

HUMAN SUBJECTS PROTECTIONS IN VA RESEARCH

HEARING BEFORE THE SUBCOMMITTEE OVERSIGHT AND INVESTIGATIONS OF THE COMMITTEE ON VETERANS' AFFAIRS HOUSE OF REPRESENTATIVES ONE HUNDRED EIGHTH CONGRESS FIRST SESSION

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HUMAN SUBJECTS PROTECTIONS IN VA RESEARCH

WEDNESDAY, JUNE 18, 2003

U.S. HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON VETERANS' AFFAIRS,
Washington, DC

The subcommittee met, pursuant to notice, at 10 a.m., in room 334, Cannon House Office Building, Hon. Steve Buyer (chairman of the subcommittee) presiding.

Present: Representatives Buyer, Boozman, Hooley, and Evans.
Also present: Representative McNulty.

OPENING STATEMENT OF CHAIRMAN BUYER

Mr. BUYER. Good morning. Welcome to today's Subcommittee on Oversight and Investigations for the House Committee on Veterans' Affairs hearing on human subjects protection in VA medical research, dated June 18, 2003.

Today's hearing deals with very crucial issues that, I believe, demands constant and consistent oversight: the issue of human subjects protection in VA medical research.

It's not a new issue, we have looked at this issue in the past, and I applaud the VA for taking several positive measures to strengthen its oversight of medical research. But we also have some lapses.

In fact, the VA announced the establishment of the Office of Research and Compliance and Assurance, an independent oversight body, to monitor VA research programs, at our 1999 hearing. Another positive step taken by the VA in 2002 was initiating the accreditation process of its human research protection programs with the National Committee on Quality Assurance, NCQA.

Hopefully, we will receive an update on these and other problem areas which Dr. Roswell outlined in previous testimony. When he testified at our May 16, 2002 hearing, Dr. Roswell stated that the most common deficiencies involved in accreditation are in three main areas: one, lack of local facility policy and procedures related to IRB structure and operations; number two, a lack of policy and procedures related to informed consent process and the conduct of informed consent documents; and number three, the evaluation and determinations the IRB must make and document during initial review of research programs.

The subcommittee is also interested in the Office of Research Development's efforts to provide guidance to VISN directors concerning staffing levels of independent review boards. It is apparent that the role of IRBs approving and monitoring research protocols

for all projects at the facility level must have the necessary support to fulfill its mission, thereby ensuring that all applicable regulations for the protection of human subjects is adhered to and followed by all VA researchers.

While the VA has made a good faith effort to address problems that are documented dating back to 1993, it does appear that there are still some recurring problems that need to be addressed immediately.

The outstanding questions are, is it systemic? Can more be done? The purpose of this hearing is not to question the good faith effort, because I think that those who are involved are doing their very best. But there are also some who are sometimes captured by their ambition or aspiration, that they are willing to dance upon the edge. And there is a human being at stake.

The groundwork for today's hearing stems from a hearing held by this subcommittee on April 21, 1999, entitled, "The Suspension of Medical Research at West Los Angeles, and the Sepulveda VA Medical Facilities and Informed Consent and Patient Safety in VA Medical Research."

At the hearing, former Chairman, Terry Everett stated, "The subcommittee demands an explanation and accountability. These outrageous crimes against our veterans must not happen again." The outstanding question is, has it happened again?

Since then, several hearings have been held by the subcommittee to ensure that necessary actions are taken to ensure that our nation's most vulnerable veterans are protected, and not subjected to any type of abuse, such as the violations imposed upon them at the greater Los Angeles medical facilities.

During today's hearing, we hope to learn what precipitated recent actions taken by the VA in its organizational restructuring within the office of research development.

I know that we have the same goals that relate to VA medical research. We do not want veterans to have their rights denied, or to place them in harmful environments. Likewise, we recognize the tremendous contributions that have been made by the VA through its medical research, and the discoveries of important life-saving drug therapies, medical devices that have benefitted not only veterans, but also all Americans and others around the world.

I also recognize that there is ongoing investigation with regard to the facility in Albany, NY. And because there is a criminal investigation, I just caution members to be careful about trying to solicit specific facts from the VA, and that we can sort of speak in tongue, vague, in generalities, and dance along the edge.

And if any of the members want any facts in greater detail, you can obtain them through me, through our office. But let's not get too far into that today.

I would ask unanimous consent that Mr. McNulty be permitted to join the subcommittee today, and be permitted to ask questions, in accordance with the committee rules. Any objections?

[No response.]

Mr. BUYER. Hearing no objection, so ordered. What that means, Mr. McNulty, is that you will be recognized after all the members of the committee are recognized, and we are pleased that you have joined us here today.

Also, before I yield, Ms. Hooley, I want to express to my colleagues on the Energy and Commerce Committee, we are marking up the Medicare prescription drug bill, and I believe the first amendment up is my amendment. So as soon as I get the notice, I am going to have to leave, and then Mr. Boozman, if you could then take the chair.

Ms. Hooley, you are now recognized for an opening comment.

OPENING STATEMENT OF HON. DARLENE HOOLEY

Ms. HOOLEY. Thank you, Mr. Chairman. I welcome our guests this morning. I also am going to join the Chairman in signing on to his bill which calls for oversight research compliance and assurance for the Veterans Health Administration.

There is a reason why every federal agency has an Inspector General. There is a reason why congressional committees have oversight and investigative subcommittees. It is our business to oversee and investigate the care and treatment of United States veterans. And as the VA well knows, this includes continuous scrutiny of VA programs and procedures.

Human subject research is no exception to this protocol. Fully funded robust research enables VA doctors to improve the physical and mental health of all Americans. Cardiac and cancer surgery, HIV and Hepatitis medication, post-traumatic stress and sexual trauma treatment, the final products of VA research are tangible examples of assisting those who have borne the battle.

As GAO points out in their testimony, VA research has a long history of success stories: the first liver transplant, the nicotine patch, and many other devices, techniques, and medicines that not only benefit this country's veterans, but also improves the lives of everyone living in the United States and throughout the world.

However, VA has not been problem-free in managing human subject research. Past problems closed the program at West Los Angeles. The GAO noted problems in a prior review of VA human subject research programs. There was a death of a human research subject in Albany, NY. Today, perhaps, we shall glean the culture that permits this type of problem to continue unchecked.

Writing training plans and promulgating policies is a necessary first step. But sometimes, when the issue and the stakes are as high as they are for human subject research, you must go and see for yourself. It takes robust oversight, supported by adequate funding. It takes vigilant managers at all levels, willing to look, listen, and to ask why.

Where veterans are the test subjects of a VA research, we need a no excuses mentality. I am stunned that the first response of VA, upon encountering a problem here in the Albany death, was to compromise the independence of the oversight agency by placing control directly under the office responsible for conducting research.

Regardless of the integrity of the principal parties involved—and I am not passing any judgement—but it seems only a matter of time until someone might try to attempt to guide or limit some future investigation. This cannot be tolerated, and alignment of oversight under the office of research and development would eliminate checks and balances needed for effective and safe management.

Again, what culture produced—an initial solution where independence is compromised. Veterans deserve the best care. Veterans who participate in research studies deserve to be treated as more than a means to an end. Veterans have protected this country from harm on foreign and domestic shores. It is the very least we can do to ensure their protection from incompetent and research improprieties.

And I yield back the remainder of my time.

Mr. BUYER. Ms. Hooley, thank you for joining on the bill, and I appreciate your contribution. This is really, truly a bipartisan effort. Mr. Boozman, do you have any opening comment?

Mr. BOOZMAN. [Shaking head.]

Mr. BUYER. Thank you, sir. The chair now recognizes Mr. Evans, ranking member of the full committee, for any comments he would like to make.

OPENING STATEMENT OF HON. LANE EVANS, RANKING DEMOCRATIC MEMBER, FULL COMMITTEE ON VETERANS' AFFAIRS

Mr. EVANS. Mr. Chairman, there is no question that I value the research at the VA. There is also no question of the high duty the VA has to protect its human research subjects.

Human research subjects must be informed of risks and consent to those risks voluntarily. Risks must be reasonable in relation to anticipated benefits to an individual or to society. The selection of research subjects must be fair. The common rule was adopted to create a system of protection for human subjects, based on written regulations.

The common rule assigns responsibilities to investigators. It establishes an oversight mechanism for research at the institutional level. It also takes agencies like the VA to ensure compliance by these other institutions.

The VA has experienced past problems with management and oversight of human subject research. Sometimes research at VA facilities was suspended due to actual harm, or because of the potential for harm.

VA must adapt rules and procedures that are foolproof, and must educate human subjects and researchers to construct a reliable incident reporting procedure.

The VA must ensure strong and independent oversight of high human subject research matters. Policy must translate into real oversight at the program level. To accomplish this, I cosponsored H.R. 1585.

I also co-sponsored H.R. 1585 after a recent possible research-related death, because the initial reaction of the VA was to place the oversight agency under the control of the very organization that they were to hold accountable.

This would obviously limit independence, and could appear as a conflict of interest. While the VA viewpoint has been favorably changed, the legislation is still needed.

Veterans are the beneficiaries of VA research. We must take all precautions to prevent them from becoming victims. And I thank you, Mr. Chairman, for allowing me the time.

Mr. BUYER. Mr. Evans, you and I signed a letter on April 24, 2003, to Chairman Simmons, the chairman of the Subcommittee on Health, to mark up H.R. 1585. I have not received a response to our letter. Ms. Hooley, I thank you for joining us in that. And hopefully, today's hearing can help get a little more momentum.

As soon as I get a response, Mr. Evans, I will let you know.

Mr. McNulty, you are recognized for any comments you would like to make.

OPENING STATEMENT OF HON. MICHAEL R. MCNULTY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW YORK

Mr. McNULTY. Thank you, Mr. Chairman. I thank you, and the ranking member of the subcommittee, the ranking member of the full committee, Mr. Boozman, and all other members of the subcommittee, for allowing me to participate today.

As I get older, Mr. Chairman, I work more diligently on trying to keep my priorities straight. One of those priorities is to remember that had it not been for all of the men and women who wore the uniform of the United States military through the years, people like me wouldn't have the privilege of going around bragging, as I often do, about how we live in the freest and most open democracy on the face of the earth.

Freedom isn't free. We have paid a tremendous price for it. I try not to let a day go by without remembering with deepest gratitude all of those who, like my brother, Bill, made the supreme sacrifice, and all of those like many people who are in this room, who are willing to put their lives on the line, put their lives on the line for all that we hold dear, and then, thankfully, came back home, and rendered outstanding service in the community, and raised beautiful families to carry on in their fine traditions.

These are the things that I am most grateful for today. And that's why, when I get up in the morning, the first two things I do are to thank God for my life, and veterans for my way of life.

I thank you for holding this hearing, because it's a very serious subject. I understand the constraints that we are under, and I will abide by those.

I just want to say that I have been in public office for 34 years, and throughout that period of time I have been associated with the Veterans Administration Hospital in Albany, NY, now named the Samuel S. Stratton VA Medical Center, after our late colleague, Sam Stratton. And I can say to you, Mr. Chairman, that throughout all those years, that facility, in my opinion, has rendered outstanding service to all of our veterans, and I am deeply grateful to all of those who have worked at that VA medical center through the years.

This latest incident which is now under investigation troubles me greatly. And that is why I am deeply grateful to you for stepping up to the plate, and recognizing this particular problem and others across the country, and working to rectify them.

And as you know, I am already a sponsor of your bill, H.R. 1585, and I just wanted to come here today to thank you for stepping forward, along with the other leaders of this committee and the other

members of this committee, to make sure that we continue to provide the best possible health care services to all of our veterans.

Thank you, Mr. Chairman.

Mr. BUYER. Thank you, Mr. McNulty. We are really privileged to serve on this committee. We sit in this committee room under these flags, and some of these flags represent a lot of sacrifice. And especially when you get to see the military's flags, and you see all of those streamers, that's a lot of battles. I appreciate your being here, and I appreciate your cosponsorship.

We will now turn to our first panel, Ms. Bascetta, from the GAO. Ms. Cynthia Bascetta, director of the Veterans' Health and Benefits Issues at the U.S. General Accounting Office. We also would like to recognize Dr. Greg Koski, senior scientist at the Institute for Health Policy, and the first director of the office of Human Research Protections. Ms. Bascetta, you are now recognized.

Ms. BASCETTA. Good morning.

Mr. BUYER. Good morning.

STATEMENTS OF CYNTHIA A. BASCETTA, DIRECTOR, VETERANS' HEALTH AND BENEFITS ISSUES, U.S. GENERAL ACCOUNTING OFFICE; AND GREG KOSKI, M.D. SENIOR SCIENTIST, INSTITUTE FOR HEALTH POLICY, MASSACHUSETTS GENERAL HOSPITAL, HARVARD MEDICAL SCHOOL

STATEMENT OF CYNTHIA A. BASCETTA

Ms. BASCETTA. Mr. Chairman, and members of the subcommittee, I am very pleased to be here today to discuss the strengths and weaknesses of VA's actions to protect the thousands of veterans who participate in its research programs.

While research offers the possibility of significant benefits to individual participants and society, we all recognize that it is not without risk to research subjects. VA and other federally-funded research programs are governed by extensive regulations to minimize these risks, and to protect the rights and welfare of human subjects.

Since many veterans are unable to afford private health care, and may fear jeopardizing their access to VA care if they do not agree to participate in research, VA has a special responsibility to safeguard their rights and protect their welfare.

Nevertheless, serious failures in human subject protections in both VA and non-VA research have come to national attention over the past several years. In September 2000, we testified before this subcommittee about the uneven but disturbing pattern of non-compliance we found in our review of eight VA medical centers.

We made recommendations to strengthen weaknesses we identified in guidance, oversight, and funding for human subject protection activities. Today, I would like to note the progress VA has made in implementing the recommendations we made nearly 3 years ago, and to comment on VA's ongoing reorganization of its research offices.

Mr. Chairman, VA has taken some important steps to strengthen aspects of its human subject protections, most notably, through its compliance office's internal oversight activities, and by leading the

research community in instituting an external accreditation program.

On balance, however, VA has not taken sufficient action to respond to our recommendations. VA still needs to update its policy to implement governing federal regulations. We learned yesterday that they plan to do this within 30 days.

VA has also not ensured that all personnel involved in human subjects research will receive periodic training. And they need to ensure that institutional review boards have information that can help them interpret reports of actual adverse events, and that sufficient funding is allocated to support human subject protection activities at all medical centers.

As you know, VA is now in the midst of reorganizing the Office of Research Oversight, formerly ORCA, and the Office of Research and Development. The reorganization began early this year without adequate planning and notice to affected staff.

For example, when ORCA was disbanded, the compliance function and staff were initially assigned to ORD. Compliance field personnel began reporting their activities to ORD. This reporting arrangement conflicted with generally-accepted government auditing standards requiring that offices with responsibility for assessing regulatory compliance be organizationally independent of the offices they review.

Consistent with the legislation that you introduced, we understand that the compliance office is now accountable to the Under Secretary for Health, not the chief officer of ORD. Although our concern about independence appears resolved, VA's reorganization raises other questions about the extent of the Office of Research Oversight's authority.

In the past, ORCA was authorized to perform for-cause investigations of alleged non-compliance, as well as routine inspections. Your bill would establish, in statute, the compliance office's authority to continue to conduct routine inspections.

Existing memoranda establishing the new compliance office, however, are silent on routine inspections. Experts tell us that the authority to conduct these inspections is important, because such inspections are essential in minimizing risk to research participants, rather than merely addressing instances of non-compliance after the fact.

The reorganization also raises questions about VA's plans for strengthening human subject protections. For example, the reorganization assigns responsibility for education and training to ORD. Although officials told us yesterday that the Office of Research Oversight would continue to provide guidance regarding specific instances of non-compliance, they have not formalized this responsibility in writing.

ORD has also been assigned the responsibility for policy development. But existing memorandum have not clarified what role the Office of Research Oversight will play in policy development.

