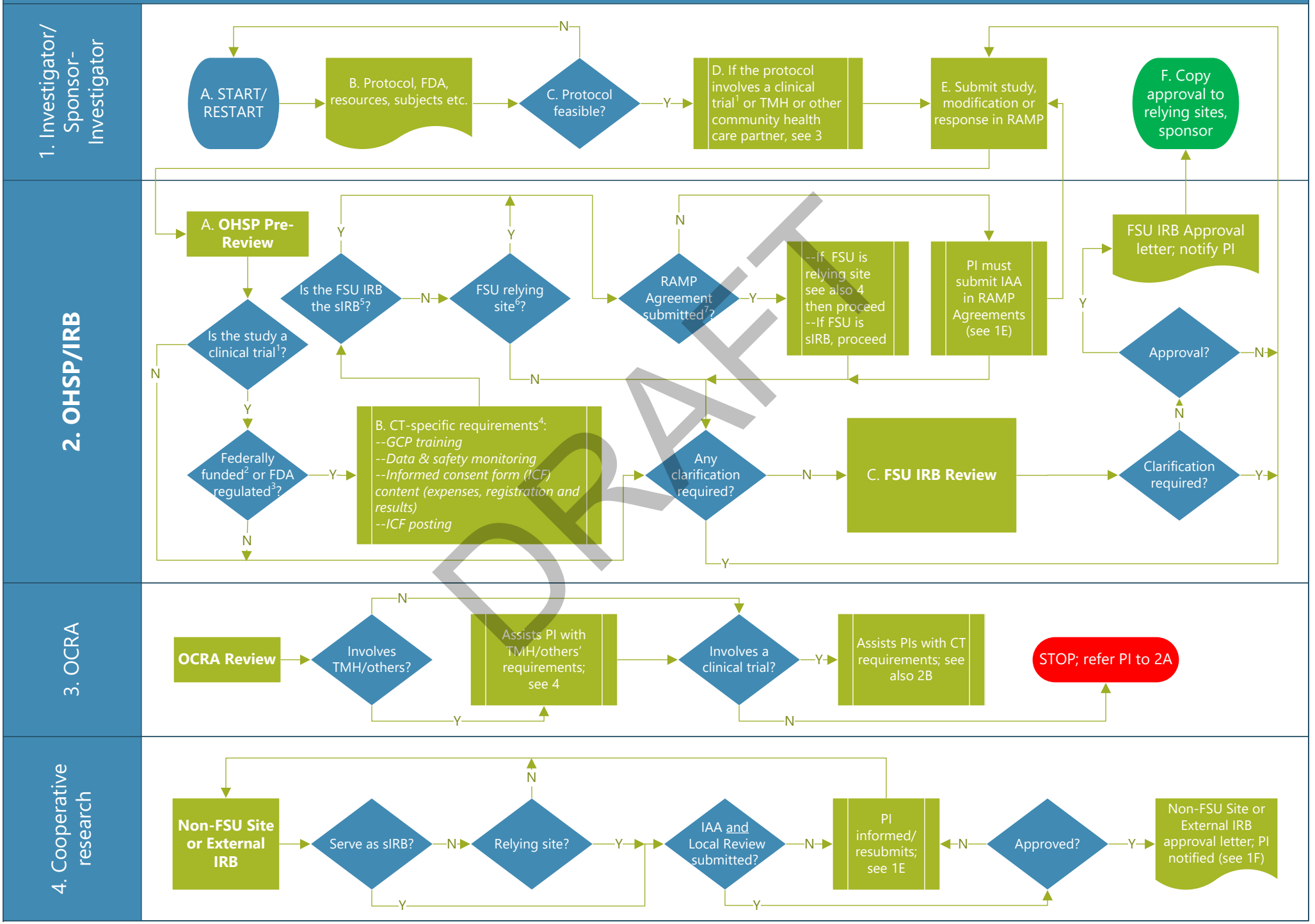
Clinical Trials ("CT")/Human Research Workflows* (April 25, 2022)



NOTES

*****This algorithm and related notes are intended to only illustrate and provide brief explanations about some select workflows, decision points and outcomes related to FSU OHSP/IRB human research review of studies involving clinical trials (see Note 1 below); not all workflows, decision points and outcomes that pertain to human research review are included. Other swim lanes are provided only as illustrations of other general processes outside of the OHSP/IRB regulatory purview that may be related to or interact with the OHSP/IRB human research review process. Other processes and specific requirements or steps may apply.

OHSP/IRB=The FSU Office for Human Subjects Protection/Institutional Review Board. The OHSP is a directorate of the FSU Office of Research. The IRB is an independent committee comprised of FSU faculty and staff as well as community members; the OHSP provides the IRB with professional, administrative and technical support.

