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Accreditation Of Human Research Protections Programs: A Validation Approach For GCPs?

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Introduction

Aside from aspects of the technology used, the world of Good Clinical Practices (GCPs) is one of human complexity and interpretation. While it may not as obviously lend itself to methods of validation with which our colleagues in laboratory, manufacturing, and packaging environments are so familiar, the primary concerns are indeed the same: to verify the essential processes and procedures that ensure quality and yield appropriate outcomes. Toward that end, accreditation can be viewed as an approach to validation.

What Is Accreditation?

Accreditation is a time-tested process used in many diverse professions, from manufacturing and engineering to education, from patient care to animal use and care. In all accreditation programs, the goal is to ensure quality and improve practice. In 2001, accreditation was introduced to the field of human subject protection in clinical research as a mechanism to demonstrate public accountability through quality assurance and improvement.

Distinguished from formal audits or inspection by government agencies or sponsors of research, the process of accreditation begins with self-evaluation and moves toward validation of policies and procedures that go beyond regulatory compliance. Accreditation requires organizations to have in place internal evaluation processes that lead to continuous quality improvement. Indeed, one of its key principles is to identify innovative, effective practices.

Simultaneous with the birth of accreditation was the introduction of the concept of a Human Research Protections Program (HRPP). Until five years ago, the locus of responsibility for protecting human subjects was the Institutional Review Board or Institutional Ethics Committees (IRBs/IECs, also know Internationally as ERCs or Ethic Review Committees). Subject protection is too important to be left to any one part of the clinical research enterprise, including IRBs/IECs/ ERCs. Through the accreditation standards, responsibility for oversight and protection has been expanded to include all parties. In its short existence, accreditation has helped in making human subject protections more robust in clinical research.

Currently, accreditation in the United States (U.S.) is a voluntary, non-governmental endeavor. Two notfor- profit organizations

offer accreditation: the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP), with which one of the authors is affiliated, and the Partnership for Human Research Protection, or (PHRP). Both organizations were created due to increased government scrutiny of research organizations, threats of additional government regulation, and concerns about the public's trust in the research enterprise.

AAHRPP was founded by seven national organizations that are major stakeholders in the research enterprise: Association of American Medical Colleges, Association of American Universities, Consortium of Social Science Associations, Federation of American Societies for Experimental Biology, National Association of State Universities and Land-Grant Colleges, National Health Council, and Public Responsibility in Medicine and Research. PHRP is a joint venture of the Joint Commission on Accreditation of Healthcare Organizations and the National Committee for Quality Assurance.

While accreditation has become closely identified with HRPP s, in reality it is separate from them. Accreditation validates HRPP s. Accordingly, HRPP s can be arranged in different ways; there is no single ideal. What is crucial to an effective HRPP is the identification of responsible individuals or organizational units, description of roles, and structuring of communications – the flow of information – among the various functional areas to ensure subject protection. In essence, what are subject to accreditation are that system flow and its checks and balances.

What Is Accredited

While the two accrediting bodies differ in what they accredit, fundamentally, all constituents of the clinical research industry, from private research sites through government agencies can and should be accredited. For example, AAHRPP 's broad approach in accrediting human research protection programs means that organizations from myriad research settings are eligible: hospitals and health systems, IRBs/IECs/ ERCs, Contract Research Organizations (or CROs), cancer centers, universities, and government agencies, among others. AAHRPP designed an accreditation program with flexible accreditation standards that could be applied across settings. Even though an independent IRB, for example, is not engaged in conducting research and would apply the standards differently than a university, the same level of accountability and organizational responsibility would apply.

Dimensions and Challenges of Accreditation

- *Help or Hindrance?*

In these early years, as the first cohort of organizations becomes accredited, there is a strong emphasis placed on building infrastructure; that is, assisting organizations in developing high-quality human research protection programs including sound policies and procedures. Accreditation is a means of applying uniform, meaningful standards for all research organizations to strive toward, regardless of setting. As that professionalization occurs, the consistent application of high regulatory and ethical standards in the research review process occurs. In other words, the "bar is raised" for subject protections.

