

Many academics are familiar with grant requirements. However, working outside the academic arena can alter the complexity and perception of the federal demands. Non-academics will need familiarity with some basics. For everyone, some basic facts are critical.

1. Institutions get grants – people don't.

Large academic medical center or 2-person corporation, funding is still directed to the company. An institution is “any public or private entity or agency (including Federal, State or other agencies).

2. Institutions give assurances to agencies – IRBs and investigators don't.

45 CFR 46. is the DHHS policy on protection of human subjects (It's FDA counterpart is 21 CFR 56.) Section .103 describes the assurance process and requirements. The opening sentence says,

“Each institution engaged in research which is covered by this policy and which is conducted or supported by a federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy.”

An FWA is granted for 3 years.

3. IRBs are registered – Institutions are not.

An FWA lists the registered IRBs with which the institution chooses to associate. An institution may designate one or multiple IRBs. Registered IRBs are listed on the OHRP website. **IRC's OHRP Registration number is IRB00000762.**

4. Institutional officials signing the assurance are making promises.

The “Terms of Assurance” describe the promises made. The central promises include development of and adherence to an institutional policy regarding protection of human subjects, a monitoring plan and a training plan. The IRB should be integrated into the larger institutional plan.

5. FWA applications and IRB applications are totally separate.

An FWA is a high-level administrative agreement. IRB approval is between an investigator and the IRB. Each relationship is independent and may be initiated at any time.

6. This simple system can be highly complex.

At this site we have only discussed the basics of the FWA. The nuances and information about more complicated relationships are on the OHRP web site

There are many documents on the OHRP website.

SEE PAGE 2 for OHRP SITES

SEE PAGES 3-7 for more detail

There are many documents on the OHRP website to explain Assurances and to provide other information.

The OHRP website also contains their training modules for institutional officers and human subjects administrators.

TOPIC	WEBSITE
OHRP site	http://www.hhs.gov/ohrp/
Assurance area	http://www.hhs.gov/ohrp/assurances/assurances_index.html
Terms of Assurance	http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm
FWA template (OHRP)	http://www.hhs.gov/ohrp/assurances/assurances_index.html#domestic
OHRP training modules	http://www.hhs.gov/ohrp/education/ (Recommendation: Print out all the documents, put them in a binder available to the people taking the course – and as a later reference book.)
45 CFR 45 (The Common Rule)	http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm



NOTE: Many independent IRBs do not work with federally funded clients because doing so is often a financial loss! The primary reason is that a large investment of unpaid consulting time is often required both for the FWA stage and the IRB review. Please read this and other guidance found on our web site.

A. GENERAL PREMISE *An assurance is a promise.*

An FWA (Federal Wide Assurance) contains several promises given by an institutional officer on behalf of the institution and made to the federal funding agency.

False statements in an assurance – including failure to follow institutional policy after assuring that it will be followed -- can be cause for:

- ⇒ **administrative action invalidating the Assurance.**
- ⇒ **Invalidation can result in the need to halt all (or all federally funded) research under this assurance, and**
- ⇒ **legal action.**

The Office of Human Research Protections (OHRP) within the office of the Secretary of the Department of Health and Human Services (DHHS) has established the standards for FWAs.

The rules apply to institutions that are “engaged in” non-exempt human subjects research. See OHRP guidance for the Terms of Engagement.

B. THE ENTITIES AND PERSONNEL INVOLVED

1. Institution:
Federal agencies give money to institutions and not to people. The assurance is from the institution.
2. Agency:
The funding agency is one of the federal agencies agreeing to accept the Federal Wide Assurance.
3. Office of Human Research Protections (OHRP)
The office within DHHS that administers the DHHS policies regarding protection of subjects is OHRP. This is the same office previously known as OPRR.
4. Institutional Official (I.O.)
A person very highly placed within the institution who has the authority to make a binding promise on behalf of the institution and to make institutional policy. (Responsibility for component parts of the policy may be delegated.)
5. Human Research Administrator (HRA)
The person with the responsibility to administer the program of protection. This may be the same person as the Institutional Official.

6. Institutional Review Board (IRB)
A committee designated to review research on behalf of the institution. The *sole* mission of the IRB is to consider protection of the human subject prospectively and on an on-going basis.
7. Investigator
The investigator is not named on the FWA. The institution is responsible for the investigator and the conduct of research in the institution. Although the investigator is responsible to the institution, his or her first concern must be for the safety, rights, and welfare of the study participants.

C. THE PROMISES REQUIRED

The assurance statement requires a number of promises to be made on behalf of the institution. The assurance is completely unrelated to any single specific grant or protocol; it represents over-arching institutional policy.

Assurances for very small institutions are generally very simple and name only one IRB and no other components. Assurances can, however, become very large and complicated. For instance, an institution with multiple cooperative research grants might work with a multitude of IRBs and even more component institutions. This document *does not address* the possible relationships established within an FWA.

1. Institutional Policies:
The institution must have a policy on how it will assure the protection of subjects. This institutional policy should include – but not be limited to – a statement of commitment, lines of authority, establishment of the IRB, monitoring, accountability and training.