OCRA=The FSU Office for Clinical Research Advancement. OCRA provides guidance, tools, resources and facilitation to help the FSU community navigate clinical and human subjects research at FSU and with its community healthcare partners.

1 ***Clinical trial*** means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes (Title 45 of the U.S. Code of Federal Regulations Part 46 (45 CFR 46) (U.S. Department of Health and Human Services), section 46.102(b), and analogous sections of other federal agencies' regulations for the protection of human subjects).

Under U.S. Food and Drug Administration (FDA) regulations, a ***Clinical trial*** means a clinical investigation or a clinical study in which human subject(s) are prospectively assigned, according to a protocol, to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on biomedical or health-related outcomes (42 CFR 11, section 11.10(a)).

To find any citation included in these Notes, see https://www.ecfr.gov/ and search for the referenced Title and sections. While the eCFR is not an official edition of the U.S. Code of Federal Regulations, the eCFR is a U.S. government online resource that provides more timely versions and ease of use.

2 ***Federally funded*** means that a U.S. federal agency conducts or supports, in whole or in part, the clinical trial. Support may include grants, contracts and cooperative or other agreements issued to a research organization or academic health science center to cover researchers' time and effort as well as clinical trial-related expenses. Federal agencies that support clinical trials includes for example a National Institutes of Health (NIH)'s Center or Institute; the U.S. Centers for Disease Control and Prevention (CDC); the Department of Defense (DoD)'s Congressionally Directed Medical Research Program (CDMRP); the Substance Abuse and Mental Health Services Administration (SAMHSA); and the Veterans Administration.

3 ***FDA regulated*** means that a product or article used in a clinical trial is subject to FDA regulations or related guidance [link]. Products or articles may include drugs, biologics, devices, diagnostics (e.g., IVDs), and in some cases dietary supplements and food additives; these may be subject to FDA approval, clearance or registration, or may be exempt from these requirements provided that certain FDA regulatory conditions are satisfied. The sponsor or sponsor-investigator of

any clinical trial involving a FDA regulated product or article is responsible for obtaining the documentation necessary to ascertain the product or article's FDA regulatory status, and making the documentation available to the IRB for review.

[4] **CT-specific Requirements.** Along with the usual human subjects protection-related requirements that apply as a condition of IRB approval, a number of other requirements apply specifically to clinical trials. If these requirements are not satisfied, the clinical trial study submission will be returned to the study team. The clinical trial specific requirements are:

a. Good Clinical Practice (GCP) training, available through the FSU CITI program of courses and training, must be completed and current. To access the training, visit the OHSP CITI Training Requirements page [link or https://www.research.fsu.edu/research-offices/ohsp/investigator-resources/citi-training-requirements/]
b. The study protocol must be based upon the current FSU-approved protocol template for clinical research studies: HRP-503 Template Protocol [external link or available in the RAMP IRB templates], and requires completion of section 18 of the protocol ("Provisions to Monitor the Data to Ensure the Safety of Subjects), to include implementing a data and safety monitoring plan and an appropriate data and safety monitoring board or committee. Board or committee members must be identified by name, credential/license and institutional affiliation, and members may not have a conflict of interest in the clinical trial. For related policy, guidance and examples of what data and safety monitoring should include, visit this NIH Data and Safety Monitoring web page [link or https://grants.nih.gov/policy/humansubjects/policies-and-regulations/data-safety.htm]. Keep in mind that a study's sponsor may have different or more specific data and safety monitoring requirements, and section 18 must be consistent with these requirements.
c. The Informed consent form (ICF) must be based upon the current FSU-approved consent form template for clinical research studies: HRP-502 Template Consent Document [external link or available in the RAMP IRB templates]. Pay particular attention to any section pertaining to clinical trials. Keep in mind that a study's sponsor or the non-FSU IRB which may serve as the reviewing or Single IRB may have different ICF requirements. Additionally, the ICF must include other specific content in addition to that which is usually required of ICFs. The required specific content is as follows:
    i. Costs. A description of ANY costs for which study participants may be responsible, such as any deductibles or co-payments that participants may be required to pay if their insurance will be charged for clinical trial-related procedures, services or items; any charge to participants' insurance for a clinical trial related procedure, service or item; any clinical trial-related out-of-pocket expenses for which participants may be responsible; and any expenses and treatment arrangements made for study participants' research-related injuries. If study participants may be responsible for such costs, then the description must be accompanied by a statement to the effect that such costs will be the participant's responsibility. Also, if clinical care that is not part of the clinical trial may occur at the same time as a research procedure, then the description must be accompanied by a statement to the effect that such clinical care will be participant's responsibility. Any description about how costs will be covered must be consistent with the applicable clinical trial or other agreement(s).
    ii. FDA-required statement.
        A. If the study is deemed an *Applicable Clinical Trial* (ACT) in accordance with FDA regulations regarding registering the clinical trial and providing study-related results, the following verbatim statement must be included: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

