

# **U.S. House of Representatives**

## **Committee on Veterans' Affairs** Subcommittee on Oversight and Investigations

### **Statement of Greg Koski, PhD, MD**

Senior Scientist  
Institute for Health Policy,  
Massachusetts General Hospital  
Harvard Medical School,  
Boston, Massachusetts

Former Director, Office for Human Research Protections  
Office of the Secretary, U.S. Department of Health and Human Services

Former Chairman, Human Subjects Research Subcommittee  
Committee on Science, National Science and Technology Council

June 18, 2003  
Washington, D.C.

**The views expressed in this statement are those of the author, based in part upon experiences and discussions before, during and after his period of government service and do not represent any official positions of the Department of Health and Human Services, the National Science and Technology Council, or of any other U.S. government agency or office.**

**This statement is based in part upon a draft statement previously prepared by Dr. Koski while he was Director of the Office for Human Research Protections, HHS.**

**Mr. Chairman and Distinguished Members of the Subcommittee:**

Thank you for this opportunity to appear before the Subcommittee as it assesses the Department of Veterans Affairs' management of human subject protections maintained in its nationwide research program. The long-standing and continuing commitment of this Subcommittee to the well being of research participants is well recognized and appreciated. Indeed, it was in testimony delivered before this Subcommittee in September 2000 that I, as the first Director of the newly established Office for Human Research Protections (OHRP) at the Department of Health and Human Services, first described to the Congress and the American people the Department's vision for the future of our nation's system for the protection of human subjects in research. Others who testified at that hearing included representatives from the General Accounting Office and the Department of Veterans' Affairs, both from the Office for Research Development (ORD) and from the VA's own newly created Office for Research Compliance and Assurances (ORCA).

Since that hearing nearly three years ago, the Department of Health and Human Services (HHS) and the Department of Veterans Affairs (VA), with OHRP and ORCA working hand-in hand under the Common Rule (45 CFR 46), implemented a new approach to the protection of human subjects in research, one based on the simple concept that the first responsibility of everyone involved in the human research process is to protect the rights, interests and well-being of the brave and unselfish individuals who voluntarily participate as subjects of study in our research activities. Among them are our veterans who have served America not only in our armed services, but also as research subjects in support of the VA health research program.

While all of the federal agencies are faced with continuing issues in human research, my comments today will focus on HHS and the VA. The new approaches pioneered by HHS and the VA are more than just an improvement of the existing oversight and corrective action approach. It is a different paradigm. It is a system focused on *prevention*. Compliance with regulations, while necessary and important, is not alone sufficient to ensure protections for human research participants. Identification and correction of deficiencies *after* someone has been harmed is simply not good enough.

We owe the American people, and particularly our veterans, more. We must have a system that minimizes the likelihood that subjects will be harmed, a system that is proactive and interactive, not reactive. The programs that were developed and implemented by OHRP and ORCA are taking us down this new road. On this road, the real goal is responsible conduct of science, not mere procedural compliance with regulatory requirements. We must do more than go through the motions.

Today, important steps are being taken both in and outside of the government to ensure that every party to research is properly trained and educated so that each can accept and fulfill his or her responsibilities for protecting research subjects as a necessary condition for the privilege of being an investigator. Today, as a complement to federal regulatory requirements, nationally

recognized performance standards have been developed to provide the basis for private voluntary accreditation of human research protection programs that review, approve, and conduct continuing oversight of human research. In fact, the VA's leadership was instrumental in efforts to launch these accreditation programs.

Some initial steps have already been taken to clarify, simplify and streamline regulatory oversight, to reduce administrative burdens and eliminate or modify procedural requirements that may impede the effectiveness and efficiency of our system without providing increased effective protections. The development of a dramatically simplified and more flexible Federalwide Assurance (FWA) process allowed OHRP, ORCA and other agencies to devote a greater and much needed portion of their limited resources to new education and quality improvement initiatives instead of non-productively processing paperwork. The flexibility of the FWA encourages collaboration and elimination of wasteful redundancy in the review through utilization of alternative review models, including central and regional review boards. Nevertheless, much remains to be done, and with cooperation among the Federal agencies, much could be accomplished.

