

## GUIDELINES REGARDING HUMAN SUBJECTS PROTECTION AND MICROBIOME RESEARCH

- A. Research involving the collection of samples (stool, skin swabs, etc.) derived from human subjects for specific studies always requires institutional review board (IRB) review. Depending on the research, the IRB may determine if full board review and approval, consent, and monitoring are needed or if the research may undergo expedited review or receive exemption from further IRB oversight. Exempt research may not require patient consent or subsequent IRB monitoring and review (<https://irb.duhs.duke.edu/forms/exemption-checklist>)
1. If samples are obtained by approaching the patient directly (e.g., research personnel give the patient a stool collection kit or swab their skin), approval, consent, and monitoring are required
    - a. Provided it is written into the protocol, subjects may be approached (e.g., over the phone) and give verbal consent over the phone (e.g., document by telephone note in Epic or alternative study log) or e-consent such as via RedCap (though the subject must have a way to ask questions of research staff). The subject can then be given a collection kit (e.g., by mail); the subject may collect the sample and bring it to an in-person visit, but the sample cannot be transferred until written consent is signed.
  2. If protected health information (**PHI**) is accessed (not just recorded) with the sample (<https://irb.duhs.duke.edu/node/4094>), approval, consent and/or HIPAA waiver, and monitoring may be required; this is likely situation specific and will benefit from IRB consultation.
    - a. For example, if there was a desire to use samples that tested positive for C. diff from the microbiology lab, IRB approval would be needed, but with a HIPAA waiver consent may be not be needed and the samples could be accessed provided no PHI is being recorded.
  3. If neither of the above (e.g. discarded samples are used such as stool in a bedside commode after it has been recorded by the nurse and before it is flushed or leftover stool in the microbiology lab after a specimen has been sent for clinical testing), then the research may be exempt. In this case, clinical data may be recorded at the time of collection (e.g. patient body mass index) but no PHI or study identifier that can be linked to PHI.
- B. Research with samples (stool, skin swabs, etc.) derived from human subjects from a biorepository always requires IRB review. However, because the biorepository manages the IRB approval, patient consent, sample collection, etc., a non-biorepository investigator (NB investigator) can use these samples without re-consenting patients (though in rare occasions, re-consent may be required for new uses that have not been included in the original biorepository consent). These “use” protocols are often exempt depending on access to PHI. Use protocols can be written to access existing (banked) specimens or also new specimens as they are added to the repository.
1. Biorepository staff may have access to PHI and biorepositories may prospectively collect patient data per biorepository protocol. NB investigators may ask biorepository staff for summary data even before submitting a “use” protocol to help determine if sufficient samples are available to answer a research question (i.e. if it is worth submitting a protocol); for example, if a NB investigator wanted to know how many stool samples were collected within 7 days prior to a bloodstream infection, biorepository staff could look up this number.
  2. Once the IRB has determined the “use” protocol is exempt, the third-party investigator may request biorepository staff to pull individual patient-level data, provided the data is deidentified, though a limited data set (e.g., treatment and sample dates) may be allowed. In this case, the biorepository staff are acting as an honest broker or firewall between the third-party investigator and subject information.
    - a. If biorepository staff were to also be on the NB investigator protocol, they would no longer be considered to be honest brokers. While this may be allowed, full IRB review may be required.
  3. In some research studies, the protocol and consent may allow “future use” of collected specimens. There are two options for this: (1) the specimens would become linked to a separate biorepository, or (2) the specific protocol would become a biorepository. In the former case, to use the specimens, proceed as above (and it is best to consent patients to both the research study and the biorepository, though if a biorepository is created later, re-consent to the new biorepository may not be needed). In the latter case, any future use would require an amendment of the original protocol as opposed to a separate “use” protocol. Often, this will not require re-consent of patients (provided they consented to future use), but this will require full IRB review.

- a. Exercise caution if language such as “samples cannot be shared outside the study” or “specifically for this study” are used

4. Requests from external investigators will be subject to institutional requirements for transfer.

C. Research involving the culturing or isolating of microbes from samples derived from human subjects (whether part of a specific study or from biorepository samples) always requires IRB review due to the interaction with human samples. However, if no PHI is included, this research will often be exempt following review. Examples of this would be taking a stool sample from an obese patient and culturing the microbes (e.g. in a petri dish) or performing a fecal transplant of human stool into a mouse.

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D. Research involving microbes already cultured or isolated and separate from human subjects is not considered human subjects research provided there is no PHI. In the above example, if an investigator wished to do further studies with the cultured microbes from the petri dish or the microbes in the stool of the mouse after fecal transplant, that would no longer be considered human subjects research and would not need IRB review. Associated clinical data (e.g. strain X cultured from this plate was originally obtained from an individual with obesity) is allowed provided there is no PHI. This is true whether with a single species or a community including multiple species.

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E. An investigator may close the IRB protocol provided all the following are met:

1. All samples are used or destroyed

2. All data analysis has been completed and results published with no further planned analyses or publications

Note that data should still be kept for 6 years after protocol closure before the data can be destroyed/deleted.