We are concerned that if VA's compliance and operational research offices do not collaborate on both education and policy, VA could miss the opportunity to bring to bear the collective expertise of these two offices.

In addition, we are concerned that if ORD takes the lead on policy relating to compliance functions, that could inappropriately interfere with the Office of Research Oversight's ability to independently oversee compliance.

Mr. Chairman, this concludes my remarks, and I would be happy to answer your questions, or those of the other subcommittee members.

[The prepared statement of Ms. Bascetta appears on p. 37.]

Mr. BUYER. Thank you. Mr. Koski.

STATEMENT OF GREG KOSKI

Dr. KOSKI. Mr. Chairman and distinguished members, thank you for the opportunity and privilege to appear at today's hearing. The longstanding and continuing commitment of this subcommittee to the well-being of research participants is well-recognized and widely appreciated.

Indeed, it was here in September of 2000 that I, then as the first director of OHRP, the new office at the Department of Health and Human Services for the oversight of human research, first described to the Congress and the American people the Department's vision for the future of our national system for the protection of human subjects.

Since that hearing nearly 3 years ago, the Department of Health and Human Services and the Department of Veterans Affairs, with OHRP and ORCA, working hand-in-hand with other federal agencies, have begun to implement a new approach for the protection of human subjects in research, one based on the simple concept that the first responsibility of everyone involved in the research process is to protect the rights, interests, and well-being of the individuals who voluntarily participate as the subjects of studies. Among these are veterans who have served America not only in our armed services, but also as research subjects in support of the VA's health research programs.

The new approaches pioneered by HHS and VA are more than just an improvement of the former oversight and corrective action approach. They represent a new paradigm. They provide a framework for a system that is focused on prevention. 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 than that.

Our system must minimize the likelihood that research participants will be harmed. We must have a system that is both proactive and interactive, and not reactive.

The programs that have been developed and implemented by OHRP and ORCA are taking us down this new road, where the goal is responsible conduct of science, not mere procedural compliance with regulatory requirements. At HHS, this focus on prevention, performance, and quality improvement has been incorporated into the Department's strategic plan, and I believe that there will be no turning back.

Over the past few months, the VA's human research program has again been subject to intense scrutiny, as new allegations of non-compliance, abuses of human subjects, and scientific misconduct have come to light. Further, the organizational restruc-

turing that last January eliminated ORCA and returned, at least in part, oversight of research activities to the Office of Research and Development, have been a source of concern.

The need for—and even more importantly, the value of—independent oversight of research activities has never been more clearly appreciated. Independent objective oversight and evaluation builds confidence and trust. We have come to realize all too well that it's erosion of this trust that poses the single greatest threat to the continuing vitality and productivity of our health research mission.

Shortly after ORCA was created within VA to provide independent oversight of research activities at VA facilities, a similar step was taken at HHS, the creation of OHRP within the Office of the Secretary. The creation of OHRP was considered by many to be a sentinel event in an effort to reform the nation's human research system.

Its creation was recommended in June 1999 by an expert review panel convened in response to continuing concerns over the organizational placement, resources, and effectiveness of the Office for Protection from Research Risks, OHRP's predecessor.

As detailed in that panel's report, even perceptions of competing commitments and conflicts of interest inherent in the placement of an oversight office in a subordinate position within the very agency that it is supposed to regulate were among the compelling arguments for the establishment of a new organizational structure, an autonomous office within HHS.

The panel's report is directly relevant to your consideration of the optimal placement of human research oversight responsibilities within VA, and I would respectfully request, Mr. Chairman, that this report be entered into the record of this hearing, along with my written statement.

(A copy of the report can be found at this website: <http://www.nih.gov/about/director/0603996.htm>)

Dr. KOSKI. The programs initiated by HHS and VA address virtually all of the major recommendations of the HHS Office of the Inspector General and the General Accounting Office focusing on strengthening oversight, but they are still at a very early stage. This is a work in progress, and much remains to be done, and the resources to accomplish these goals must be forthcoming.

Upon review of the progress that is being made, it's clear that the important contributions of ORCA have helped us along this road. And that calls into question the rationale, motivation, and justification for its dissolution.

Independent oversight is critical to accountability. Unfortunately, recent events at some VA medical centers have demonstrated that some programs and investigators have yet to embrace their responsibilities. Of course, even the most effective system of oversight cannot eliminate the possibility of mishap or misconduct. But the research community and the Federal Government cannot tolerate those who are unwilling to fulfill their responsibilities.

Based upon the activities of the VA and HHS, the need for a more independent and consistent, integrated approach to human research oversight at the federal level has been discussed for sev-

eral years. At the executive branch, the Human Subjects Research Subcommittee of the NSTC's¹ Committee on Science has made a valiant effort to proceed with integration under its new charter.

But I do not believe that it has yet reached its full promise, largely because of administrative barriers and conflicting priorities, or opportunities within the various federal departments. It may be simply impossible to achieve the goals of integration and consistency under the existing federal statutory framework.

As we have seen in the case of homeland security, the only way to achieve these goals may be for the Congress to take action toward creating a comprehensive system for oversight of human research, one that includes a single federal commission that can operate with authority and autonomy that's unencumbered by competing interests of individual federal agencies trying simultaneously to fund and conduct the research, while also bearing responsibility for oversight of those activities.

This commission must also be sensitive to the changing environment of science and be responsive to both the public and the research community it serves.

This was the challenge that fostered the creation of both OHRP and the ORCA at VA. Mr. Chairman, the bill that you have introduced with bipartisan support provides a statutory resolution to the problem within the VA, but it may not go far enough.

The American people can reap the benefits of biomedical research and technology only through human studies, and they deserve the best efforts of 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 individuals upon whom our research mission is absolutely dependent. As with the creation of OHRP and HHS, the creation of an autonomous oversight office within VA was and remains today an important step toward ensuring the integrity of its human research programs and enhancing the system for protection of human subjects.

The same must be said for oversight at the federal level, more broadly, and I believe that the time for action is not only now, but in fact, it's overdue.

In closing, I would like to acknowledge and thank the many friends and colleagues who have contributed, both inside government and outside, in the private sector, to these efforts over the years, and to the ideas that I have expressed and shared with you today.

I am happy to entertain any questions, Mr. Chairman.

[The prepared statement of Mr. Koski appears on p. 55.]

¹NSTC: National Science and Technology Council of the White House. (EOP)

Mr. BUYER. Ms. Bascetta, thank you for your contribution, along with Dr. Koski. Dr. Koski, your testimony was excellent.

You got my attention, Dr. Koski. I take it from your testimony, that you would concur that an independent oversight body should be codified into law.

Dr. KOSKI. Yes, Mr. Chairman, I do.

Mr. BUYER. Now, please specify your recommendations to me when you said that, "I like what you are doing, but you don't go far enough." Please express your opinions and recommendations.

Dr. KOSKI. Mr. Chairman, I believe that the action that your bill would take with respect to VA would address the problem within that agency. But the problem that I see is larger than simply at one federal agency.

I think the need is to create a uniform system for oversight of human research, all human research, regardless of the source of funding, under a common federal regulatory structure, and to have an independent, autonomous agency within the government that would be subject to the oversight of a board of overseers that would include representatives from both the public, as well as the government, in order to ensure that the activities of that commission are fulfilling its goals, and also to include an independent advisory committee that would be able to provide balanced and authoritative advice on the ethical, scientific, and policy issues that are going to continue to face us in human research as we go forward.

Mr. BUYER. All right, help me out here. You were at NIH, and then you pulled this out of NIH at HHS, and you are saying, "Wait a minute, Steve, don't do this just for the VA, think bigger."

So, obviously, I serve on the health subcommittee in Commerce. So what you are saying is that this bill is too narrow and we should go back to the drawing board?

You know, I feel like I am now going beyond the jurisdiction of this committee—but are you also saying that there are concerns with regard to how we fund research within NIH and—you name it, FDA, DOD? I mean, the list goes on. We fund many types of research out here, and you tell me we are just too narrow and we should think in broader terms?

Dr. KOSKI. Mr. Chairman, I am not the first to voice these concerns about the largely fragmented approach to human research oversight across the Federal Government. The National Bioethics Commission and several other expert commissions that have been convened over the years have recognized the need for greater integration, and the calls for a uniform approach to oversight and independence of the oversight office are not new.

So, I am simply restating them. And I believe that the experiences that we have seen over the last 3 years, as efforts have been made to strengthen these programs, validate the pre-existing concerns, and also the recommendations that have been made.

Again, not to attack this problem on an agency-by-agency basis, but rather, to take a comprehensive and wide-ranging approach that would basically provide independent oversight of human research activities across the entire Federal Government in a coordinated and effective manner.

Mr. BUYER. Well, I didn't come to Congress to grow government, but you have gotten my attention because we fund research in so

many different areas. I never thought about creating a separate federal agency. We have the FBI doing one thing, and now what, create another agency that has overlapping jurisdictions?

Not that I am against it, I am just telling you you are taking thoughts where I was not prepared to go. I am going to be a good listener, though.

Let me ask this. Of all research—since we place a lot of trust on the honesty and integrity of the researcher and their data, could ORCA or the Office of Human Research Protection, or any other oversight body, actually detect research misconduct in the form of data fabrication? Can you actually detect that?

You are asking us to be proactive. But when you actually go in, could you actually catch that ahead of time?

Dr. KOSKI. Misconduct, in terms of fabrication of data, is something that is, obviously, very difficult to catch, because the very intelligent individual who wants to try to do so is clearly positioned in a way to do that.

However, there are, of course, times in which there are hints that some impropriety has occurred, and there needs to be a process that can investigate those when they do occur. And they are often painful investigations.

But to ensure that when there is an allegation or a concern that arises—and they usually come from whistle-blowers or publications that raise questions about the voracity of the data—the investigatory process has to proceed in a way that the science is—the scientific community is basically removed from the investigation to the extent necessary to ensure the autonomy and integrity of the investigational process.

Mr. BUYER. All right. My time has expired. Ms. Hooley?

Ms. HOOLEY. Thank you. Ms. Bascetta, the Office of Research and Compliance and Assurance, ORCA, has been disbanded. And the Office of Research Oversight is set up as a replacement for VA research oversight. The often referenced catalyst for this change is a recent death of a human research subject.

Your testimony points out that many of the completed recommendations from your 2000 report were fulfilled by the Office of Research, Compliance, and Assurance. I want to know that—did ORCA need to be revamped, were policies adequate, was training adequate, was oversight adequate, were upchanneled communications effective, and will the new management realignment improve human subject protection for veterans?

Ms. BASCETTA. That is a very important question, and we have thought about that a lot in the last few weeks, as we have been looking at the reorganization.

We really can't find a compelling reason for the reorganization. We would certainly agree that VA had not done enough to implement our recommendations, but we wouldn't have foreseen that a reorganization would be necessary. We thought that the organization that they had with ORCA and ORD was appropriate, and that within that construct, those two offices could have taken the necessary actions to move more quickly to implement our recommendations in all of the areas that you listed.

Mr. BUYER. Doctor, you have got my head spinning, trying to figure this out.

Mr. BOOZMAN. The question I would have is that there are many institutions, you know, that do human testing. Is there a good model out there to—I mean, you know, rather than reinvent the wheel, is there a good model out there of somebody that does an excellent job of doing this?

Ms. BASCETTA. I think that the federal regulations that govern human subject protections are the model. The problem is that not enough research is conducted in a manner that complies with those regulations, both within VA and outside VA.

And we have noted within our own work that some of the medical centers that we have reviewed have done a much better job in implementing those regulations, and in funding the institutional review boards to, in many ways, carry out the most important activities to protect patients' rights and welfare.

On the other hand, other organizations that were in the scope of our review did a much poorer job.

Mr. BOOZMAN. Are there strong penalties for those that do falsify, both corporately and individually, that falsify data?

I mean, you know, we have had instances where people did falsify data. Are there strong penalties for those that do that? Is that legislated somewhere?

Dr. KOSKI. There are penalties, sir, but generally they are an exclusion from participation in various activities within the scientific community. They will also carry with them the preclusion of research funding, federal funding for research to an investigator for a period of time. But perhaps the greatest penalty that any investigator can, you know, bear is the penalty that comes along with the destruction of a reputation and a career as a scientist that almost inevitably results after scientific misconduct that includes fabrication of data.

Mr. BOOZMAN. So, if a person is found guilty of fabrication, they can't any longer work in a federally-funded situation?

Dr. KOSKI. At least for a period of time, yes. Generally, an investigator who is found to have engaged in misconduct will enter into an agreement of some sort with the funding agencies that define the conditions under which they will conduct their activities for a period of time.

Mr. BOOZMAN. Is the ORO, is that basically ORCA without the training and the things you mentioned, without the training, without the policy component and the spot checks?

Ms. BASCETTA. Our understanding at this point is that ORO, the Office of Research and Oversight, is responsible for the previous compliance functions that ORCA had.

Mr. BOOZMAN. Without those three things?

Ms. BASCETTA. Correct.

Mr. BOOZMAN. But everything else is basically the same?

Ms. BASCETTA. It seems to be.

Mr. BOOZMAN. Okay, thank you.

Mr. BUYER. Mr. Evans?

Mr. EVANS. Thanks again, Mr. Chairman. Ms. Bascetta, VA worked with academic institutions to develop an optional web-based training program for researchers requiring a score of 75 percent correct before certification—was an optimal program coupled with the 75 percent passing score adequate?

Ms. BASCETTA. It is hard for me to comment on whether the 75 percent score is a good measure or not. I would really like to examine the test, as well as have a better appreciation for the effectiveness of the testing itself.

But on its face, it would seem that a higher score certainly would not be an inappropriate measure.

Mr. EVANS. I yield back, Mr. Chairman.

Mr. BUYER. Mr. McNulty, if you will indulge me for one moment.

Ms. Bascetta, I want to tap dance around this for a second, about the incident in Albany, NY, in thinking about what occurred in Los Angeles. Reflecting on my days as a prosecutor at the U.S. Attorney's office, you know, there is a lot of information that can be gathered during a grand jury process, much of which is relevant, and then that which is material for the specific charge which may be handed down in a specific indictment.

But there will be a lot of information which is not within the public domain. I don't mind having this public conversation with you, because I want to figure out a way in which the subcommittee works with you in doing a bottoms-up review.

Because my instincts are going to tell me that there were perhaps individuals who may have had knowledge, or should have known, and perhaps under the criminal aspects of the law. Perhaps the prosecutor will exercise a judgement that he could not prove a particular charge beyond a reasonable doubt.

So there is a huge gap between the indictment standards of probable cause, and then actually obtaining beyond a reasonable doubt. So the prosecutor will exercise his discretion on whether to ask the grand jury to return an indictment on particular incidents.

That does not mean that this committee is going to let it go. So, in regard to the civil side and administratively, I want to work with you and with the Department of Justice, for us to gain that access to that information, for us to be able to review through it, and for us to come to our own judgements about who was responsible within the chain of command.

I make no allegations. One thing that I know about facts is that they are very cold and that they are very stubborn. And you can finesse them, you can try to hide them, but they keep coming. They don't go away.

And when we have an incident like this that erodes the trust and confidence of even the human subjects, and by the population at large, this subcommittee must act, and GAO, and the VA, and those who want to make corrections. And I think it's the best way for us to do it, Ms. Bascetta.

Do you have any comments, relative to mine?

Ms. BASCETTA. Only that as Dr. Koski said earlier, it is very difficult to prevent someone who has malicious intent from perpetrating harm. But we do have to wonder whether or not, if the human subject protection systems in place are more robust, whether we could detect those kinds of problems more quickly.

And of course, the quicker we can detect them, the quicker we can take patients out of harm's way. So, I would definitely support your action to look on the—I think you called it the administrative side, or the civil side, to work this problem from all directions, and see how we can improve what is a very grave situation.

Mr. BUYER. You know what I also love about the facts —this is my last comment, Mr. McNulty—what I also love about the facts is that if individuals have been wrongly accused, those facts are able to exonerate them.