With this increased flexibility, there must be greater accountability and openness. Over the past few months, the VA's human research program and its oversight has again been the subject of intense scrutiny as new allegations of non-compliance, abuses of human subjects and scientific misconduct have come to light. Further, the organizational restructuring at the VA that eliminated ORCA and returned, at least in part, oversight of research activities to the ORD, has caused great concern.

The need for, and even more importantly, the value of independent oversight of research activities have never been more clearly appreciated. Shortly after ORCA was created to provide independent oversight of human research in VA facilities, a similar step was taken at HHS, the creation of OHRP within the Office of the Secretary. The creation of OHRP, of which I was honored to serve as the first director, was considered by many to be a sentinel event in an effort to reform the nation's human research system after twenty years of largely neglected calls for such reform emanating from several distinguished groups, including the President's Advisory Committee on Ethical Problems in Human Research, the Advisory Committee on Human Radiation Experiments, and the National Bioethics Advisory Commission among others. The creation of OHRP was recommended in June 1999 by an expert review panel convened by Dr. Harold Varmus, then director of the National Institutes of Health (NIH), in response to concerns expressed over the organizational placement, resources and effectiveness of the Office for Protection from Research Risks (full report available at <http://www.nih.gov/about/director/060399b.htm>, accessed June 9, 2003; see Appendix 1). The competing commitments and conflicts of interest inherent in the placement of an oversight office in a subordinate position within an agency that it is supposed to regulate were compelling arguments for the establishment of a new organizational structure and an autonomous office within HHS. Acting upon the panel's recommendations, then Secretary of HHS Donna Shalala announced the creation of OHRP in June 2000 and charged it with leading the Department's human subjects reform initiatives. While HHS and VA are different in many ways, the panel's

report is directly relevant to the ongoing consideration of the optimal placement of human research oversight responsibilities within the VA.

Although I stepped down as the director of OHRP at the end of November 2002, today's hearing affords an opportunity to review some of the important issues requiring our continuing attention, and the status and progress of initiatives that have been undertaken to date. The programs initiated by HHS and VA over the first three years of this remodeling of our human research oversight system specifically address all of the major recommendations of the HHS Office of Inspector General, as detailed in its 1998 Report entitled "IRBs: A Time for Reform", and many of those included in the report of the General Accounting Office to this Subcommittee focused on strengthening the VA's oversight processes. Upon review of the remarkable progress that has been made in a very short period of time, the important contributions of ORCA are readily evident, calling into question the rationale, motivation and justification for its dissolution.

Among these recommendations in the above referenced reports are the following:

***Recommendation 1: Grant institutions and institutional review boards (IRBs) greater flexibility, but hold them more accountable for results.***

OHRP, working with FDA, implemented in December 2000, a unified Federal registration system for all human research review boards, that allows registration regardless of the source of funding of the research they oversee. Prior to my departure from OHRP, FDA planned to propose a rule to require registration of all IRBs subject to its regulatory authority. I presume that the agency still intends to do so. Already, OHRP has made this database accessible to all Federal agencies relying upon FWA's. This system provides an important database for improved communications with IRBs across the country and around the world, and is an important first step toward establishing greater uniformity and connectivity in the IRB process.

As mentioned earlier, the federal assurance process for human subjects protection has been dramatically simplified. Since the implementation of federal regulations for protection of human subjects in research, grantee institutions have negotiated assurances, a process through which they commit to the Federal government that they will comply with human subject protection regulations as a condition of receiving federal support. In December 2000, OHRP initiated a simplified assurance process that avoids time-consuming negotiations that distract attention and resources from more effective and desirable approaches to achieving true protection of human research subjects. Presently, the registration and assurance processes have been converted to an electronic web-based process, almost totally eliminating the mountains of paperwork formerly generated. The VA, as a signatory to the Common Rule, utilizes this assurance process for its own research facilities and all have benefited from its simplicity. With the resources freed by streamlining the former unnecessarily complex assurance process, OHRP, and ORCA, implemented new programs of education and support as part of a broad continuous quality improvement (CQI) initiative. These programs are administered through a combination of proactive site-visits, videoconferences and directed self-evaluations that are then reviewed by the staff of the oversight offices. Feedback from these consultations helps programs identify their strengths and weaknesses, a necessary condition for improvement. The QI assessment tools and

procedures underwent pilot testing and refinement in voluntary cooperation with institutions across the country. The CQI Tool Kit developed by ORCA provided a remarkable resource to the research community.

