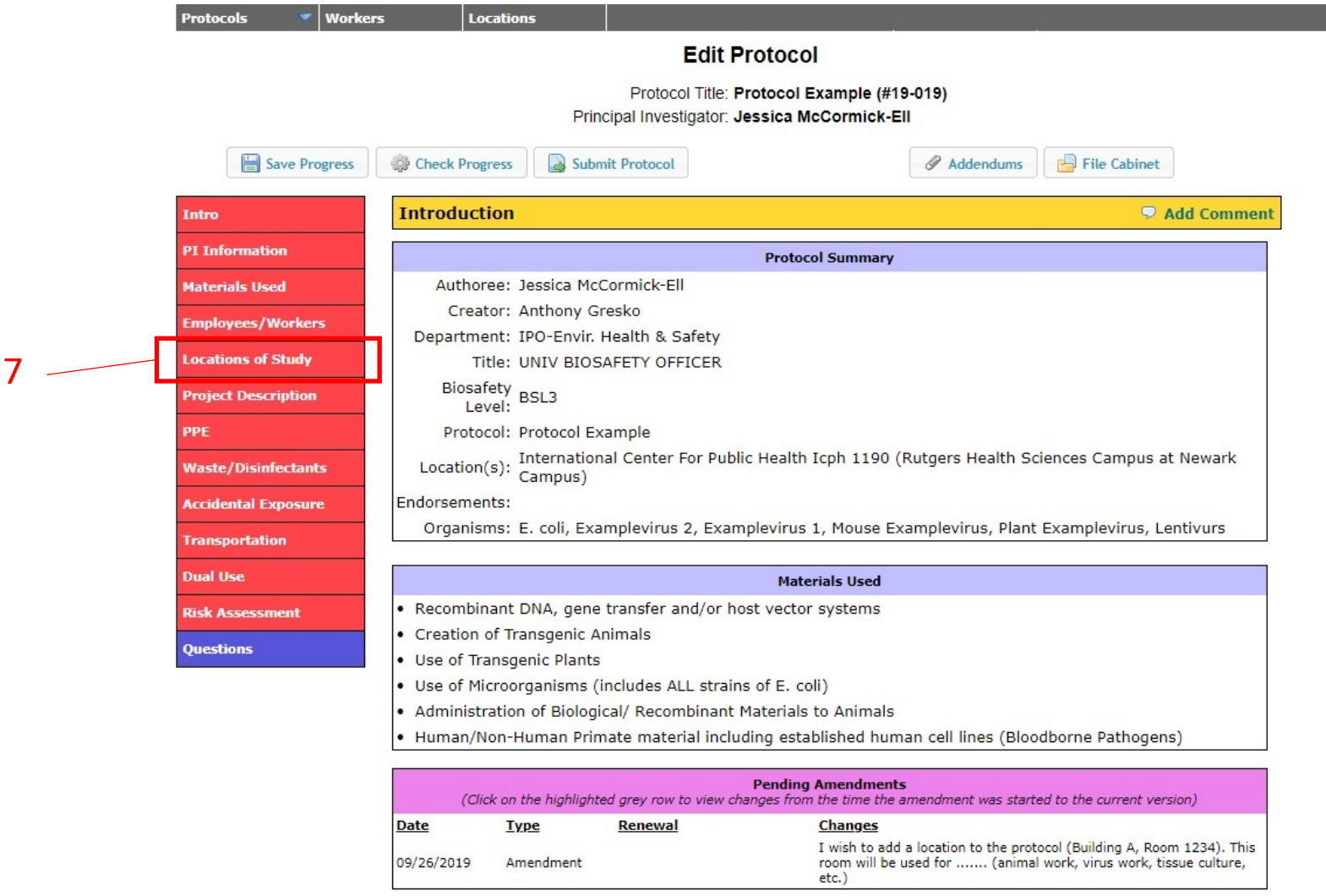
4. Type into the dialogue box the location you wish to add and what the location will be used for.
5. As you will need to add it in the protocol itself, click "**I still need to make changes to my protocol**".
6. Once all boxes have been appropriately checked and/or answered, click on the "**Save Amendment**" button.



Adding a Location

To add a location to a protocol:

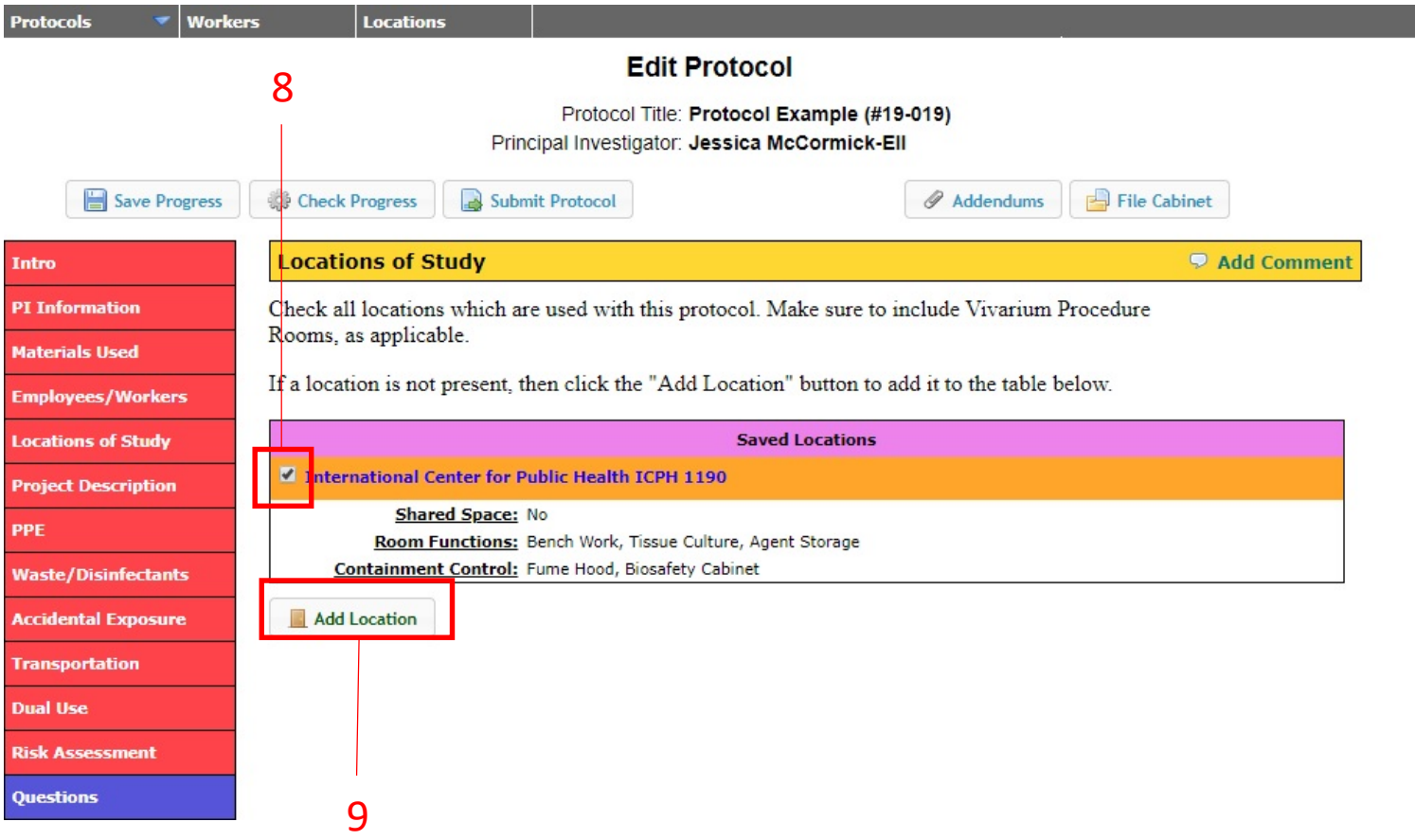
7. Click on the **Locations of Study** tab.