And it is hard for them to refute any attacks or defamations upon their character by allegations that others may have made, but when we go through this process, it is a way for them to exonerate themselves from allegations that have been made against them.

At the same time, we get to the bottom in finding out who specifically—those who were responsible and accountable. We will let the Department of Justice handle one side, but we have a responsibility to clean up the other. Those are just my thoughts.

Dr. Koski, do you have anything?

Dr. KOSKI. Well, I would just add that perhaps the best protection, security that there won't be problems, is when an institution or an organization has clearly established a norm of conduct and a culture within its own walls, it simply will not tolerate the individuals that may engage in that kind of misconduct.

And I think, in all honesty, sir, that we are seeing this movement begin at institutions across the country, as they recognize their responsibilities and take steps to fulfill them. But it is not something that happens over night, so it will take time to do it. But I think progress is being made there, and we need to encourage that.

With respect to the broader issue that set your mind reeling before, I might just mention, in closing, that Representatives DeGette and Greenwood last year introduced a bill that, in fact, would move very much down the road that I had mentioned of creating an independent oversight office, in a coordinated fashion, under a consistent and uniform regulatory structure.

Mr. BUYER. That would be very challenging. Mr. McNulty?

Mr. McNULTY. Thank you, Mr. Chairman, and I thank both of the witnesses for their excellent testimony, and for their care and concern for our veterans.

And let me ask a practical question, which either or both of you can respond to. As I said in my opening comments, it has been my experience that the vast majority of folks who work, at least at the Veterans' Affairs Medical Center in Albany, are capable, hard-working, caring, giving individuals who do a tremendous job for our veterans who need quality health care.

And what really frustrates me is that when an incident occurs—and as the chairman pointed out, they are actually few and far between, but sometimes they are very serious—that it has an impact on the whole system, and all the employees, and their morale, and so on. And that troubles me greatly.

Also in keeping with the chairman's admonition and not getting specific, I know I can say in general terms that there have been allegations in particular instances at facilities across the country that certain individuals were hired for positions who would not have been hired for those positions had their full background been known.

And my question is, just as a practical matter, before we get to any new legislation, or any new commissions, or anything like that, what can and should be done internally within the Department to

make sure that there is a better job done with regard to researching the background of individuals who are hired for sensitive positions within the VA system?

Ms. BASCETTA. I wish I had a good answer for you right now. I can tell you that we have a current request from the chairman to review, top to bottom, their credentialing system, and we will be starting that work very soon.

Dr. KOSKI. There are already in progress efforts to establish mechanisms for training and certification of clinical investigators that are arising in several organizations across the country.

And it seems to me that the expertise that is required to be a competent clinical investigator who is going to have the well-being of subjects in their hands is something that warrants this degree of training and certification, and I support those programs.

Indeed, some would argue that for certain types of a very risky human research, it may be very appropriate to not allow individuals who have not achieved a demonstrated degree of competency through certification to participate in those activities.

So, again, we see this developing as the bar is raised for everyone. And again, it will take time. But to me, the most satisfying part is that these efforts are arising within the research community itself. These are physicians organizations and others who are working to raise the bar and establish these programs.

I find it ironic that there have been such certification programs for clinical research coordinators, research nurses, IRB managers, and so on, so that those parts of the system have already responded. And perhaps the latest people to arrive at the party are, indeed, the scientists and investigators themselves. But it is good to see them doing it.

Mr. McNULTY. But it seems to me that there is a problem of mechanics here, because before you even get into the quality of the investigators and the investigative techniques and so on, that there are instances out there—again, not mentioning any in particular—where if the investigation had just gone back to the person's previous job or two jobs, that person never would have been hired.

So it is not a really complicated thing, as far as the level of investigation, or their certification, or qualifications, or anything like that. It seems to me that just making sure that somebody picks up the damn phone and calls the previous employer or two employers to ask a couple of simple questions could reveal information which would prevent the hiring of an individual who could cause harm or even death to a veteran.

Dr. KOSKI. That concern has been expressed more broadly within the medical profession, with respect to medical practice, as well as conduct of human research.

Mr. McNULTY. Thank you, Mr. Chairman.

Mr. BUYER. Mr. McNulty, I had passed an article to you that outlines some of the investigations we are going to do into these hiring practices.

Mr. McNULTY. And I thank you for it, Mr. Chairman. I thank you for all your work.

Mr. BUYER. Thank you. Ms. Bascetta, in the GAO's opinion, if the VA had implemented all of your recommendations from your

2000 report on human subject protections, would the VA have been better able to respond to the Albany incident?

Ms. BASCETTA. It is hard for me to know that without knowing the specifics of Albany, but I can say that it does make us wonder whether or not, if the recommendations had been implemented, whether the detection of a problem would have occurred sooner.

Mr. BUYER. Using the same evaluation criteria GAO used in 2000, would you find similar, less than, or greater than level of patterns of non-compliance with human subjects protections?

Ms. BASCETTA. Well, unfortunately, I think I have to respond that if we were to do a review now, because of the weaknesses that still exist, I believe that the pattern of compliance would continue to be uneven. So I think it would be similar to 3 years ago.

Dr. KOSKI. If I may add, please, Mr. Chairman?

Mr. BUYER. Yes.

Dr. KOSKI. Over the last 3 years, the Office for Human Research Protections engaged in some 300 for-cause compliance oversight investigations. Some of those involved actual site visits, many were resolved through correspondence, but they all involved a comprehensive review of the programs where the alleged problems had occurred.

And if one looks at the pattern that has emerged from an analysis of those, there is clear evidence that the research community—at least at institutions that are under the oversight of OHRP—are taking steps to correct deficiencies in their programs, because we found that since many of these were investigations of complaints that were already 2 years old, they had already taken steps necessary in order to correct those.

But in the final analysis, I think this—the necessity of direct interaction, the need to have people going in one mechanism or another, either through compliance oversight, through quality improvement, or other processes that involve direct interaction and evaluation with feedback and all, are absolutely essential. If we simply sit in Washington and wait for something bad to happen, and then go investigate, we will never get to the point that we will have well-functioning systems that achieve their goals.

Mr. BUYER. Ms. Bascetta, your testimony states that the VA does not have a mechanism for handling adverse event reports to ensure that the IRBs have the information they need to safeguard the rights and welfare of human research participants. Are these events reported to the VA's patient safety center?

If you do not know, I will ask Dr. Koski.

Ms. BASCETTA. I do not know for sure, but I would imagine that there is duplication of at least serious adverse events, that there should be a parallel reporting of those events to both the patient safety center in Ann Arbor, as well as to the researchers.

Mr. BUYER. Since we are going to have Dr. Roswell up here next, let me have your opinion, please. I have your statement, we have gone over this in the past before, but in an open conversation here with me, with Dr. Roswell, and the audience, what should the VA's top priorities be? Give us your one, two, three. What is, quick, the one, two, three, the top priorities of the VA for rectifying these deficiencies? What are they?

Ms. BASCETTA. First of all, issue the revised policy, as they told us yesterday, within 30 days, so that the current guidance is clear and available to everyone.

Second of all, require training in policy, periodic and recurrent training, so that the personnel who are involved in human subject research are required to stay current with ways to assure that they are complying with all applicable regulations.

And thirdly, to continue, in a vigilant way, oversight through both for cause and prospective inspections.

Mr. BUYER. Thank you. Dr. Koski, what would be your one, two, three recommendations to the VA?

Dr. KOSKI. I would say requirements for education, training certification of all who are engaged in the human research process, continuing with interactive, proactive quality improvement activities in order to help programs improve, and to use compliance oversight tools, both for cause and not for cause investigative techniques or evaluations as necessary, to supplement and actually promote the full adoption of those practices.

Mr. BUYER. Thank you. I yield to any members who would have follow-up questions, a second round. Ms. Hooley?

Ms. HOOLEY. Yes, thank you, Mr. Chair. Mr. Koski, or Dr. Koski, I appreciate your comment in your statement that we must do more than just go through the motions regarding compliance. What are the tell-tale signs of an organization that is merely going through the motions? How do we know?

Dr. KOSKI. When a program that has a large research endeavor underway has very limited resources dedicated to the management of that process at their institution, I believe that is as strong a sign as any that, in fact, there is a deficiency in the commitment of that institution to the necessary process.

Of course, it could be just a limitation of resources. Those often go hand-in-hand in this world of competing interests, financially. But nevertheless, I think that, as we have seen time and time again, a hallmark.

The failure of the leaders of institutions to make very clear to every member of the organization exactly what the expected norm is, to truly lead by example, and convey the message, is another tell-tale sign. And increasingly, we are seeing the people at the top being the ones to convey the message and set the tone for the institution. I think that's where it has to come from.

You know, when there is also a lack of respect for those who are actually participating on the front lines for the process, where they truly minimize what they need to do in order to meet their obligations and responsibilities, where, in fact, they are simply going through the motions, that's another indicator that, in fact, there is not a robust process in place, there is not an appropriate culture at that institution.

Just because you discover those things doesn't mean that they can't change. But I think that they are tell-tale signs that there will be a problem at that institution.

Ms. HOOLEY. Let me ask you another question. You were at the Office for Human Research Protection, HHS. How many research improprieties did your office investigate? And do you feel that any

of these could have been prevented by the new approaches implemented by VA?

Dr. KOSKI. Within HHS, the organizational structure is somewhat different, in that allegations of research impropriety and misconduct are actually carried out by another office, the Office for Research Integrity. So they are separated there, so I can't comment on that.

I will say, however, that the Office of Research Integrity operates under the existing regulations with the actual research sites themselves, with the institutions that make an assurance to the government that they will have an effective process in place for the adjudication of allegations of misconduct in research.

So that, again, it is a hand-in-hand thing. The institutions bear major responsibility in all of these areas, including the oversight of animals, human research, and scientific conduct.

Ms. HOOLEY. Thank you, Dr. Koski.

Mr. BUYER. I want to thank you both for your contributions here today. This is really an important subject.

I just think it has all been very well said today. And there was a word that was used earlier, and it was in your testimony, describing the patients as a "vulnerable" population. It is so true.

And whether—Dr. Koski, whether they were patients within NIH, I have said this before and I have to say it again, you can have—because of our compassion and our love, family members will do desperate acts, through love, to hold on to life, in that they are willing to participate in research, even cutting edge, even having been informed of the risks, for life. So, that makes them vulnerable.

But when I also then say that that individual is a veteran, to me, they are even more vulnerable, because that veteran comes with a different dimension. "I am going to do it not only for myself but also for my country," which makes them an extraordinarily vulnerable individual. And for that reason, we are going to be tough.

And Ms. Bascetta, I look forward to working with you. And we are not going to let this one go. Thank you for your testimony.

Ms. BASCETTA. Thank you.

Dr. KOSKI. Thank you.

Mr. BUYER. We now have concluded the first panel. If the second panel would come forward, we recognize Dr. Robert Roswell, the Under Secretary of Health, Department of Veterans Affairs.

Also with him will be Dr. Wray, chief of research and development for the VA, and I would ask Dr. Roswell to introduce others who will be with him here today.

Dr. ROSWELL. Good morning, Mr. Chairman. With me today are my Deputy Under Secretary for Health, Dr. John Perlin. On my left, your right, Dr. John Mather, the previous director of the Office of Research, Compliance, and Assurance. On my right, Dr. Nelda Wray, the chief officer for—chief research and development officer, head of ORD. And to her right, Dr. David Weber, acting director of the Office of Research Oversight.

Mr. BUYER. Very good. Dr. Roswell, you may begin your testimony.

STATEMENT OF ROBERT H. ROSWELL, M.D., UNDER SECRETARY FOR HEALTH, DEPARTMENT OF VETERANS AFFAIRS; ACCOMPANIED BY NELDA P. WRAY, M.D., CHIEF RESEARCH AND DEVELOPMENT OFFICER, DEPARTMENT OF VETERANS AFFAIRS; JOHN H. MATHER, M.D., SPECIAL ASSISTANT TO THE UNDER SECRETARY FOR HEALTH, DEPARTMENT OF VETERANS AFFAIRS; DAVID A. WEBER, ACTING CHIEF OFFICER, OFFICE OF RESEARCH OVERSIGHT; AND JOHN PERLIN, DEPUTY UNDER SECRETARY FOR HEALTH, DEPARTMENT OF VETERANS AFFAIRS

Dr. ROSWELL. Thank you, Mr. Chairman. It is a pleasure to be here today, and I want to acknowledge your leadership on an issue that is very near and dear to my heart, as well.

Sadly, despite aggressive efforts that date back to 1999 and even before, including the creation of an independent office of research, compliance, and assurance, VA has continued to experience problems with the conduct of human research that have placed veterans in harm's way.

This is simply not acceptable. Accordingly, we are in the process of changing our policies and operations to ensure that unethical research behaviors will not be tolerated in this Department.

We will ensure that patients are optimally informed when they consent to participate in research, and that research activities are safe and ethical. Thus, we have developed and are implementing new programs and training to support successful research conduct, management, and oversight at every level of the organization.

Today, I would like to give you a brief progress report. Just since VA announced a research stand-down on March 6th of this year, we have made significant changes in the requirements for the conduct of research, many of which have been alluded to by the members of the previous panel and members of the committee.

First, we have required that leadership at each VA facility that conducts human research certify that local institutional review boards, or IRBs, and research and development committees are in place, are working appropriately, and are effectively overseeing the conduct of all human studies.

Second, we have required training of over 15,000 individuals involved in human study research in good clinical research practices. Human studies research personnel are now also required to take refresher courses on an annual basis.

Third, we have required credentials verification, not just on the physicians involved in research, where we have always completed a credentialing and privileging process and background check, but on all research personnel with any degree of patient contact or programmatic responsibility.

The Office of Research and Development is also creating an electronic means of tracking all employees involved in human subject research to facilitate checking these individuals against exclusionary lists.

Following review of our experience with the external accreditation program for human research programs, revised standards were published in April 2003, and the accreditation process that is conducted by the National Committee on Quality Assurance, or NCQA, will begin again this summer, and all VA facilities will have

human research programs complete the accreditation process by the summer of 2005, an external accreditation process, I might point out.

We have also revised the organizational structure for research oversight to align policy and training with the Office of Research and Development, and to focus the Office of Research Oversight on compliance with regulatory and policy aspects of human subjects protections, animal welfare, research safety, and research misconduct.

Since its inception in 1999, ORO's predecessor, the Office of Research, Compliance, and Assurance, or ORCA, under the leadership of Dr. John Mather, contributed in many ways to the improvement of VA's protection of human subjects participating in research.

ORCA provided prospective compliance consultations, retrospective compliance reviews, a compliance program, and a training, education, and development function.

However, our experiences have compelled us to establish mechanisms for more rapid, broad, and effective development and dissemination of policy and education. These actions are directed to go beyond insurance of compliance, and assure adequacy and integrity of research programs.

The VA has established the program for research, integrity, development, and education, or PRIDE, within the Office of Research and Development. PRIDE is a ground-breaking program that is responsible for all education, training, and policy development related to human research protection in the VA.

PRIDE is already serving as a resource for providing guidance and policy development for responsible research conduct. These activities coordinate with and require collaboration with the policies and work of other agencies and organizations involved in the protection of human subjects, both inside and outside the VA.

Such entities include NCQA, the Food and Drug Administration, the National Institute of Health, the Office of Human Research Protection, and other components within VA, as well as quality assurance and patient safety organizations.

While a new infrastructure has been developed in the Office of Research to support effective, rapid improvement in research conduct, VA believes strongly in independent oversight. As described, policy and programmatic educational activities now reside in the Office of Research and Development.

Oversight of compliance and—with policy regulation law and ethics is the responsibility of the Office of Research Oversight. All human resources of the predecessor office, ORCA, are contained in the new Office of Research Oversight, and are now devoted to these three oversight activities.