In the case of AAHRPP , achieving accreditation provides organizations an assurance of regulatory compliance. The federal shutdown of research programs between 1999 and 2001 had to do with systemic problems often resulting from failing to follow the federal regulations for protecting human subjects.

Since that time, organizations have been working on developing and implementing all necessary policies and procedures to meet federal standards. Engaging in accreditation puts organizations on a fast track to achieve compliance. As accreditation becomes widespread, the focus will necessarily shift to subject protection outcomes, but always with regulatory compliance as a floor or basic requirement.

Some have argued that regulatory compliance is not synonymous with research ethics, or even with high ethical standards. For example, the federal regulations do not apply to all research involving human beings, they provide minimal protection for individual privacy interests and confidentiality of data, and they provide no additional protections for adults who are unable to make decisions about participating in research.

The goal of HRPP accreditation is to make research more ethically sound by improving the quality of ethics reviews conducted by IRBs/IECs/ERCs, by improving the capacity of investigators to understand ethical issues and apply ethical principles; to engage sponsors more fully in ethically sound research practices; and to reduce any influences that might inhibit the voluntary nature of research.

Accreditation standards should evaluate human research protection programs in terms of how well they protect research

participants in a context that regards research as important and necessary for the advancement of science. High-quality protection programs should not prevent or hinder ethically sound and scientifically meritorious research from moving forward. Instead, they should streamline IRB/IEC/ERCs and other protection functions to remove unnecessary burdens, and build capacity so that research protocols move more quickly to implementation.

- *Consistency*

Accreditation programs prove worthwhile when standards are interpreted consistently across research settings over time. Accrediting bodies are largely dependent upon the model they use for site visits (e.g., only peers, exclusively staff, or a blend of the two). No one way is more effective than another. Regardless of the model, consistency improves when site visitors are knowledgeable and trained. Evidence suggests that peers are more influential because they are well respected and can speak to individuals at organizations seeking accreditation in their own language and with an empathy that encourages response.

In the field of human subject protection where the federal regulations often require interpretation, it is important that site visitors be especially knowledgeable about federal regulatory requirements.

- *Self-evaluation Process*

A major component of effective accreditation programs is the incorporation of a self-assessment phase, wherein organizations perform an intensive internal examination of their protection programs' strengths and weaknesses. Self-improvement is an intended goal of the self-assessment process, because a "gap analysis" naturally occurs as a major component of internal review. Not only are policies, procedures, and practices examined, revised, and improved upon, the aspects of an organization's corporate culture related to human subject protection may change. Oftentimes, organizations begin the self-assessment with the IRB/ IEC/ERCs as the target, but end with decisions about resources, commitment, and priorities at the highest levels of the organization. Conducting a self-assessment means the status quo will change.

Of course, organizations must gauge themselves as they move through the self-assessment and not become paralyzed or overwhelmed by the need for change. Accreditation is an on-going activity with quality improvement occurring over years, even decades, not overnight.

- *Resources*

Preparing the self-assessment requires devoted resources. The costs in terms of dollars allocated and staff time are directly related to an organization's readiness, which may best be measured by its current level of regulatory compliance. An organization with well-developed policies and procedures, adequate staffing, and devoted resources will be in a better position to expediently complete a self-assessment. Like most accreditation programs, the majority of effort is required for initial accreditation; re-accreditation activities are typically less intensive.

Based on the nature, size, and complexity of their programs, organizations take various approaches to completing the self-assessment. Some assign individual staff members to lead the process; others employ a team or task force approach. In these early years of accreditation, a self-assessment may take as little as 6 or as long as 18 months.

Looking to the Future

- *Planning and Accreditation*

Beyond achieving accreditation – indeed, what may well become part of any organization's preparations for accreditation or re-accreditation – is the importance and value of what Dr. Jeffrey Cooper (Deputy Director, AAHRPP) calls a "Strategic Human Research Protections Program Plan" (or, Strategic HRPP Plan).