Adding a Location

To add a location:

8. You can click or unclick a location that is already in the protocol
9. You can click on the **"Add Location"** button to add a new location to the protocol.



PI assurance

When a proxy under a PI submits a protocol, the PI must acknowledge that the proposed work in the submitted protocol is indeed correct. Protocols will not be approved until the assurance is completed.

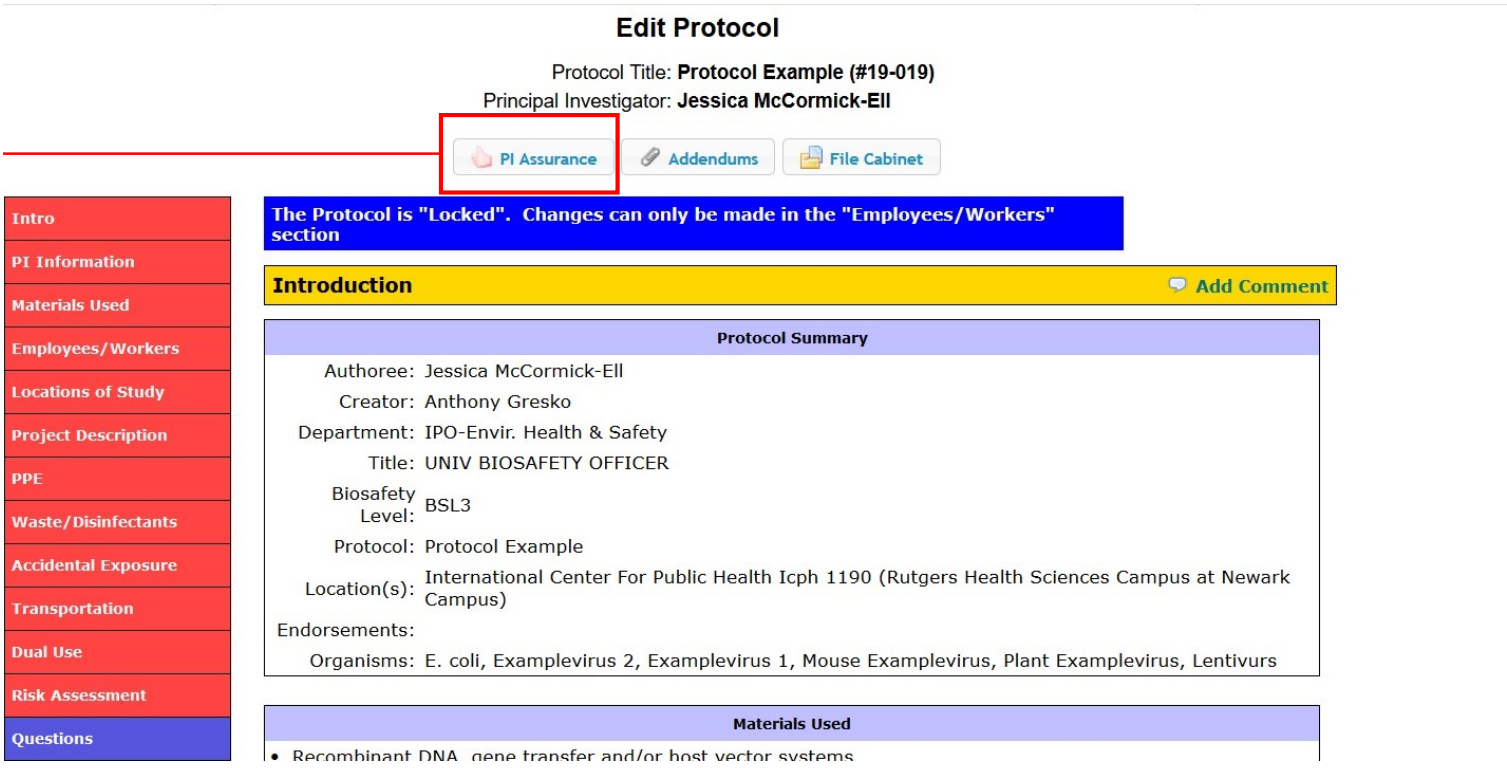
To give PI assurance:

1. When the proxy submits a protocol, the PI will receive an email asking to provide assurance that they approved the submission of the protocol. An example of this email is shown below.

From: biosafety@rutgers.edu <biosafety@rutgers.edu>
Sent: Thursday, September 19, 2019 10:24 AM
To: Jessica McCormick-Ell <jessica.mccormickell@rutgers.edu>
Subject: Rutgers Biosafety Protocol Management System - PI Assurance Required

Anthony Gresko has created, renewed or amended a biosafety protocol on your behalf.
Please use the link at the bottom of the email to access your protocol
Protocol Code: 19-019
Protocol Title: Protocol Example
Please review the protocol, and if all is accurate, click on the "PI Assurance" button to read and complete the agreement statement. Your protocol will be reviewed and processed but will not be finalized until you have taken this action. Please contact biosafety@rutgers.edu with any questions or concerns!
https://myrehs.rutgers.edu/index.php?bpms_protocol=XWlm55fyawWxRK47

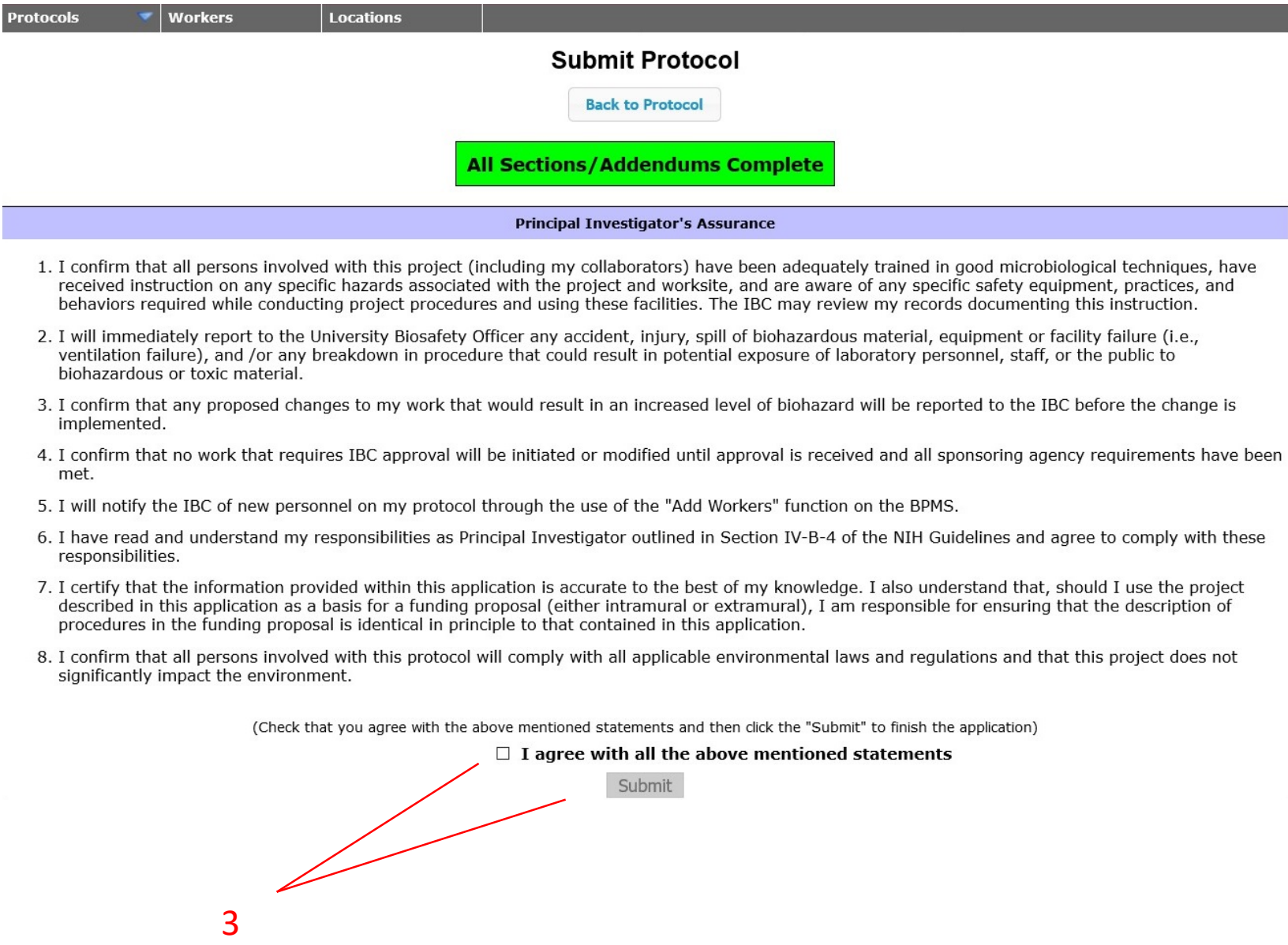
2. The PI will need to click on the link sent to their email address which will bring them to the protocol in question. Click the "**PI Assurance**" button