The activities of the research office and the oversight office are increasingly complementary with problems identified through oversight being met with aggressive solutions by the research office. The skill set embodied by the oversight office staff, in its five regional offices around the nation, and guided by the central office component, is well capable of informed consultative intervention.

Because of its own oversight mission, the Office of Research Oversight will continue to serve as VA's governing body for Federal Wide Assurance for VA facilities, in partnership with the Office of

Human Research Protection in the Department of Health and Human Services.

In our revised program protections, the oversight office will enjoy greater role clarity in discharging the oversight functions of its predecessor organization. This increased focus on oversight activities will assure that problems are investigated and, with the Office of Research as a committed peer office, provided effective and timely policy and training and are corrected.

Research programs that fail to appropriately safeguard patients and the values of ethical research conduct will have funding terminated. We commit to this so that the Department of Veterans Affairs maintains the highest quality research programs in the country, and most responsibly serves the needs of our nation's veterans.

Mr. Chairman, my colleagues and I are prepared to answer questions you may have.

[The prepared statement of Dr. Roswell appears on p. 72.]

Mr. BUYER. Before I respond to your statement, Dr. Roswell, with questions, Dr. Roswell, I have some concerns and haven't been able to discuss this with everyone on the subcommittee, but I bring it to everyone's attention now.

There is a company called Guidant Corporation that has pled guilty to criminal activity, with regard to hiding information and data that should have been reported to the FDA. And 12 people have died because of their stents. And well over 1,000 patients were affected.

And I have made a request of the VA. I would like to know who are veterans, and whether or not the VA had purchased this medical device from Guidant Corporation. And Dr. Roswell, if you have any comments with regard to our request?

Dr. ROSWELL. We are aware of your request. We are aware of the circumstances of the product, and it does appear that a number of VA patients—a small number—of VA patients, on the order of 15, to possibly as many as 30, have received that particular endovascular prosthesis.

We are currently involved in a series of aggressive efforts to identify patients who may have received the prosthesis, or the endograft, and take appropriate actions. I will ask Dr. Perlin to detail the various databases that are currently being queried to ascertain which VA patients may have received such a product, and if, in fact, there have been any adverse outcomes in VA patients.

Mr. BUYER. At this point, we don't know whether or not any of the 12 deaths, whether any of those were veterans, or received this at a VA—

Dr. ROSWELL. We have no indication of a death of any VA patient as a result of a defect or malfunction of this product.

Mr. BUYER. But you are checking the adverse outcomes, Dr. Perlin?

Dr. PERLIN. Mr. Chairman, thank you. As Dr. Roswell mentioned, we have identified that we have purchased 15 of these devices. We also can tell you that we believe we have three inpatients, through a cooperative studies program.

I can tell you that we are actually working through six discrete databases to try to identify any particular patients who may have

been affected by any of the endovascular stints, or the specific product, in particular.

In fact, in our RCA database of over 60,000 adverse events in the last couple of years, we have identified no patients who have had a death attributable to this particular device.

I have to offer a caveat. The caveat is this device goes into people with significant vascular disease, and if they died of a vascular cause, it may not flag even the clinician it may be something that's related. So we're not satisfied that that's the absolute answer.

Of the 15 acquisitions we pulled up through our acquisitions and prosthetics database—and we're going in further detail, not only to ascertain those before the 2001, before that particular model of the device was terminated, but also devices up to the present.

In addition to the RCA database, the acquisitions and prosthetics database, we are working with our national surgical quality improvement program, our clinical patient records—computerized patient record system, including the surgical package, as well as the CPT, or procedure codes, as well as the cooperative studies program.

We are aware of a particular cooperative study trial that randomized patients between a traditional open procedure and the stint, and we believe that there were approximately 32 patients who got one of the stints, and 3 of those stints are the particular model.

We hope to have all of the information back to you within the next 10 days to 2 weeks. And of course, for any patient who might have received this device, we will contact them and will relay not only the manufacturer's information, but FDA recommendations regarding not just the particular device in question, but the category of devices.

Mr. BUYER. With regard to VA's business practices, hypothetically, Dr. Roswell, you and I are in business together in my home town, and we are dealing with a business, and we have now learned that this business which we were dealing with has pled guilty to criminal charges.

And we purchase their product, and maybe one of our clients which we were interlocutor here has been harmed. I don't think you and I are going to be doing business with this individual until certain things perhaps have to happen.

So, with regard to your business practices and your reviews, I am curious about what actions are being taken with regard to your relationship with Guidant Corporation for the fact that a corporation now has pled guilty to such criminal misconduct. Is a review taking place, or what is happening? Could you please tell me?

Dr. ROSWELL. Well, I would agree, and there is actually precedent where VA has suspended business dealings with—

Mr. BUYER. The VA has suspended business dealings with Guidant Corporation? Until what?

Dr. ROSWELL. In this particular case, the Food and Drug Administration is the responsible government agency with oversight that basically licenses, certifies the safety of the product.

We, obviously, will defer in all cases, to guidance from the Food and Drug Administration concerning product safety, particularly in plantable devices.

Clearly, though, in this case, where there is criminal activity involved, and patients may have been harmed, we are not only following—as Dr. Perlin said—FDA guidance, but we are also identifying patients and contacting them, and are not doing business, currently, with Guidant.

Mr. BUYER. Okay. Thank you very much. Ms. Hooley, you are now recognized.

Mr. HOOLEY. Thank you. Dr. Roswell, VA has not formally commented on H.R. 1585. But after some growing pains, VA seemingly has adopted a process that would conform to H.R. 1585. Why did it take so long for you to endorse the wisdom of H.R. 1585, and if that is not in place, if it doesn't pass, what would prevent the VA from returning to a less rigorous oversight scheme?

Dr. ROSWELL. Ms. Hooley, I think we do embrace the principles embodied in H.R. 1585. I think we have shared that with the committee staff director, Mr. Wu, on numerous occasions since the issues came up.

We have taken what we believe is bold and aggressive action to not only refocus and safeguard the safety of veterans, but send a loud and clear message to everyone within the Department of Veterans Affairs that this is a very serious issue, and that it requires not only responsibility, but accountability at all levels in the organization.

H.R. 1585 reflects the commitment and the structural changes that have already taken place within the Department of Veterans Affairs. And so, as I said, we support the concept of the bill.

Ms. HOOLEY. But—say we don't pass H.R. 1585; will you go back? What is to prevent you from going back to where you were?

Dr. ROSWELL. Well, it certainly won't be on my watch.

Ms. HOOLEY. Okay. Are there any new improprieties that we don't know about?

Dr. ROSWELL. The short answer is I don't know about what I don't know about. And I don't mean to be flip. The problem with human research is that it actually affords a better level of care when we make it available to our veterans.

Veterans are very special to me, and I know they are to you, as well.

Ms. HOOLEY. They are.

Dr. ROSWELL. Participation in human research yields access to cutting edge technologies before the Food and Drug Administration may have approved them. And as the chairman pointed out, it often offers life-saving medications, techniques, and procedures where, otherwise, the prognosis is very grim.

So, to me, it is very important in looking out for veterans, that we do everything we can to make research participation an option for them. But by the same token, participation in that research cannot place them in harm's way.

Because of the complexity of research, because of the nuances, it is likely that there will be problems associated with human research. But let me point out that human research will have adverse events that may not be the result of misconduct, that may not be the result of lack of compliance or oversight, that may not be the result of deficient policy, education, or training, because the

very nature of disease is that it leads to untoward events, despite the best interventions of man.

So our goal is to safeguard the process, to identify problems where they exist, but more importantly, to seek to prevent those problems with the emphasis we placed on leadership throughout the entire research community and the Department of Veterans Affairs.

Ms. HOOLEY. Well, I understand about research, and that's why your protocols in oversight and investigation are so important. My question is, though, why has it always been reactive instead of proactive?

Dr. ROSWELL. Well, again, I am going to ask Dr. Nelda Wray to address that. But I think that it must be proactive, and I think we have made some fundamental changes that shift our research oversight towards a proactive approach.

As I said, the challenge is not only identification, but ultimately, it is prevention. And the Office of Research, Compliance, and Assurance was very effective at identification. But research policy, research education, research leadership commitment to safeguard the welfare of our patients is the effort that must be focused at prevention, and I have charged Dr. Wray with that responsibility.

Ms. HOOLEY. Thank you. Go ahead.

Dr. WRAY. May I answer?

Ms. HOOLEY. Yes, please.

Dr. WRAY. Thank you, Ms. Hooley, and thank you, Dr. Roswell. First, I want to commend ORCA, the previous institution, because they were not just reactive, they did several not-for-cause, but simply on a scheduled basis, site visits to oversee those sites.

I think the separation, however, of the policing function and the education function is very, very important. I want to point out that the federal regulations simply categorize what the IRB should be, what the membership should be, what the IRB protocols should look at, as far as risk/benefit ratios, what informed consent should be.

It stipulates that we, on a regular basis, re-review the protocol, and it also stipulates that we look at adverse events. It does not stipulate that we do credentialing, it does not stipulate that we do quality assurance, it does not stipulate the type of proactive quality assurance program that was talked about in the last panel.

Clearly, that is what we need. We need to start with education and training. We have, as Dr. Roswell said, trained 15,000 individuals in the last 6 weeks. We created a software package for good clinical practices. We put it—within 2 weeks, we put it up, and now we have trained over 15,000.

I agree with GAO, that we don't have a policy out yet that requires, but we have guidance out that says they will repeat it every year. And before it is time to do it again, I will have that policy out.

Regarding moving towards this compliance program, I took the job 5 months and 12 days ago. Since that time, we have put seven individuals in the PRIDE office in ORD in Washington, DC. Four of those are new hires and three are transfers. I have hired five individuals at Little Rock, one of which is considered the leading IRB expert within the VA, to create our team for education.

I have moved eight individuals from our cooperative trial program, an additional two-and-a-half individuals from an educational program, and several large consulting grants into an educational effort. If you take that, that's a salary commitment of approximately \$2.2 million I have already committed, and we are still interviewing to increase ORD's commitment to education.

We have developed an e-mail list of our compliance officers. That compliance officer group has 100 names on it. Those are individuals in the field doing compliance. Ninety of our sites already have an electronic IRB to be able to quickly manage their IRB.

So, as of yesterday, we have a formal policy in the field that will create an establishment of a facility level human protection program. What I want to make clear—we are moving beyond the federal regulation. We are going to put in place a quality assurance program at each site which will establish that culture that the last panel talked about that will do ongoing oversight.

There are two things I think you can do regarding fabrication of data. Number one, you can have in place on-site individuals who are doing continuous quality assurance, so people are worried about falsifying that data. If they don't think they are going to get caught, they may not worry about it.

And then you provide them the quality assurance itself. You look directly at the charts. We found—excuse me—the problem in Albany was found. It was sad that it was so long before those charts were reviewed.

We are going to put in place a procedure which will have quality assurance, regularly spot-check for human studies consent, regularly check for the quality of the data, the maintenance of appropriate records on all the studies that are conducted at sites on an ongoing basis.

I don't want to leave anyone with the impression that we are going to look at every patient put into every study, but we are going to make sure we do enough of a probability sample by quality compliance at each site that we know what is going on.

If I could just make one other point, and then I will shut up, this memorandum, 40 percent of all the human studies that we do in the Department of Veterans Affairs are funded by the manufacturing drug industry, yet we have not had a systematic policy to ask those to help to fund our compliance problem.

We do at least \$60 million worth of pharmaceutical studies. It is not only 40 percent of all human studies, but if you take out the chart reviews, it is fully 90 or 95 percent of all the studies that have the potential to really put patients at risk.

What we are doing is starting to charge a compliance fee to the pharmaceutical studies which are done in the VA to help fund, at the site, in addition to the resources we are going to be putting in, help fund at the site the compliance program I have talked about. On a yearly basis, every site will have to report to our office the monies that they have been able to obtain for this function, and their compliance program. So I wanted to make that point.

Ms. HOOLEY. Thank you.

Dr. WRAY. Oh, and I can submit this for the record.

Ms. HOOLEY. Thank you.

[The information follows:]

Department of Veterans Affairs
Veterans Health Administration
Washington, DC 20420

VHA DIRECTIVE 2003-031

June 13, 2003

ESTABLISHMENT OF A FACILITY HUMAN PROTECTIONS PROGRAM

1. PURPOSE: This Veterans Health Administration (VHA) Directive establishes a new policy for the establishment of a Facility Human Protections Program (FHPP) to help Department of Veterans Affairs (VA) medical centers fully cover costs associated with human subjects protection. This policy applies to all newly funded and VA approved industry-funded studies conducted at VA facilities. *NOTE: This policy is not retroactive and thus does not apply to previously negotiated agreements.*

2. BACKGROUND

a. Clinical research involving human subjects requires intensive oversight in order to ensure the protection of study participants; as a result, human subjects research incurs substantial costs. Top professional staff must perform necessary, labor-intensive activities associated with research involving human subjects, including education and training of clinician investigators and research staff, ensuring compliance with applicable regulations, credentialing of research staff, and operation of Institutional Review Board (IRB) committees. In addition, VA medical center staff must perform heavy regulatory administrative duties.

b. Forty percent of all VA research involving human subjects is funded by industry, with funds (hereafter referred to collectively as "grants") accepted by VA in accordance with the gift acceptance authority in Title 38 United States Code (U.S.C.) § 8301. When simple chart reviews are excluded, 80 percent of all human subjects research conducted at VA facilities is industry-funded. Compliance costs associated with these trials have been estimated to be approximately 10 percent of the funds spent in direct support of these studies, excluding IRB-related costs.

c. University affiliates and VA non-profit corporations (NPCs) administer industry-funded grants that are conducted at VA medical centers. The university affiliates typically charge an indirect rate of approximately 26 percent for industry-funded trials, while NPCs charge variable indirect rates ranging from 5 to 25 percent.

d. A review has revealed the existence of systemic weaknesses in the human research protections program, especially in studies funded by industry. There is a clear need for ongoing quality assurance at every VA research site. To address these weaknesses the Office of Research and Development (ORD) has identified four broad compliance-related activities that need to be carried out at every research site:

- (1) Training and education of lead investigators and research staff,
- (2) Credentialing of research staff,
- (3) Ensuring compliance with applicable human research protection standards, and

THIS VHA DIRECTIVE EXPIRES JUNE 30, 2008

VHA DIRECTIVE 2003-031
June 13, 2003

(4) Accrediting of the facility Human Subjects Protection Program by the National Committee for Quality Assurance (NCQA)

e. Existing methods used by the entity administering study funds for the collection of fees to cover IRB-related costs need to continue. *NOTE: IRB-related costs, including initial and continued review, are not to be included with the compliance-related activity costs identified in the preceding.*

3. POLICY: As of July 1, 2003, it is VHA policy that VA medical centers can not accept industry grants (including grants funded through NPCs) that are not sufficiently funded to support the Facility Human Protections Program (FHPP).

4. ACTION

a. **Facility Associate Chief of Staff for Research (ACOS/R)**. The facility ACOS/R is responsible for:

(1) Notifying, in writing, the entity administering the study funds about the implementation of the new FHPP policy.

(2) Ensuring that any grant accepted by VA includes an amount equal to 10 percent of the direct cost of the study, or a flat fee of \$1200, whichever is greater, to be applied towards FHPP-related costs incurred by the VA medical center.

(3) Obtaining from the entity administering the study funds an annual accounting of the total amount of direct costs of industry-funded studies conducted at VA medical center(s) as well as the amount of funds that were made available for support of FHPP costs. This accounting will be compared to records maintained by the local R&D Office.

b. **Facility R&D Office**. The facility R&D Office annually reports to the Director of Finance, ORD:

(1) The information received from the entity administering the study funds, and

(2) An accounting of all expenditures in support of the compliance-related activities.

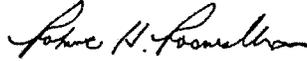
NOTE: ORD annually verifies that sites have complied with this directive and assesses the appropriateness of FHPP rate.