Formal implementation of these QI programs was a significant milestone in the reform process. According to plans, and with sufficient resources, once this program is fully implemented, OHRP would interact with every program under its jurisdiction at least once every 5 years. To maximize the effectiveness of this program, as a first priority, OHRP should work with the 174 institutions that receive 90% of HHS research support, the same group toward which NIH has recently directed \$28.5 million in new infrastructure support for human subjects protection. But smaller programs cannot be neglected. The more limited scope of the VA system makes even more intensive interaction possible, and these efforts were well underway. The continuing deployment and impact of these programs on the performance of human research protection programs warrants close attention as data collected as a by-product of the evaluations becomes available.

Oversight and communication are critical to accountability. Both HHS and VA have taken this responsibility very seriously. Everyone engaged in the research endeavor is expected to act responsibly—every review board, every institution, every investigator, and every sponsor. A single irresponsible investigator or institution harms not only individual subjects, but also science itself. The research community cannot, and the federal government's oversight offices must not, tolerate those who are unwilling to take seriously their responsibilities for protection of human subjects.

Since OHRP was created in June 2000, it has engaged in more than 300 for-cause compliance oversight investigations. Although most compliance cases can be appropriately resolved without the need for physical site visits, OHRP conducted at least seven such visits over the past three years, five of these in relation to specific complaints. ORCA conducted at least as many. Importantly, in addressing the majority of these cases, OHRP and ORCA conducted not only a review of the specific complaint, but also a comprehensive review of each institution's human research protection process and worked with the institutions to develop effective plans for corrective action and offered helpful guidance on best practices.

OHRP and ORCA also introduced not-for-cause compliance surveillance programs that will enhance the effectiveness of their voluntary QI programs. FDA has contributed as well to the oversight of clinical research through its Bioresearch Monitoring Program, conducting over 1000 on-site inspections each year of clinical investigators, study sponsors, monitors, contract research organizations, and Institutional Review Boards that ensure the integrity of clinical research submitted in support of product applications to FDA. With the recent creation of a new Program for Good Clinical Practice within the Office of the Commissioner, FDA is working more closely across its Centers and together with OHRP and the Department to increase the coordination, quality, and effectiveness of its inspection programs.

During my tenure at OHRP, plans were made to host a special task force that would bring together representatives of the federal agencies, offices and departments involved in human

research with representatives from every facet of the human research community to discuss current regulations, policies and procedures as part of an effort to identify and eliminate inconsistencies and inefficiencies that do not contribute effectively to the protection of human subjects. This task force would focus upon four specific goals: simplicity, uniformity, efficiency and effectiveness (SUEE) of our nation's system for protection of human research subjects. The individual participants would be asked to identify *real* steps that the government could take to achieve these goals without reducing the effectiveness of the system of protections for research subjects as effort continue to build a new system focused on *performance*. I remain hopeful that this initiative will go forward under new leadership at OHRP, and that all of the Federal agencies will actively participate.

***Recommendation 2: Re-engineer the federal oversight process.***

The entire research community has recognized the need for greater uniformity and public accountability of human research protection programs. Toward fulfillment of this goal, HHS commissioned the Institute of Medicine (IOM) of the National Academy of Sciences to recommend uniform performance and resource-based standards for private, voluntary accreditation of human research protection programs (HRPPs).