For those familiar with the business world, the value of a strategic plan is to project where an organization is going from a foundation in the present, with particular and equal emphases on the organization's strengths now and what is anticipated to be essential for the organization's survival in the longer-term.

Achieving accreditation provides a firm foundation for the future. But, simply assuming that, because one's organization is accredited there is no further need for refinement, is a mistake. Such an assumption fails to take into account improvements necessary in both efficiency and effectiveness of current processes, not to mention anticipating regulatory, legal, and social change.

One approach to a Strategic HRPP Plan is sketched in *Exhibit A*.

- *The International Scene*

Accreditation already exists in some European countries, although it is defined and determined differently. In contrast, what we are discussing here emphasizes an approach to integrating diverse functions within an organization that has an impact on protecting research subjects. In light of the European Union's (EU) Clinical Trials Directive and the EU emphasis on building drug and biological development capacity, as well as the momentum accreditation is gaining in the U.S., a more thoroughgoing version may be anticipated to spread internationally.

Interestingly, key leaders in developing and redeveloping nations wishing to expand their economic bases to include clinical research and its attendant industries, may become aggressive in pursuit of accreditation as well. Accreditation provides a means by which the services of a country can be judged in comparison to certain international standards.

Most important, though, is the internationalization of the research enterprise as a whole. Major research sponsor companies, such as GlaxoSmithKline, are committed to broadening the base of their clinical research trial presence.1 The Chief Executive Officer (CEO) of that company has said that doing so is an attempt to ensure "that the dollars spent on Research and Development (R&D)… are spent on finding new drugs and not on unnecessary infrastructure or bureaucracy."2 Accreditation may become an essential part of any strategy for going global in order to ensure subject protection that emphasizes efficiency as well as effectiveness through a meaningful approach to risk management for both subject and sponsor.

Principles of AAHRPP Accreditation of Human Research Protection Programs

1. Regulatory compliance is a minimal expectation for a human research protection program.
2. Protecting the rights and welfare of human research participants must be a research organization's first priority. Beyond assessing compliance with applicable regulations, accreditation standards should promote a research environment where ethical, productive investigation is valued.
3. Accreditation must approach the human research protection program from a broad organizational perspective, moving beyond a narrow focus upon Institutional Review Board (IRB) operations to examine whether policies and procedures of the organization as a whole result in a coherent, effective scheme for the protection of human research participants.
4. The accreditation process should be flexible and responsive to changes in federal and state regulation of research. The accreditation process must also accommodate continuing evolution of the standards in response to growing experience in their application across the multiple disciplines and settings in which research involving human participants takes place.
5. Accreditation should be primarily an educational process involving collegial discussion and the provision of constructive feedback. The accreditation process must identify areas in which a human research protection program does not yet meet established standards, and it should afford inspected organizations the opportunity to discuss potential program improvements.
6. Standards should be performance-based, assessed through an evaluation scheme that is sufficiently detailed to support the accreditation process, yet capable of effective and efficient implementation. Program evaluation should result in a grade of pass or fail for each standard, but should also include commendations or recommendations for meeting standards, as appropriate.
7. Standards should be applicable to human research protection programs across the full range of settings (e.g., university-based biomedical, behavioral and social science research, independent review boards, hospitals, government agencies, and others). Standards should address any special concerns (e.g., the use of vulnerable populations or heightened risk to privacy and confidentiality) that may arise in each setting.
8. The accreditation process should provide a clear, understandable pathway to accreditation, along with equally clear pathways for appeal and the remediation of identified shortcomings.
9. Standards should promote the development and implementation of outcome measures that can provide a basis for demonstrating quality improvement over time.

The Ethics of Accreditation

The ethical case for accreditation is intimately related to public accountability of the clinical research enterprise. Not only are public expenditures a major source of funding for research, the public itself is the source of the most precious ingredient in the

clinical research recipe – subjects volunteering to participate in trials.