PI assurance

To give PI assurance:

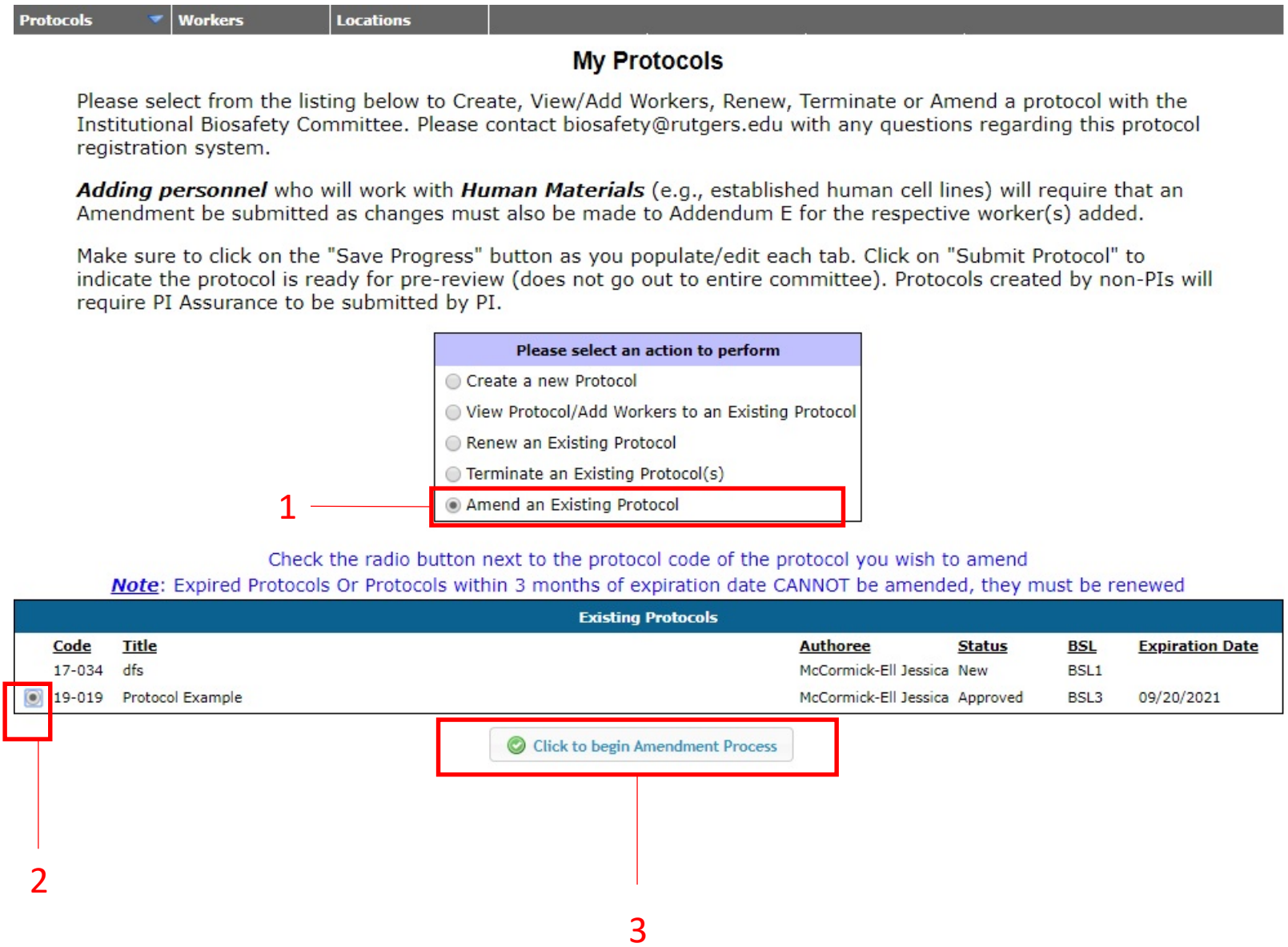
3. Read the PI assurances and click on “I agree with the above mentioned statements” to acknowledge and approve of the research proposed in the submitted protocol. Then click “Submit” button.



Amending a Protocol

To amend a protocol:

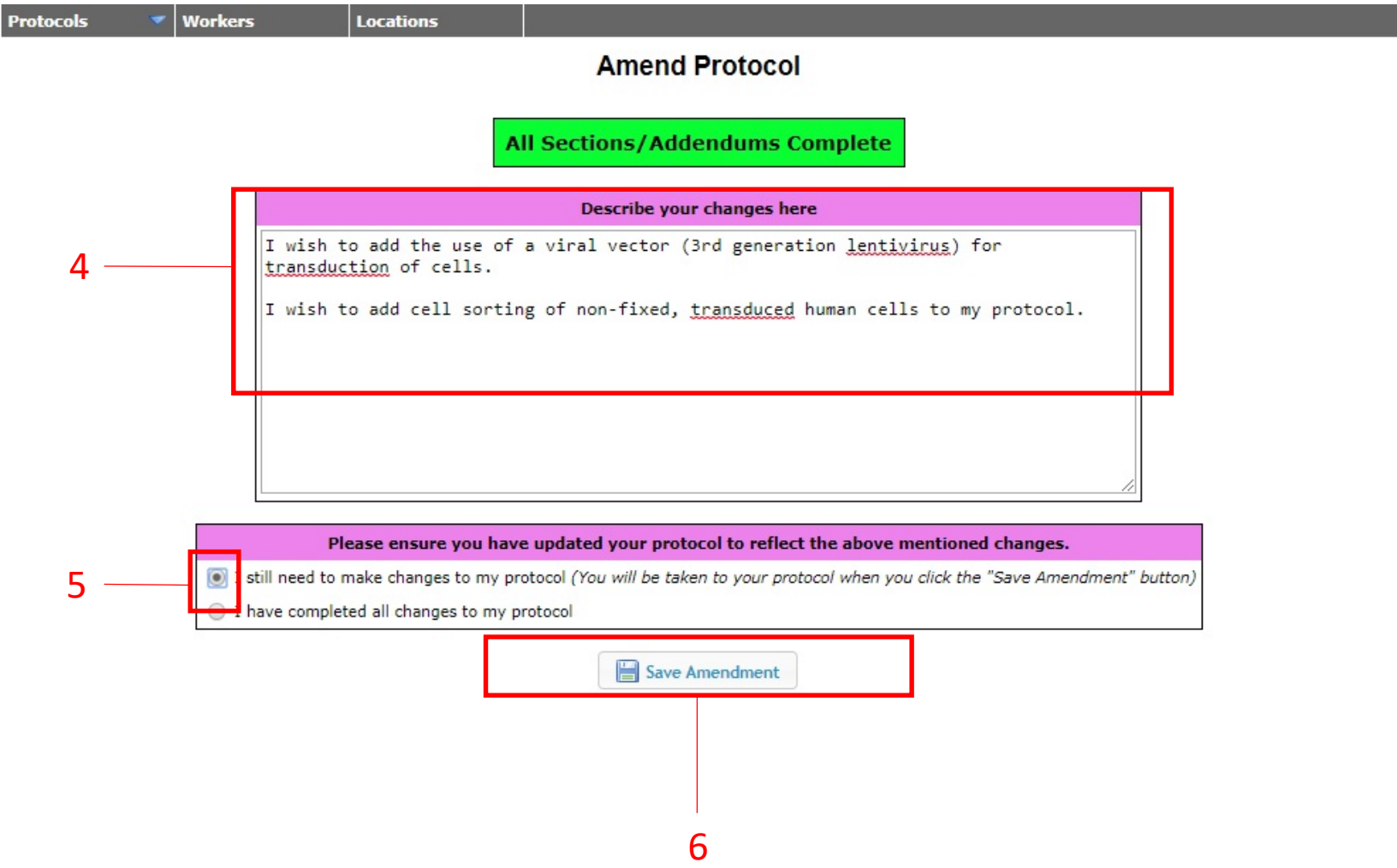
1. In "**My Protocols**", click on "**Amend an Existing Protocol"**
2. Click on the protocol that you wish to amend.
3. Click on the "**Click to begin Amendment Process**" button



