

ORIGINAL REPORTS: EMERGING BEST PRACTICES FROM RCMI

THE RESEARCH SUBJECT ADVOCATE AT MINORITY CLINICAL RESEARCH CENTERS: AN ADDED RESOURCE FOR PROTECTION OF HUMAN SUBJECTS

In early 2001, the National Institutes of Health (NIH) created the research subject advocate (RSA) position as an additional resource for human subjects protection at NIH-funded Clinical Research Centers (CRCs) to enhance the protection of human participants in clinical research studies. We describe the RSA position in the context of clinical research, with a particular emphasis on the role of the RSA in two of the five CRCs funded by the NIH Research Centers in Minority Institutions (RCMI) program. Through participation in protocol development, informed consent procedures, study implementation and follow-up with adverse events, the RSA works closely with research investigators and their staff to protect study participants. The RSA also conducts workshops, training and education sessions, and consultation with investigators to foster enhanced communication and adherence to ethical standards and safety regulations. Although we cannot yet provide substantive evidence of positive outcomes, this article illuminates the value of the RSA position in ensuring that safety of research participants is accorded the highest priority at CRCs. On the basis of initial results, we conclude that the RSA is an effective mechanism for achieving the NIH goal of maintaining the utmost scrutiny of protocols involving human subjects. (*Ethn Dis.* 2005;15 [suppl 5]:S5-107-S5-110)

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INTRODUCTION

In September 1999, 18-year-old Jesse Gelsinger died while participating in a clinical trial at the University of Pennsylvania's Institute for Human Gene Therapy. His highly publicized death led to intense government scrutiny and heightened public suspicion of medical research in the United States. Following Jesse's death, the National Institutes of Health (NIH) received delayed reports of >650 dangerous adverse reactions, including several deaths, that had occurred in other studies around the country.^{1,2} Upon investigation, the NIH learned of widespread noncompliance with federal requirements for clinical research studies. Most disturbing was that several NIH-supported investigators had violated federal mandates by deviating from approved study design, taking risks involving human subjects, and not reporting adverse events to the appropriate authorities. Clearly, the NIH system of review, oversight and reporting, including involvement of institutional review boards (IRBs) and scientific advisory committees, while comprehensive and extensive, was failing to protect all research participants.^{2,3} In response, the Food and Drug Administration (FDA) and the Office of Human Research Protection (OHRP) shut down human research at several

major medical centers and issued sanctions for noncompliance with human subject regulations, dealing a blow to the medical research enterprise.^{4,5}

ESTABLISHMENT OF THE RESEARCH SUBJECT ADVOCATE POSITION

In an attempt to restore public confidence by alleviating safety concerns in the clinical research setting, various federal agencies enacted programs designed to protect human research participants. For example, in 2000, the Department of Health and Human Services empowered OHRP with the authority to regulate research through written assurances from institutions and to investigate complaints and take corrective action. To complement the role of the OHRP, the FDA set up the Office for Good Clinical Practice to monitor individual investigators, industry sponsors, and IRBs. One of the most important federal measures was the creation of the research subject advocate (RSA) position by the NIH National Center for Research Resources (NCRR). The RSA, with training in human subject protection and medicine, nursing, pharmacy, or other appropriate fields, would ensure that all research conducted in NCRR-supported General Clinical Research

Centers (GCRCs) complied with federal regulations and prevented harm to research participants.

In early 2001, the NCRF funded the RSA position through the 80 GCRCs across the country and soon required that all five Research Centers in Minority Institutions (RCMI) Clinical Research Centers (CRCs) also hire an RSA.⁶ More than 10,500 NIH-supported investigators conduct nearly 8,000 research projects each year at the GCRCs. In addition, >100 projects are conducted at the RCMI CRCs each year.⁷ Thus, the RSAs are instrumental in protecting thousands of individuals participating in research studies in the United States. As of 2005, nearly 150 RSAs are working in research centers throughout the nation.⁸

ROLE OF THE RSA

RSAs report directly to the principal investigator of each GCRC (the medical school dean) or RCMI CRC (the medical school dean or university president), thereby eliminating any potential conflict of interest that might arise by reporting to the GCRC or CRC program director. The primary responsibility of the RSA is to educate investigators and research staff on human subjects protection, ensure compliance with regulatory obligations, and establish data and safety monitoring plans for all NIH-funded clinical studies that pose more than minimal risk. The RSA periodically serves as an unbiased observer during the informed consent process. The RSA may communicate directly with research participants to help them understand study risks and ensure that their safety receives the highest priority.⁸

RSAs must be available on a 24-hour basis to assist with resolution of adverse events if they occur during a study. An aspect of the RSA's role is to oversee reporting of adverse events and conflicts of interest. If an adverse

event arises during a study, the RSA is involved in the decision-making process related to restoring the patient's well-being. The RSA communicates with emergency medical staff as necessary. The RSA also works with the investigator and their staff in reporting serious adverse events to the appropriate agencies. Moreover, in order to preserve patient safety, the RSA has the authority to halt any study if risk to research participants is deemed to be too high.

In sum, RSAs monitor research activity through involvement in all stages of the clinical study process, from protocol design and recruitment to implementation. The goal of the RSA is not simply to ensure that investigators adhere to regulatory requirements, but ultimately to prevent harm or injury to individuals participating in research.