Ultimately, accreditation is founded on ethical principles – the same principles characterizing federal regulations in the U.S. (found in the Belmont Report) and underpinning various international guidance, such as those of the International Conference on Harmonisation (ICH), the Declaration of Helsinki, and the ethics codes of the Organization of International Medical Societies (CIOMS).

In closing, accreditation is being embraced by various sectors within the research community: hospitals and health systems, independent IRBs, universities, cancer centers, and Veterans' Affairs medical centers. Industry support is also emerging: The Pharmaceutical Research and Manufacturers of America (PhRMA) supports the movement toward the voluntary accreditation of human research protection programs.

Increasingly, organizations recognize accreditation's value: improved protections for research participants, a clear path to regulatory compliance, and, in the current environment of litigiousness and public scrutiny, the benefits for risk management. Finally, from an ethical standpoint, accreditation is "the right thing to do."

References

1. The headline of one of the lead pieces in the FDA News Drug Daily Bulletin (Vol. 1, No. 213, Monday, November 8, 2004) reads: "GSK CUTS COSTS WITH MORE R&D ABROAD, ELECTRONIC DATA CAPTURE." The article indicates, "GlaxoSmithKline (GSK) is on track to move as much as 30 percent of its human clinical drug trials to lowcost countries, according to the drug-maker's top executive." The article goes on to quote the company's CEO as saying: "'We used to do 10 percent; now we're between 10 percent and 30 percent, closer to 30 percent,' [regarding] the trials conducted in countries such as India and Poland."
2. The full quote alluded to in our text, and from the same article cited above, reads: "It's [expanding GSK's clinical trials network overseas] not necessarily lowering the envelope, but making sure that the dollars spent on R&D… are spent on finding new drugs and not on unnecessary infrastructure or bureaucracy."

Exhibit A

Introduction

To create a strategic plan for an organization's Human Research Protections Program (HRPP), a variation on a standard business tool (SWOT (Strengths, Weaknesses, Opportunities, and Threats) analysis) may be employed. This may be called a "S-C-O-T" analysis, standing for Strengths, Challenges, Opportunities, Threats, where Challenges are internal and Opportunities and Threats are external challenges.

Outline

Strengths

To demonstrate sound ethical business practices, as well as one's Human Research Protections Program strategy, what can be sketched in a Strategic Plan for HRPPs in this section is what has been done, is currently being done, and what will be done to plant seeds for the future as it impacts industry standards, while serving clients, employees, and the community.

Chalenges (Internal)

To illustrate this section, there are four particular areas of internal challenges that can be addressed: technology, professional development, proactive planning, and public outreach. The last is especially crucial to the clinical research enterprise as a whole.

Opportunities (or External Challenges, I)

To illustrate this section, there are three key areas for increasing opportunities to improve human research protections that can be addressed:

1. Industry-wide interest in applied bioethics
2. National and international concerns about “public awareness and the understanding of clinical research”
3. Greater acceptance of the value of independent IRBs within the larger research community (including institutions such as Academic Medical Centers)

Threats (or External Challenges, II)

To illustrate this section, there are three dramatic threats to the clinical research enterprise as a whole, and to human research protections efforts in particular, that can be addressed:

1. Public mistrust of the clinical research enterprise
2. Federal and international government de-emphasis of the importance of human subject protection
3. Ethical and compliant conduct of clinical research internationally, especially in redeveloping and developing countries

Attachments

Both for accreditation purposes and for the viability of any strategic plan, a balance of description and documentation is most effective. Below are suggested four approaches to documentation to flesh out the descriptions of the S-C-O-T analysis:

1. Bibliography and examples of publications by organization personnel who are involved in the organization’s HRPP (and who may range from investigators and IRB administrators through IT, education, and contracts individuals)
2. Examples of presentations by the same types of personnel as noted in item one
3. Graphics describing human research protections-related communications and interactions within the organization, both current and anticipated
4. Overview timeframe of key organization goals for future years – including proactive responses to anticipated regulatory, legal, and social change

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