

What is the NIH Federalwide Assurance (FWA) and how does this relate to multi-site research conducted by the NIH Intramural Research Program (IRP)?

This guidance is to help investigators of the NIH IRP gain a better understanding of what an FWA is, which researchers the NIH considers to be covered under the NIH FWA, and the distinctions between FWA coverage and reliance agreements.

### Federalwide Assurance

A Federalwide Assurance (FWA) is a written commitment by an institution to comply with the federal regulations that relate to the protection of human subjects under 45 CFR 46. The FWA is filed with the Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) and is approved for all human subjects research (HSR) conducted or supported by HHS. For extramural institutions, not all research may fall within the scope of the FWA, as some research may not be supported by federal funds. However, since NIH is an agency within HHS, all HSR conducted by the NIH IRP falls within the scope of our FWA and therefore must be conducted in accordance with this commitment.

Institutions have the authority to determine, through the setting of institutional policy, which investigators conducting human subjects research are considered “covered” under their FWA. Being “covered” under the FWA means that investigators are acting on behalf of the institution that holds the FWA, and that the institution is responsible for the actions of those investigators who are conducting HSR. Institutions typically limit this to their employees, as it is the employer/employee relationship that provides the mechanism for accountability and oversight. Institutions may choose to “extend” their FWA coverage to non-employees if they so desire, but there is no legal obligation to do so.

How the NIH determines who is and is not covered under the NIH FWA is discussed below. Importantly, investigators do not have the authority to determine who is covered under the NIH FWA. That determination can only be made by the Institutional Official, or his or her designee.

Before addressing more about FWA coverage, it is important to understand what is meant when we refer to conducting research that involves human subjects. An investigator is conducting human subjects research if he or she does the following:

- Obtains information or biospecimens through intervention or interaction with the research subject, and uses, studies, or analyzes the information or biospecimens;
- OR
- Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens;

OR

- Obtains the informed consent from a prospective research subject.

If an investigator is conducting human subjects research, as defined above, then that investigator's activities "engage" their institution in human subjects research. Further, by regulation, if the research is either conducted or supported by the federal government, the institution must hold an FWA. Therefore, as a federal agency, NIH must hold an FWA. In addition, NIH may only collaborate on research with other FWA-holding institutions, whether those institutions are domestic or international. In limited circumstances, the NIH may choose to extend its FWA to cover the activities of individual investigators or small private practices that do not hold an FWA, if it is in the interests of the NIH to do so.

### The NIH FWA

By the policy of the NIH IRP, only the following individuals are covered under the NIH FWA:

1. NIH investigators are covered with no additional agreement. This includes NIH federal employees (intramural or extramural), NIH Special Volunteers and Intramural Research and Cancer Research Training Awardees<sup>1</sup>.
2. Unless otherwise specified by the terms of the contract, NIH contractors are only covered by the NIH FWA without an additional written agreement, if:
  - a. The contractor is working at an NIH site (e.g., at the NIH Clinical Center or at NIDA in Baltimore) with an NIH federal employee; or
  - b. It has been determined by the OHSRP Director or designee, in writing, that the contractor's activities are covered by the NIH FWA.
3. All other investigators (e.g., external collaborators, Guest Researchers, rotating fellows and rotating students) conducting human subjects research, who are not

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<sup>1</sup> Note: Trainees such as IRTA/CRTAs and [Visiting Fellows](#) have additional restrictions on the research activities that they are permitted to conduct based on other NIH policies. Per the [manual chapter](#), Non-FTE trainees are prohibited from having any patient/human subject contact unless they are entirely under the direct supervision at all times by an appropriately clinically credentialed NIH employee (must be an FTE). Thus, unless there is a Clinical Fellow, Staff Clinician or above with the trainee at all times, this is not allowed. These restrictions are based upon the Office of Intramural Research (OIR) policies and legal considerations, such as the applicability of the Federal Tort Claims Act. For additional information on this, please contact Dr. Arlyn Garcia-Perez, Director of Policy and Analysis, OIR, OD.

described above, are not covered under the NIH FWA unless through a written agreement. (For more information See NIH Policy Manual Chapters [2300-308-1 - Guest Researcher/Special Volunteer Programs](#); [2300-320-7 - Intramural Research Training Award \(IRTA\) Program Automated Fellowship Payment System](#) and NIH HRPP Policy 100, *NIH Intramural Research Program's Human Research Protection Program*.)

Only the Institutional Official, or designee, is authorized to determine who is covered under the NIH FWA or to execute an agreement to extend the NIH FWA to those who are not automatically covered.

The NIH FWA, Reliance Agreements and mandates for Single IRB review for Multi-Site Research

The concepts of FWA coverage and reliance agreements are often confused. FWAs are the commitments made by institutions to the federal government to follow the human subjects protection regulations (45 CFR 46). Reliance Agreements are legal agreements between two or more FWA holding institutions that give permission for the IRB of one institution (or a commercial, independent IRB) to review the research activities being conducted by investigators at a different institution(s).

