HUMAN SUBJECT MEDICAL RESEARCH

HEARING

BEFORE THE

SUBCOMMITTEE OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON VETERANS' AFFAIRS
HOUSE OF REPRESENTATIVES

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September 28, 2000

HUMAN SUBJECT MEDICAL RESEARCH

THURSDAY, SEPTEMBER 28, 2000

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

The subcommittee met, pursuant to call, at 10:04 a.m., in room 334, Cannon House Office Building, Hon. Terry Everett (chairman of the subcommittee) presiding.

Present: Representatives Everett and Brown.

OPENING STATEMENT OF CHAIRMAN EVERETT

Mr. EVERETT. The hearing will come to order.

Good morning. This subcommittee's second hearing on VA research will follow up on what progress the VA has made in protecting veterans volunteering in its medical research programs since the suspension of all medical research at the West Los Angeles VA medical facilities 18 months ago.

Chairman Cliff Stearns of the Health Subcommittee, Ranking Democratic Member Corrine Brown of the Oversight and Investigations Subcommittee and I were extremely concerned with what we heard last April. VA obviously failed to protect our veterans at the West Los Angeles medical research facility.

At the hearing, I asked GAO to investigate whether the research violations at the West LA VA were isolated incidents or whether the lack of protections for human subjects could be widespread in VA medical research. The General Accounting Office's written statement today describes a disturbing pattern of noncompliance at eight VA medical centers for ensuring the protection of human research subjects.

I will ask GAO what the implications of this finding are systemwide for the VA facilities engaged in medical research and what should be done. We will hear from the Department of Health and Human Services' new Office of Human Research Protection, which is now responsible for overseeing protection of human subjects in research throughout the Federal Government; and, finally, we will hear from the VA.

I had hoped that the last 18 months would allow the Department to proactively identify and correct all the serious violations delivered at West Los Angeles or elsewhere that they might be occurring within the VA. The VA did announce the creation of its own research compliance organization called the Office of Research Compliance and Assurance. I would like to note that this was announced 1 day before this subcommittee's hearing last April.

I certainly expect the VA to tell this subcommittee that it is truly committed to the safety and welfare of veterans participating in medical research. These veterans are one of the most vulnerable populations of in all of human medical research. Their protection must be a top priority for the Department. But what has the VA actually done? That's what counts.

The VA should have the specifics and definite completion dates for their initiative that isn't already complete and be able to convince us that ORCA will be an effective watchdog. What I have seen so far leaves me skeptical about how aggressive the VA has been. So I look forward to hearing today's testimony and the answers of the witnesses to the subcommittee's questions.

Because of the nature of today's testimony, the witness panels will be sworn in for their testimony.

At this point, I would like to yield to my ranking member for any comments she may have.

OPENING STATEMENT OF HON. CORRINE BROWN

Ms. BROWN. Thank you and thank you for holding this hearing.

VA medical research is an important part of VA's health care, but the research should include safeguards for veterans who receive new treatment and drugs. This is the cost of doing business. Last year, we examined issues raised by the suspicion of human subject research at the West Los Angeles Medical Center. At today's hearing we'll review the steps VA has taken since last year.

The issues boil down to two questions: One are VA research rules adequate to protect veterans? Two, are the rules seriously in force? I want to know that VA has specifically planned to accomplish GAO recommendations with completion dates. We are making progress and can we measure it? I'm looking forward to some detailed answers this morning, Mr. Chairman.

Mr. EVERETT. Thank you.

I will now, as I said, swear in all witnesses on all panels today; and I will ask each panel to limit their oral testimony to 5 minutes. The complete testimony will be made a part of the official hearing record.

Myself and Ms. Brown will hold our questions until the entire panel has testified.

At this time, I'd like to call on Dr. Greg Koski, the Director of HHS's new Office of Human Research Protections.

[Witness sworn.]

Mr. EVERETT. Thank you. Please be seated.

Sir, you will please present your testimony. Again, I ask you to please hold it to about 5 minutes. I know we're going to be probably be interrupted to go to the floor during the hearing.

STATEMENT OF GREG E. KOSKI, Ph.D., M.D., DIRECTOR, OFFICE OF HUMAN RESEARCH PROTECTIONS, OFFICE OF THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. KOSKI. Thank you, Mr. Chairman and distinguished members of the committee. I know that many who come before you start out by saying that they're delighted to be here. In what is perhaps a radical departure from the norm, in fact, I would like to assure

you I truly am delighted to be here. Because in fact this provides an opportunity for the first time to publicly actually discuss some of the specifics of the initiatives of the new Office of Human Research Protections. I appreciate that opportunity.

As you know, the Office of Human Research Protections is a new office. The office was created within the Office of the Secretary by Secretary Shalala as part of her overall initiatives to increase protections for human subjects in research. The office was placed within the Office of the Secretary believing that from that position the office would be better able to both exercise its authority as well as to have greater autonomy and to provide leadership for the efforts to reform and train in the human subject's protection process in a more global manner.

The Office for Human Research Protections is new in many ways. In addition to its new positioning, it has a new structure, new personnel, new leadership and, of course, new responsibilities. The new office, unlike its predecessor, is devoted entirely to protection of human subjects in research and no longer has any responsibility for oversight of animal research.

I have, as you know, submitted an extensive written statement and will not recite that here. Instead, I would like to take this time to specifically discuss our goals and our plans and to bring forward the approach that we intend to take in the new office in order to realize our goals.

I would also like to discuss some of the enormous opportunities that we currently have available to us, given the intense interest in this particular topic at this time.

Now the members of this subcommittee certainly know well that the system for protection of human subjects has been under intense scrutiny and some criticism for several years. The HHS Inspector General's record that was issued formally in 1998 called to our attention many of the challenges that the IRB process has been facing and attributed many of these to the changed research and environment that we've witnessed since the original process was established. That report also makes specific recommendations for strengthening the system.

I'd like to say unequivocally that OHRP endorses that report, is taking steps to ensure that all the recommendations made there are acted upon in timely fashion. Many of the specific initiatives that I have described in my written statement are crafted—specifically organized within that to demonstrate how they address the concerns raised by the OIG. I would be happy to provide additional details on any of those during the question period. But first I'd like to describe in broad terms the vision that drives this reform initiatives and how that vision differs from what we've known before.

The OIG report states that the IRBs are the sole bodies within the system of protection of human subjects that bears their primary responsibility for protection of human subjects. Mr. Chairman and members of the committee, I submit to you that this notion is fundamentally flawed; and indeed I would like to reject that notion in the strongest possible terms. Because I believe that in many respects it may be at the heart of some of the problems that we've been facing.

Put bluntly, the IRBs do not bear sole protection for protection of human subjects. Indeed, that responsibility is one that is shared by everyone—I mean, every party engaged in the research endeavor. It's the responsibility shared by the investigators and the members of their research teams, by the research institutions and sites as well as the sponsors and funding as agencies.

It's a responsibility that's also shared by our society as a whole. We all reap the benefits of biomedical research, even though only a few members of society actually take the risks and bear that burden. Consequently, we all must share the responsibility for ensuring that the interests of the research subjects take precedence over the interests of either science or society. Responsibility means that we take personal initiative to know what we must do to acquire the proper training and education to ensure competency and that we act accordingly.

We must also incorporate into our actions a sense of caring. When we care about individuals, we put their interests ahead of our own; and in biomedical research we must demonstrate that we care about the research subjects.

At the same time, I am sure we all recognize that our society values science strongly; and our goals are not to put up a roadblock to stop the progress of science. Instead, we want to promote science. But we must ensure that it's done right, so that we can all rightly take pride in its accomplishments.

Now with the responsibility also comes the need for accountability. We must do all that we can to ensure that all human research is performed according to appropriate standards for responsible conduct. We must move from a culture of compliance to a culture of conscience and responsibility. The system that we will work to establish along with our collaborators in the other agencies is one that operationalizes this concept.

We envision a system of standards that includes certification of individuals, accreditation of review boards and assurances from institutions that are based upon a dedication to meeting those standards. The program at OHRP will work to build emphasizes education as well as enhanced oversight. Our goals are to support to the fullest extent possible those institutions and investigators as well as IRBs that are driving to accept and meet their responsibilities, and I will say that we simply cannot tolerate those who are unwilling to do so.

Already, great progress has been made. I believe that this is in part due to the efforts that have already been undertaken by the NIH, by the FDA, by the VA, the DOD and other agencies who have already recognized the need to improve their actions in these areas.

Clearly, OHRP cannot do there alone. We can only do it if we recognize that our goals are shared and we work together. Doing so will require both cooperation and compromise, but I believe that we have an opportunity before us now to bring the common rule to bear in a way that will serve our interests to a much greater extent than it ever has before. I look forward to your advice and support as we do so. Thank you.

[The prepared statement of Dr. Koski appears on p. 31.]

Mr. EVERETT. Thank you very much. Let me first offer my congratulations on your recent selection as Director of the Office for Human Research Protections in the Department of Health and Human Services. OPRR, your predecessor organization under NIH, was responsible for shutting down all medical research at West LA in the spring of 1999. It took 6 years of noncompliance by the VA for OPRR to take action. I understand that this was directly related to a severe long-standing funding and staffing situation. How is this being addressed and corrected?

Dr. KOSKI. Mr. Chairman, I am not at liberty today to talk about specific details with respect to funding since the budget process is still moving forward.

Mr. EVERETT. Fine. You're not prepared or not at liberty?

Dr. KOSKI. However, I can speak to specific steps that have been taken when the new office was reconstructed.

Mr. EVERETT. Excuse me. I asked for some clarification. You're not at liberty or you're not prepared to talk about it?