Although many questioned the aggressive time frame HHS proposed for this work, in April 2001, the IOM issued its report on accreditation of human research protection programs. Since then, two entities, the Association for the Accreditation of Human Research Protection Programs (AAHRPP) and the National Council for Quality Assurance have implemented their accreditation processes, the latter specifically targeting VA programs. Recently, NCQA has formed a new partnership with the Joint Commission for the Accreditation of Hospital Organizations (JCAHO) to enhance the scope and effectiveness of its accreditation process. Pilot testing was performed at selected medical centers in the Department of Veterans Affairs and other institutions, including NIH. The standards are flexible enough to be applied in all research settings regardless of the source of funding or the nature of the research. The accreditation process is the cornerstone of the new system, one based on a true public-private partnership in which private accreditation complements the regulatory and oversight responsibilities of government. This approach will allow the research community to achieve new standards of excellence in performance without the burden of new regulations. Accreditation will do much to build confidence within the research community and foster trust among the public at large.

Having completed the first phase of its project on human research oversight under its contract with HHS, the IOM engaged in a second phase of its work, a study of the evolving human research system to determine the extent to which the issues and concerns raised by the HHS Office of Inspector General, the General Accounting Office, the National Bioethics Advisory Commission, and other national groups are being addressed within the current program of reform. The IOM working group was also charged with developing objective measures for the effectiveness of the system for protection of human subjects in research. Such criteria could then be used on an ongoing basis for continuing assessment of the system's effectiveness, updating of the accreditation standards, and reporting to the Congress and the public on the performance of the system. The working group report, issued last October, underscores the need for a system approach to human subjects protection, a position strongly expressed by both the OIG and the GAO and central to the remodeling initiatives of both HHS/OHRP and VA/ORCA.

Last year, HHS also established an interagency working group to review recommendations contained in NBAC's final report on human research oversight to ensure that all appropriate actions are being taken to develop an optimal system for responsible conduct and oversight of human research. That working group has not yet issued its formal report; it should provide useful insight into continuing efforts by the Department to improve the human research process.

***Recommendation 3: Strengthen continuing protections for research subjects in ongoing approved studies.***

The FDA, NIH and other federal agencies have launched an effort to carefully examine the continuing review process and to develop guidance for institutions and review boards regarding appropriate mechanisms for ongoing monitoring of approved research, particularly recognizing the need for more effective monitoring and management of adverse events. As of last winter, the Office of Biotechnology Affairs and the FDA had made very significant progress toward deployment of a prototype research safety system, a protected but searchable clinical research

data warehouse served by a uniform, web-based reporting system. The system could be an enormously valuable resource to the research community and make possible for ‘real-time’, continuous monitoring of safety in ongoing clinical trials. This is an effort that should be supported by HHS and the Congress with sufficient resources to adapt it for all clinical research over the next five years, using the already perfected lexicon and infrastructure. In this effort, teams led by Drs. Amy Patterson at NIH and Phil Noguchi of the FDA demonstrated unparalleled cooperation between their agencies, setting a standard for everyone in government.

Last year, OHRP and ORCA took steps to clarify, through guidance and compliance oversight activities, the elements of a more effective continuing review process, widely considered to be one of the greatest weaknesses of the current process. Together, ORCA and OHRP produced a video program on continuing review that was made available as an educational tool to the IRBs across the country. Already, institutions have taken steps to strengthen continuing oversight of approved studies, and an increasing number are developing their own internal auditing and quality assurance programs. This emphasis on quality assurance and quality improvement is a promising trend, one that will be reinforced by the accreditation process.

***Recommendation 4: Enhance education for research investigators, administrators and IRB members.***

In an effective system for human research, every participant--whether a subject or a member of the research team, whether an IRB member, manager, or chair, or a vice-president for research or medical school dean must know what his or her responsibilities are and must be appropriately trained and prepared to fulfill them. We have seen too clearly the results of allowing inadequately prepared individuals to perform and oversee human research activities. Many observers have recognized that education is a key to our success, and it is accordingly a major focus of our efforts to improve the system for protection of human research subjects.

Each agency has conducted major outreach programs to their respective stakeholders. In collaboration with other federal agencies, OHRP, NIH, FDA and the Department of Veterans Affairs' ORCA conducted numerous conferences, workshops and town meetings across the country. Since June 2000 OHRP staff members have given over 150 presentations to institutions, IRBs, investigators, and professional societies. Since October 2000, OHRP has co-sponsored with FDA and the VA at least six national workshops on human protections issues including in places like Washington, D.C., Honolulu, HI, and Newark, NJ; four town meetings and two video town meetings. Also, as part of this campaign of reform, as the Director of OHRP, I made "ambassadorial visits" to dozens of research institutions across the nation and several VA regional meetings.

