Tip Sheet for Completion of eIRB section 21 (Drugs)*

(* for new applications submitted or approved after the effective date of the DHHS Revised Common Rule in January 2019)

The purpose of this tip sheet is to provide instructions for study teams in completing the eIRB application, section 21. This tip sheet outlines each item in Section 21 and provides guidance on completion of each item.

Question 1: Will participants receive any drugs, substances, or biologicals that are specified by name and regimen in the protocol (FDA approved or investigational)?

- **Respond "Yes" when the research protocol requires the use of any drugs, substances, or biologicals specified in the protocol by name and regimen, i.e. they are "protocolized." This applies both to investigational products and to any products which would be administered as per standard of care.**
- **In thinking about what are "drugs, substances, or biologicals" for this purpose, it is helpful to consult the definition of a "drug" in the FD&C Act –**

    - **(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).**

  Put simply, if the product is to be of use in the research setting such that it falls into these broad categories and is protocolized as described above, you should respond "Yes" to this question and list the product(s) where appropriate in the subsequent items that appear.

- **Please Note: there is a new question in this section (Question 11), which will appear and asks: "Will any other products or drugs not specified by name or regimen in the protocol (e.g. rescue medications, pre-medications, others) be required for this study that have not been listed in a category above?" You should answer "Yes" to Question 1 if the study requires rescue medications or pre-medications even if not specified by name or regimen in the protocol.**

Question 2: Are any of the drugs, substances, or biologicals used in this study subject to a REMS?

- **Under the FDA Amendments Act of 2007, the FDA may issue a Risk Evaluation Strategy (REMS) for particular drugs to ensure that their benefits outweigh their risks. The FDA maintains a list of drugs subjects to a REMS and this list is linked in the text of Question 2. If you are uncertain whether products to be used in your research are subject to these requirements, you should consult with the list.**
- **When responding "Yes" to this question, you will be prompted to describe your plan for management in compliance with the product's REMS requirement.**
- **Generally, if your research involves the use of one of these products and you propose to deviate from the REMS requirements for prescribing and handling, you or your sponsor should submit an IND (Investigational New Drug) application to the FDA.**

Question 3: "Will any of the drugs, substances, or biologicals used in this study be prepared or manipulated by anyone outside of a JHM pharmacy after initial product manufacturing?"

- **When responding "Yes" to this question, you will be prompted to list the products in question and detail the facility(ies) at which the manipulation or preparation will occur.**

Question 4: "Select all facilities where the drug is stored, dispensed or manipulated. Please check all that apply."

- **Once selecting the applicable site(s) in this question, you will now be prompted to provide more specific details. For example, if drugs for your research will be dispensed at the Johns Hopkins Hospital, you will need to indicate at which of the hospital's various pharmacies the drugs will be stored, manipulated, or dispensed.**
- **Investigators should take care to select all applicable pharmacy sites. If selecting a non-Hopkins site or a Hopkins site not appearing among the options, you will be asked to describe the site(s). It is suggested in these cases that you also provide a brief explanation or justification for the IRB/P&T as to why the products will not be managed by one of the Johns Hopkins pharmacies.**

Question 5: "Are any of the drugs, substances, or biologicals used in this study classified as Controlled Substances (Schedule I-V per DEA)?"

- **Responding correctly to this question is important to the pharmacies involved with your research so that they can ensure they are meeting all legal and regulatory requirements for their management. Guidance from the DEA may be found here: https://www.dea.gov/drug-scheduling.**
- **Please be aware also that if your research will use a product classified by DEA as Schedule I, there are additional requirements you will need to meet in order to conduct the study, including approval by the DEA of your protocol after the IRB has granted approval. For questions concerning this process contact the OHSR and ask to speak with a member of the Compliance Team.**

Question 6: "FDA-approved product and formulation (e.g. a prescription drug or over the counter drug) used according to the FDA-approved indication (e.g. dosage, route of administration, population, etc.)"

- **Select this option as applicable. Create an individual entry for each product. When doing so, you will be prompted to provide the name of the manufacturer(s). If your study does not require the use of a study-specific supply of these products to be used "on-label" you may indicate "various" for the manufacturer if accurate.**
- **Be aware that this option applies to products marketed specifically as drugs in the United States. This option is not appropriate for other substances, e.g. dietary supplements, unless those substances also have concurrent marketing clearance from the FDA as drugs.**
- **When considering how to enter the name of a marketed product, use of the generic name is preferred unless the protocol specifically requires use of a specific trade name. For example, if ibuprofen will be administered, but the protocol specifically details that Motrin is to be used, then the trade name would be preferable to the generic. This is recommended because the product may have a formulation particular to that corresponding with the trade name that it may not for other generic versions. You may choose to consult with either Micromedex or Lexicomp, which may be accessed from Hopkins clinical workstations, if you have questions about generic products and naming convention.**

Question 7: "FDA-approved product and formulation (e.g. a prescription drug or over the counter drug) used for an indication that is not FDA-approved and an IND application WAS NOT submitted to the FDA. This section is intended to apply to use of products that could qualify for an IND exemption as determined by the IRB or have been determined to be exempt by the FDA."

- **Select this option as applicable for products marketed as drugs but which will be used "off-label" in your research for which you are not seeking an IND. You should list products here both when you are requesting an IND exemption determination from the IRB or when you or your sponsor have sought or will seek the exemption from the FDA.**
- **When creating an entry for a product, you will be prompted to name the product and the manufacturer and will be asked to confirm whether you or your sponsor have sought or will seek an IND exemption from the FDA. If you will be seeking an exemption determination from the IRB, respond "No" to sub-question 3 and make the confirmations concerning the IND exemption criteria in sub-question 5, which will appear.**
- **If an IND exemption from FDA has been sought or obtained, respond "Yes" to sub-question 3, and upload the formal documentation from FDA granting the exemption in sub-question 4, which will appear. If you will be seeking an IND exemption**

determination from the FDA you are strongly encouraged to do so prior to your submission of the eIRB application. If this documentation is pending at the time of your submission to the IRB, you may submit your application, though the IRB will be unable to approve until it has been provided.