Dr. KOSKI. Not at liberty to discuss.

Mr. EVERETT. Why are you not at liberty?

Dr. KOSKI. I have been advised that while the budget process is moving forward it would be inappropriate for me to address specific issues related to, you know, that process.

Mr. EVERETT. Thank you for that clarification. Please continue.

Dr. KOSKI. When the new office was constructed, one of the things that occurred immediately was the increase in the complement of staff devoted to human studies from the original 15 to 26 people in the new office. And of course a request for additional resources to support the enhanced efforts has gone forward. We're also looking forward to, apart from the, as I mentioned in my written statement, the opportunity to rededicate resources that will become available within the office due to the reorganization of certain processes such as the assurance process that will allow us to devote a greater effort to the oversight and compliance activities.

We also look to using new mechanisms for working with the agencies to—or not the agencies, excuse me, the institutions and the IRBs to ensure that they know exactly what their responsibilities are and to provide technical assistance to help them both evaluate what they're doing and to put necessary policies and procedures in place to be sure that they are effective.

So that I think that already these are steps that have been taken, and there will be additional steps that will be forthcoming.

Mr. EVERETT. Sir, your testimony states, "We envision a system in which every party to research is properly trained and educated to fulfill their responsibilities and in which every individual personally acknowledges and accepts responsibility for protecting research projects as a condition of participation." How do you plan to get there when so many researchers consider these requirements as nothing more than an "administrative inconvenience"?

Dr. KOSKI. I think the perception of the investigators that this is purely at administrative inconvenience has changed radically since the time of the last hearing. Already, the National Institutes of Health has issued specific requirements for appropriate documentation of education prior to receiving funds for their research grants.

There are enhanced educational initiatives occurring not only in OHRP but also within several of the other agencies. I've seen work done by the CDC, by VA, by Department of Defense. This is an area that clearly is receiving dramatic attention; and we look to development of specific resources that will make it possible to actually avoid redundancy and spread the available resources more widely in order to accomplish this goal, in particular the development of shared web sites and links that will direct individual investigators and institutions to tools for education, providing generic lectures, to institutions that they can use as part of their educational programs.

What we need to do initially is to establish through clear guidance that's developed in cooperation with all of the other agencies a minimum set of educational standards that everyone would meet, and then we will be calling together—convening an education summit that will bring all of the parties to the table to more clearly define what expectations there would be beyond the minimal level to ensure that everyone is working to an appropriate standards. We then will move to both support private accreditation programs and certification programs for individuals that will ensure that each party is up to the standard before they are, in fact, allowed to participate in the research.

This is a system that will have to evolve over time, but steps can be taken immediately that can begin to reenforce what is already there and make it more effective.

Mr. EVERETT. You mentioned a minute ago that you need to inform IRBs about their responsibilities—are you saying that they didn't know what their responsibilities are? Also, are IRBs simply rubber stamps or just operating pro forma?

Dr. KOSKI. The IRBs are not rubber stamps. I believe that IRBs have been working diligently to try to meet the enormous burden and responsibility that they carry. There——

Mr. EVERETT. Do they know what they were doing?

Dr. KOSKI. I believe that IRBs do, by and large, know what they are doing. But the complexity of some of the Federal regulations and some of the inconsistencies that develop because of the lack of uniformity can lead to situations where there are apparent inconsistencies.

I think we should remember also that the IRB process is one that's based on exercise of judgment, interpretation of regulations; and that's not going to be consistent necessarily across the board. So I believe that, as I said, the IRBs are working to do their jobs as best they can. I believe that the IRBs will benefit from greater guidance that will simplify certain situations and certainly from increased resources to help them do their jobs. I think that we must meet that responsibility.

Mr. EVERETT. You state you're working closely with ORCA to build a strong relationship within the VA. How many times in your short tenure have you or OHRP met with Dr. Feussner, the head of research at the VA, or Dr. Mather, the director of ORCA?

Dr. KOSKI. In my 2 weeks here as director of the new office we have already met formally with Dr. Mather and his group for a lengthy discussion; and I have had additional conversations since then. He, Dr. Mather, has already picked up on certain initiatives

that we have under way. He's also picked up on leads that we've given to him that I was able to make available from my former civilian life, and we've also learned certain things from the programs that he's already developing.

I think that the—I have not met until today Dr. Feussner and Dr. Garthwaite, but we have done that. And my boss, Dr. Satcher, the Assistant Secretary for Health, is also going to be contacting Dr. Garthwaite to cement that relationship.

I think that we have a wonderful opportunity to work together, and I have sensed a strong commitment on behalf of Dr. Mather and his group to do so.

Mr. EVERETT. Did you say you have met with Feussner?

Dr. KOSKI. No.

Mr. EVERETT. Doctor, I'll have, and I'm sure Ms. Brown may have, additional questions for the record. We would ask for a timely submission of the answers to those questions. Ms. Brown.

Ms. BROWN. Thank you, Mr. Chairman. You have done such a thorough job I just have one question.

Are the IRBs set up in a way that make them responsible for the safety of the human subjects?

Dr. KOSKI. I don't believe that the IRB system, as it currently functions, provides sufficient protections during the conduct of the research. It's an area that was cited in the OIG's report as an area that needs additional attention. That is certainly what it's going to receive from our office. There are tools and mechanisms that can be conducted not just as the IRB—remember that the IRB is a committee that exercises its function. There is a broader human—system for protects of human subjects. I think that we need to work to build upon that system concept in order to bring new approaches to improving the continuing oversight of studies after they have been approved by the IRB and then a more effective process for communications back to the committees so that they can more effectively exercise that oversight role. Some institutions have already made significant progress in that direction, and this is going to be one of the areas of greatest attention as we move forward.

Ms. BROWN. Thank you.

Mr. EVERETT. Thank you. Thank you, Doctor; and thank you for your testimony today.

Dr. KOSKI. My pleasure. Thank you.

Mr. EVERETT. At this point I'd like to call Mr. Rezendes, the Assistant Controller General of the General Accounting Office, and his staff.

Prior to being seated, sir, would you please raise your right hand.

[Witnesses sworn.]

Mr. EVERETT. Thank you. Please be seated.

Mr. EVERETT. Mr. Rezendes, we're honored to have you here today; and we appreciate the interest of GAO by having you come over to attend this meeting. If you would now proceed, I would ask you also to adhere to the 5 minute clock.

STATEMENT OF VICTOR S. REZENDES, ASSISTANT COMPTROLLER GENERAL, U.S. GENERAL ACCOUNTING OFFICE; ACCOMPANIED BY CYNTHIA A. BASCETTA, ASSOCIATE DIRECTOR, HEALTH, EDUCATION AND HUMAN SERVICES; AND BRUCE D. LAYTON, ASSISTANT DIRECTOR, HEALTH, EDUCATION AND HUMAN SERVICES

Mr. REZENDES. Thank you, Mr. Chairman.

I have some slides here to bring focus to my presentation, and I really appreciate the opportunity to talk about the report we are issuing to this committee today.

Based on our review of eight medical centers, we conclude that VA needs to strengthen its protections for human subjects in research. While some centers are performing better than others, we documented a disturbing pattern of noncompliance. The cumulative weight of the evidence indicates failure to consistently safeguard the rights and welfare of research subjects.

We found various degrees of noncompliance in four basic areas.

First, we found problems in IRBs. The Institutional Review Board, as you've already discussed, is a key oversight mechanism. One board held meetings without having all the required members in attendance. As a result, studies on new drug treatments for unstable coronary symptoms and pneumonia were initiated without legitimate approval.

We found some boards did not have adequate staff or sufficient space to keep confidential information. At one site file folders were stacked loosely on top of file cabinets and on the floor. We found incomplete documentation, such as minutes of meetings that did not document substantive discussions. Although inadequate documentation alone does not place subjects at risk, such failures do prevent adequate oversight and monitoring.

We found informed consent problems at all the centers we went to. In a study for the treatment of esophageal cancer, the consent form did not mention the possible risk of a biopsy. The ability of subjects to make their own informed decisions is undermined when not all of the requirements and the information is made available to them to make informed decisions.

At the five sites we visited that had VA-run boards, as this chart shows, we found more extensive problems than those that relied on the university-run boards. I should point out, however, that the university-run boards were not without problems.

We identified three specific weaknesses in VA's system which to us indicates that protection of subjects has historically not received adequate attention.

The first is that VA headquarters did not provide guidance and, therefore, had little assurance that research staff had all the information they needed to protect subjects.

The second weakness is that VA did not have an effective system for monitoring protections, allowing noncompliance to go undetected and uncorrected. In fact, VA was generally unaware of regulatory investigations by other Federal agencies against university-run boards until after the regulatory sanctions became effective.

The third weakness relates to ensuring adequate funding. Five centers told us they did not have sufficient resources to accomplish their mandated responsibilities.

As this chart shows, we found that funding responsibility is diffused across several decisionmakers, with different sources of funding and competing priorities for the use of those funds. The result is that no one official was accountable.

The good news is that substantial corrective actions have been implemented at some sites, as you can see on this chart here.

Since VA is going to focus on why the glass is half full, let me talk to you a little bit about why we think the glass is still half empty.

Our primary concern is that VA's system-wide efforts have been slow to develop. For example, the officials at the West Los Angeles Medical Center were particularly slow to respond to problems identified over a 5-year period, including not having written procedures.

Only recently has headquarters begun to implement system-wide changes to identify which centers use their own VA boards, and which rely on the universities.

In addition, VA is making two organizational changes to enhance its oversight. First, it awarded a contract, as you mentioned, for external accreditation of its board and created the Office of Research Compliance and Assurance. While these are positive steps, staffing for the compliance and assurance office is still incomplete.