In February 2001, OHRP and the HHS Office of Research Integrity (ORI) hosted the first Human Research Education Summit, an HHS-sponsored meeting attended by representatives from both the academic and corporate sectors, as well as representatives from almost every federal agency subscribing to the Common Rule. This meeting was an initial step toward developing a system of shared resources and best practices. Such a system could serve as an approach toward education for both human research and for the responsible conduct of research. A second meeting took place in August 2001, resulting in the creation of a new national council for education in responsible conduct of research. This non-governmental group, the Responsible Conduct of Research Education Consortium (RCREC) is now a reality. It will work to establish standards for education in human research and shared educational resources for the research community. A formal announcement of this new organization will be forthcoming soon.

Among its many education and support initiatives, OHRP developed and implemented web-based educational modules for institutional officials, IRB managers and IRB chairs to ensure that these individuals are fully cognizant of their responsibilities under their assurances. Video-conferencing is being used to enhance educational outreach activities in a cost-effective manner. As mentioned earlier, ORCA also produced and distributed a wealth of education materials, including its Continuous Quality Improvement Toolkit, which has become a valuable resource for programs both in and outside of the VA system.

To support institutions in their efforts to educate their investigators and research teams, Public Responsibility in Medicine and Research (PRIM&R) allowed OHRP to make available to all federal assurance holders a site-license for the PRIM&R training CD, "Investigator 101".

For the past two years, OHRP, FDA, the VA, and Department of Energy have been working on a new federal handbook for human research. This “Millennium Edition”, intended to replace the now outdated Guidebook issued in 1993 by the former Office for Protection from Research Risks (OPRR), will serve as a reference source for IRBs, investigators and institutions. Ideally, such a guidebook should be referenced to the Common Rule and be applicable to all of the signatory agencies, noting where appropriate those issues that may be unique to individual agencies and research programs. IRBs need more uniform guidance, with less ambiguity if they are to function more effectively. When and if completed, this handbook should be available in paper, electronic and CD format to optimize its usefulness and accessibility and minimize its cost. The government, working with the private sector, should continue to search for additional effective ways to enhance education at all levels, including efforts to foster and support programs for private training and certification of every individual engaged in the research process, including investigators.

Several dedicated private organizations, such as the Association of American Medical Colleges (AAMC), the Association of Clinical Research Professionals (ACRP), Public Responsibility in Medicine and Research (PRIM&R), the Society of Clinical Research Associates (SOCRA), the National Council of University Administrators (NCURA), and the Society of Research Administrators (SRA) have actively engaged in the education process, and some have instituted programs for certification of those individuals who complete their training programs successfully, whether they are IRB managers, clinical research associates, clinical research coordinators or investigators. Currently, a number of private organizations including the ACRP, the American Academy of Pharmaceutical Physicians (AAPP), the Drug Information Association (DIA) and the American Society of Clinical Oncologists (ASCO) have developed programs specifically for investigator training and certification at a national and international level in support of harmonized Good Clinical Practice (GCP) guidelines. Ultimately, recognition of clinical investigation as a formal subspecialty of medical practice is a sensible and laudable goal.

***Recommendation 5: Moderate the workload of institutional review boards and to ensure adequate resources for their activities.***

IRBs and institutions are still trying to shoulder what seems to be an ever-increasing burden of administrative activities. The NIH, through its Administrative Burden Reduction working group, has taken some steps to reduce this burden, such as the “just in time” policy for IRB review, but much more needs to be done. An initiative like the “SUEE Task Force (Simplicity, Uniformity, Efficiency and Effectiveness)” mentioned earlier could also identify and recommend additional opportunities for reducing unproductive administrative burdens, but this will not be enough to bring the system into balance.

For too long, government and the scientific community have viewed programs for protection of research subjects as simply an administrative process. It is time to change this thinking. The system for protection of human subjects is not optional--it is the very *foundation* of responsibly conducted, ethical human research. To fully recognize the proper and essential role of these

programs in research, institutions must provide appropriate resources. At the same time, the government must work to reduce unproductive administrative burdens and costs, while maintaining an effective system of protections.