IMPORTANCE OF THE RSA AT MINORITY CLINICAL RESEARCH CENTERS

Accomplishing this goal is particularly important in institutions that support research involving minority populations. The CRCs at the Charles R. Drew University of Medicine and Science in Los Angeles (Drew) and at the University of Hawai'i John A. Burns School of Medicine in Honolulu (University of Hawai'i) are among the five RCMI-funded centers that provide infrastructure for clinical research with a particular focus on minority health. Both CRCs support studies involving racial and ethnic minority populations. The Institute of Medicine (IOM) report released in March 2002 reports that racial and ethnic minorities tend to suffer from higher rates of cardiovascular disease, cancer, diabetes, infant mortality, and other serious diseases.

Compounding this problem, minorities tend to receive lower quality of care even when healthcare insurance, health

condition, income, and age are controlled for. For example, the IOM states that racial and ethnic minorities are less likely to receive cardiac medication, aggressive treatment for HIV/AIDS, or kidney dialysis.⁹ Indeed, one of the NIH's primary objectives for the coming years is the reduction of health disparities in under-served and under-represented populations in the United States, and effective research programs are vital to achieving this objective. Unfortunately, though, because of general mistrust of traditional research and fear of being induced to serve as "guinea pigs," many individuals of racial and ethnic minority descent are reluctant to participate in research studies.^{10,11} In addition, given the increased incidence of serious diseases that lead to health disparities, racial and ethnic minorities tend to be more targeted by investigators for studies, which can further amplify attitudes of suspicion and mistrust.

The presence of an RSA at minority-serving institutions appears to help reduce such suspicion and provides additional assurances that may contribute to more successful recruitment and retention of participants in research studies designed to benefit minority populations. For example, the RSA at Drew is bilingual in Spanish, enabling her to address concerns of Spanish-speaking participants. Similarly, at the University of Hawai'i CRC, in cases where language or cultural barriers impede proper communication regarding a study, the RSA may determine the need for translators or translated consent forms as part of the process of obtaining valid informed consent. At each site, issues regarding gender, generation, literacy, culture, and language are periodically assessed by the RSA to ensure that consent to participate in studies is truly informed. With increased public awareness of the RSA's ability to advocate on behalf of participants, community members may be more willing to consider taking part in research activities.

As a key element of the emerging community-based participatory research paradigm, both Drew and the University of Hawai'i CRCs invite community representatives to actively engage in the development of community-academic partnerships. These involve community participation in all phases of research projects to ensure cultural competence and tangible community benefit and foster links to the community being served.^{12,13} This approach is critical since the remarkable advances in biomedical sciences and medical therapeutics in recent decades have not led to anticipated improvements in patient outcomes, largely because of the inability to translate scientific advances into clinical practice at a provider and community level.^{14,15} One of the goals for the next few years is to promote increasing interaction between RSAs and community representatives as they work together to enhance community outreach, address cultural and ethical concerns, enact appropriate recruitment procedures, and monitor study implementation and follow-up activities. This interaction will facilitate more effective translation of clinical research findings to improved practice in the healthcare setting.^{16,17}

At both institutions, the RSA provides an additional protective resource for those participating in the clinical research process. This protection has implications for any research involving human subjects but is perhaps even more vital to reassuring members of minority communities that volunteering for research studies is safe. Clinical investigators must provide assurances to community members in order to establish a trusting relationship and encourage participation in research studies. As the RCMI CRCs embark upon more community-based participatory research projects, the presence of the RSA will hopefully strengthen this element of trust. In turn, minority-based research programs can more effectively achieve results that will lead

to improved prevention, treatment, and health outcomes for this target population.

CONCLUSION

Due to the novelty and innovation of the RSA position in the research setting, it may be too early to offer a valid assessment of its success. It is clear, though, that the number of data and safety monitoring plans and boards at GCRCs and RCMI CRCs has increased since 2001, and a recent survey conducted by the President of the Society of Research Subject Advocates (SRSA) demonstrated that RSAs are accomplishing their goal of helping clinical investigators comply with data and safety monitoring requirements.¹⁸ The SRSA has established several working groups, including a Quality Assurance Committee, and offers mentoring, educational tools, and other resources to assist RSAs in their evolving role.¹⁹ The NCRR has also noted a positive institutional response to RSAs and plans to continue RSA support for all NIH-funded patient-oriented research at GCRCs and CRCs.⁷

Unfortunately, risk to participants is often inherent to the conduct of clinical research. Regardless of improvements in federal oversight, institutional support, IRBs, and investigator-initiated safety measures, adverse events will inevitably occur within the context of research. Nevertheless, RSAs around the country are demonstrating positive results as they strive to reduce risks to human participants. The RSA is one of the key components of a broad strategy to regain public trust by creating a safe environment that is conducive to medical research designed to benefit all human subjects. At both the University of Hawai'i and Drew CRCs, the RSA has become an integral part of the clinical research process, hopefully contributing to a greater

sense of community-wide confidence in safe study design and implementation. With the knowledge that an individual is wholly dedicated to protection of research participants' interests, it is likely that we will begin to see an increased willingness of individuals representing diverse ethnic communities to volunteer for and participate in clinical studies. This will no doubt enhance the efforts of minority CRCs to reduce and ultimately eliminate the disproportionate burden of health disparities upon minority populations.

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