Amending a Protocol

To amend a protocol:

4. Type into the dialogue box a summary of what you intend to change with the amendment. This is referred to later in this guide as “Summary of Changes”.
5. Depending on your changes, you may need to go into the protocol and edit the necessary sections where the changes are (i.e. project description, risk assessment, addendums, etc.). If further changes must be made, click on the appropriate box.
6. Once all boxes have been appropriately checked and/or answered, click on the “**Save Amendment**” button.

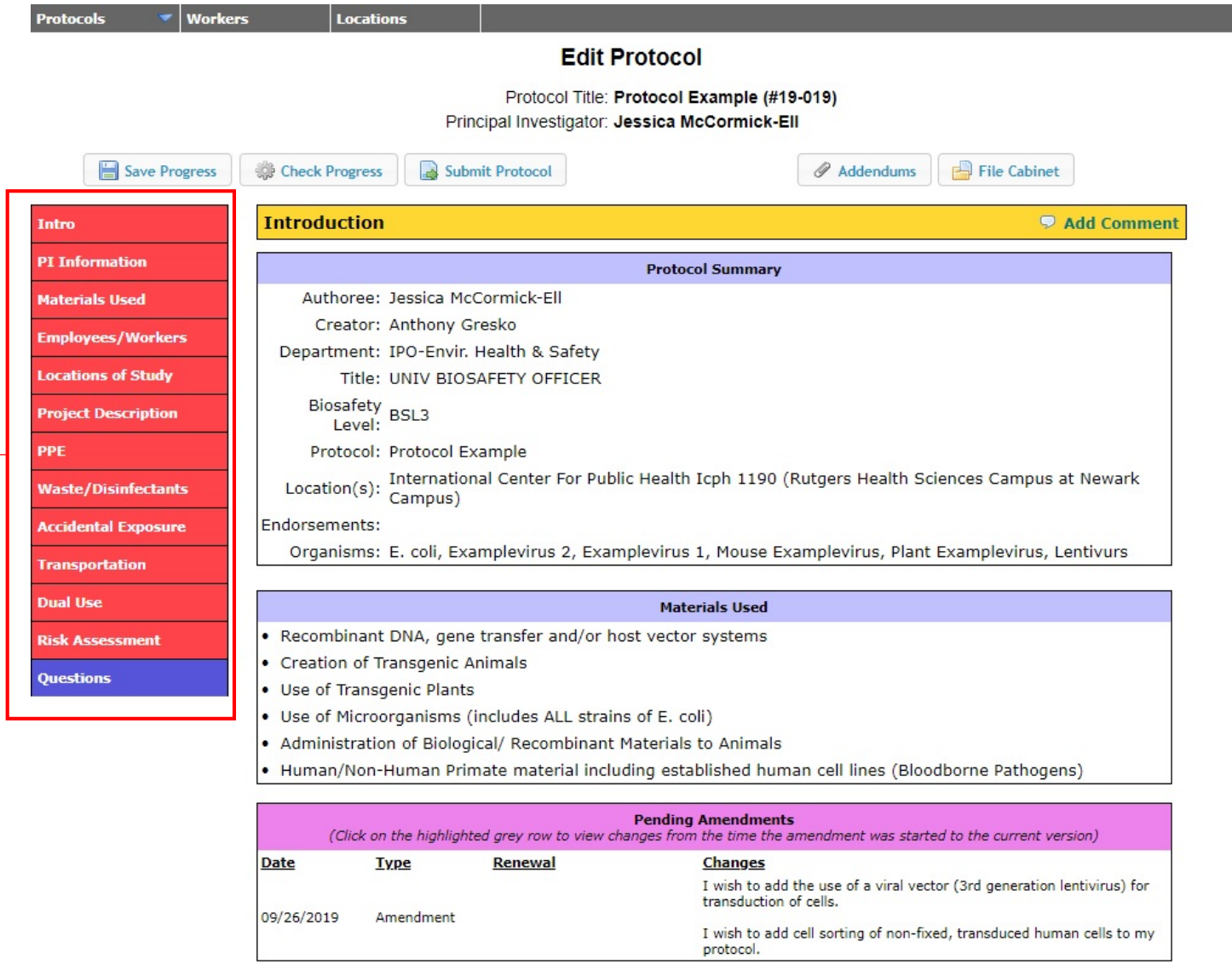


Amending a Protocol

To amend a protocol:

7. Go into the Sections that need to be changed and make the necessary changes that you described in your "Summary of Changes" that was in Step 4. An example of making the changes is shown in step 8.

NOTE: You will ALWAYS need to update the Project Description and Risk Assessment sections.



Amending a Protocol

To amend a protocol:

8. Example Amendment: In the project description, describe the changes you wish to make to the protocol. *It helps to mark the date of these changes to distinguish when this part of your research was added to your protocol.

Pending Amendments

(Click on the highlighted grey row to view changes from the time the amendment was started to the current version)

Date	Type	Renewal	Changes
09/26/2019	Amendment		I wish to add the use of a viral vector (3rd generation lentivirus) for transduction of cells. I wish to add cell sorting of non-fixed, transduced human cells to my protocol.

2. Provide a step by step "walk-through" of your research methodology. Be sure to explain how and why specific agents are used. If there is a connection between this IBC protocol, IRB, ESCRO and/ or IACUC be sure to describe the links.

immunoregulatory in nature. Recombinant plants will be generated using CRISPR techonology. Recombinant cell lines will be generated using RNAi and lentiviral systems. Both siRNA and miRNA will be used for transient gene knockdown.

Amendment 9/20/2019
A lentivirus containing CRISPR gRNA library will infect both cell types (Cell A and Cell B) to achieve stably knock-out and knock-in cell lines. The lentivirus packaging system (3rd generation, acquired from this company (website)) is split into 4 total plasmids. One plasmid encodes Rev, one encodes Gag and Pol, one encodes the envelope protein (VSV-G), and the last plasmid encodes the shRNA or cDNA for Cas9. This 4 plasmid system is replication incompetent and having 4 separate plasmids further decreases the possibility of recombination and creation of replication competent particles. Also, the 5' LTR region of the transfer plasmid contains self-inactivation mutations to further decrease possibility of replication competent particle generation.