In recognition of this need for resources, HHS introduced a new \$28.5 million NIH-funded program of awards to institutions for building and strengthening infrastructure for human research protections. While well intended, this alone is not sufficient, but only a first step. It is the responsibility of the federal agencies and the Congress to continue to explore mechanisms to provide appropriate resources for these critical parts of the research process. Funding programs for prevention of harm to research participants as part of the scientific mission, rather than as an administrative process, would be a worthwhile investment in the national infrastructure for responsible human research.

**Recommendation 6: Establish an independent advisory committee for human research.**

In June 2000, HHS promised to create a National Human Research Protections Advisory Committee (NHRPAC). That promise was fulfilled, at least for a time. To many, NHRPAC was a national resource, providing a forum for balanced public discourse on the challenging issues being faced in the human research arena, and providing expert advice as government and the research worked to develop a more effective system for human research oversight. The balance and depth of its membership served NHRPAC well as it has offered advice on such complex issues as financial relationships and conflicts of interest in human research, children as research subjects, appropriate protections for subjects of social and behavioral research, and third parties in research. Regrettably, NHRPAC was inexplicably dissolved last summer and replaced with a new Secretarial Advisory Committee on Human Research Protections (SACHRP) amidst accusations that the advisory process was being manipulated to promote specific ideological viewpoints. The new committee has yet to have its first meeting, but there is little doubt that there is much at stake as we face the challenges of global research, genomics, the process of informed decision-making, special protections for decisionally impaired individuals, compensation for research-related injuries and other important issues. Many will be watching closely as this important committee begins its important deliberations and one can only hope that it will be up to the challenges it faces, able to approach them with reason, wisdom and balance.

**Recommendation 7: Foster greater integration of federal oversight of human research.**

Over the past three years, new working relationships developed inside and outside the Department; relationships based on collaboration. The close collaboration between OHRP and FDA's new Office for Good Clinical Practice was one such example. With those collaborations came opportunities for better communication, coordination, efficiency, and effectiveness, benefiting not only HHS, but also more broadly benefiting all those who interact with government in the process of protecting research subjects.

At the Executive Branch level, with the leadership of HHS, the National Science Foundation and the Office of Science and Technology Policy, the Human Subjects Research Subcommittee (HSRS) of the National Science and Technology Council's Committee on Science was revitalized under a new charter. The HSRS, which brings together representatives from all of the federal offices and agencies involved in human research, strives to better coordinate the policies and practices of the federal government's oversight of human research. Whether it can do so under the fragmented system of federal oversight that has been assembled under the Common Rule remains doubtful to many, including the National Bioethics Advisory Commission. Increasingly, the need for a uniform regulatory framework and a single, independent oversight office seems evident.

For several years, the HSRS has been working to integrate the activities of a score of federal offices, agencies and departments that share responsibilities in this oversight process. Through its efforts, the common Federal Policy for Protection of Human Subjects in Research, generally known as the Common Rule, was established. Under its revised charter approved in January 2001, the HSRS had an opportunity to become a powerful engine of progress. Its working groups took on a host of issues including conflicts of interests in clinical research and appropriate application of the federal policy for protection of human subjects in non-biomedical, social and behavioral sciences research. The HSRS had an opportunity to become the "central nervous system" of the federal system for human research oversight, but its effectiveness has not as yet lived up to its promise. Administrative hurdles and differences in perspectives and priorities of individual agencies limit its effectiveness, and these may be insurmountable, as noted by others.