B. This legally required FDA statement is important, for which the failure to include in an ICF will be considered by the FDA as non-compliance. Check first with the FSU Office for Clinical Research Advancement (OCRA) [link], which office may provide study teams with assistance with these requirements. Neither the OHSP nor IRB is the FSU proponent office regarding this ClinicalTrials.gov requirement.

C. For the definition of an *Applicable Clinical Trial*, refer to this U.S. Federal Register web page [link]; to learn more about what clinical trials must be registered and their descriptions and results made available at the ClinicalTrials.gov web site, visit this ClinicalTrials.gov web page [link].

d. Informed consent form (ICF) Posting.

i. Federal law requires that for any federally funded clinical trial, that the IRB-approved ICF that is used to enroll study participants be posted by the PI/grantee on a publicly available Federal Web site (e.g., ClinicalTrials.gov), which site is established as a repository for such informed consent forms. The ICF must be posted after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any study participant, as provided by the study protocol (45 CFR 46, section 46.116(h)).

ii. FSU IRB approval letters for studies that involve clinical trials include the following template language to remind study teams of this requirement:

A. *Please note that the approved IRB consent form must be posted to a publicly available Federal web site by an awardee of federal department or agency funding and for any study that is an applicable clinical trial under FDA regulations. The consent must be posted after the research has been closed to recruitment and no later than 60 days after the last study visit of any subject. Visit this FSU Office for Clinical Research Advancement (OCRA) page and related procedure for additional and OCRA contact information as well as specific instructions*.

[5] A ***sIRB,*** or Single IRB, is the IRB that serves as the reviewing IRB of record for multiple sites that are involved in cooperative research (i.e., a research project that involves more than one institution). The sIRB may be an IRB that is internal to one of the cooperative research institutions, or may be an IRB that is independent of the institutions. Institutions in the U.S. that are involved in cooperative research are required by law to rely upon a single IRB for approval for that portion of the cooperative research that is conducted in the U.S. An sIRB may be identified by the federal department or agency that is funding the research, or proposed by the lead research institution (subject to acceptance by the department or agency) (45 CFR 46, section 46.114). The lead research institution should identify the proposed sIRB at the time of application for federal funding. The FSU IRB may serve as the designated sIRB for cooperative research pursuant to a written agreement (IRB Authorization Agreement, or IAA, sometimes referred to as a reliance agreement) between FSU and the sites relying upon the FSU IRB; however, the FSU IRB must decline to serve as the sIRB if in accordance with federal law the FSU IRB lacks the requisite knowledge, experience and expertise to conduct the review (45 CFR 46, sections 46.103(e), 46.107).

[6] A **relying site** is an institution involved in cooperative research that relies upon another IRB for approval of the cooperative research. Designation of FSU as a relying site should be made at the time of application, or afterwards when a sIRB that is not the FSU IRB is identified or designated. In all cases, such reliance requires a written agreement (IRB Authorization Agreement, or IAA, sometimes referred to as a reliance agreement) between the relying sites and the institution or organization with the IRB (45 CFR 46. Section 103(e)). For FSU studies that may not involve cooperative research, FSU may nonetheless rely upon another IRB for approval of the research when the FSU IRB lacks the requisite knowledge, experience and expertise to conduct the review (45 CFR 46, sections 46.103(e)).

[7] Whether the FSU IRB serves as the sIRB for cooperative research, is designated as the reviewing IRB of record for any FSU study involving other institutions, or relies upon another institution or organization's IRB for review of research involving FSU, the FSU study team must submit an IAA or reliance agreement in the FSU **RAMP Agreements** module for review and approval before a study that is subject to FSU IRB review (where the FSU IRB serves as the sIRB) or subject to another IRB's review (where FSU is a relying institution) may begin. If the former, local context information (e.g., local informed consent-related materials; study team's human subjects and GCP training documentation; communication procedures) and the IAA indicating relying sites' agreement to rely upon the FSU IRB must be provided by the relying sites to FSU for approval; if the latter, the FSU study team should provide local context information to the reviewing IRB as well as submit the reviewing IRB's IAA or reliance agreement for FSU approval.

(Revised April 24, 2022)