We are encouraged that VA concurs with our recommendations which we have listed here and included in our report. While timely effective implementation of these recommendations is critical, so is sustained commitment to a heightened vigilance in this program. Without this, participants in VA research will remain at risk.

Thank you, Mr. Chairman. I would be happy to answer any questions.

[The prepared statement of Mr. Rezendes appears on p. 38.]

Mr. EVERETT. Thank you very much. On your chart there, you show us graphically that no one was accountable. Does that also mean no one was responsible?

Mr. REZENDES. That is really part of the heart of what we saw as some of the problems here. We saw pervasive problems at just about all of the facilities we went to which I would say are indicative of what OHRP is finding in the private sector. But what we have here is a system where a lot of people are responsible—the individual investigators are responsible for the research, the IRBs are responsible for overseeing the investigators, you have the medical facilities that are in charge of the IRBs, and you have VA responsible for everything. What we've not seen with great clarity is how accountability flows down through there when something goes wrong, who is held accountable and responsible for making sure that the failures are corrected. When it gets very diffused, when you have diffused responsibility and accountability, you can end up having problems.

Mr. EVERETT. Well, it's one of the sad things about—in committee we often find that we have problems, but we can't find out who's responsible. There is no one to end up saying, the buck stops here. You should have done that.

Mr. REZENDES. I think that's a classic problem with Federal programs in general and specifically in this one, also.

Mr. EVERETT. You state that GAO documented disturbing patterns, some of which you mentioned, of noncompliance in eight

medical centers. Could you elaborate just briefly on some that you have may not have put up on the board?

Mr. REZENDES. At each of these facilities we found routine problems that were in varying degrees of noncompliance. While we only went to eight facilities, I want to say that the noncompliance we found was indicative of the noncompliance that OHRP finds in the private sector. But what really disturbed us was that, when you look at the noncompliance at these selected facilities which we selected to effect differences in VA research programs and look at the system-wide failure, it points to a disturbing pattern here.

Mr. EVERETT. You state there is a lack of adequate guidance to medical centers about human subject protection. What guidance have been issued since April of 1999?

Mr. REZENDES. As I said, there is good news. VA is making progress. They've held bimonthly conference calls to share information. They did a plan and began an education program. They had a nationwide video conference, and they are redrafting their policies. While all this is going on, it's still definitely a work in progress. But I'm sure VA will amplify on this more for you when they get here.

Mr. EVERETT. The second weakness was insufficient monitoring of local protection. What evidence of any monitoring activity could you document?

Mr. REZENDES. They are making progress there, also. They have these assurances that they receive from the 120 centers which are attesting to the fact that they're complying with the various regulations and requirements. They have surveyed their regional offices to assess the needs, and they're conducting site visits. But, again, they still have limited resources; and until they become fully staffed that's still a work in process.

Mr. EVERETT. And funding is a problem?

Mr. REZENDES. Absolutely. The funding is particularly a problem because you have three people responsible for deciding how much needs to be there. They're coming from three different sources of funding—the research account, the medical care appropriation, as well as from nonprofits. There's not clarity as to who is accountable to ensure that the funds are allocated down to the medical centers and the IRBs that need these monies.

Mr. EVERETT. Recognizing you selected eight facilities and recognizing that you could have found many if not all of the same problems at other facilities, would you please identify the facilities that you looked at?

Mr. REZENDES. Sure. I really appreciate your caveat, and I think these eight facilities were not selected because they had problems. We don't want to imply these are particularly bad. We selected them for a variety of reasons.

But I have on the chart here, it shows the ones in blue at the top are the VA-run IRBs that we selected. The next color down, the purple I guess, is for those run by the universities; and the last three in green are the three centers in addition to the eight that we went to that had regulatory sanctions against them and we went to determine what kind of follow up actions and what kind of aggressive action is happening there.

Mr. EVERETT. What are the most serious problems with the VA-run IRBs?

Mr. REZENDES. There were a whole host of them, as I mentioned earlier, from a variety of issues. I guess the most disturbing part for us was the pervasiveness that we found at all the facilities. But if I had to single out a single piece it would probably be the consent form. That probably is the heart of the research controls where you have patients that have—you want to make sure that the subjects involved have an awareness and an agreement and concurrence to what's going to happen.

Mr. EVERETT. I will get one final question in here.

Your testimony states that VA's authorization or resumption of research operations less than 1 month after being sanctioned by HHS was premature. I find GAO's opinion very disturbing in relationship to that. Please explain why you think resumption of research activities was indeed premature.

Mr. REZENDES. That's an excellent question. The actions that were taken against West Los Angeles were a result of cumulative problems over a 5-year period, including things like no written procedures. What disturbed us was, while the center had committed to make reforms and was in the process of making reforms, those reforms had not come to fruition. Given the past track record of 5 years of noncompliance, of having these problems, making them aware of the problems, and having promises to make corrective actions and not seeing those corrective actions followed through, we didn't think that demonstrated enough aggressive positive corrective action at that facility to warrant putting them back in business.

Mr. EVERETT. Thank you very much. Ms. Brown.

Ms. BROWN. Thank you, Mr. Chairman.

Let me just ask you straight out, should veterans and their families refuse to take part in VA research?

Mr. REZENDES. I want to make that clear. I appreciate the opportunity to answer that question.

What we're talking about here is a system of controls and a process for assuring the integrity of the entire research process. I want to make it very clear that throughout the centers we went through, these eight and the other three that had sanctions against them, by and large, we were impressed that a lot of researchers are hard-working, sincere, dedicated people doing a noble cause. In no way do we want to imply that the subjects involved there were being harmed and they should not participate.

But we are talking about system failures. We are talking about the assurance that VA and others should have that the safeguards that Congress and regulations have imposed are in fact being carried out. We think we have a confidence gap here in terms of what we can actually tell the subjects involved in terms of what kind of assurance they could have that these are being complied with.

Ms. BROWN. Would you discuss with me in your report that you didn't think the VA was given sufficient funding for human subject protection? Can you explain that a little bit more?

Mr. REZENDES. I'd like to clarify that. I don't want to align myself that they have inadequate funding, but rather what we did find was the allocation of the funds wasn't getting to everybody

that needed them. Five centers told us clearly that they didn't have the resources they need to carry through the protection programs that we thought that they had. That doesn't mean that VA doesn't have the resources, but what we do know clearly is that the money wasn't getting to the people who needed it.

Ms. BROWN. You also found VA, quote, VA had not provided adequate counseling.

Mr. REZENDES. Guidance. Absolutely right.

Ms. BROWN. Counseling, guidance.

Mr. REZENDES. It's a critical piece here. We have to make sure that everybody who is involved in the program knows specifically what they're responsible for, and the researchers as well as the IRBs need to have guidance from VA.

Ms. BROWN. One last set of questions. I am concerned about the VA's new Office of Research and Compliance. You indicated that you think it is vastly understaffed.

Mr. REZENDES. We're saying it's not up to full staff yet. The office was just recently established. Only recently have they appointed a director. They're going to have four regional offices and headquarters staff, and they're still in the process of hiring the requisite people to bring it up to full strength.

Ms. BROWN. Thank you.

Mr. EVERETT. I have a few additional questions here.

You characterize VA's corrective actions as slow. Why do you believe progress has been at this slow a pace? When does the GAO think the VA will have all its patient protection safeguards in place? Is everything being done that should be done and how could things be speeded up?

Mr. REZENDES. We've seen a flurry of activity, a lot of great initiatives. But, as I mentioned earlier, these are works in process. We're seeing them at two levels, at the local level with the IRB as well as at the headquarters level with VA. We see positive actions, and we see an aggressive sincere effort on their part to move forward. What is missing for us is a clear time frame as to when things will be done, who's going to be held accountable if they're not done, and who this committee can call up to ensure that the progress is being made that you want made.

Mr. EVERETT. The way I understand your report, you're saying deficiencies in VA's protection of medical research subjects puts them at risk. Is that correct?

Mr. REZENDES. Yes, sir.

Mr. EVERETT. I should say continued risk.

Mr. REZENDES. Correct. That's really the issue we have. We did not go forward and it wasn't our methodology to go out and find out whether research subjects were being harmed. The thrust of our objective was to see whether the structure, the process, the systems that are in place to ensure that the research subjects are protected, that it did provide us a degree of confidence that that system worked. And our sad answer is, no, we don't have confidence that it's working. To the extent that that system is important, and isn't working, then it places the subjects at risk.

Mr. EVERETT. You state that the VA is planning to use a contractor to provide external accreditation for IRBs. I understand a $5.8 million contract has been awarded to the Washington-based Na-

tional Committee on Quality Assurance. I understand this organization does not accredit research programs. I also understand that they don't even have an established criteria for accreditation. How can they expect to do any accreditation of IRBs anytime soon?

Mr. REZENDES. I don't think it will happen anytime soon. This is going to be a first-of-a-kind activity. I'm sure VA will testify to that very soon. We think that's a positive thing. But there are a lot of issues to address—it's an ambitious program that requires a meeting of the minds in terms of what are the criteria they're going to use, how you establish the certification, what the certification of accreditation really means.

Suppose someone doesn't achieve accreditation? Does that mean they lose their right to do research? They need to engage the community. I would think that would be a long process before that comes to fruition. But VA may have a more aggressive agenda than we're aware of.

Mr. EVERETT. To your knowledge, is there another organization that might already have the ability to do accreditation for the IRBs?

Ms. BASCETTA. There is another organization, Public Responsibility in Medicine and Research (PRIM&R), that is contemplating going forward with——

Mr. EVERETT. I'm sorry, ma'am. Would you move that mike up just a little bit?