As we have seen in the case of homeland security initiatives, the only means to achieve the necessary and desirable coordination and effectiveness of federal oversight of human research may be to establish an independent federal commission for this purpose, a commission not unlike the Securities Exchange Commission or the Federal Reserve Board that can function with authority and autonomy unencumbered by competing interests of individual federal agencies that have been asked to simultaneously fund and conduct research while concurrently bearing responsible for oversight of those research activities. This was the challenge that fostered the creation of OHRP, removing OPRR from its subordinate position within the organizational structure of NIH. This is also the problem that was solved within the VA by creating ORCA and placing it outside ORD. The recent action at VA that abolished ORCA and would have returned the oversight process to ORD was unfortunate, ill conceived and ill timed. The legislation recently introduced by Mr. Buyer with bipartisan support (H.R.1585) provides a permanent statutory solution to this problem within the VA, but may not go far enough. If we are to promote the integrity of the research process and preserve public trust in it, it is essential to ensure that the oversight of human research and responsibilities for protection of human subjects across the government not be subordinated to those who conduct and support that research, however well intended they may be.

**Recommendation 8: Issue guidance regarding financial relationships and conflicts of interest that may impact the interests and well being of human subjects.**

Over the past two years, the conscience of the nation awakened with growing concern over the potential negative impact of financial relationships that may undermine our system for protection of research subjects and compromise the integrity of our science. After a very successful August 2000 HHS-sponsored conference on financial conflict of interest and human subject protection, an HHS working group developed a draft interim guidance document for IRBs to stimulate public discussion of the steps that could be taken by IRBs, investigators, and institutions to strengthen human subject protections through the disclosure, management, and whenever possible, avoidance of elimination of financial relationships that pose conflicts of interest.

OHRP presented this draft interim guidance document to the first meeting of NHRPAC in December 2000, and in January 2001, OHRP disseminated the draft widely for public comment.

In response, the Association of American Universities (AAU) and the Association of American Medical Colleges (AAMC) accelerated their efforts to issue guidelines for their members, which they did in 2002. Many, including HHS, applauded their responsible initiatives and will be watching to see how the research community responds to them. A sensible and effective approach to identification and management of potential conflicts that might otherwise undermine public confidence in, or even the integrity of, the human research process is essential. Recent revelations that Harvard Medical School might take steps to loosen its restrictions on financial relationships of investigators with companies sponsoring their research are not reassuring, coming only weeks after HHS issued its final draft guidance document calling for more careful consideration of such financial relationships and the conflicts of interest they can create. That monetary considerations can and do affect investigator behavior and may compromise the safety and interests of human subjects remains a serious concern. The AAMC and the AAU have made this point very clearly in their published guidelines and it is now up to the research community to take the lead. Congress should continue to monitor developments in this area closely. Failure of the research community and industry to act responsibly in this arena may require regulatory remedies.

**Recommendation 9: Promote international harmonization of standards for human research and capacity development.**

The international community of scientists and physicians is intensifying its efforts to address the complex challenges of international, cross-cultural research. The HHS Inspector General recently issued a report on oversight of international human research, and identified the many challenges that exist. Last March, OHRP created a new interdisciplinary Program for International Activities to lead and coordinate the Department's human subjects protection activities in the international domain. HHS, through OHRP and FDA, has taken a leading role as a partner alongside other international organizations to encourage and support education and the development of capacity for ethical review and oversight of human research throughout the world's research community.

In December 2001, the Department hosted the Third Project Development Team meeting of the Strategic Initiative for Developing Capacity for Ethical Review (SIDCER), an initiative fostered by the World Health Organization and the European Forum for Good Clinical Practice. Under the auspices of SIDCER, regional fora have been established around the world to promote and support local development of ethics review committees and to establish standard operating procedures and criteria for surveying their operations to ensure quality. In 2002 HHS, including OHRP and FDA, sponsored and participated in five regional international workshops as part of SIDCER's initiative in Best Health Research Practices. OHRP already extended its quality improvement initiative to the international domain at the request of the major universities of South Africa, where a team visited six centers last summer. FDA has also increased its international Bioresearch Monitoring Program, reflective of the globalization of clinical research and submission of multinational studies as part of product applications. As globalization

continues, more intensive oversight efforts must also be pursued. As in the United States, independent international accreditation of human research protection programs may be an effective mechanism to enhance their effectiveness and facilitate the acceptance of data to support the drug approval process globally, even in the absence of a uniform global regulatory framework, something that is unlikely to develop any time soon.