Question 8: "FDA-approved product and formulation (e.g. a prescription drug or over the counter drug) used for an indication that is not FDA-approved and an IND from the FDA is required."

- **Select this option as applicable for products to be used "off-label" in the research pursuant to an IND issued by FDA. Typically this will be implicated if a pharmaceutical company will be seeking a new indication for product labeling from the FDA, or the use of the product in the research does not otherwise meet all requirements for IND exemption (e.g. its use in the study will involve a route of administration, dosage level, use in a patient population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) of its use).**
- **Once you have created an entry for a product, you will need to respond to several drill-down sub-questions, primarily focused on documentation of the IND number and provision of product information for consideration by the IRB/P&T Representative.**
- **With respect to sub-questions 8 and 9, please be aware that if the Hopkins PI or other Hopkins staff will be the sponsor-investigator of the IND, formal documentation of the IND issued by the FDA is required and you should select "Written communication from FDA documenting IND number has been uploaded" in sub-question 8 and upload in sub-question 9.**
    - **If you will be seeking an IND from the FDA you are strongly encouraged to do so prior to your submission of the eIRB application. If IND issuance is pending at the time of submission, you may submit your application to the IRB, though the IRB will be unable to approve until this is provided.**
    - **If the FDA in its issuance documentation has provided comments of either a clinical hold or non-clinical hold variety, please upload any subsequent correspondence in sub-question 9, including any responses to FDA or any subsequent correspondence from FDA conveying that its concerns have been sufficiently addressed.**
    - **The FDA permits the conduct of multiple research protocols under a single IND. If the Hopkins PI or other Hopkins staff is the sponsor-investigator of the IND and the protocol being submitted is an amendment to an existing IND, please consult the following guidance from FDA: https://www.fda.gov/drugs/investigational-new-drug-ind-application/ind-application-reporting-protocol-amendments. The FDA will not typically issue documentation demonstrating that it has accepted a new protocol under an existing IND. For such studies, you should upload the following:**

        - **The original IND issuance documentation from FDA; and,**
        - **The complete submission packet for the IND amendment, which includes the cover letter to FDA, the protocol submitted, and the completed FDA Forms 1571 and 1572.**
    - **In the rare cases for which the FDA has issued documentation of approval for a new protocol being added to an existing IND, please upload this documentation as well.**
- **With respect to sub-question 10, as all IND products to be listed in this question have marketing clearance for some purpose, they may or may not be accompanied by an Investigator's Brochure. If not, you should upload the product's most recent package insert.**
- **With respect to sub-questions 12 and 13, the IRB/P&T Representative will typically require this documentation (FDA Forms 1571 and 1572) only if the Hopkins PI or other Hopkins staff will be the sponsor-investigator of the IND.**
- **All IND products require the submission of a completed Investigational Drug Data Sheet (IDDS) in sub-question 14 (excepting in certain cases radiotracers which will not be dispensed by a pharmacy). If you will be conducting the research at multiple Hopkins sites and drug will be dispensed from multiple pharmacies, then you must upload an IDDS specific to each site. For example, if drug will be dispensed from both a Johns Hopkins Hospital pharmacy and a Sibley Memorial Hospital pharmacy, you will need to complete and upload two IDDSs, one per site.**
- **With respect to sub-question 15, if you plan to charge participants/their insurers for the cost of the IND product, FDA approval may be required. Please consult the following FDA guidance if you intend to charge: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/charging-investigational-drugs-under-ind-questions-and-answers. If FDA approval to charge is required, upload documentation of its approval where prompted.**

Question 9: "Non-FDA-approved product or formulation (e.g. a dietary supplement, a nutraceutical, a cosmetic) and an IND application WAS NOT submitted to the FDA."

- **Select this option as applicable for products which will be used as drugs in the research (see FD&C Act definition above), but which will not require an IND. The instances for which you may select this option will be very limited. For example, if using an experimental radiotracer, the FDA permits an institutional Radioactive Drug Research Committee (RDRC) to approve its use in a research product as a substitute for an IND. Another example will be an exception detailed by FDA in its guidance for dietary supplements. If a dietary supplement without marketing approval as a drug will be used strictly to measure its effect on the structures and functions of the body, it will still be deemed a drug, but no IND will be required. If its use, on the other hand, would be to assess its therapeutic value, an IND would be required and this would not**

be the appropriate location for such products. See FDA guidances for reference: https://www.fda.gov/media/79386/download and https://www.fda.gov/drugs/science-research-drugs/radioactive-drug-research-committee-rdrc-program.

Question 10: "Non-FDA-approved product or formulation (e.g. an investigational new drug, a dietary supplement, a nutraceutical, a cosmetic) and an IND application WAS submitted to the FDA."

- **Guidance with respect to the selection of this item is essentially identical to that provided for question 8 above, the primary difference being that the products here have no marketing clearance in the United States for any indication. (The numbering of some of the latter drill-down sub-questions is slightly different however the content of the questions addresses the same issues).**

Question 11: "Will any other products or drugs not specified by name or regimen in the protocol (e.g. rescue medications, pre-medications, others) be required for this study that have not been listed in a category above?

- **As stated in the guidance for Question 1 above, you should answer "Yes" to Question 1 if the study requires rescue medications or pre-medications even if not specified by name or regimen in the protocol. You should then select the box next to Q. 11 and create an entry for each product as applicable.**