Ms. BASCETTA. There is another organization, Public Responsibility in Medicine and Research (PRIM&R), that is engaged in considering how this could be done. But we're not aware of how far along they are in that process.

Mr. EVERETT. Well, thank you for your testimony. I remain disturbed at the West LA Situation, how it was handled, the fact under California law the doctor who performed the experimentation on at least one of the patients if he had been done that outside the VA he would have been subjected to a year in jail and a $10,000 fine. It's my understanding that absolutely nothing other than maybe a 7-day suspension occurred to this doctor. That's very disturbing.

We're talking about the veterans who have no other choice. That's the only reason that sometimes they're in these programs. So I thank you very much for your testimony today. Thank you.

Mr. REZENDES. Thank you.

Mr. EVERETT. Dr. Garthwaite, thank you. Would you and your panel please raise your right hands?

[Witnesses sworn.]

Mr. EVERETT. Please be seated. If you will introduce your staff, sir.

STATEMENT OF HON. THOMAS L. GARTHWAITE, M.D., UNDER SECRETARY FOR HEALTH, DEPARTMENT OF VETERANS AFFAIRS; JOHN R. FEUSSNER, M.D., CHIEF RESEARCH AND DEVELOPMENT OFFICER; JOHN H. MATHER, M.D., CHIEF OFFICER, OFFICE OF RESEARCH, COMPLIANCE AND ASSURANCE; AND JAMES P. BAGIAN, M.D., DIRECTOR, NATIONAL CENTER FOR PATIENT SAFETY

Dr. GARTHWAITE. Thank you, Mr. Chairman.

To my left is Dr. John Mather. He is the head of our Office of Research Compliance and Assurance. To the right is Dr. John Jack Feussner, who is the head of our Research and Development Office. Dr. Jim Bagian is the head of our National Center for Patient Safety.

Mr. Chairman and Congresswoman Brown, we appreciate the thorough and thoughtful review of the General Accounting Office. We have concurred and responded to each of the their recommendations.

My entire statement has been provided for the record. I would like to make just three points:

First, we acknowledge that events surrounding the suspension of research at West Los Angeles were a wake-up call to the entire academic community of the need to significantly improve the process to protect human research subjects. VA should have done a better job there and system-wide in monitoring and enforcing the rules, and we are putting into place unprecedented systems to assure that we will in the future.

Second, following the events at West Los Angeles and your hearing in April, 1999, we, like you, recognized the need to take significant steps to enhance the protection of human subjects. Beginning in May of 1999, we have told our field research administrators that they must improve our compliance, we have signed contracts with facility and research leadership detailing what is necessary to assure compliance, and we have created mechanisms to provide independent, on-site review of our research programs and accreditation of our human subjects' protections.

We believe VA is the first research institution to commit to these independent review mechanisms, and we believe that such independent review is necessary to assure veterans and the public that the process works. I regret that the implementation of these two new efforts has taken so long to put into place, but they are in place now, and real progress is being made.

Third, I will personally hold researchers and research administrators and line officials accountable for meeting not only the letter of the laws and regulations governing human research but also the intent. If we cannot assure the protection of human subjects, we cannot do research. If we cannot do research, we all lose. In their testimony, GAO notes that the VA has a long history of important contributions to medical research and that VA could set important precedents in improving human research protections. We welcome that challenge and believe we are on course to meet it.

Thank you.

[The prepared statement of Dr. Garthwaite, with attachments, appears on p. 50.]

Mr. EVERETT. We're going to depart from the normal procedure here. At this point, I want to yield to Ms. Brown.

Ms. BROWN. Thank you, Mr. Chairman.

I want to take a minute, since this is our last hearing, to thank you for your leadership, your guidance and oversight. You know, I don't think we differ on anything. We are just different parties. But I just strongly feel that when we're dealing with veterans it should be bipartisan. I mean, when veterans serve all of us and they've committed themselves to make America free, then when they need

us we need to be here. I just want to commend you for your leadership in this area. I am really happy—and that's not just saying that, what I really feel, being ranking member on this committee—working with you over the past year. Thank you again.

Mr. EVERETT. I appreciate the gentlelady's comments, and there is certainly no way that this committee could be as successful as it's been without the input from you. I appreciate working with you.

I will also yield to the gentlelady to do your questions first.

Ms. BROWN. I just want to say I'm fully in support of the new efforts of VA that you've issued in your report. I think they're sensible and needed.

I just have two questions. Why are they taking so long and what are we doing in the meantime?

Dr. GARTHWAITE. Well, we have a long list of things that we've done in the meantime. We've not only planned and instituted the Office of Research, Compliance and Assurance, a unique approach to oversight of research programs; we planned and instituted the external accreditation contract for human subjects' protection. It takes time to develop and advertise such a unique contract, time to allow bidders to respond, and more time to fairly evaluate the bids. All of those things have contributed to the time that it has taken. These are unique efforts that will be of prime importance as we move forward.

We have conducted multiple educational initiatives, as both the GAO mentioned and we mentioned in our written testimony. Beginning January of 2001, we're mandating that all applicants for VA research and all IRB members will be certified for their knowledge concerning human subjects' protection in research. I think we're also the first research institution to take that significant step.

We've conducted a study and issued guidance on staffing and funding. We've developed and signed multiple project assurance contracts will all 120 VA facilities that do research. We've developed and instituted a requirement for research performance plans, which include concurrence by the Office of Research and Development at headquarters.

We placed compliance with certification procedures in all our network director performance agreements. We've instituted an accounting mechanism so we can track the dollars that are spent on the research support related to these procedures. We've instituted in our cooperative studies, SMART teams that go out and review ongoing research to assure compliance in our cooperative studies programs. They have already made 242 site visits.

We've updated our research policy. It's out for comment now. We anticipate publishing it in the next few months as soon as we can complete the review process.

Finally, we've instituted very significant interagency coordinations. Dr. Mather and his staff receive copies of letters from the Office of Human Research Protection and from the FDA that involve VA's affiliates and VA's research program directly so we can detect any problems that are found by other agencies.

Those are a few of the—how many pages do you have now, Jack—30 some pages of detailed information regarding actions that

we have taken. I think we're on the right road and the right track. Some of the things have taken longer perhaps than they should have, certainly longer than we wish they would take. I think part of that is the nature of meeting various Federal procedural requirements. I won't detail those for you unless you really want.

Ms. BROWN. Would you attribute it to tight budgetary matters?

Dr. GARTHWAITE. I don't see that the budget should affect this. This is a building block, a foundation. If we don't do this right, we don't do research. This just has to be done and done right. It's the first dollar spent. You can overkill any project and you can put too much money into certain administrative oversight that isn't effective, so we have to make sure that what we do is effective. But the dollars are there, and they have to be here. I think the performance contract with the network directors and holding the facility and network directors accountable to meet these standards will make sure that those who control the dollars spend the dollars to get it done.

Ms. BROWN. Thank you.

Thank you, Mr. Chairman. I yield back my time.

I have some questions that I would just submit for the record.

Mr. EVERETT. I will probably also have questions for the record also, and ask that you reply to those questions within 2 weeks.

At this point, I'm going to recess the subcommittee until we can get to the floor and do whatever it is that we're supposed to be doing out there. I'll be back shortly.

Thank you. Hearing is recessed.

[Recess.]

Mr. EVERETT. The hearing will come to order.

Thank you for waiting. That's part of, as you know, what we have to do up here.

Dr. Garthwaite, you state that ORCA has been assigned a full scope of responsibilities and is currently recruiting a level of eight staff and headquarters and staffing for four regional offices with an initial staff of 24. When is this going to happen?

Dr. GARTHWAITE. Well, Dr. Mather can give you probably a little more precise detail, but he's hard at work at doing that. I believe he has already recruited the leadership for three of those field units.

I'll make one brief comment, that in bringing this up from scratch we had to go out and try to hire the best people we could for a job for which there is no role model, for which there has never been anybody who has done the job. So we had to convince people, first of all, that it is a valuable thing to do, an important thing to do, and to join the VA to do that. Then, following that, we had to get other people—at a fairly high level to buy—in. Also—once they knew who their boss might be. John has been exceptionally aggressive at trying to make this all happen within the Federal personnel regulations.

John, can you give us any sense of the timing?

Dr. MATHER. Mr. Chairman, at this point we have seven of the eight headquarters staff on board. Some time in the early part of next month I expect we'll complete the full complement of eight people here in headquarters.

We have been putting together the Regional Offices for the four designated Regional Office Directors. We have three selected. One is physically in place in Atlanta and the two at Washington, DC, and West LA VA Medical Centers will be in place next week, assuming the personnel system will allow us to get all this done. But I think they'll be in place next week.

We're hot on the heels of a person to select for Director of the Chicago Regional Office, and I expect that that will be closed out towards the end of October.

The other staffing for each of these offices, the three additional staff in each of these offices, we eventually received earlier this month the certificates to continue the interviews of those that are listed. My expectation is that, with the Regional Office Directors in place, we'll be in a good position to make those selections momentarily, and I have every intention that by the end of this calendar year we will have the Regional Office staffs fully staffed up.

Mr. EVERETT. Thank you.

Dr. Garthwaite, again, what was the original staffing supposed to be and is that level of staffing adequate?

Dr. GARTHWAITE. Well, I'm not sure there's supposed to be a certain level—there are various proposals. Because it's never been done before. I don't think we know what the actual required staffing is. The deal that John and I have is that he's going to staff up to his currently approved level that he just mentioned. Then we'll re-assess that as soon as we get going. If we need more, we'll put in more.