The globalization of human research is clearly accelerating and the US must be a partner in that process. HHS is continuing to work with the World Medical Association, the European Forum on Good Clinical Practice, the Council of International Organizations of Medical Societies and other international organizations to refine the interpretation and application of the revised Declaration of Helsinki. FDA has played a leadership role in the adoption of Good Clinical Practice guidelines as a harmonized international framework for responsible conduct of clinical trials. The NIH, through its Fogarty International Center, and the Centers for Disease Control and Prevention (CDC) are partners in these efforts. A working group was convened prior to my departure from HHS to propose guidelines for evaluating the basis of 'equivalent protections' for human research participants as called for in the Common Rule when federally supported research is conducted outside the US. A report from this group should be finalized soon. As international efforts to build capacity for responsibly conducting ethical human research around the world grow and expand, we must be part of them, even if this means clarification or modification of existing regulatory requirements.

### **Concluding Remarks**

The American people can reap the benefits of biomedical research and technological discovery only through human studies and they deserve the best efforts of the Congress and the Administration to increase our national investment in research and development. But without an effective system for protection of human subjects, we risk losing the trust of those individuals upon whom our human research is absolutely dependent.

Too often, our attention has focused on deficiencies and tragedies, often to the exclusion of the positive. Accordingly, OHRP commissioned an independent consultant to develop a national award program to recognize programs of excellence in protection of human research subjects. This program, the Awards for Excellence in Human Research Protections (AEHRP) is now in place and the first award was announced at the Public Responsibility in Medicine and Research (PRIM&R) annual meeting in December of last year, going to the Baylor College of Medicine for its development of an information system to support the human research protection program.

Such approaches are consistent with a performance-based system that focuses not on regulatory compliance *per se* as an end, but truly on the effectiveness of the process for its real goal, protection of human research subjects.

While HHS and the other federal agencies, and the research community at large can rightfully take pride in what has been accomplished or initiated during the initial phases of an ongoing remodeling effort, much remains to be done. The magnitude of the task is enormous, as is its complexity. Obviously, changes in leadership can shift priorities, and some of the initiatives that have been started could fall by the wayside. I hope that they do not...only time will tell.

As this remodeling of our system for protection of human research subjects continues, we must be cognizant both of the progress being made and of the impediments that continue to stand in the way. As new programs of quality improvement, education, expanded not-for-cause compliance oversight and private accreditation are being implemented, there is a critical need to collect data that will help allow objective evaluation of the effectiveness of these reforms. In the end, the responsibility will likely fall to Congress to take comprehensive legislative action to promote and coordinate initiatives directed toward promoting responsible conduct of human research, including protection of human subjects, and ensuring that the resources provided for these efforts are commensurate with their importance to the realization of our human research mission.

Creation of an autonomous oversight office within the VA was, and today remains, an important step toward ensuring the integrity of its human research programs and enhancing its system for protection of research participants. The same can be said for oversight of all human research across the federal government. I believe, as do many others, that time has come, in fact, is overdue, for definitive and comprehensive action to create a single regulatory framework for all human research regardless of the source of funding and a single, autonomous office, agency or commission to implement the process, with oversight of the office by an independent board of overseers composed of representatives drawn from both the public and private sectors, and a truly independent and balanced advisory committee based outside of the political influence of government that possesses the wisdom and insight to tackle the challenging ethical and policy issues facing human research today and tomorrow.

In closing, I would like to acknowledge and thank my many friends and colleagues both in government and in the private sector who have contributed to the ideas expressed in this statement, and in some cases to the actual text through their thoughtful comments and suggestions. In particular, I would like to thank Dr. Arthur Lawrence, Deputy Assistant Secretary for Health, HHS for his strong support and invaluable counsel and advice during my period of government service.

This statement is not intended to represent an official position of the U.S. Department of Health and Human Services, National Science and Technology Council, or any other federal offices or agencies.

Thank you, Mr. Chairman and Subcommittee members for this opportunity to share these views.

Appendix 1: Report to the Advisory Committee to the Director, National Institutes of Health, from the Office for Protection from Research Risks Review Panel; Nancy Dubler and Renee Landers, Co-Chairs, June 3, 1999.

Full text available at <http://www.nih.gov/about/director/060399b.htm>, accessed June 12, 2003.