5. REFERENCES: None.

6. FOLLOW-UP RESPONSIBILITY: The Office of Research and Development (12) is responsible for the contents of this Directive. Questions may be addressed to (202) 254-0201.

VHA DIRECTIVE 2003-031
June 13, 2003

7. **RECISSIONS:** None. This VHA Directive expires June 30, 2008.



Robert H. Roswell, M.D.
Under Secretary for Health

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Mr. McNULTY. Mr. Chairman, I thank the members of the panel. I would just with regard to something Dr. Wray just said—and again, I want to comply with the request of the chairman about being too specific—but you said you caught the problem in Albany.

Well, the fact of the matter is that if the allegations eventually prove to be true—and I'm not prejudging anything—you caught it too late.

Now, beyond that, what I want to say to Dr. Roswell is that I am very pleased with both the content and the tenor of your testimony here today. Because with regard to the seriousness of the allegations that have been made in these very limited number of circumstances, and the need to do something about it now, you get it. And I am grateful for that.

And you were in the room during the previous testimony, and I expressed my concern about doing things now. I mean, we want to do the chairman's bill, we want to create commissions, and do these other things, all of which may have impacts way down the line. But I want to see things done now to protect veterans at VA medical facilities. And I think you understand that.

And I am particularly pleased that you have verified what was told to me by VA officials in Albany about these background checks. Because when I talked to them, I was saying, "How can this happen, and what are we doing about it in the future, and so on?"

And they told me that the background checks on the medical researchers will be strengthened and be more stringent in the future, and you have verified in your testimony today that you have ordered that to take place, and that is taking place now.

And the only question I would have in that context, Dr. Roswell, would be I know that you're saying the background checks on the medical researchers, and so on, are more stringent now. Are they as stringent as the background check on doctors? Is that something that can be compared?

Dr. ROSWELL. They are as stringent as we can make them. The databases that record and track physician training, such as the national practitioner data bank, which is a statutory requirement that was implemented and applies to all physicians, there is no equivalent counterpart for that for people involved in research who are non-physician investigators.

But by querying a number of existing data banks, looking at exclusionary lists, doing a formal background check, we are making the process as rigorous as we can, under the circumstances.

Mr. McNULTY. I just want you to know that I am very grateful for that, and very grateful for you to take that proactive step, absent any new legislation, or anything like that, because that is something that can accrue to the benefit of veterans all across this country. I thank you for doing that.

That is all I have, Mr. Chairman.

Mr. BUYER. I would like to clarify something. Number one, in response to Ms. Hooley's question, Dr. Wray, you said within the last 6 weeks you have trained 15,000 people. In regard to Dr. Roswell's testimony, Dr. Roswell says, "We have required training of over 15,000 individuals," which is it?

Dr. WRAY. Which is true?

Mr. BUYER. Which should I follow?

Dr. WRAY. Yes. I could get you the absolutely exact number. We created what is called a——

Mr. BUYER. No, I just needed to know have you trained them, or have you required——

Dr. WRAY. Just less than 15,000 are certified for having been trained.

Mr. BUYER. So Dr. Roswell's testimony is not accurate?

Dr. WRAY. I am sorry?

Mr. BUYER. Sorry, Doctor, but whoever wrote this—this was not accurate, then. That's what I'm correcting, because on page two of Dr. Roswell's testimony, it says, "Second, we have required training of over 15,000 individuals." So what it should say is, "We have completed training of 15,000."

Dr. WRAY. That is correct.

Mr. BUYER. Okay? I just want to make sure. Okay.

Dr. ROSWELL. Mr. Chairman, I apologize.

Mr. BUYER. No, that is all right.

Dr. ROSWELL. We required training of 15,000, we have now a 98 percent completion rate for that.

Mr. BUYER. And is this per—I have the memo here that was sent from the Secretary of the VA to you, specifically, outlining this training program. This is what it is in reference to? And are you saying—it is not?

Dr. WRAY. No. The stand-down requirement, which I believe you should have——

Mr. BUYER. Yes.

Dr. WRAY (continuing). And if not, we will get you a copy of it—required that everybody involved in research receive ethical IRB training as one issue, and good clinical practice training.

The 15,000 researchers we are talking about have received that. The letter you have from Secretary Principi required the training of VISN directors, the head clinical person of the VISN——

Mr. BUYER. All right. Has this taken place?

Dr. WRAY. We have given one session of that to all hospital directors, which was 136 individuals who participated at the Ann Arbor patient safety meeting on May the 28th and 29th. The last day of July and the first day of August, we will train everyone else at our senior management conference in Chicago.

Mr. BUYER. All right. Dr. Roswell or Dr. Wray, when the GAO submitted its report in September of 2000, "While Protection for Human Subjects Need to be Strengthened," the VA agreed to promptly fill five recommendations.

The VA agreed to issue a current, comprehensive, and clear guidance, including the new handbook on human subject protections. Has that been published?

Dr. ROSWELL. No, it has not. The—obviously, this is a broad and comprehensive document that requires a lot of concurrence. And I acknowledge that we have not been as responsive as we should have been, under the circumstances, with the hiatus created by the organizational change, and refocusing the departmental commitment on research.

I have asked that we do everything we can to expedite the publication of that research handbook, the policy guidance that——

Mr. BUYER. What is your time line?

Dr. ROSWELL. Thirty days.

Mr. BUYER. Thank you. An additional agreement with GAO is to determine the funding levels needed to support human subject protection and insure appropriate allocations of funds. Has the assessment been made?

Dr. ROSWELL. It has.

Mr. BUYER. And is this with regard to this new policy about charging the pharmaceutical manufacturers a particular fee?

Dr. WRAY. That is simply the first part of it. We also are currently conducting a survey of all of our sites to determine the volume at each of the sites, and make a plan, which we are doing with a process engineer, on exactly how many people need to be at each site.

We will fund this and have it in place by this coming—with the distribution of the next fiscal year 2004 budget.

Mr. BUYER. Dr. Mather, on page six of Dr. Roswell's testimony, he stated that ORO, and its predecessor office, negotiated over 100 Federal Wide Assurance and related agreements with VA facilities to ensure their commitment to carry out the common rule protections afforded to human subject research.

Can you tell us how many of these agreements were negotiated by ORCA?

Dr. MATHER. The former ORCA negotiated all of those agreements. There are 114 Federal Wide Assurances that we worked through. We also have human research protections at HHS to put into place. At the same time, the institutional review boards, or the IRBs, were simultaneously appropriately registered under those Federal Wide Assurances.

There are two VA medical centers pending that have joint arrangements with their affiliate medical schools. And when those are completed some time this summer, all of the 115 or so medical centers will hold Federal Wide Assurances which will authorize them to conduct human subjects research.

Mr. BUYER. On page four of the GAO testimony, Dr. Mather, it states that the VA awarded a contract to the National Committee on Quality Assurance to provide external accreditation of its medical centers, and human research programs in August of 2000.

How is this process going, and while you were the director?

Dr. MATHER. Mr. Chairman, I would ask to defer the answer to that question to Dr. Wray or Dr. Roswell, since the Office of Research, Compliance and Assurance had no lead responsibility for that accreditation program.

Mr. BUYER. All right. In 20 seconds?

Dr. WRAY. I am very—Dr. Mather's report, I agree with much of what is in it. I believe that the prior NCQA process was both unfair and irrational. We have met with NCQA extensively since I started up here. The process is now both fair and rational. The pause has been lifted. The training will start this week. The review process starts this summer, and all will be reviewed by 2005.

Mr. BUYER. All right. Dr. Roswell, in 15 seconds, do you agree or disagree with the recommendations by the previous panel regarding their one, two, three?

Dr. ROSWELL. Yes, we do.

Mr. BUYER. The hearing is concluded.
[Whereupon, at 11:48 a.m., the subcommittee was adjourned.]

APPENDIX

PREPARED STATEMENT OF CHAIRMAN BUYER

Hearing on Human Subjects Protection in VA Medical Research

June 18, 2003

Good morning. Today's hearing deals with a very crucial issue that demands constant oversight. The issue of human subject protection in VA medical research. This is not a new issue. We have looked at this issue in the past and applaud the VA for taking several positive measures to strengthen its oversight of medical research. In fact, the VA announced the establishment of the Office of Research Compliance and Assurance, an independent oversight body to monitor VA research programs, at our 1999 hearing.

Another positive step taken by The VA in 2002 was initiating the accreditation process of its human research protection programs through the National Committee on Quality Assurance (NCQA). Hopefully, we will receive an update on these and other problem areas which Dr. Roswell outlined in previous testimony. When he testified at our May 16, 2002 hearing, Dr. Roswell stated that the most common deficiencies involved in accreditation are in three main areas:

- Lack of local facility policy and procedures related to IRB structure and operations,
- The lack of policy and procedures related to the Informed Consent process and the conduct of the informed consent document, and
- The evaluation and determinations the IRB must make and document during the initial review of research programs.

The Subcommittee is also interested in the Office of Research Development's efforts to provide guidance to VISN Directors concerning staffing levels of Institutional Review Boards. It is apparent that the role of IRBs—approving and monitoring research protocols for all projects at the facility level, must have the necessary support to fulfill its mission thereby insuring that all applicable regulations for the protection of human subjects is adhered to and followed by all VA researchers.

While the VA has made a good faith effort to address problems that are documented dating back to 1993, it does appear there are still some recurring problems that need to be addressed immediately.

The groundwork for today's hearing stems from a hearing held by this Subcommittee on April 21, 1999, entitled, the Suspension of Medical Research at West Los Angeles and Sepulveda VA Medical Facilities and Informed Consent and Patient Safety in VA Medical Research. At that hearing, former Chairman, Terry Everett, stated: "The subcommittee demands an explanation, and accountability. These outrageous crimes against our veterans must not happen again."

Since then, several hearings have been held by the Subcommittee to insure that necessary actions are taken to ensure that our nation's most vulnerable veterans are protected and not subjected to any type of abuse such as the violations imposed upon them at the Greater Los Angeles medical facilities.

During today's hearing, we hope to learn what precipitated recent actions taken by the VA in its organizational restructuring within the Office of Research Development.

I know that we all have the same goal as it relates to VA medical research. We do not want veterans to have their rights denied, or to place them in a harmful environment.

Likewise, we do recognize the tremendous contributions that have been made by VA through its medical research and the discoveries of important life saving drug

therapies and developing medical devices that benefited not only veterans but all Americans.

United States General Accounting Office

GAO

Testimony
Before the Subcommittee on Oversight
and Investigations, Committee on
Veterans' Affairs, House of
Representatives

For Release on Delivery
Expected at 10:00 a.m.
Wednesday, June 18, 2003

VA RESEARCH

**Actions Insufficient to
Further Strengthen Human
Subject Protections**

Statement of Cynthia A. Bascetta
Director, Health Care—Veterans'
Health and Benefits Issues



June 16, 2003

VA RESEARCH

Actions Insufficient to Further Strengthen Human Subject Protections



Highlights of GAO-03-917T, a testimony before the Subcommittee on Oversight and Investigations, Committee on Veterans' Affairs, House of Representatives

Why GAO Did This Study

Every year thousands of veterans volunteer to participate in research projects under the auspices of the VA. Research offers the possibility of benefits to individual participants and to society, but it is not without risk to research subjects. VA studies, like other federally funded research programs, are governed by regulations designed to minimize risks and protect the rights and welfare of research participants. VA must ensure that veterans have accurate and understandable information so that they can make informed decisions about volunteering for research.

In September 2000, GAO reported on weaknesses it found in VA's systems for protecting human subjects. VA concurred with GAO's recommendations that its human subject protections could be strengthened by taking actions in five domains—guidance, training, monitoring and oversight, handling of adverse event reports, and funding of human subject protection activities. (*VA Research: Protections for Human Subjects Need to Be Strengthened*, [GAO/HEHS-00-155, Sept. 28, 2000]).

GAO was asked to assess whether VA has made sufficient progress in implementing the recommendations and to examine the recent changes in VA's organizational structure for monitoring and overseeing human subject protections.

www.gao.gov/cgi-bin/getrpt?GAO-03-917T.

To view the full product, including the scope and methodology, click on the link above. For more information, contact Cynthia A. Bascetta at (202) 512-7101.

What GAO Found

VA has not taken sufficient actions to strengthen its human subject protection systems since GAO made recommendations nearly 3 years ago. Continuing weaknesses VA has not sufficiently addressed include ensuring that

- its policy for implementing federal regulations for the protection of human subjects is up to date;
- training occurs periodically for all personnel involved in human subject protections;
- those charged with reviewing risks have information that can help them interpret reports of adverse events; and
- sufficient funding is allocated to support human subject protection activities.

VA has taken some important steps to strengthen aspects of its human subject protections by providing some necessary guidance and offering training to research personnel. Moreover, it strengthened its internal oversight and instituted an external accreditation program, with reviews of all its medical centers' human subject protection programs scheduled through summer 2005.

VA is now in the midst of a reorganization of its headquarters research offices that was begun without adequate planning and notice. VA did not initially ensure the independence of compliance activities although more recent actions appear to have restored the integrity of the compliance function. VA has not clarified responsibilities for education, training, and policy development. Until it does so, it is unclear how the reorganization will affect VA's efforts to further strengthen its human subject protections.

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here to discuss the protection of human subjects who participate in research conducted through the Department of Veterans Affairs (VA). Every year thousands of veterans volunteer to participate in research projects under the auspices of VA. Research offers the possibility of benefits to individual participants and to society, but it is not without risk to research subjects. VA studies, like other federally funded research programs, are governed by regulations designed to minimize risks and protect the rights and welfare of research participants. VA must ensure that veterans who agree to become subjects in VA research are given accurate and understandable information about procedures, risks, and benefits so that they can make informed decisions about volunteering. Concerns about VA's protection of its human research subjects came to national attention in March 1999. At that time, all human research was suspended at the West Los Angeles VA Medical Center after officials there failed to correct long-standing problems with its system for protecting human subjects.¹ Recently, serious concerns were raised about the safety of research programs at several VA medical centers, including the Albany VA medical center, where the possibility of patient deaths related to research is under investigation.

In September 2000, we testified before this subcommittee on weaknesses we found in VA's systems for protecting human subjects.² VA concurred with our recommendations to take immediate steps to ensure that human subjects would be protected in accordance with all applicable regulations. We made specific recommendations for actions in five domains—guidance, training, monitoring and oversight, handling of adverse event reports, and funding of human subject protection activities. You asked us to assess whether VA has made sufficient progress in implementing our recommendations and to examine the recent changes in VA's organizational structure for monitoring and overseeing human subject protections.

¹The West Los Angeles VA Medical Center is now part of the VA Greater Los Angeles Healthcare System.

²See U.S. General Accounting Office, *VA Research: System for Protecting Human Subjects Needs Improvements*, GAO/HEHS-00-203 (Washington, D.C.: Sept. 28, 2000) and *VA Research: Protections for Human Subjects Need to Be Strengthened*, GAO/HEHS-00-155 (Washington, D.C.: Sept. 28, 2000).

My testimony is based on an update of VA's progress in implementing our September 2000 recommendations and a review of VA's recent and ongoing reorganization of its research offices. To do our work, we reviewed documents, including VA memorandums, policies, and guidance and interviewed key officials in VA headquarters. We conducted our work from May through June 2003 in accordance with generally accepted government auditing standards.

In summary, VA has not taken sufficient action to strengthen protections for human subjects, although it has made some progress. VA needs to address continuing weaknesses we identified nearly 3 years ago. Specifically, VA has not revised its policy for implementing federal regulations for the protection of human subjects. VA also has not established training requirements, in policy, to ensure that all research personnel will be informed of, and stay current with, ways to comply with all applicable regulations for the protection of human subjects. VA actions regarding two other recommendations are incomplete. VA has not ensured that those charged with reviewing risks related to ongoing research activities have information that can help them interpret reports of actual adverse events that research subjects experience while participating in studies. VA has also not ensured that sufficient funding is allocated to support human subject protection activities. On the other hand, VA has strengthened aspects of its human subject protections by providing some necessary guidance and offering training to research personnel. Moreover, it strengthened its internal oversight and instituted an external accreditation program, with reviews of all its medical centers' human subject protection programs scheduled through summer 2005.