Mr. EVERETT. Please explain why the ORCA funding comes from the research funding.

Dr. GARTHWAITE. It's been our interpretation from discussions with General Counsel that the funding in the medical care account, the only other place we could take it, has to be closely assigned to the clinical care that we give. That's a justification for providing research support out of the medical care appropriation. So we've tried to be very true to that and have used General Counsel guidance to do that.

Mr. EVERETT. Does Dr. Feussner have to approve of this funding level?

Dr. GARTHWAITE. If it's out of his budget he gets a chance to do it.

Mr. EVERETT. He has to approve of it.

Dr. GARTHWAITE. Yes. If I ask Jack to give the money——

Mr. EVERETT. Here's the problem with that. Here's my problem with that. He's funding the very people that are supposed to be overseeing him. Isn't that not true? I see a real problem.

Dr. GARTHWAITE. I see what you say. It comes back to me. The reason we structured it to have ORCA report directly to the Under Secretary was to avoid that problem. I simply can direct Jack to fund them at the level. So although it comes out of his budget—I see what you're getting at—it's not something that he really has control over. We're going to get what John Mather and I believe is necessary to do the job.

Mr. EVERETT. I sure hope you're right, and pardon me for being skeptical. We've seen this kind of thing too often in government, and this is not the first type situation where has existed. There

needs to be an assurance of independence, and that's pretty much where I'm driving.

The GAO identifies three systemic weaknesses: inadequate guidance, insignificant monitoring, and inadequate funding. Who's responsible for this and who is accountable after these 18 months that very little has been done, frankly, to ensure that veterans are protected? Is it Dr. Feussner? Who besides yourself?

Dr. GARTHWAITE. Well, I have—I would argue that.

Mr. EVERETT. Let me break it down a little bit to simpler, in multi-questions, let me just ask you who's responsible for the systemic weaknesses of inadequate guidance, insufficient monitoring and the funding and insufficient funding? Whose shoulder does that fall on?

Dr. GARTHWAITE. Well, I would say I'll take some responsibility, but I think that we all have some joint responsibility.

We have done I think an incredible amount in a short time, although not as fast as I or you would like.

The issue of how to distribute the funds, there have been no guidelines as to how much funds are adequate. Jack did a study to find out how much funds are needed, and we've provided that guidance. But there was previously no guidance. Obviously, what was being funded, at least at the front end, didn't feel like enough, but that's true of almost every program we run. People would like more funds for the things they do. We needed some objective data to find out how much we should invest in that. I think we've made significant progress. I recognize that it's not as fast as anyone would like.

Mr. EVERETT. I do appreciate the fact that for the first time in memory somebody sitting before me has taken some direct responsibility. That doesn't happen often here. So I appreciate you having done that.

Do you disagree with the GAO's findings in this regard?

Dr. GARTHWAITE. No, their review goes back fairly far. I think we're in agreement that the protections and especially the processes and the adherence to the specific rules has not been what it should be. There is no question about that.

I would say also that I have no tolerance for investigators who overstep their authority, and I will not be tolerant of anybody who doesn't believe that they must get informed consent or feels that they're above these rules and regulations.

Mr. EVERETT. Let me get back to responsibility. Who is responsible under you?

Dr. GARTHWAITE. I would agree with the first witness who said that the investigator has a responsibility to know. We have a responsibility to tell the investigator who must know and to make sure they do know and that's why we're going to have certification when they put forward a grant. They're going to have to demonstrate that they are aware of the rules. The research administrators who organize the IRBs have responsibility, the chairs of those IRBs have responsibility. I used to do that. I know it's an important responsibility.

The person who runs the hospital has a responsibility, especially for the funding and the resources available. At the central office level or headquarters level, Dr. Feussner has a responsibility for

education, some oversight of the programs. I believe I have a significant responsibility and I created an office with Dr. Mather and ORCA to really provide me expert guidance and to make the whole process go forward.

I think there's an additional responsibility. I think there's a responsibility that goes beyond internal oversight. We're doing the research and we run it, therefore, we can never be seen as completely without a conflict of interest. We've tried to overcome that conflict of interest by introducing an accreditation standard. So we're asking people from outside of government, outside the VA to set up the most honest and rigorous process they can have to come into our facilities on a regular basis, recurring basis, to conduct on-site investigations and make sure rules are followed. I think it has a reasonable chance of succeeding.

Mr. EVERETT. If I ask you a question, if everybody is responsible then nobody is responsible, how would you reply to that?

Dr. GARTHWAITE. Well everyone is responsible but there are different levels.

Mr. EVERETT. Is everybody an equal among equals here, or is there someone who finally says, the buck stops here?

Dr. GARTHWAITE. If responsible parties don't take those responsibilities honestly and seriously and go about making that happen, the buck moves up the chain of command to my office.

Mr. EVERETT. Abnormality.

Dr. GARTHWAITE. Right. If the researcher was certified to do certain research protections and failed to do those, then on average that could easily be that the system was bad or that the individual researcher either had ill intent or wasn't—didn't get the message. They're responsible.

Mr. EVERETT. Or not qualified.

Dr. GARTHWAITE. Right. They're responsible. If the system—if there is no system in place to get independent outside review, or if they recommend things and no action are taken, you should look at me.

Mr. EVERETT. Dr. Feussner, the VA testimony states that VHA established a requirement for all VA investigators to provide documentation that they are participating in educational programs of human subjects' protection before their research projects can be approved. How is this different from certification?

Dr. FEUSSNER. Well, the education process would flow something like this: You would submit a grant project to be considered for funding. Before you would be able to submit that grant for funding, you would have to provide information that said you took part in this educational activity with this organization on this date. As that requirement is construed today, that is the end of the story.

What we intend to do after January is to require some mechanism of assessing that you learned something when you took that educational activity and that you took a test or you took a quiz or you passed some measure that says you are certified. That requirement will go into effect January.

Now, we are in a bit of a conundrum with that issue in the same way that we are with the IRB—the Institutional Review Board certification and accreditation. There are no other groups that require these steps as yet and so we are working with the contractor on

the IRB side to set up the guidance and the criteria for the accreditation, and we are also working and will be done by the end of the calendar year having guidance set up that will say what the certification requires.

Mr. EVERETT. And you are responsible for this new requirement?

Dr. FEUSSNER. Well, Dr. Garthwaite is required to approve the new requirement. The three of us have essentially worked on this issue.

Mr. EVERETT. Why is the VA waiting until January 1, 2000, to make this effective, when HHS is doing it in the next several weeks?

Dr. FEUSSNER. I am not sure that's correct, Mr. Chairman. I believe that what HHS is requiring is that you take an educational course—for example, if you take the course that is on the NIH web site, at the end of taking that course, you could actually print a certificate. Technically, I guess that would mean you are certified. We think the certification process is going to be more complicated than that.

Mr. EVERETT. In other words, we're not comparing apples to apples.

Dr. FEUSSNER. That is correct.

Mr. EVERETT. Dr. Garthwaite, what is the difference in mission for ORD and ORCA?

Dr. GARTHWAITE. With regards to the human subjects' protection, ORCA exists especially to provide independence directly to the Office of the Under Secretary. Dr. Feussner and the Office of Research and Development manage the Research program. They provide the guidance; they provide education. They're obviously part of the policy development.

But just as we have an office of the medical inspector to take the point of view of the patient, as opposed to the clinician caring for the patient, we've developed this Office of Research Compliance and Assurance to take the point of view of the research subject and to make sure that they're viewing it all from that point of view. They also have an ancillary role for continuing education and evaluation and on-site review.

I don't know if I've characterized it well, but at least in my mind that's how I view the difference.

Mr. EVERETT. Let me ask you this: Hasn't ORCA now inherited part of the problems and issues that ORD had failed to address or been slow to address?

Let me also bring up the issue of funding. Let me ask again, are they adequately funded?

Dr. GARTHWAITE. Is ORCA adequately funded? Again, I would say that, I believe that they're adequately funded to start. We'll know as John gets his teams up and out in the medical centers and we find out how much work there is to do, how much education, how hard it is to do that, how much we can leverage off of what HHS and others are doing. We will understand much better the magnitude of the problem. But sort of like in surgery, until you get in there, you don't know exactly what you're going to find. So I saw the current funding of this to really to get them up and running.

Mr. EVERETT. So the issue of inheriting problems——

Dr. GARTHWAITE. I'm not sure if you inherit it. I think they come in with a different view. We're all attacking, I think, the same problem.

Mr. EVERETT. But no problems existed that were passed down to him?

Dr. MATHER. Well, Mr. Chairman, I think what we're talking about is a matter of degree. We certainly now receive all of the reports that come out of OHRP, Dr. Greg Koski's office. We now are sent all of the FDA information. We're now in a good position to sift and sort out all that information. So it becomes a certain level of increased emphasis in that regard.

Have I assumed the problem of West LA? Yes, to a certain extent I've assumed that problem, because my office is now the compliance and assurance office. We have a full spectrum of making sure that there is a new program of VA "assurances." This program was initiated by the Office of Research and Development. So to that extent I have this problem now, because I administer the VA assurance program.

The compliance issues I think are very significant. And we initiated, wherever we had brought to our attention issues that need to be examined. We have put together these very Special Inquiry Force Teams, or SIFT teams—it's a very deliberate acronym—to sift out what the problems are. We are not coming with an attitude to knock you around a little bit and see what's going on. We're there to find out what the problem is, get to the root of the problem. It's sort of like a root cause analysis and focused review.

We have done a half a dozen of them. Yes, we've turned up issues that might have been turned up earlier, but I think there's another side to this. That is, the people now in the field are beginning to get trust in this office that's only existed for 9 months. People are calling ORCA, calling me, and saying, we have these sets of issues; how can you help us?