Cell Sorting will also be performed to sort for stable knock-outs and knock-ins from the lentiviral transduction. Additional information is found in Addendum I.

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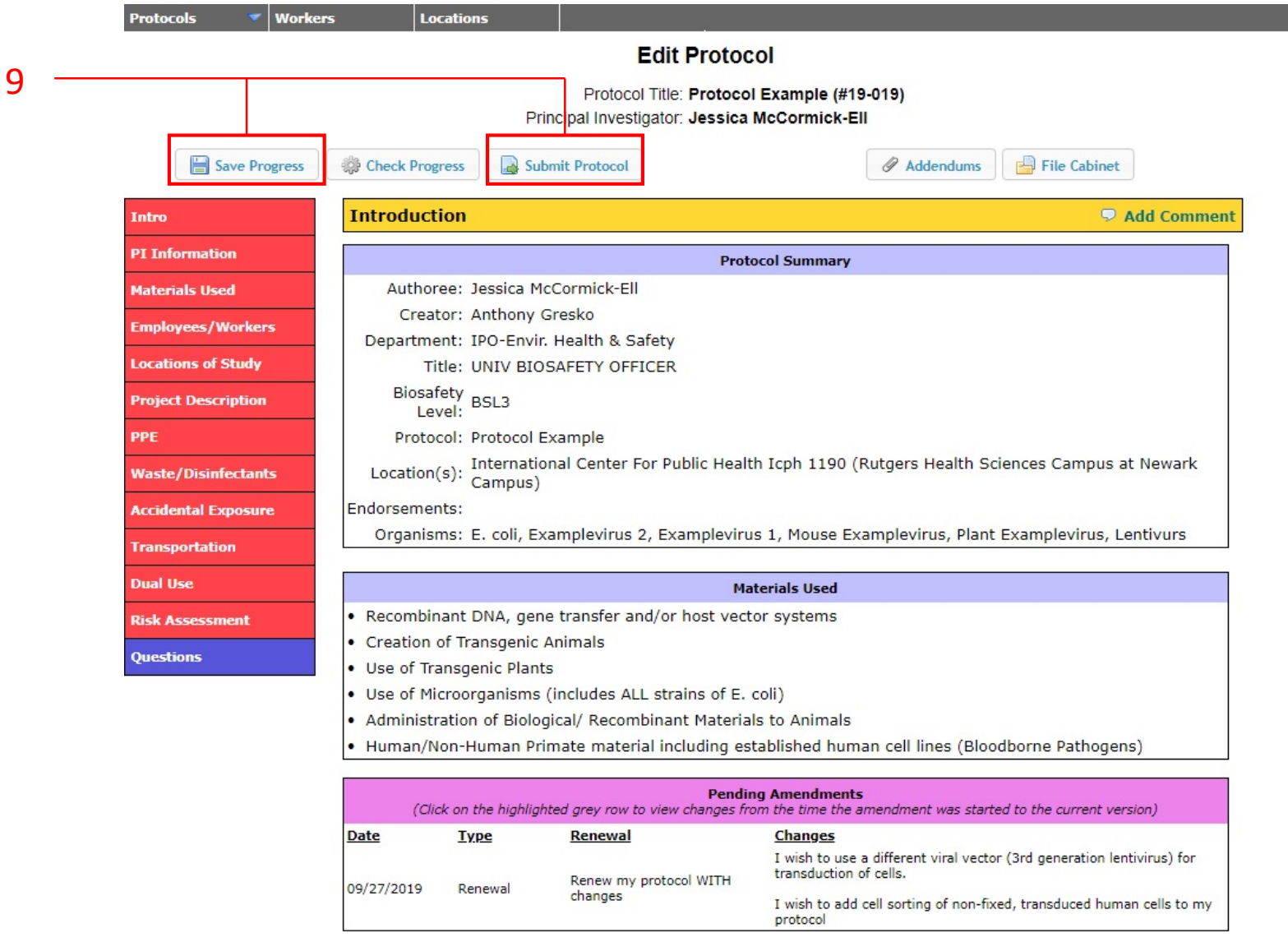
******* NOTE: In addition to describing the changes in the Project Description, Addendums A, A-1, and B must be updated for the use of the Lentivirus, as well as creating an Addendum I for cell sorting. The Risk Assessment section will need to be updated to reflect any change.**

Amending a Protocol

To amend a protocol:

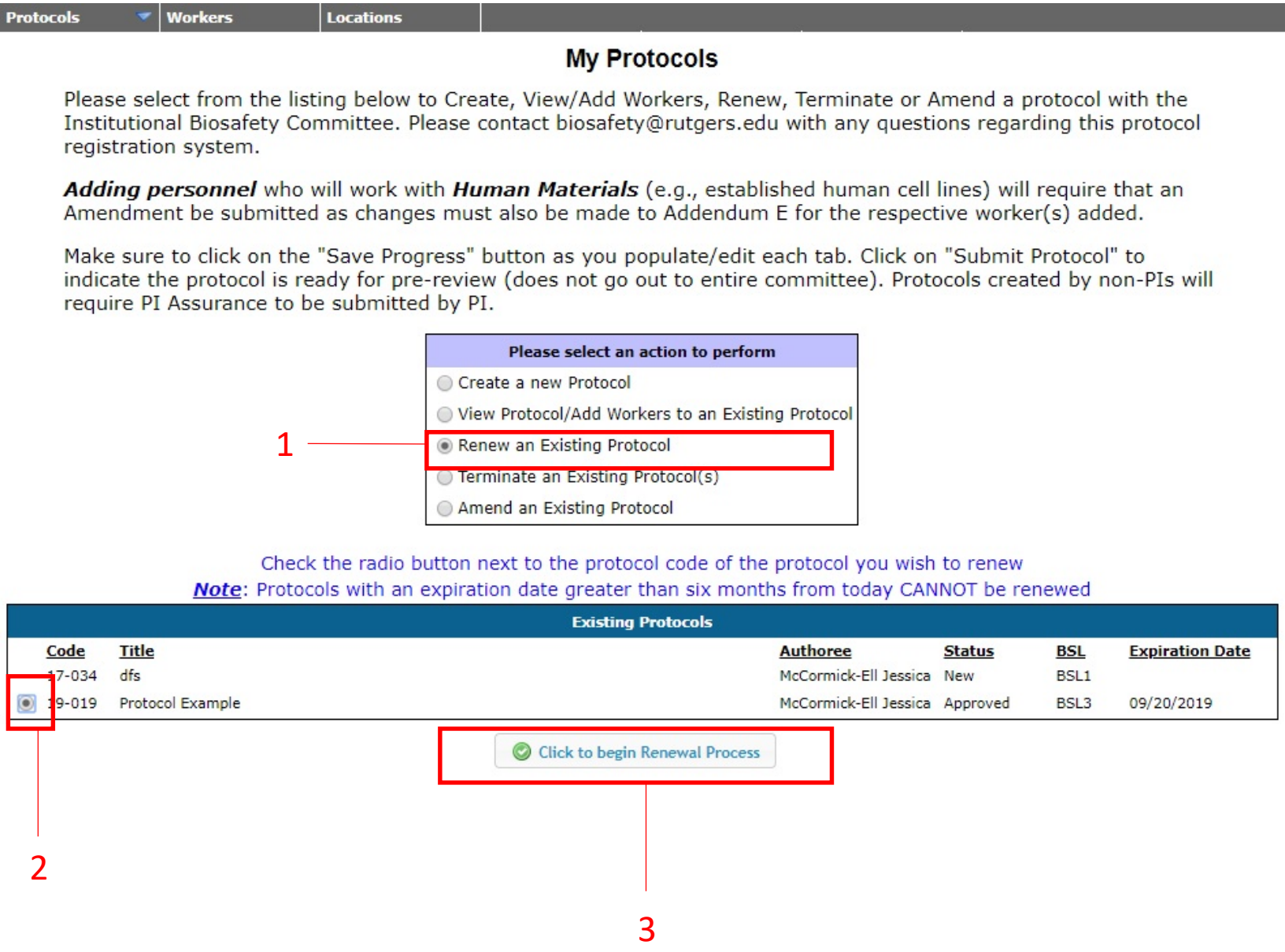
9. When finished editing ALL sections needed, click "**Save Progress**" and "**Submit Protocol**".