Prior to implementation of the [NIH Single IRB \(sIRB\) policy](#), multi-site protocols for which different sites were conducting HSR on the same protocol were permitted to use different IRBs. Since the effective date of the NIH sIRB policy (January 25, 2018), review by a single IRB is required (there are some [exceptions](#), e.g., when such a requirement is prohibited by tribal law). (For more information, see the NIH sIRB [guidance webpage](#).) The [revised Common Rule](#) also requires single IRB review for cooperative (multi-site) research projects that are subject to the revised rule but only for the portion of the research taking place within the US.

To comply with the sIRB requirements, in many instances, institutions must cede IRB review to an IRB that is not part of their own institution. This necessitates the execution of a reliance agreement between the institution(s) that is ceding IRB review, and the institution that is providing the IRB review. A reliance agreement does not place the other institution's researchers under the FWA of the reviewing IRB's institution. It merely spells out the terms and conditions for research conducted by institution "A" to be reviewed by IRB "B". Each investigator remains under their home institution's FWA, and their home institution remains obligated to fulfil the terms of their FWA as it relates to the research covered by the agreement.

For multi-site research being conducted by the NIH IRP, the Office of Human Subjects Research Protections (OHSRP) will determine if a multi-site research protocol is subject to the requirement for a single IRB. If it is, OHSRP will work with the investigator to execute the needed reliance agreement(s) or seek an exception to the NIH sIRB policy. Whether or not the

NIH will serve as the reviewing IRB for multi-site research is determined by the OHSRP Director, and only the DDIR or designee, (usually the OHSRP Director) is authorized to execute a reliance agreement. Investigators may not sign any reliance agreements. Furthermore, research may not commence at a site until the necessary agreements and IRB approval are in place.

**Example Scenarios:**

- A. *A researcher with the NCI intramural program wishes to conduct a single site, phase 1 trial to determine the safety and efficacy of a new investigational drug for the treatment of metastatic prostate cancer. All subjects will be enrolled at the NIH Clinical Center (CC), and all research activities will occur at the CC. All investigators and staff working on the project are full time NIH federal employees.*

Are any agreements needed?

**No.** All NIH investigators are covered under the NIH FWA. As it is a single site study, no reliance agreements are needed.

- B. *The study is recruiting lots of subjects, and the Principal Investigator (PI) needs to hire a new research coordinator. The PI does not have any FTE slots available, so she hires a contractor. The contractor will start tomorrow. The new staff member's work will occur entirely at the CC under the direction of the PI.*

Are any agreements needed?

**No.** The contractor is covered under the NIH FWA without additional agreement, unless this is contrary to the terms of the contract. The new research coordinator only needs to complete the required HSR training and be added to the protocol via an amendment before the research coordinator can begin work on the study.

- C. *Recruitment has slowed down, and the PI wishes to reach into the community to identify more potential subjects. She decides to engage contractors that work for a private firm to go to community events to identify people that may be eligible. The contractors will provide study information, have the potential subject sign a consent document, then collect screening health information and a blood sample that will be used to determine eligibility.*

Are any agreements needed?

**Yes:** As described above, the contracting firm is “engaged” because the outside contractors are conducting human subjects research. These contractors would not be covered by the NIH FWA, because they are not conducting research at an NIH site, under the supervision of an NIH employee. For the researcher to use this contracting

firm, the firm would need to have filed its own FWA with OHRP.<sup>2</sup> In addition, the activities of these contractors would need to be overseen by an IRB. Since the contracting firm is not part of NIH, the NIH IRB would not automatically be the reviewing IRB for their work. The PI should request that NIH enter into a reliance agreement with the firm, so that the NIH IRB can serve as the reviewing IRB.

- D. The phase 1 study was successful, and the PI now wishes to conduct a phase 2 study, enrolling 300 participants. To meet the enrollment goal, the PI wishes to make this a multi-site project with Johns Hopkins (JHU) and Medstar Washington Hospital Center (MWHC) as collaborating sites.*

Are any agreements needed?

**Yes:** This is now multi-site research and is subject to the requirement for a single IRB, both by NIH policy and under 45 CFR 46. As well established academic medical centers, both JHU and MWHC have already filed an FWA with OHRP. Before research can commence, the investigators will need to determine which IRB will be the reviewing IRB for the study, and reliance agreements will need to be executed to finalize the arrangement. The investigator should contact OHSRP early in the planning stage, to seek guidance and to give OHSRP the time to determine if NIH can serve as the reviewing IRB and to execute any necessary agreements.

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<sup>2</sup> By contracting regulation, the contract with the NIH should already include the HHSAR clause Subpart 370.3 (which requires proof of an active FWA). For more information, check with your COR or Contracting Officer.