Which may be a little bit of a surprise, that somebody can even call headquarters and think there's somebody there to help them, Mr. Chairman, but we're sincere in trying to help put the pieces together. We have different ways in which we do that, with consultation from our office, through recruiting ORCA staff that understand the FDA regulations, a person that used to work in OHRP and so forth. So we bring together this level of expertise that probably didn't exist before.

Mr. EVERETT. Dr. Bagian, first of all, it's good to see you again. I hope the trip today is more fruitful than the last one we had when we had to cancel because of votes on the floor.

Can you tell us how and when your patient safety center is going to capture adverse events in the VA research?

Dr. BAGIAN. Yes, sir. The way the system—we look at as far as looking at adverse events or close calls, we don't look at it in a specific category, say, research being different from normal clinical care. We're concerned about any problem that comes up, regardless of what stripe, to understand what happened and how do we prevent it in the future and understand it.

A root cause analysis, as Dr. Mather described, what we have on the new version of the root cause analysis computer aided tool that guides the teams through what they do and what the proper steps

are, et cetera, is there's a question that we've put in there, a pointer, if you will, that we've done in consultation with Dr. Mather's group where it specifically, you know, inquires or reminds the team—it says, did this event involve a research protocol in any way? And if it has, you have a duty to talk to ORCA to pursue that further for that.

That does not change our team's—that is the safety side, looking at how do we make it better. You know, they become blind in a sense to whether it's research or not. But it informs the people who are reporting it and working on it that if it is an ORCA, you know, under the ORCA scope that you need to pursue that. We make that separate because there are certain potential enforcement issues that rise out of ORCA, which is different from the safety system. They need to be separate. Otherwise, you just won't find out about the other things. You have to separate those two. That's why we've done it in that way.

Mr. EVERETT. How many times have you formally met with Dr. Feussner?

Dr. BAGIAN. Formally? You mean, like face to face? I don't know. More than a few times. I haven't kept count.

Mr. EVERETT. Dr. Mather?

Dr. BAGIAN. Dr. Mather, tons of times. John was one of the first people I talked to when I took this job. Because he was in OHI in the OIG at the time. I thought it was extremely important that I meet OHI as well as OMI to understand what they thought were issues so we would be able to address those. We are on the same team.

Mr. EVERETT. You've met with him. Have you had any formal agreement on what gets reported and who should report? And if you don't have a formal agreement when will you?

Dr. BAGIAN. We do. As I was describing, you know, with Dr. Mather and Dr. Weber, who is here in the audience who works for Dr. Mather, we've been talking to them for the last several months about what would go into our system to direct things that belong to ORCA. So we've done that, and we've already gone over the actual language that's in the form. So, yes, we've done that.

Dr. MATHER. Could I pick up that story briefly, sir?

This past spring we worked with Dr. Feussner to assume responsibility from his office for reviewing at all adverse events and serious adverse events involving research subjects. Prior to that time, these reports had come from the field to his office. They now come directly to my office.

But that doesn't absolve them at the local level of the VA medical center. The investigator has the responsibility and the local IRB has clear responsibility to look at these issues. It's only when they get to a threshold of seriousness that they become classified as a serious adverse event. We get them—Dr. Weber, my deputy, who is a Ph.D. Scientist in physics, is working with the FDA at this time to try and figure out more precisely what should be the appropriate processes.

FDA itself is in the mode of reexamining Policies and Procedures.

There's other things called Data Safety Monitoring Boards, DSMBs, that figure into this picture as well. So while we've already established a mechanism whereby Dr. Weber goes back and

finds out from the investigator at the VA Medical Center that they've done the right thing, which includes reporting to the appropriate agencies, such as the FDA, we are actively working with FDA so that there will be a little more of a seamless process. I have to say, right now, it is a little haphazard.

Mr. EVERETT. As long as you're standing at the plate, let me throw you a couple more pitches. Is the current funding arrangement adequate for you to do your job?

Dr. MATHER. As this point in time, as Dr. Garthwaite has pointed out, we're in the process of putting all of the pieces together. With the funding levels that I've been assigned, he has promised me, an appropriate time in the not-too-distant future, we'll review the funding needs. If it comes about that we don't have the staff to do the job, particularly in the Regional Offices, then we will revisit that issue in a serious mode.

Mr. EVERETT. Has the ORCA original staffing requirements changed?

Dr. MATHER. I'm not quite sure what is the benchmark here, Mr. Chairman. Going way back to last year, there were plans put together for a staffing level that is more than what our Regional Offices right now——

Mr. EVERETT. Did you get what you requested?

Dr. MATHER. Did I get what I requested? Dr. Garthwaite has already indicated that I didn't get what I requested, and that's for the record, and that's clear.

Mr. EVERETT. Last April, Dr. Kaiser testified to this committee and stated, "I want to particularly emphasize the ORCA will be independent, objective and unbiased in its oversight activities." how can ORCA be independent when you have to bite the hand that feeds you?

Dr. MATHER. Mr. Chairman, I think when you bite that hand, that hand had better be prepared to be bitten. We have already, using our funds mainly out of headquarters at this point in time. I think it's a generic issue. It's not just where the money comes from. It's ORCA itself overseeing the research enterprise. Yes, in some ways I think the source of ORCA's money out of the research appropriation can be viewed as some sort of quasi conflict of interest.

But I want to assure you that we have been given, under Dr. Garthwaite's leadership, the independence, the separateness and the specific responsibility to call it the way it is. We have filed now five of these SIFT reports, and I don't know whether I'm pleased to report, but as Dr. Garthwaite has received them, he has signed every one without a change or an amendment, which means probably we're fulfilling our job of independence, separateness and objectivity.

Dr. GARTHWAITE. At the risk of volunteering, I would add that, you know, ultimately, the independence part comes back to the Office of the Under Secretary. If we don't treat it with independence, we can't separate the creators of research and their own inherent belief that they're doing the right thing from an outside objective review from someone who isn't quite as close to the issue.

I think that the additional step of having the outside accreditation contracts will help to provide that additional layer of objectiv-

ity, but we can't wait for all those to occur. We have to get in there deeply and quickly and put into place a lot of things, including a lot of education, before that can occur.

Mr. EVERETT. Well, of course, we had this conversation a little earlier, but I did want to return to it. Dr. Mather, what are the roadblocks, hurdles or resistance that you have encountered to try to establish ORCA, if any?

Dr. MATHER. I think the simplest thing I can say, sir, is that the personnel process and the need to run through all the hoops and links through that process has been a real challenge for us. We have, as Dr. Garthwaite alluded to, been aggressive in engaging with the human resources side of the VA. They have limitations as well. OPM needs to get the word to us. But we have worked as quickly and as smoothly as we can to get the support from them that we need.

I would even go on record as saying that we had a VA Medical Center's human resources staff that stepped up and said that they would help us. I would honestly say if they had not stepped up to help us we may not be as far along as we are right now.

Mr. EVERETT. This is a draft VA handbook that the subcommittee, by the way, received last Monday. Have you ever seen this draft?

Dr. GARTHWAITE. Have I?

Mr. EVERETT. No, Dr. Mather.

Dr. MATHER. Yes, I have seen it.

Mr. EVERETT. Did you participate in input and drafting of the document?

Dr. MATHER. No, I did not, sir.

Mr. EVERETT. Okay. When is the last time, Dr. Garthwaite, that this policy was updated?

Dr. GARTHWAITE. 1992.

Mr. EVERETT. My information is it's 1985.

Dr. FEUSSNER. If I may volunteer, sir.

Mr. EVERETT. Go ahead.

Dr. FEUSSNER. The larger policy documents were last updated in 1985, that is correct. The human studies component of that was updated in 1992. The current updates are a work in progress. We have updated the—well, we have created a preliminary version of an updated policy manual that is currently going through review in the field. We have put that document on our web site. Once—and we have been getting quite a lot of commentary back from the field. Once that is updated and we have revised the policy manual based on the feedback, then the next step in the process will be for the manual to go through a formal headquarters concurrence process.

Mr. EVERETT. '85 and '92. Is that frequent enough?

Dr. FEUSSNER. I certainly would say now the answer to that question is, no, it is not frequent enough. The policies at the national level, for example, our guidance from the cooperative studies program has been undergoing revisions so frequently that we've actually stopped publishing a final version and have just put it on the web site and revised it pretty much continuously.

Mr. EVERETT. Dr. Mather, what facilities have you visited since the ORCA's inception? And would you please share your findings?

Dr. MATHER. Mr. Chairman, I probably would have to give the full list for the record, but the staff, as they have joined ORCA, have been encouraged to visit, and—I've made sure of this, that they get around to a number of places so they can see what a full research program is.

But specifically with respect to our assurance and compliance responsibilities, we've visited again several sites but more specifically five where we have conducted these Special Inquiry Force Team reviews; and those are the ones that we concentrated our efforts on because problems surfaced. Those problems, if I can generally characterize them as being a lack of understanding, a lack of appreciation for what it is they were supposed to be doing. I found in none of these sites, Mr. Chairman, somebody who has willfully decided they're not going to ensure the informed consent forms get signed by human subjects or willfully decided that the particular research project should not come to the IRB and so forth.

Mr. EVERETT. Did you visit West LA?

Dr. MATHER. Yes, sir, I visited West LA, but not in any capacity in my current roll of investigating anything there.

Mr. EVERETT. The situation there was that consent forms were not signed and, as a matter of fact, one veteran had denied the signing of a consent twice.