Renewing a Protocol

To renew a protocol:

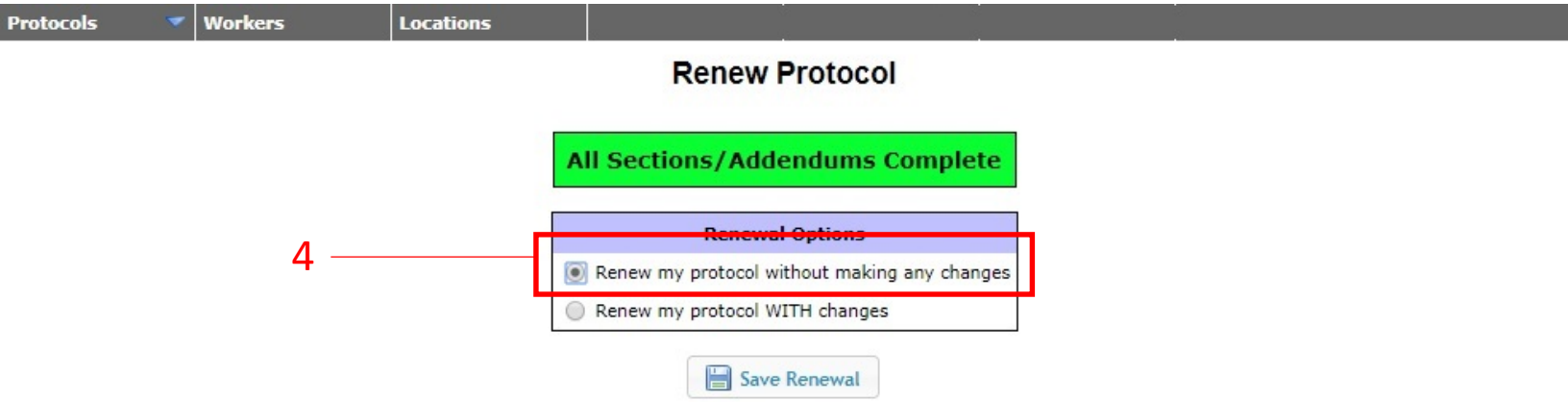
1. In "**My Protocols**", click on "**Renew an Existing Protocol"**
2. Click on the protocol that you wish to renew.
3. Click on the "**Click to begin Renewal Process**" button

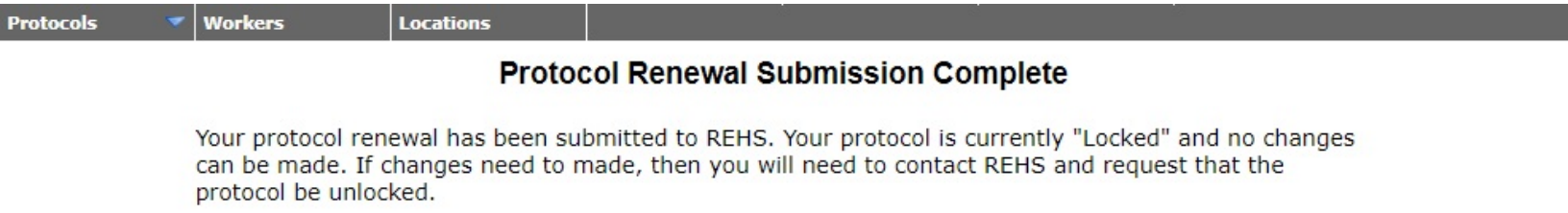


Renewing a Protocol

To renew a protocol:

4. If you have no changes to your protocol, click "**Renew my protocol without making any changes**". If you do not have changes and click "**Save Renewal**", you will see the screen at the bottom and will NOT be able to make any changes in your protocol. If you have changes, proceed to step 5 on the next page.

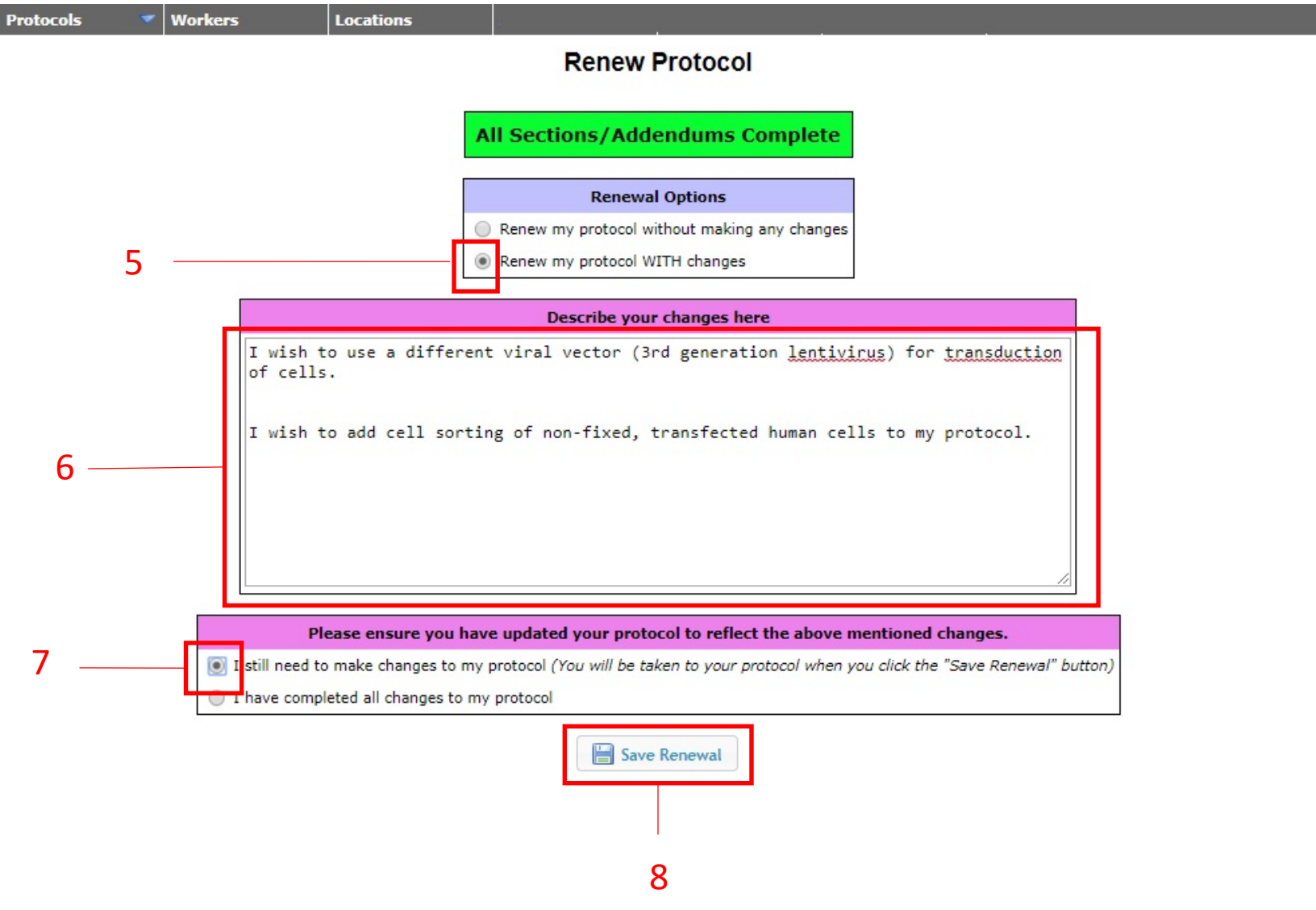




Renewing a Protocol

To renew a protocol:

5. If you have changes to your protocol, click "**Renew my protocol WITH changes**".
6. Type into this dialog box a summary of what you intend to change with the renewal. This is referred to later in this guide as "Summary of Changes"
7. Depending on your changes, you may need to go into the protocol and edit the necessary sections where the changes are (i.e. project description, risk assessment, addendums, etc). If further changes must be made, click on the appropriate box.
8. Once all boxes have been appropriately checked and/or answered, click the "**Save Renewal**" button.