Institutional policies should be clear about which IRB(s) its investigators are permitted to use. If the institution names IRC as its only IRB, then that is the only permissible IRB to use. The institution has the option of naming multiple IRBs.
2. Ethical Codes:
The institution must adopt one or more codes of conduct. As some codes conflict with others, and some codes are inappropriate for some types of research, an institution should be careful in their selection. All IRC clients will, at a minimum, adopt the use of the Belmont Report.
3. Regulatory standards (domestic):
The institution must adopt a set of federal rules to be followed. If DHHS money is involved, the institution must adopt 45 CFR 46 (The Common Rule) and its three subparts regarding specified vulnerable populations.

Agencies other than DHHS require compliance with their regulations.

The institution must also decide whether it will apply these rules only to federally funded studies or to all studies within the institution. This is an institutional preference; to do so establishes one consistent standard throughout the institution, not to do so allows greater flexibility.
4. Regulatory standards (international)
A number of national and international standards are listed in the OHRP document; the institution should promise adherence to the appropriate one(s).
5. Monitoring:
This part of the institutional policy involves two questions: how does the institution assure review of all regulated research and how does it assure that approved research is conducted

appropriately? The institution must adopt a policy appropriate to its needs. The assurance statement requires a statement about whether or not there is such a policy.

6. Education:

There are two levels of training addressed in the assurances.

- (a) The institutional officer and HRA must have had training regarding their roles and responsibilities. This is *not* training in the ethics and conduct of research; it is about institutional roles and responsibilities. The training modules on the OHRP website are required. OHRP has published a few courses that can substitute.
- (b) Education and training regarding the ethical and responsible conduct of research is necessary for protection of subjects. The institutional policy must address the categories of people who must receive basic education about protection of subjects. The categories found in the “Responsible Conduct of Research” (RCR) are considered fairly basic. The tenets of Good Clinical Practice are an excellent start to RCR training but are not sufficient.

7. Institutional Interactions:

There are a multitude of ways in which institutions collaborate; they can use each others IRB, can be responsible for other institutional components and can share responsibilities. An assurance can be used to document such relationships. OHRP has alternative forms on its website.

D. REGISTRATION OF IRBs

Registration of an IRB is not required unless the IRB is named in an assurance. Any IRB may elect to be registered. In order to register, the IRB roster must be submitted and updated as necessary. The IRB chair and the person responsible for the IRB must complete the OHRP Training Modules.

IRC is a corporation. IRC supports a registered IRB. IRC does no research and receives no federal funding; thus it is not required to have an FWA. **Our IRB’s registration number is IRB00000762.**

E. IRC AND OUR INVOLVEMENT IN YOUR FWA

Relationship and Process



1. Client:

IRC (the business entity) has a business relationship with a client (another business). Clients range from small professional corporations to large pharmaceutical companies. IRC clients are assigned a client number when a relationship between business entities has been established.

The client file should contain

- Indemnification agreement
- Evidence of means to provide indemnification (e.g., insurance)
- Information about the client’s business

2. Client Seeking an FWA:

Institutions receiving federal funding must seek an FWA. The FWA will name IRC’s IRB as the IRB of record. An FWA is general; it allows submission of multiple grants and conduct of multiple studies. In signing an FWA naming IRC, the client institution is promising to treat the IRC IRB as if it were its’ in-house IRB; to have it review all studies from that institution.

To sign or to be listed on an FWA, IRC needs to have:

- the client number (see above)
- A completed IRC FWA application Form (Form 4.53)

Conditions: the client must notify IRC of

- the outcome of the OHRP submission
- any changes in the I.O. or the HRA
- any serious and related adverse events

On an annual basis IRC will require an update of the information plus a list of all studies and approvals under that FWA.

Multiple IRBs can be named in one FWA.

If the Client seeks to rely on an existing IRB it must do two things:

- amend its FWA to list the additional IRB
- have an Institutional Affiliation Agreement signed by both institutions or its IRB.

3. Grant Application from an Investigator Associated with a Client with an FWA:

An FWA allows submission of multiple grant applications. Grant applications are not likely to be sufficient alone.

Content: The grant application is a justification of value, need, and ability but it often does not contain the wealth of information necessary to make an IRB decision. When the IRB reviews a grant application it is rarely sufficient for approval. For instance, it often does not specify recruitment processes, logistics and training of staff. See below for the protocol information.

Timing: Most grant applications must be submitted to the agency far in advance of funding. Most agencies require IRB approval prior to consideration of the grant. This means grants are IRB reviewed before funding is assured – an expense for a non-academic applicant.

Review: Grant applications will be accepted for review by the expedited process. The questions raised is whether there is reasonable evidence of protection of subjects and whether it is something that IRC is willing to submit to the IRB review under the terms of the FWA.

Approval, if granted, will be a “general” approval and will have several conditions attached:

- Annual review of the status of the grant.
- IRC must be told of funding priority, status and questions.
- An abstract must be submitted with the grant.

4. Protocols for Specific Activities involving Human Subjects:

A single grant application may encompass multiple studies. Some cannot even be designed until the first studies are completed. Each individual study will need individual IRB approval. The investigator (or the institution on the investigator’s behalf) must submit specific studies to the IRB.

Each protocol will be reviewed independently with its own approval number assigned.