Dr. MATHER. It may not be a good thing for me to say, but that didn't happen on my watch. I joined ORCA in December, and I have certainly read the full record. I have every concern that you have and Dr. Garthwaite has expressed, particularly the concern about the investigator who engaged in some of the most egregious behaviors that I've seen. As I understand it, there is still litigation going on for the removal of that individual pending two boards of investigation that have been completed, have found exactly the same things, and that this individual engaged in totally inappropriate behaviors.

Mr. EVERETT. Would you describe for the record exactly what you understand had been done?

Dr. MATHER. What has been done at West LA?.

Mr. EVERETT. By that doctor when he performed his experiments on the patient who had twice denied him the right to do so.

Dr. MATHER. I'd like to defer to Dr. Feussner to give you the specifics, but you asked me for my understanding. My understanding is that the individual failed to respect the patients and the human subjects' program. He failed to abide by the requirements of an investigator. He failed to look at the human subjects' protection and the ethical responsibility that he bore in that regard and, indeed, failed to perform the appropriate informed consent, in fact, sidled around the informed consent in the desire to enroll people in those projects. That's what I understand.

But I would defer to Dr. Feussner to give you more details.

Mr. EVERETT. Please.

Dr. FEUSSNER. Yes, sir. The specific details is the physician involved is a heart specialist and as part of his clinical responsibilities he would evaluate a heart that would have electrical problems to see where the electrical problems might be fixed. In the process of doing a clinical study called an electrophysiology study on the patient that was clinically indicated, he asked the patient for in-

formed consent to do additional study after the study that was required for clinical care was completed. The patient declined to participate in the research project.

Mr. EVERETT. Once or twice?

Dr. FEUSSNER. I believe it was twice.

When the patient went to the electrophysiology laboratory to have the clinically indicated procedure, in addition to the clinical procedure the patient had the additional research procedure performed, the procedure to which he specifically did not consent. A board of inquiry was developed. The physician was reprimanded.

Mr. EVERETT. In what way, please?

Dr. FEUSSNER. Well, I would actually also have to go back to the lengthy details.

Mr. EVERETT. I understand that he was given 7 days suspension.

Dr. FEUSSNER. That is correct.

In the process of the subsequent situation at West LA With the investigations that went on in February and March of and April of 1999, we learned that the reprimand was not properly enforced. So that while the investigator was reprimanded or at least was intended to be reprimanded, the reprimand was not implemented the way it was supposed to have been implemented.

The reprimand was then carried out. The official who was responsible for implementing the reprimand was herself reprimanded. Subsequent to this, initially a board of inquiry had been undertaken which led to this initial reprimand.

Mr. EVERETT. Was a second investigation or any subsequent action taken after this action?

Dr. FEUSSNER. Yes, sir, that is correct.

Mr. EVERETT. Would you describe what happened there?

Dr. FEUSSNER. Well, my recollection is that when the issue was revisited the initial board of inquiry was perhaps not as explicit, documented as well as might need to be documented for legal purposes; and so a second board of inquiry was undertaken to more completely document that, in fact, the information in the first board of inquiry was correct.

Mr. EVERETT. And what happened with the second board?

Dr. FEUSSNER. The second board of inquiry confirmed that the initial board's findings were correct.

Mr. EVERETT. And what happened to the doctor?

Dr. FEUSSNER. Well, the physician—the intention subsequent to the second board of inquiry was that the physician be removed from his position. The physician has not been removed from his position.

Mr. EVERETT. And why not? You recognize in civilian life that would be subject to a $10,000 fine and a year in prison. That was an assault, a felony assault on this patient.

Dr. FEUSSNER. We've discussed this before, Mr. Chairman; and I can't disagree. The physician is currently litigating the action—the adverse action that the VA has taken. In the interim, the physician has been put on administrative leave, I believe, since January.

Mr. EVERETT. With pay?

Dr. FEUSSNER. Yes, sir. I think that is required under the circumstances.

Mr. EVERETT. It is. I just wanted to make a point.

Dr. FEUSSNER. His clinical responsibilities have been interrupted, his research responsibilities have been interrupted, and, actually, another physician had to be hired to do the procedures that the incident physician that we're discussing would normally have done. The issue is not resolved at of this date. The litigation is ongoing.

Mr. EVERETT. I'm glad to hear you say that, because I understand the litigation of not ongoing. But you're telling me it is.

Dr. FEUSSNER. Well, I called—I have been in communication with the CEO at the hospital. The last time I knew, the litigation was ongoing. Some material was going to be presented to the CEO for him to perhaps adjudicate. But as best I know, the litigation continues.

Mr. EVERETT. And I know you'll be glad to hear this.

Finally, Dr. Garthwaite, when did you request approval from Secretary West of Dr. Mather's appointment?

Dr. GARTHWAITE. I think we sent the paperwork forward asking for——

Mr. EVERETT. I'm sorry, I didn't hear.

Dr. GARTHWAITE. I think we sent the paperwork forward asking for his appointment in late September.

Mr. EVERETT. Late December.

Dr. GARTHWAITE. September.

Mr. EVERETT. When was it approved?

Dr. GARTHWAITE. Early December.

Mr. EVERETT. Okay. Gentlemen, thank you very much for your hearing. I recognize it's been long. I know that you agree this is one of the most important subjects that we can discuss, the huge problems involved in this; and we're talking about some of the poorest of our patients who have no choices involved in it.

So at this point I'll dismiss this panel, and my closing statement will be as follows: The results of the GAO's review leave me very disappointed in VA's progress toward adequate protection of veterans who participate in medical research. I conclude that the VA has not yet done everything it should have in the last 18 months. GAO testified that progress has been slow and that lack of protections continues to put veterans at risk.

This is not acceptable. The VA does not have a choice. It must do better in complying with human subject research protections for veterans and do it quickly or face the prospect of outside regulation of the research, as valuable as it has been.

The next report from GAO will be critical. The Congress cannot allow VA to continue putting veterans at risk in medical research.

Thank you, and this hearing is dismissed.

[Whereupon, at 12:01 p.m., the subcommittee was adjourned.]

APPENDIX

Statement of the Honorable Lane Evans
Ranking Democratic Member
Committee on Veterans Affairs

Hearing on Human Subject Protections in VA Medical Research
Subcommittee on Oversight and Investigations
September 28, 2000

This hearing follows up two landmark hearings held during the 106th Congress by the House Committee on Veterans' Affairs Subcommittee on Oversight and Investigations.

- Last year, on April 21, this subcommittee held a ground-breaking hearing on medical research conducted by the Department of Veterans Affairs (VA), prompted by problems with patient safety management at the West Los Angeles VA Medical Center. Based on that hearing, the Subcommittee on Oversight and Investigations commissioned a General Accounting Office (GAO) study of human subject research safety concerns, on which we expect to hear a great deal in testimony this morning.

- Secondly, the Subcommittee on Oversight and Investigations held a hearing on Patient Safety and Quality Management in the Department of Veterans Affairs on July 27 of this year. That hearing examined a report from VA's Office of the Medical Inspector (OMI) which reported a total of 2,927 medical errors in a period of a year and a half, of which over 700 resulted in accidental patient deaths or suicides.

In both hearings, this subcommittee looked with VA and the American public at unsettling subjects. These hearings overlap, though VA cannot tell how much they overlap, because many veterans who receive treatment through VA's Veterans Health Administration (VHA) take part in medical research.

Today's witnesses will tell us what VA has learned to date, and what progress it has made in installing systems that may lead to identifying and minimizing medical misadventures. It is an important hearing, and there will be more in the future.

As a veterans advocate in Congress, I appreciate the contributions VA research has made in diagnosing and treating problems such as:

- geriatric health,
- alcohol and drug dependency,
- the special health problems of women veterans,
- brain injuries,
- spinal cord injuries,
- heart disease,
- post-traumatic stress disorder,
- prostate disease,
- schizophrenia, and
- conditions associated with Agent Orange and service in the Persian Gulf War.

I am particularly proud of the follow-up assessment the Subcommittee on Oversight and Investigations requested from GAO, which will be presented in testimony this morning. It discloses problems that still need resolution. More than that, it has laid out recommendations that I believe will allow VA – under the watchful eye of Congress – to create and implement plans that can make human subject safety a secure part of standard operating procedures at VA.

VA must make certain these details are done right. GAO found three weaknesses that compromise human subject safety protections.

1. VA headquarters has not provided adequate guidance on human subject safety protections.
2. VA has not exercised sufficient oversight.
3. VA has not ensured there is sufficient funding for human subject protections.

Let me be clear that I am not saying it is unsafe for veterans to act as human subjects for VA medical research. On the contrary, veterans often obtain new and important break-through treatment through such participation, and they advance medical science by doing so. What concerns us today is making certain that such treatment is as safe as possible, and that it adds minimal risk to the veteran. Proper procedures and records -- often missing, according to GAO – are as much a part of good research as proper disposal of used needles.

STATEMENT OF

GREG KOSKI, PH.D., M.D.
DIRECTOR, OFFICE FOR HUMAN RESEARCH PROTECTIONS
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Chairman Everett and distinguished members of the Subcommittee:

Thank you for this opportunity to discuss the new Office for Human Research Protections (OHRP) and to outline some of the initiatives the office is undertaking toward fulfillment of the Secretary's committment to enhance protections for human research subjects and to improve the biomedical research process.

Although the American people and Congress have long been avid supporters of biomedical research, events of the past several years threaten to further undermine the already shaken public confidence in this important endeavor. Although some real progress has been made as a result of steps taken by NIH, FDA and other federal agencies, the need to continue effective reform is great, and the pace of the reform effort needs to be accelerated. Ensuring the public trust in the biomedical research endeavor must be one of our highest priorities.