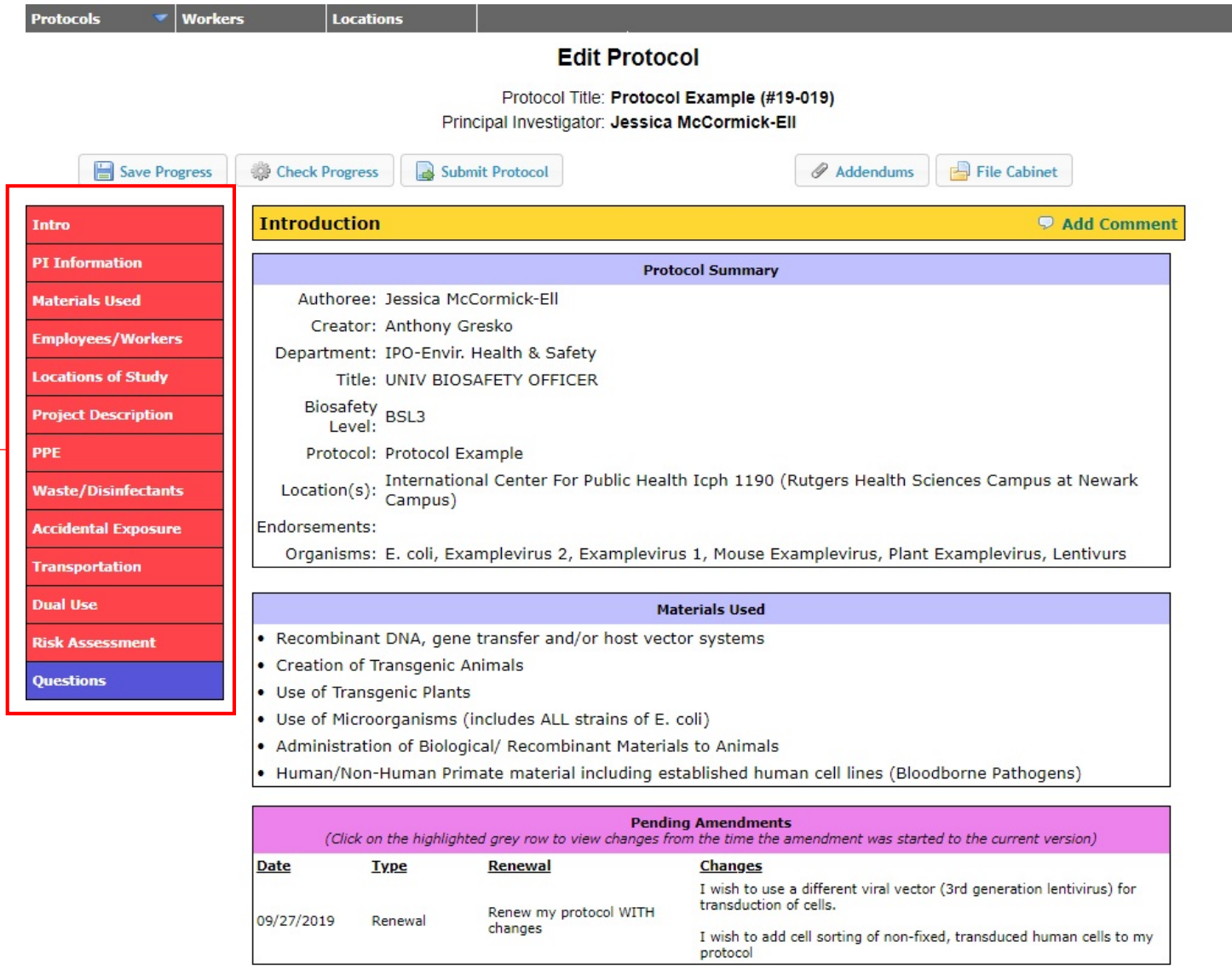


Renewing a Protocol

To renew a protocol:

9. Go into the Sections that need to be changed and make the necessary changes that you described in your "Summary of Changes" that was in Step 6. An example of making the changes is shown in step 10.

NOTE: You will ALWAYS need to update the Project Description and Risk Assessment sections.



Renewing a Protocol

To renew a protocol:

10. Example renewal/amendment: In the project description, describe the changes you wish to make to the protocol. *It helps to mark the date of these changes to distinguish when this part of your research was added to your protocol.

Pending Amendments

(Click on the highlighted grey row to view changes from the time the amendment was started to the current version)

Date	Type	Renewal	Changes
09/20/2019	Renewal	Renew my protocol WITH changes	I wish to use a different viral vector (3rd generation lentivirus) for transduction of cells. I wish to add cell sorting of non-fixed, transfected human cells to my protocol.

2. Provide a step by step "walk-through" of your research methodology. Be sure to explain how and why specific agents are used. If there is a connection between this IBC protocol, IRB, ESCRO and/ or IACUC be sure to describe the links.

neither of which are oncogenic or immunoregulatory in nature. Recombinant plants will be generated using CRISPR technology. Recombinant cell lines will be generated using RNAi and lentiviral systems. Both siRNA and miRNA will be used for transient gene knockdown.

Renewal/Amendment 9/20/2019
A lentivirus containing CRISPR gRNA library will infect both cell types (Cell A and Cell B) to achieve stably knock-out and knock-in cell lines. The lentivirus packaging system (3rd generation, acquired from this company (website)) is split into 4 total plasmids. One plasmid encodes Rev, one encodes Gag and Pol, one encodes the envelope protein (VSV-G), and the last plasmid encodes the shRNA or cDNA for Cas9. This 4 plasmid system is replication incompetent and having 4 separate plasmids further decreases the possibility of recombination and creation of replication competent particles. Also, the 5' LTR region of the transfer plasmid contains self-inactivation mutations to further decrease possibility of replication competent particle generation.

Cell Sorting will also be performed to sort for stable knock-outs and knock-ins from the lentiviral transduction. Additional information is found in Addendum I.