In 2003, VA began a reorganization of its research offices without adequate planning and notice. We found that VA did not initially ensure the independence of compliance activities although more recent actions appear to have restored the integrity of the compliance function. In addition, VA has not clarified responsibilities for education, training, and policy development. Until these responsibilities are clarified, it is unclear how the reorganization will affect VA's progress in further responding to our recommendations to strengthen its human subject protections.

Background

Conducting research is one of VA's core missions.³ VA researchers have been involved in a variety of important advances in medical research, including development of the cardiac pacemaker, kidney transplant technology, prosthetic devices, and drug treatments for high blood pressure and schizophrenia. In fiscal year 2002, VA supported studies by more than 3,000 scientists at 115 VA facilities. VA researchers receive additional grants and contracts from other federal agencies, such as the National Institutes of Health, research foundations, and private industry sponsors, including pharmaceutical companies.

To protect the rights and welfare of human research subjects, 17 federal departments and agencies, including VA, have adopted regulations designed to safeguard the rights of subjects and promote ethical research. These regulations, known as the Common Rule, establish minimum standards for the conduct and review of research to ensure that studies are conducted in accordance with certain basic ethical principles. These principles require that subjects voluntarily give their informed consent to participate in research, that the risks of research are reasonable in relation to the expected benefits to the individual or to society, and that procedures for selecting subjects are fair.⁴

The Common Rule creates a system in which the responsibility for protecting human subjects is assigned to three groups:

- Investigators are responsible for conducting research in accordance with regulations.
- Institutions are responsible for establishing oversight mechanisms for research, including committees known as institutional review boards (IRB), which are to review both research proposals and ongoing research to ensure that the rights and welfare of human subjects are protected. VA medical centers engaged in research involving human subjects may establish their own IRBs or secure the services of an IRB at an affiliated university or other VA medical center.
- Agencies, including VA, are responsible for ensuring that their IRBs comply with applicable federal regulations and have sufficient space and staff to accomplish their obligations.

³VA's four core health care missions are patient care, education, research, and backup to the Department of Defense health system in war or other emergencies.

⁴38 C.F.R. pt. 16. VA regulations provide additional protections to those participating in human subjects research. See 38 C.F.R. §17.85.

VA is responsible for ensuring that all human research it conducts or supports meets the requirements of VA regulations, regardless of whether that research is funded by VA, the research subjects are veterans, or the studies are conducted on VA grounds. In addition, two components of the Department of Health and Human Services (HHS) have oversight responsibilities for some VA research. The Food and Drug Administration (FDA) is responsible for protecting the rights of human subjects enrolled in research with products it regulates—drugs, medical devices, biologics, foods, and cosmetics. HHS-funded research is subject to oversight by its Office for Human Research Protections (OHRP). Both FDA and OHRP have the authority to monitor those studies conducted under their jurisdiction, and each can take action against investigators, IRBs, or institutions that fail to comply with applicable regulations. To facilitate assurance of compliance with federal regulations for the protection of human subjects, VA awarded a contract to the National Committee for Quality Assurance (NCQA) to provide external accreditation of its medical centers' human research protection programs in August 2000.

Two VA headquarters offices have responsibilities that are directly related to human subject protections. Responsibility for the administration of VA's research program rests with its Office of Research and Development (ORD), which allocates appropriated research funds to VA researchers. To help ensure that VA research is conducted ethically, legally, and safely, VA created an independent office to conduct compliance and oversight activities—the Office of Research Compliance and Assurance (ORCA)—in 1999. This office was given responsibilities for promoting and enhancing the ethical conduct of research and investigating allegations of research noncompliance; it reported directly to the Under Secretary for Health. In early 2003, VA reorganized its research offices and replaced ORCA with a new office, the Office of Research Oversight (ORO). ORCA's responsibilities for education, training, and policy guidance were transferred to ORD. ORCA's responsibilities for compliance activities were assigned to ORO.

In March 2003, ORD issued a memorandum announcing a 90-day national "stand down" for VA human subject research to be effective from March 10 through June 6, 2003, although research was permitted to continue during this period. The stand down was intended to focus efforts on identifying and correcting problems with VA's systems for protecting human subjects and to notify investigators that disciplinary actions may result from noncompliance with federal regulations governing the conduct of their research. ORD also asked medical center managers to attest that their IRBs are constituted as required by VA regulations and that they meet

regularly enough to review research protocols and adverse events; that their research staff has obtained training in human subject protections; and that they have checked the credentials of all personnel involved in research, including investigators, research team members, IRB members and staff, and research and development committee members.

**Earlier Evaluation Showed
VA Needed to Strengthen
Human Subject
Protections**

In 2000, we concluded that medical centers we visited did not comply with all regulations to protect the rights and welfare of research participants. Based on our review of eight medical centers, we documented an uneven, but disturbing, pattern of noncompliance with human subject protection regulations. The cumulative weight of the evidence indicated failures to consistently safeguard the rights and welfare of research subjects. Among the problems we observed were failures to provide adequate information to subjects before they participated in research, inadequate reviews of proposed and ongoing research, insufficient staff and space for IRBs, and incomplete documentation of IRB activities. We found relatively few problems at some sites that had stronger systems to protect human subjects, but we observed multiple problems at other sites. Although the results of our visits to medical centers could not be projected to VA as a whole, the extent of the problems we found strongly indicated that human subject protections at VA needed to be strengthened.

Although primary responsibility for implementation of human subject protections lies with medical centers, their IRBs, and investigators, we identified three specific systemwide weaknesses that compromised VA's ability to protect human subjects. First, VA headquarters had not provided medical center research staff with adequate guidance about human subject protections and thus had not ensured that research staff had all the information they needed to protect the rights and welfare of human subjects. Second, insufficient monitoring and oversight of local human subject protections by headquarters permitted noncompliance with regulations to go undetected and uncorrected. Third, VA had not ensured that funds needed for human subject protections were allocated for that purpose at medical centers, with officials at some medical centers reporting that they did not have sufficient resources for the staff, space, training, and equipment necessary to accomplish their mandated responsibilities.

To strengthen VA's protections of the rights and welfare of human subjects, we recommended that VA take immediate steps to ensure that VA medical centers, their IRBs, and VA investigators comply with all applicable regulations for the protection of human subjects. The specific

actions we recommended involved guidance, training, monitoring and oversight, handling of information about adverse events, and funding of human subject protection activities. VA concurred with our recommendations.

Insufficient Action Taken to Strengthen Protections for Human Subjects, Although VA Has Made Some Progress

VA has not taken sufficient action to strengthen protections for human subjects since we made our recommendations nearly 3 years ago although it has taken some important steps. ORD has not revised its policy on human subject protections, and it has not established training requirements, in policy, to ensure that research personnel obtain periodic training. Moreover, VA has not established a mechanism for handling adverse event reports to ensure that IRBs have the information they need to safeguard the rights and welfare of human research participants and it has not ensured that sufficient resources are allocated to support human subject protection activities. On the other hand, VA has strengthened aspects of its human subject protection systems. ORCA developed a training program and conducted oversight activities by investigating claims of research improprieties or noncompliance and restricting or suspending four medical centers' research activities when it found evidence of serious problems. VA also instituted an external accreditation program that has the potential to further strengthen VA's oversight of human subject protections.

Policy for Human Subject Protections Has Not Been Revised, but Other Important Guidance Was Issued

In 2000, we reported that we had found problems with VA's policy for implementing federal regulations for the protection of human subjects. These problems included requirements for obtaining and documenting informed consent. For example, the policy requires use of a particular form to document a subject's consent to participate in research. This form calls for the signature of a witness, but does not indicate who may serve as a witness, to what the witness is attesting, or the circumstances under which a witness is needed.

In its comments to that report, VA indicated that ORD was in the process of updating its policy on human subject protections and that it expected to submit that policy for internal review by the end of August 2000. When we followed up in September 2001, VA reported that comments were being incorporated into the draft policy. In September 2002, VA reported that it was awaiting final review but has not issued its revised policy as of June 2003. As a result, investigators, IRB members and staff, and other research personnel do not yet have a clear, up-to-date policy to follow when implementing human subject protections. Consequently, VA cannot ensure

that research staff know what they need to do to protect the rights and welfare of human research subjects.

In addition to the problems we noted with VA's policy, we reported in 2000 that VA headquarters had not provided medical center staff with adequate guidance to help them ensure the protection of human research subjects. VA has made some progress in this area. For example, ORCA had begun distributing some information to medical centers in early 2000. By January 2003, it had posted about 60 information letters and 14 alerts on its web page and through electronic mail to research facilities. These letters and alerts provide information about new HHS guidance and policies regarding human subject protections, reports on research ethics, and problems that ORCA staff observed during site visits to VA medical centers. In addition, ORCA developed guidance about human subject protections. For example, ORCA published a best practices guide for IRB procedures in September 2001 and a tool for medical centers to use to assess their human subject protection programs in October 2001.

**Training Requirement Not
Established in Policy,
Although Training
Opportunities Offered**

In 2000, we found that VA did not have a systemwide educational program focused on human subject protection issues. Although VA's human subject protection regulations do not include any specific educational requirements, we concluded that periodic training for investigators, IRB members, and IRB staff is necessary to ensure that they can meet their obligations to protect the rights and welfare of human research subjects.

VA has not established training requirements in policy, although on two occasions it has issued memorandums that required training. In August 2000, ORD issued a memorandum to medical center associate chiefs of staff for research stating that all VA investigators had to meet specific education requirements before submitting research proposals during 2001. ORD's memorandum regarding the March 2003 stand down stated that all research personnel must provide documentation that they have completed both a course on the protection of human research subjects and a course on good clinical practices within the past year; otherwise all research personnel must complete this training by June 6, 2003. These additional personnel include research coordinators and research assistants involved in human research; all members of VA research offices, research and development committees, and IRBs; and IRB staff (except secretarial staff). According to VA's policy for distributing information, however, memorandums are not used to establish permanent requirements or policy, and education and training requirements for investigators were not published in a directive or handbook, which are the documents VA uses to

communicate policy requirements. As a result, headquarters cannot systematically ensure that all VA personnel involved in human subject research will be informed of, and stay current with, ways to comply with all applicable regulations for the protection of human subjects.

Despite the lack of policies requiring human subject protections training, both ORD and ORCA have provided information since we made our recommendation about available educational programs to investigators and other research personnel. ORCA worked with academic institutions to develop an optional training program for use by VA investigators, IRB members, IRB staff, research administrative staff, and medical center officials. This web-based training program includes quizzes after each module; certification of successful completion requires achieving a score of at least 75 percent correct. ORCA also presented a seminar on research compliance and assurance to senior managers of each of VA's networks,⁴ and ORD recently began providing training to senior managers about their responsibilities regarding human subject protections.

Internal and External Oversight Strengthened

In 2000, we reported that VA had not identified widespread weaknesses in its human subject protection systems because of its low level of monitoring. VA has made progress in strengthening its oversight. ORCA, which was created in 1999, was charged with advising the Under Secretary for Health on all matters related to human subject protections, promoting the ethical conduct of research, and conducting prospective reviews and "for cause" investigations. Since becoming operational, ORCA has investigated claims of improper conduct of research and noncompliance. In about a dozen cases, it sent teams to medical centers to conduct intensive for cause reviews. ORCA also conducted six on-site reviews to follow up on findings from external accreditation reviews. As a result of its investigations, ORCA restricted or suspended research at four VA medical centers until identified problems were corrected. For example, in March 2001, ORCA restricted one medical center's human research activities by suspending enrollment of new subjects in research after its investigation revealed noncompliance with several regulations pertaining to IRBs.⁵

⁴VA has 21 Veterans Integrated Service Networks that coordinate the activities of, and allocate funds to, VA medical centers, nursing homes, and other facilities in each region.

⁵The IRB of this medical center served as the IRB-of-record for a second VA medical center. Therefore, human research at two medical centers was affected.

ORCA lifted this restriction in February 2002 after the medical center corrected the identified problems.

In addition to its internal oversight mechanisms, VA became the first research organization to arrange for external accreditation of human subject protection systems. External accreditation has the potential to significantly strengthen oversight of human subject protections. In August 2000, VA awarded a \$5.8 million, 5-year contract to NCQA to operate an accreditation program to assess medical centers' compliance with federal regulations for the protection of human subjects. VA's contract with NCQA requires it to develop accreditation standards, to conduct a site visit every 3 years to each VA medical center conducting human research, and to decide on the accreditation status of each facility. According to a 2001 report by the Institute of Medicine, the accreditation standards developed by NCQA provide a promising basis for accreditation because they are explicitly linked to federal regulations and pay attention to quality improvement.⁷ The Institute of Medicine recommended that the NCQA standards be strengthened, for example, by specifying how research subjects will be involved in human subject protection systems.

NCQA began accrediting VA medical centers and has revised its accreditation process. NCQA conducted accreditation visits to 23 VA facilities from September 2001 through May 2002. An ORD official told us that, of those 23 facilities, 20 were accredited with conditions, 2 were not accredited, and 1 withdrew from the process. A facility accredited with conditions met most of the accreditation standards. On the basis of its experience and feedback on its standards, NCQA proposed—and ORD approved—revising the standards. NCQA discontinued accreditation reviews while it revised its standards for evaluating human subject protection programs. Revisions involved clarification of standards, reduction of redundancies, and changes to the scoring system. Some revisions were designed to respond to comments from the Institute of Medicine. For example, NCQA adopted standards to encourage a facility to obtain input from research subjects to improve its human subject protection system. ORD approved a new set of standards in April 2003. Site visits are expected to resume in October 2003, with accreditation reviews of all VA facilities involved in human subject research planned for completion by summer 2005.

⁷Institute of Medicine, *Preserving Public Trust: Accreditation and Human Research Participant Protection Programs* (Washington, D.C.: National Academy Press, 2001).

**Actions Regarding Adverse
Event Reports and
Funding for Human
Subject Protection
Activities Are Incomplete**

In 2000, we reported that IRBs have difficulty handling adverse event reports and often lack key information necessary for their interpretation. Since then, VA has not developed a mechanism for handling adverse event reports to ensure that IRBs have information that can help them interpret reports of actual adverse events that research subjects experience while participating in studies. Federal regulations require investigators to report to the IRB unanticipated problems involving risks to subjects. In turn, IRBs are to review these adverse event reports as part of their continuing assessment of the adequacy of a study's protections for human subjects. ORD issued guidance stating that analyses of adverse events should be provided to IRBs for those clinical trials that VA funds at multiple medical centers. ORCA staff participated in interagency discussions about how to help IRBs handle adverse event reports and developed guidance regarding what adverse events IRBs are to report to ORCA. As of June 2003, this guidance has not been issued and VA still lacks comprehensive guidance to help IRBs interpret reports of adverse events.

In 2000, we reported that VA did not know what level of funding was necessary to support human subject protection activities and research officials at five of eight medical centers we visited told us that they had insufficient funds to ensure adequate operation of their human subject protection systems. In May 2000, ORD provided networks with suggestions for the level of administrative staffing of IRBs. ORD also commissioned a study of the costs of operating IRBs within VA, which was completed in June 2002. On June 13, 2003, VA issued a policy regarding funding for human subject protection programs that medical centers are to obtain from external sponsors of VA research. Specifically, the sponsor of each industry-funded study is to be charged 10 percent of the direct costs of the study or a flat fee of \$1,200, whichever is greater, by the medical center to help cover the costs of the human subject protection program. We have not had the opportunity to study the potential for this mechanism to help ensure sufficient funding. VA has not specified a procedure for ensuring that its medical centers—which conduct VA-funded research and research funded by federal agencies and research foundations as well as industries—will be allocated the funds necessary for their human subject protection programs.