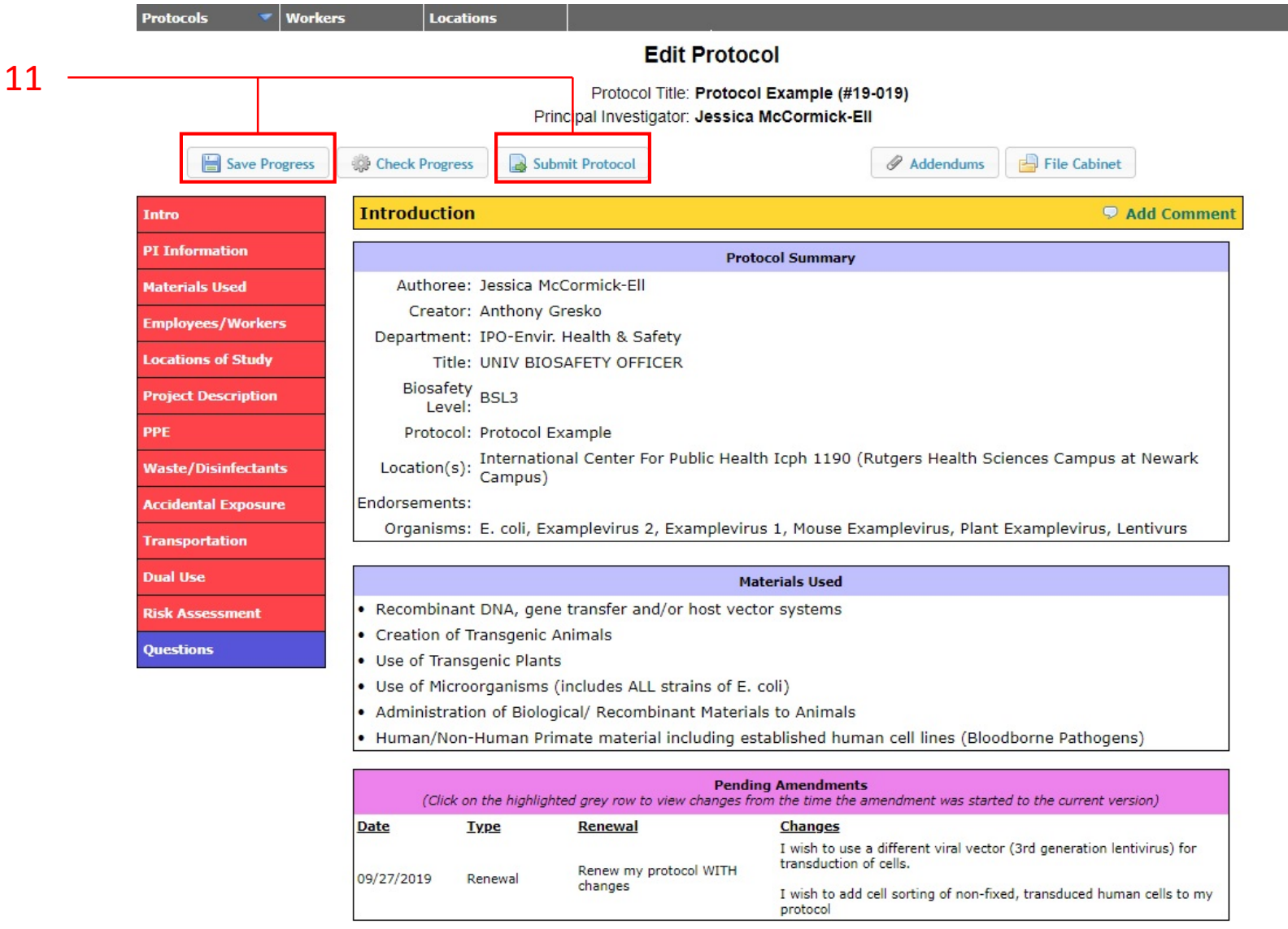
10

******* NOTE: For this example, in addition to describing the changes in the Project Description, Addendums A, A-1, and B must be updated for the use of the Lentivirus, as well as creating an Addendum I for cell sorting. The Risk Assessment section will need to be updated to reflect any change.**

Renewing a Protocol

To renew a protocol:

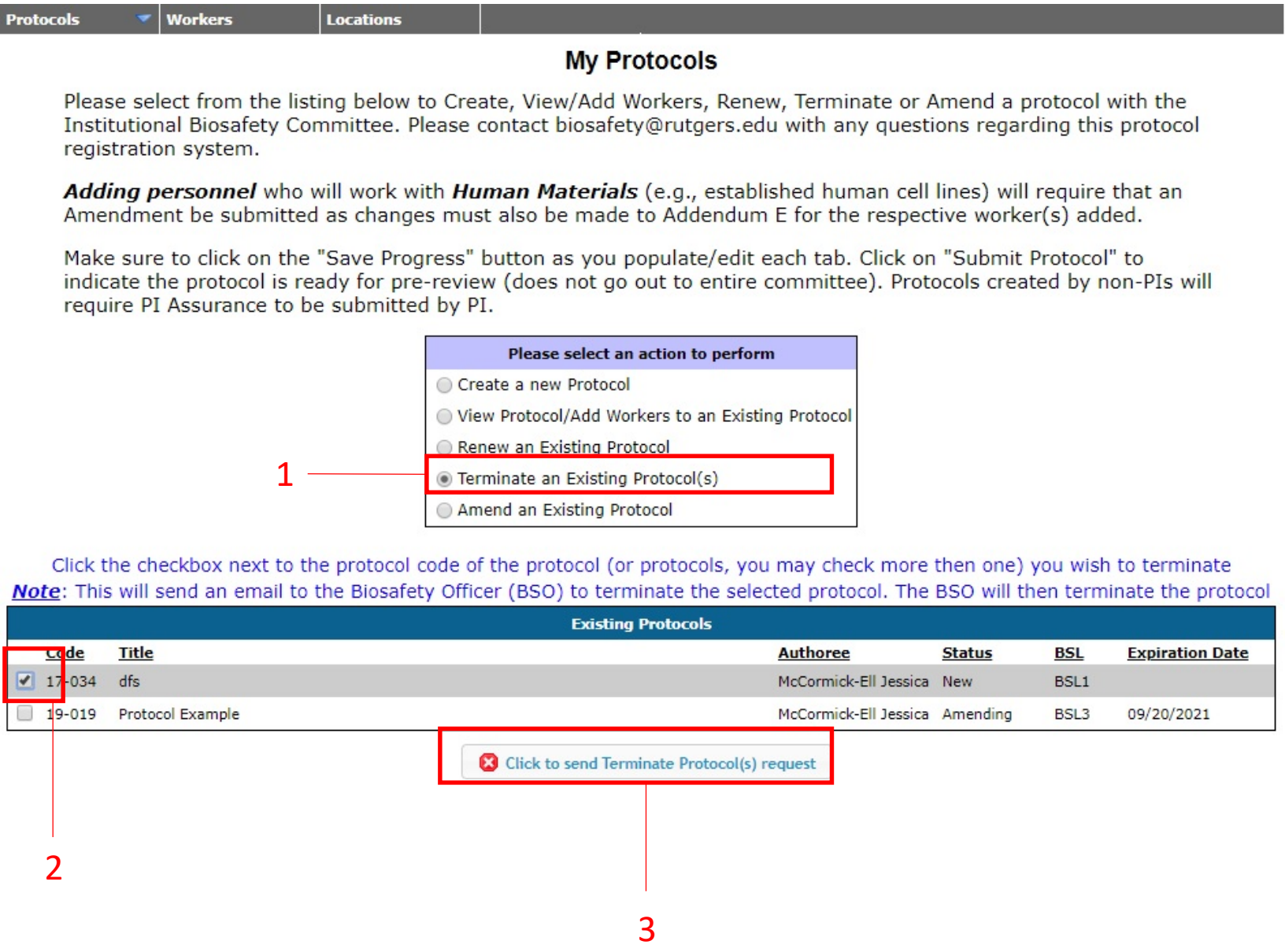
11. When finished editing ALL sections needed, click "**Save Progress**" and "**Submit Protocol**".



Terminating a Protocol

To terminate a protocol:

1. In "**My Protocols**", click on "**Terminate an Existing Protocol(s)"**
2. Click on the protocol that you wish to terminate.
3. Click on the "**Click to send Terminate Protocol(s) request"**" button



Terminating a Protocol

To terminate a protocol:

4. If you are certain you wish to terminate the protocol, click OK to confirm.