**Recent
Reorganization
Appears to Maintain
Independent
Compliance Function,
but Other Roles and
Responsibilities
Unclear**

In 2003, VA began a reorganization of its research offices without adequate planning and notice. We found that VA did not initially ensure the independence of compliance activities, although more recent actions appear to have restored the integrity of the compliance function. In addition, VA has not clarified responsibilities for education, training, and policy development.

VA's initial action to reorganize its research offices failed to ensure the independence of compliance activities. In January 2003, officials announced that the existing compliance office, ORCA, would be disbanded and the compliance function and staff reassigned to ORD. As a result, compliance field personnel began reporting their activities to ORD, potentially compromising the independence of their compliance investigations. In a series of memorandums issued from March through May of 2003, VA announced that a new office, ORO, would replace ORCA. VA memorandums indicated that ORO, like ORCA, would be independent of ORD, and that ORO would be organizationally responsible to the Under Secretary for Health.

According to generally accepted government auditing standards, offices with responsibility for assessing regulatory compliance should be organizationally independent of the offices they review and should report to, and be accountable to, the head or deputy head of the government entity.⁸ Because VA considered making ORD responsible for compliance activities—where its independence would be compromised—legislation was proposed in the House of Representatives to establish an independent office within VA to oversee research compliance with federal regulations.⁹

According to VA memorandums and discussions with agency officials, ORO will have responsibility for investigating allegations of research noncompliance, misconduct, and improprieties. However, it is not clear whether ORO will have authority to review a medical center's human subject protection program in the absence of a prior allegation of a problem; that is, whether it can conduct prospective investigations. While

⁸HHS separated its compliance office from its administrative office after we voiced similar concerns about independence. As a result, instead of reporting to the National Institutes of Health, which conducts and funds research, OHRP has been reporting to HHS's Assistant Secretary for Health since June 2000. See U.S. General Accounting Office, *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects*, GAO/HEHS-96-72 (Washington, D.C.: Mar. 8, 1996).

⁹H.R. 1585, 108th Cong. (2003).

VA memorandums indicate that ORO will have the same compliance responsibilities that ORCA had and specify that for cause inspections will be conducted; they are silent on routine inspections. Experts in human subject protections have said that these routine inspections, sometimes referred to as prospective inspections, are an essential way to help prevent noncompliance. As of June 2003, a directive to formalize the authorities and responsibilities of ORO has not been issued. Consequently, ORO's compliance responsibilities remain unclear.

Other roles and responsibilities are also unclear. For example, ORCA previously had responsibilities for education and training. VA's reorganization now assigns these responsibilities solely to ORD. The implications of this transfer of responsibilities for strengthening human subject protections are unclear. For example, when ORCA conducted compliance reviews or followed up on results of accreditation reviews, it provided instruction about what steps would be necessary to correct identified problems. It is not clear whether or to what extent such instruction, including technical assistance regarding a specific area of noncompliance, would be considered to be education and training and therefore not within ORO's responsibilities.

ORCA also had responsibility to participate in the development of policies involving human subject protections. Under the reorganization, ORD would have responsibility for policy development. Existing memorandums are silent on whether ORO will have any role in, or can contribute its expertise to, policy development. ORCA had been created with the understanding that it would collaborate with ORD on dissemination of information, communication, and policy development. It is not clear to what extent VA's efforts to strengthen its human subject protections will bring to bear the collective expertise of the staff in its compliance and operational research offices. However, having ORD take the lead on policies regarding compliance functions or activities could be inappropriate to the extent that it interferes with ORO's independence in executing its compliance functions.

Mr. Chairman, this concludes my prepared remarks. I will be pleased to answer any questions you or other members of the subcommittee may have.

**Contact and
Acknowledgments**

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Related GAO Products

Human Subjects Research: HHS Takes Steps to Strengthen Protections, but Concerns Remain. GAO-01-775T. Washington, D.C.: May 23, 2001.

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U.S. House of Representatives

Committee on Veterans' Affairs Subcommittee on Oversight and Investigations

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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 nations' 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.

Statement
of
Robert H. Roswell, M.D.
Under Secretary for Health
Department of Veterans Affairs
on
Human Research Participant Protection Program
before the
Subcommittee on Oversight and Investigations
of the
Committee on Veterans' Affairs
U.S. House of Representatives

June 18, 2003

Mr. Chairman and Members of the Subcommittee, I appreciate the opportunity to appear before you today to discuss the Department of Veterans Affairs (VA) human research participant protection program. We share your concern about research activities that placed patients at inappropriate risk or resulted in actual harm. The simple truth is that because of inappropriate research activities, some VA patients were placed in harm's way. It is unconscionable that any man or woman who wore a uniform in defense of our country be placed in jeopardy once again because they volunteered for research. We are in the process of changing our policies and operations in a manner that demonstrates that unethical research behaviors will not be tolerated. We will ensure that patients are optimally informed when they consent to participate in research, and that the research activities are safe and ethical. Thus, we have developed and are implementing new programs and training to support successful research conduct, management, and oversight at every level of the organization. Today, I would like to give you a progress report.

Since VA announced a research stand-down on March 6, 2003, we have made significant changes in the requirements for the conduct of research. First, we have required verification of appropriate Institutional Review Board (IRB) operation. In this process, leadership at each VA facility that conducts human research were required to certify that the local institutional review board (IRB) and research and development committee oversee human studies effectively. This process assures that research

protocols were adequately reviewed by an appropriately constituted IRB committee and that forceful provisions for ethical research conduct, such as good informed consent, are present.

Second, we have required training of over 15,000 individuals involved in human studies research in good clinical research practices. The good clinical practices program addresses the responsible, ethical, and accepted conduct of research. It provides particular focus on assuring the adequacy of informed consent and the increased responsibility for the care of patients in research protocols. Human studies research personnel are now also required to take refresher courses on an annual basis.

Third, to assure appropriate training and no history of illegal or unethical behavior, we have required credentials verification and background checks of VA research personnel with any degree patient contact or programmatic responsibility. Facilities were directed to confirm the credentials of all VA research personnel that come into contact with patients, not just those of independent health care providers. Sites are independently verifying education and professional certifications and have annual checks of all licenses. Facilities now repeatedly review the Department of Health and Human Services exclusionary lists to assure that they do not include any research staff. ORD is also creating an electronic means of tracking all employees involved in human subjects research to facilitate checking these individuals against exclusionary lists.

In the past 90 days, VA has achieved 98 percent compliance with the IRB verification requirements, 93 percent compliance with the training requirements, and 85 percent compliance with the credentialing responsibilities. As outliers have correction plans in place, we will achieve 100 percent compliance.

While VA demonstrated leadership in establishing an Office of Research Compliance and Assurance (ORCA) in 1999, our experiences have compelled us to establish mechanisms for more rapid, broad and effective development and dissemination of policy and education. These actions are directed to go beyond assurance of compliance and assure adequacy and integrity of research operations.

Recently, VA established the Program for Research Integrity Development and Education (PRIDE) within the Office of Research and Development (ORD). PRIDE is a

groundbreaking program that is responsible for all education, training, and policy development related to human research protection at the VA. Although it has been in existence for only a few weeks, PRIDE already has assisted in:

- Staffing the research "stand down";
- Creating a blue ribbon advisory committee on ethical research conduct;
- Reinitiating the accreditation process for human research programs at VA facilities;
- Creating new programs for education and assistance;
- Establishing links with other organizations involved in the protection of human research subjects; and,
- During the three-month period of the research stand down, VA instituted credentialing standards for research personnel that exceed any in place anywhere in the United States.

VA has already sought, and is receiving, external guidance in setting the agenda for PRIDE. A nationally prominent panel to advise ORD and PRIDE on important issues pertaining to the protection of human subjects has been established. One of the foremost research ethicists (with particular expertise in informed consent), Dr. Baruch Brody from the Baylor College of Medicine, is heading the Blue Ribbon Panel on Maximizing Human Protection in VA Research. The panel includes members representing bioethics, health law, industry, and academia. The panel is charged with articulating the necessary structures and process for insuring ethical research. They are charged to base their work upon review of all relevant U.S. and international documents governing human subjects research.

PRIDE is already serving as a resource for providing guidance and policy development for responsible research conduct. These activities coordinate with, and require collaboration with, the policies and work of other agencies and organizations involved in protection of human subjects, both inside and outside the VA. Such entities include NCQA, the Food and Drug Administration, the National Institutes of Health, other components of VA, and quality assurance and patient safety organizations.

Policy development and education are only useful to the degree that they inform the actions of managers and researchers. One of PRIDE's most critical initiatives is the

Center On Advice and Compliance Help or "COACH." This new center is directed toward providing training and educational resources on all aspects of the ethics and the logistics of human research protection. COACH will communicate with local VA facilities and investigators in person, by phone, by e-mail, and will provide educational materials on the Internet and at local, regional and national meetings. COACH will also provide training in research conduct that will lead to successful research program accreditation.

In 2000, VA became the first Federal department or agency to seek independent, external accreditation of human research programs. Following a competitive selection process, VA contracted with the National Committee on Quality Assurance (NCQA) to develop and implement a comprehensive program. Based on a review of first-year evaluations, VA and NCQA placed this program on "pause" in the spring of 2002 to refine the logistics and better standardize the review criteria. Revised standards were published April 2003. The accreditation process will begin again this summer, and all VA facilities that have human research programs will complete the accreditation process by the summer of 2005.

While a new infrastructure has been developed in the ORD to support effective, rapid improvement in research conduct, VA believes strongly in independent oversight. As described, policy and programmatic educational activities now reside in the Office of Research and Development. Oversight of compliance with policy, regulation, law, and ethics is the responsibility of the Office of Research Oversight (ORO). All human resources of the predecessor office, ORCA, are contained in ORO and devoted to their charged responsibility for oversight of compliance with regulatory and policy aspects of human subjects protections, animal welfare, research safety, and research misconduct. ORO reports to the Office of the Under Secretary for Health.

Since its inception in 1999, ORO's predecessor, ORCA, contributed in many ways to the improvement of VA's protection of human subjects participating in research. ORCA provided prospective compliance consultations, retrospective compliance reviews, a compliance assurance program, and a training, education and development function.

Despite ORCA's remarkable contributions since 1999, continuing and intolerable breaches of human research conduct compelled us to make changes in office responsibilities. These changes modify, not abandon, the principles that brought ORCA forth. Oversight is required, but as Deming taught, quality cannot be inspected into a process. For improved outcomes, processes must be changed. As the Office of Research and Development has responsibility for the management of research processes, clear alignment of policy and training with ORD is critical. The diffusion of role responsibilities has unacceptably delayed necessary policy on human subjects protection. Moreover, reluctance of field managers and researchers to rapidly seek corrective assistance from the authority that imposes sanctions is understandable.

As all personnel in the former ORCA are now exclusively devoted to oversight in ORO, VA's capacity for research oversight is effectively increased. While we fully expect and are observing that ORO's investigations and reviews are educational, the Office of Research and Development's PRIDE and COACH programs have already established successful relationships with the responsible facility officials and researchers. Their early work, including training in good clinical research practices and policies requiring certification of IRP function and researcher credentialing, is proactively addressing and resolving potentially – and manifestly – problematic situations. As described, the progress in the past 90 days alone has been remarkable.

The legacy of ORCA's accomplishments will be used to facilitate the roles of both ORO and ORD in improving research. In addition to providing seminars for researchers and leadership, ORCA developed compliance information and tools for regulatory compliance, research program self-assessment, and continuous quality assurance. ORCA developed invaluable compendia of linked regulations, policy, and accreditation standards that were published on compact disk, a template for standard operating procedures in research compliance, and a web-based training program. ORCA also provided outreach to veterans about their rights in research.

Both ORO and ORD will benefit from ORCA's history of active participation at national meetings regarding ethical research conduct and regulatory initiatives. Both offices also benefit from established linkages with other Federal regulatory agencies and professional organizations such as the Office of Human Research Protections and

the Food and Drug Administration that help ensure consistent approaches to compliance oversight within VA, appropriate external reporting, and rapid correction of noncompliance.

ORD and ORO activities are increasingly complementary with oversight problems identified by ORO being met with aggressive solutions by ORD. It is also indisputable that ORO's oversight and investigative process is invariably educational. The skill set embodied by ORO staff in its five Regional Offices around the nation, and guided by ORO's Central Office component, is well capable of informed, consultative intervention.

ORO operations will continue in the tradition of ORCA which visited nearly all VA Medical Centers and Health Care Systems that conduct research and provided 10 formal prospective overview visits, 9 systematic post accreditation team visits to sites found not accredited by the National Committee for Quality Assurance, 19 major for-cause onsite reviews, 13 more limited visits to focus on issues of serious noncompliance in human subjects protections, and investigations of hundreds of compliance issues identified from sources within and outside of VA amenable to correction through compliance advice or action plans developed collaboratively with local facility personnel.

Because of its oversight mission, ORO will continue to serve as VA's governing body for Federal Wide Assurance (FWA) for VA facilities. ORO, in partnership with the Office of Human Research Protections in the Department of Health and Human Services, administers this assurance of compliance process, without which no IRB or human research program can operate.

Notably, ORO and its predecessor office negotiated over 100 Federal Wide Assurances and related agreements with VA facilities to assure their commitment to carrying out the Common Rule protections afforded to human subjects of research, and set forth in the VA regulations at 38 C.F.R. Part 16

While compliance is critical, ORD's now explicit responsibilities for policy, training, program management, and funding are linked in a manner that provides support for rapidly correcting deficiencies. Research programs that fail to appropriately safeguard patients and the values of ethical research conduct will have funding

terminated. In parallel, this transition affords ORO the opportunity to focus on oversight activities. In the past four years, ORO has laid extensive groundwork for a sound research oversight program to better assure compliance with policy, law, and ethical research conduct. Not surprisingly, ORO's increased oversight and assessment activities have resulted in increased numbers of findings and have revealed that ORO will need to continue its vigilance in the years and months ahead. As compliance issues are identified, the ORO compliance staff have worked closely with local facilities, research personnel, and the Veterans Integrated Service Networks to correct both isolated and systematic problems through prescribing and ensuring remedial actions.

In our revised program of protections, ORO will enjoy greater role clarity in discharging the oversight functions of its predecessor. The increased focus on oversight activities will assure that problems are investigated and – with ORD as a committed peer office, providing effective and timely policy and training – corrected. We commit to this so that the Department of Veterans Affairs maintains the highest quality research programs in the country, and most responsibly serves the needs of our nation's veterans.

WRITTEN COMMITTEE QUESTIONS AND THEIR RESPONSES



**DEPARTMENT OF VETERANS AFFAIRS
UNDER SECRETARY FOR HEALTH
WASHINGTON DC 20420**

JUL 28 2003

The Honorable Steve Buyer
Chairman
Subcommittee on Oversight and Investigations
Committee on Veterans' Affairs
U.S. House of Representatives
Washington, D.C. 20515

Dear Chairman Buyer:

Enclosed are the Department of Veterans Affairs' responses to the 18 post-hearing questions you submitted as a follow up to the Subcommittee on Oversight and Investigations' hearing on Human Subject Protections held on June 18, 2003. A complete set of responses (redacted and unredacted number 4) were provided electronically to your staff on July 21, 2003.

If you have further questions, or need additional information, please have a member of your staff contact Doug Dembling, in the Office of Congressional and Legislative Affairs. He may be reached at 202-273-5615.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Robert H. Roswell".

Robert H. Roswell, M.D.

Enclosures

**Post-Hearing Questions for
Robert H. Roswell, M.D.
From Chairman Steve Buyer
Regarding the June 18, 2003, Hearing
On Human Subject Protections**

1. The GAO's testimony is highly critical of VA's efforts to implement the recommendations made in its September 2000 report on human subjects protections. It does, however, praise ORCA for the actions its staff took during the same period of time. In light of this, please explain VA's rationale to abolish ORCA?

Response: The Office of Research Compliance and Assurance (ORCA) contributed in many ways to the improvement of VA's protection of human subjects participating in research. However, despite ORCA's contributions, recurrent issues related to human research conduct compelled VA to make changes to both ORCA and ORD. VA's experiences led to the establishment of mechanisms for more rapid, broad and effective development and dissemination of policy and education. These actions go beyond assurance of compliance, and are directed to assure the adequacy and integrity of research programs. The changes modify and strengthen the principles that brought ORCA forth. All personnel in the former ORCA are now exclusively devoted to oversight in the new Office of Research Oversight (ORO), expanding VA's capacity for research oversight.

2. Dr. Wray recently held a training seminar for senior VHA officials in Ann Arbor, MI. Before that training seminar, how many similar seminars were held since 1999?

Response: Veterans Health Administration (VHA) officials from ORCA conducted eleven one-day regional leadership seminars since 1999. No national research training seminars were previously held for senior leadership. Additional information is included in the response to number 12.

3. Does the VA believe it is essential to give the Office of Research Oversight the authority not only to monitor situations where there may be problems, but also to give it the authority to initiate random checks?

Response: Yes. ORO will visit some facilities even when there is no evidence to suggest there are compliance problems. In the past, ORCA visited at the invitation of leadership in the facilities and the Networks and performed multi-assessment visits to review compliance at the facilities.

4. For researchers who violate either the Common Rule or VA's internal policy on human subject protections, but do not actually commit a crime, does the Department have a set procedure concerning disciplinary actions? Does VA have a minimum level of discipline? What disciplinary actions were taken against the researchers at West LA in 1999?

Response: 4. For researchers who violate either the Common Rule or VA's internal policy on human subject protections, but do not actually commit a crime, does the Department have a set procedure concerning disciplinary actions? Does VA have a minimum level of discipline? What disciplinary actions were taken against the researchers at West LA in 1999?

Response: The facility director determines disciplinary action on a case-by-case basis. Sanctions can include termination. ORD can bar individuals from receiving VA funding, and ORO can suspend the assurance of a facility (but not individual) until the site is in compliance.

Several individuals received disciplinary action at West LA in 1999. The Chief of Staff received a reprimand - this action has expired. The _____ received a reprimand; this action has expired and was purged from the individual's personnel file. The _____ received a demotion, but the action was overturned upon review of the Merit Systems Protection Board. One _____ was suspended. However, the grievance process overturned the suspension. The _____ resigned in August 2001 and is not currently a VA employee.

5. Did the VA consult with [the] Office of Human Research Protection (OHRP) when it moved to create a new organizational structure within the Office of Research and Development?

Response: No. VHA had access to the policies of OHRP and other organizations involved in research protections.

6. Is the VA familiar with the *Report to the Advisory Committee to the Director, NIH from the Office for Protection from Research Risks Review Panel*, published in 1999? Was this gold plate standard utilized during VHA's reorganization of ORD and ORCA?

Response: VHA is familiar with the report and has consulted closely with one of its authors. While some analogies can be drawn between the relationship of the former Office for Protection from Research Risks (OPRR) to the National Institutes of Health and that of ORCA to ORD, the scope of oversight of OPRR and its successor, the Office for Human Research Protections differ greatly from ORCA. Unlike the NIH, VA conducts an intramural research program. In addition to funding grants, VA employs its principal investigators and maintains responsibility for ensuring that its patients get the highest quality care. Therefore, ORD's first moral obligation is to preserve and ensure the health of our veterans—in short, to ensure the protection of human subjects.

7. Secretary Principi issued a memo on April 15, 2003 expressing great concern about the lack of training in ten crucial areas. Did the training session conducted by Dr. Wray address all ten of his concerns? Please provide the Subcommittee with VA's written plan that responds to this mandate.

Response: Yes, additional details are presented in the reply to question 12 below.

8. VA's written testimony discussed the "stand down" which was completed on June 6th with the submittal by each VAMC of a written report to central office. Since you have established the new Office of Research Oversight to check on research compliance, what is ORO's role in evaluating the reports for their adequacy? When will ORO provide the Under Secretary for Health with an assessment of the adequacy concerning actions taken by the VAMCs during the "stand down?"

Response: Directors of 107 of 109 facilities have attested "that their active Institutional Review Boards (IRBs) and Research and Development Committees are functioning effectively, are appropriately constituted, and meet regularly to provide timely review and oversight of new and continuing protocols as well as review adverse events and serious adverse events." ORO is discussing with ORD activities at the two facilities where additional work may be needed.

The remainder of the report focuses on areas within the purview of ORD. ORD briefed the Under Secretary for Health through the Deputy Under Secretary for Health on June 26. ORD briefed the Secretary on June 26, and the Deputy Secretary on June 27.

9. When GAO submitted its report in September 2000, entitled "Protection for Human Subjects Need to Be Strengthened," the VA agreed to promptly fulfill the five recommendations. The VA agreed to issue current, comprehensive and clear guidance, including a new Handbook on Human Subjects Protections. Despite commitments made by VA at three previous hearings before this committee, the Handbook has not yet been published. Why has it not been published? When will it be published?

Response: VHA has been preparing a handbook that accurately reflects Federal human research protection policies. Changing standards and varying interpretations complicated and lengthened the concurrence process. VHA delayed publication of the handbook and two others dealing with research protections this winter to incorporate the provisions of the Health Insurance Portability and Accountability Act. This has been accomplished and the handbook was published on July 15 (copy enclosed).

10. VA also agreed to determine the funding levels needed to support human subjects protection and ensure the appropriate allocation of funds. When was this assessment made? What funds are now allocated to adequately support the resources needed at VAMCs to support a robust human subject protection program?

Response: Health services researchers from VA, the University of Rochester, and the University of California at Los Angeles completed the study in June 2002. However, they restricted their assessment to institutional review boards (IRBs). The study found that a biomedical institutional review board is an expensive operation. Changes in regulations and the push to accredit IRBs and to certify IRB administrators have increased board costs. Over time this will place greater burden on small IRBs,

particularly those at academic medical centers where administrative reimbursement from the National Institutes of Health is capped at 26 percent.

IRB costs throughout the VA are estimated to be nearly \$20 million per year. In addition, annual research participant oversight and compliance costs have risen to over \$3 million. VHA provides partial funding for IRBs through VERA. ORD has funded the oversight and compliance costs (\$5 million has been transferred from the FY '03 Medical and Prosthetic Research budget to cover anticipated costs) and invested more than \$3 million per year in other research participant costs such as National Committee for Quality Assurance (NCQA) accreditation, researcher training and education, and computer equipment and software. ORD funding will increase with the full implementation of the Program for Research Integrity Development and Education (PRIDE). Implementation of VHA Directive 2003-031, Establishment of a Facility Human Protections Program (FHPP), will increase the funds available for this program. When accepting this type of grant/gift, VA officials will be required to ensure that the funds provided through such grants include an amount equal to 10 percent of the direct cost of study, or a flat fee of \$1200, whichever is greater. The purpose of this policy is to assist VA facilities in fully covering the costs associated with protecting human subjects who participate in such research studies. The policy applies to all newly funded and VA-approved industry-funded studies conducted at VA facilities

11. VA's testimony briefly discussed the status of the external accreditation program for the Human Research Protection Programs at VAMCs through a contract with the National Committee for Quality Assurance (NCQA). At the September Hearing last year, VA testified that it had directed the former ORCA to complete an evaluation of this accreditation program. The Subcommittee was provided with a copy of the program evaluation last December with one overall recommendation and eight general recommendations. Did VA endorse the recommendations and what has been done to implement them? How is the NCQA Certification process progressing?

Response: ORD endorsed the recommendations and has been implementing them by working very closely with NCQA since January 2003, through contract changes, and by Research and Development Accreditation Consulting Team (ReDACT) training. ReDACT training for six VA facilities was held June 25, 2003. The revised standards (Version 2.1) were posted on the NCQA website in April 2003, and the revised policies and procedures were posted in June 2003. VHA will work with each site individually to ensure that it is capable of being fully accredited.

NCQA accreditation activities will resume by early September 2003, when two sites (Memphis and Hines) will submit their required paperwork. On-site surveys will begin in October, and NCQA will speed up the process so that by spring 2004, approximately four facilities per month will begin the accreditation process. All VA facilities will have gone through the accreditation process by August 2005.

12. Secretary Principi issued a memo on April 15, 2003 expressing great concern about the lack of training for the senior level in management of VA research training in ten

crucial areas. Has ORD's training addressed all ten of his concerns? Please provide the Subcommittee with its written plan that responds to the Secretary's memo.

Response: The training plan (see attached course outline) addresses each of the Secretary's concerns. One hundred thirty-six medical center directors received one day of training on May 29, 2003 in Ann Arbor. They will receive another half day on July 31. Other senior management will also attend the July 31 session, and the May 29 program will be repeated for them on August 1.

13. During Dr. Wray's teleconference on March 10, 2003 she stated that "the Office of Human Research Oversight will be a much, much smaller office and have responsibility only to do focus reviews for cause when I report to them for cause." Is this still the Department's position about ORO's role?

Response: No. ORO will have a broader role than implied during early discussions of the transition for the office. ORO will retain the responsibilities of the former ORCA for matters related to research compliance and oversight involving protection of human research subjects, research misconduct, animal welfare, and research safety.

14. When the VA established the former ORCA, now ORO, it was stated to the Committee during the April 21, 1999, hearing that "ORCA will be an independent, objective and unbiased entity in its compliance and oversight activities." In particular, ORCA would not be a part of the Office of Research and Development (ORD) to ensure that there would be no jeopardy to its impartiality and credibility. In January 2003, VA's original plan was to incorporate ORCA as a component of ORD. What precisely were the reasons for this change of direction?

Response: In January 2003, as issues continued despite the creation of ORCA, VHA began to carefully explore a range of possible organizational structures to more effectively achieve compliance at all research sites. In particular, there was concern that the effectiveness of ORCA was being undermined by the fact that sites were reluctant to seek consultation from ORCA for fear of triggering an investigation. One option that was considered was to incorporate ORCA into ORD.

After reviewing different possible structures, and in consultation with VA's congressional oversight committees, VHA determined that the compliance and oversight functions should remain outside of ORD to ensure complete faith in the independence, objectivity and lack of bias. Further VHA deemed it essential to the effectiveness of the human protection program that all policy and education functions be removed from the office responsible for oversight and compliance, and placed in ORD so that there could be undivided focus on developing policy, guidance, training and prevention of human protection problems before they occur.

15. During the four hearings this committee has held since 1999, including the two that the current VA Under Secretary for Health testified at last year, there was unequivocal support for the former ORCA. Without consulting with Congress, VA decided to

eliminate ORCA and incorporate it in the Office of Research and Development (ORD). Now we have a new organization the Office of Research Oversight. What assurances can you give the Subcommittee that ORO will be able to conduct its work with the independence needed to ensure that it is a credible entity, beyond reproach and of the highest integrity.

Response: I am committed to keeping the Office of Research Oversight independent from the Office of Research and Development. ORO has retained all of the authorities of the former ORCA, with the exception of education and training activities. A Chief Officer reporting to the Office of the Under Secretary for Health heads the office. The new directive for ORO will reflect its independence from ORD.

16. H.R. 1585 would require the entity, and I presume it will be ORO, to provide regular counsel to the Under Secretary for Health on all matters within its scope of responsibility. In order to avoid any conflict in this role vis-à-vis ORD, should it state that ORO is the primary advisor to the USH in these matters?

Response: ORO should be the primary advisor to the USH on research subject protection issues involving compliance and Federal-Wide Assurances. ORD should be the primary advisor to the USH on research subject protection issues involving education and policy development.

17. H.R. 1585 would require that ORO conduct periodic inspections and evaluations of research integrity at VAMCs. Is ORO able to immediately conduct such prospective investigations and evaluations?

Response: ORO is prepared immediately to conduct prospective investigations and evaluations of research integrity at VAMCs. The Office has a comprehensive protocol that provides for the inspection and evaluation of human research protection, animal welfare, research misconduct, and research safety programs.

18. H.R. 1585 would require the Director of ORO to suspend, restrict, or modify research as determined to be appropriate. The Subcommittee understands that the former ORCA did make such determinations in consultation with OHRP/DHHS. How did that process work and do you think that the Director of ORO can appropriately discharge this responsibility.

Response: In ORCA, any suspensions or restrictions on the assurances for the protection of human subjects were discussed in advance with OHRP to assure consistency with their policies. OHRP is a cosignatory on the Federal Wide Assurances that ORCA/ORO negotiate with the VA facilities. The Chief Officer also discussed the actions with the Under Secretary for Health and/or the Deputy Under Secretary of Health. This was done by telephone or in person prior to the facility and the Network offices being notified that these actions would be taken. ORCA/ORO does not require "modifications" in the research in a broad sense, but may require or recommend that additional protections for human subjects be included in the research being carried out

or to be carried out. Depending on the nature of these modifications, ORO staff may consult with OHRP in advance and keep the office of the Under Secretary informed. Under the authority of the Assurance required by regulation and signed by both the ORO Chief Officer and a representative of OHRP, ORO will retain the responsibility for discharging any suspension or restriction of the Assurance.

**ENCLOSURE FOR
QUESTION
NUMBER 12**



Department of Veterans Affairs Employee Education System

presents

COURSE NO. 03.ST.OT.RES.A

**EFFECTIVELY MANAGING RESEARCH:
TODAY'S VA RESEARCH LEADING TOMORROW'S HEALTH CARE**

July 31, 2003 – August 1, 2003

in cooperation with

The Office of Research and Development

Place: Hilton Chicago
720 South Michigan Avenue
Chicago, IL 60605

Phone: 312-922-4400
FAX: 312-922-5240

Purpose: The purpose of this program is to present participants with the importance of research to the future of clinical care and with critical safety issues related to human research.

Topics will include research ethics; principles of conducting human research, informed consent, legal issues, research participant protection; compliance requirements, research credentialing and privileging, legal issues, managing Institutional Review Boards (IRBs), managing research funding, non-profit research corporations, HIPAA, and the Privacy Act. Also discussed will be the new vision of the Office of Research and Development (ORD). Participants will have the opportunity to meet with ORD staff to discuss how ORD can help them achieve the objectives of this program.

Outcome Objectives: At the completion of the program, the participant will be able to:

1. discuss the new research vision;
2. identify how VERA dollars for FY2004 will be distributed;
3. identify the roles of foundations;
4. discuss their responsibility for the success of the research mission;
5. discuss the ethical and regulatory guidance related to research;
6. develop skills to identify, assess, and ensure the structural components of the Medical Center Research Program to ensure the protection of

For more information about the products and services provided by the Employee Education System (EES), visit our website at <http://vaww.ees.irn.va.gov/>.

- human subjects, e.g., informed consent, compliance, managing IRBs, credentialing and privileging, HIPAA, and the Privacy Act; and
7. identify resources for human studies compliance; and develop systems to identify problems and implement solutions to research-related problems.

Target Audience: Medical Center Directors, Associate Directors, Chiefs of Staff, VISN Directors and their Chief Medical Officers and others involved in managing research activities.

Accreditation/ Approval: Accreditation Council for Continuing Medical Education (ACCME)
The VA Employee Education System is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

American Nurses Credentialing Center (ANCC)
VA Employee Education System is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Credit: Accreditation Council for Continuing Medical Education (ACCME)
The VA Employee Education System designates this educational activity for a maximum of 9.5 hours in category 1 credit towards the American Medical Association Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

American Nurses Credentialing Center (ANCC)
VA Employee Education System designates this educational activity for 11.4 contact hours in continuing nursing education.

A Certificate of Attendance will be awarded for 9.5 hours to all other participants. The Employee Education System maintains responsibility for the program. A certificate of attendance for 9.5 hours will be awarded to participants and accreditation records will be on file at the Employee Education System. In order to receive a certificate from EES, you must sign in at the beginning of this activity, complete an evaluation, attend 100% of the program, and pick up your own certificate at the conclusion of the program (certificates will not be mailed). EES cannot issue certificates for less than 100% participation as required by accrediting body regulations.