Although I officially assumed my position as director of OHRP only two weeks ago, the Office has been working to develop an ambitious action plan for reform that I am happy to describe for you today. I would also like to emphasize that OHRP is not alone in its concern over these issues, nor does it bear sole responsibility. OHRP will join with and help to build upon those actions already being taken by other offices and agencies within the government and by private groups that share these goals.

In my first weeks on the job, I have sensed an inspiring level of commitment and a spirit of cooperation that bodes very well for the future; indeed, creation of an effective system for protection of human subjects depends upon cooperation among all of the agencies that fund, conduct or regulate human research, and our very first priority is to establish solid collaborative relationships through which we can work toward realization of our common goals.

First, I'd like to say a few words about the new office. OHRP was created by Secretary Shalala earlier this year as part of her program to enhance protections for human subjects. Based upon recommendations of a review panel convened in 1999 by the Director of NIH, OHRP, which supersedes the former Office for Protection from Research Risks (OPRR), was created within the Office of the Secretary. This move was intended to provide a more effective platform from which the new office could lead reform, both within HHS and across all federal agencies and departments subscribing to the federal regulations for protection of human subjects in research known as the Common Rule (Title 45 CFR Part 46, Part A).

OHRP differs from it predecessor in several important ways. First, OHRP is responsible for oversight of research involving human subjects only; animal research will be overseen by the Office for Laboratory Animal Welfare (OLAW) which remains within the administrative structure

of the National Institutes of Health (NIH). Second, OHRP's responsibilities include protection of human subjects in all human research funded or regulated by HHS, and the office is intended to provide leadership for all agencies conducting or funding research under the Common Rule. It is nevertheless important to understand that individual agencies have specific regulatory and oversight responsibilities that remain unchanged, such as FDA's enforcement authority in FDA-authorized drug and medical device trials. OHRP also has a new organizational structure and new leadership that will afford greater effectiveness of its programs and greater efficiency of its operations.

The office, and the country at large, will benefit from a newly established National Human Research Protection Advisory Committee (NHRPAC). Currently, the membership of this committee is being selected by the Secretary from a group of nearly 130 nominees representing all viewpoints of the human research community. An Executive Director is being sought to convene the group which will soon begin its important work.

Among the challenges it faces will be consideration of important matters related to informed and voluntary consent, vulnerable populations of research participants, genetics research and conflicts of interest. OHRP and the Department will look to this advisory committee to provide guidance as policies and procedures are developed. Its advice will ensure that we follow a route that facilitates conduct of responsible research while optimally protecting the interests and welfare of the participants.

The time has come for us to take a new approach, one based upon recognition that the primary responsibility of every party to the biomedical research process is to protect the well-being of those brave and unselfish individuals who voluntarily participate as subjects of our research. By their doing so, all of us can reap enormous rewards from this endeavor, including better understanding of human physiology and disease, safer and more effective treatments and diagnostic procedures, and new drugs, devices and biological agents that will improve our health and the quality of our lives.

The model envisioned, a model that resonates with the recommendations of major professional, industrial, academic and advocacy groups, as well as those of the OIG, is based upon achieving greater responsibility and accountability at every level of participation.

We envision a system in which every party to research is properly trained and educated to fulfill their responsibilities and in which every individual personally acknowledges and accepts responsibility for protecting research subjects as a condition of participation.

Further, we envision a system in which objective, uniform, nationally recognized performance standards provide the basis for certification of individual competencies and accreditation of groups conducting review, approval and continuing oversight of research. And while we will be working to strengthen these processes, we will also work with our colleagues throughout government to clarify, simplify and streamline the regulatory environment, to reduce

administrative burdens and eliminate or modify rules and regulations that impair the effectiveness and efficiency of our system without adding commensurate value.

While compliance with regulations is essential, compliance alone will not achieve our goals. We must focus on responsible conduct rather than compliance per se. We must establish a research environment in which every individual does the right thing because it is the right thing to do. And those who will not accept their responsibilities must not be allowed to participate, as the cost to society is simply too great. Biomedical research, like the practice of medicine itself, involves relationships that must be founded upon and sustained by an enduring sense of trust and mutual respect between subject and investigator. Anything less is not enough.

In April of this year, the OIG issued a follow-up report on the status of its earlier recommendations. That status report acknowledges that the creation and positioning of OHRP affords a significant new opportunity for HHS to exert broad federal leadership in protection of human subjects. The status report goes on to "urge the new office to give significant attention to our previous recommendations and to those that will be forthcoming from NBAC".

That, Mr. Chairman, is precisely what OHRP intends to do. These recommendations, and the need for a balanced approach, one that combines efforts to simplify regulatory requirements and facilitate compliance with enhanced education and heightened oversight are the heart of OHRP's vision of the future, a vision that I believe is broadly shared. And I will reiterate, OHRP cannot realize this vision alone. We must take a collaborative approach toward integration of activities with all who share this vision if we are to succeed. Needless to say, we understand the need to carefully coordinate the activities of this office with those already being undertaken by NIH, FDA, CDC, AHRQ, and other HHS entities. OHRP recognizes and appreciates the efforts being made as an encourging sign. A number of working groups have been working in several areas, and we hope to join these efforts.

I would like to discuss in more concrete terms specific steps that are being taken or are planned to give substance to this vision so that everyone can better appreciate where we hope to go.
To a large extent, the road to success has been thoughtfully mapped by the Office of the Inspector General's (OIG) report originally issued in 1998, entitled *Institutional Review Boards: A Time for Reform* (US Government Printing Office). Although the recommendations are general in nature, they provide a useful framework for discussing specific initiatives that are in various stages of planning and implementation.

- **Grant institutional review boards greater flexibility but hold them more accountable for results.**

  1. We will implement a simplified assurance process that will avoid the time-consuming negotiation process that has distracted attention and resources from more effective and desirable approaches to achieving true protection of human research subjects, such as more effective education and oversight programs. We hope to be able to implement the

new system as soon as possible.

2. OHRP will devote additional resources, including those freed by implementation of a simplified assurance process, to enhance oversight and educational activities. These will include a dramatic expansion of not for cause technical support visits to assist institutions, investigators and IRBs in fulfilling their responsibilities.

3. In cooperation with FDA and other federal agencies, including the Department of Veterans Affairs (VA), we will work to develop and implement a unified registration system for all human research review boards.

4. An inter-agency working group will be established to review current regulations and guidance as part of an ongoing effort to identify and eliminate inconsistencies and inefficiencies that do not contribute effectively to protection of human subjects.

- **Re-engineer the Federal oversight process**

1. Recognizing the need for and value of greater uniformity and public accountability in the review and approval process, OHRP, with the support of the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention(CDC) and the Agency for Healthcare Research and Quality (AHRQ), will engage the Institute of Medicine (IOM) to recommend uniform, performance and resource-based standards for private, voluntary accreditation of human research review boards. This effort will draw upon work already undertaken by major national organizations to develop and test these standards by the spring of 2001, followed by initiation of a formal accreditation process before the end of next year.

2. As part of this effort, IOM will also be asked to conduct a study of the human research system to determine the extent to which they address issues raised by the OIG and the recommendations of the forthcoming National Bioethics Advisory Commission's (NBAC) report.

3. IOM will also be asked to develop objective criteria for measuring the effectiveness of the system for protection of human subjects in research. These criteria will then be used on an ongoing basis for continuing assessment of the system and regular reports to Congress and the public.

- **Strengthen continuing protections for research subjects**

1. Working with FDA and NIH and other agencies, we will carefully examine the continuing review process and develop guidance for institutions and review boards regarding appropriate mechanisms for ongoing monitoring of approved research. These

must include more effective monitoring of adverse event reports, development and implementation of quality improvement processes, and programs for on-site inspections and evaluations of research programs and IRB processes.

2. OHRP will establish a publicly accessible 'hotline' to provide information and to address complaints or concerns raised by subjects, investigators, IRB members or the general public in real time on an on-going basis. This will serve as a national resource for human subjects protection.

3. We will work vigorously to improve inter-agency communications and integrate each agency's existing oversight processes to develop an enhanced 'safety net' for research subjects that will optimize ongoing oversight without redundancy.

- **Enhance education for research investigators and IRB members**

1. Recognizing the need for enhanced education, essentially all of the federal agencies and OHRP have already enhanced and will continue to expand their educational programs. OHRP's programs will include national and regional workshops and conferences, 'town meetings', technical assistance support visits, and 'ambassadorial visits' by the director and senior staff. The latter are intended to help institutions and review boards develop a culture that embraces human subject protection as an integral part of the research process and as a responsibility shared by all.

2. While the OIG has called for enhanced education of investigators and IRB members, OHRP does not believe this to be sufficient. To achieve the goals outlined above, there must be more effective education and training for all members of the research team, institutional officials, research subjects and the general public. Indeed, education of the public at large is one of the most important steps that can be taken toward improving the informed consent process and toward enhancing public awareness and accountability of the research process.

3. In collaboration with NIH, FDA and other agencies, OHRP will develop guidance for uniform, minimal educational requirements applicable to *all* clinical investigators regardless of the source of funding or sponsorship of their research.

4. OHRP, NIH, FDA and other federal agencies, and the Office for Research Integrity (ORI), will work to integrate and coordinate their educational programs with those of institutions and sponsors to achieve maximal effectiveness of these programs and optimal utilization of resources. Toward this end, OHRP will convene an 'educational summit meeting' to clarify educational goals for each party to the research process and will issue appropriate guidance on this topic.

5. OHRP will encourage and support efforts to develop independent certification programs

for investigators, and to expand existing programs for certification of clinical research coordinators (CRCs), clinical research associates (CRAs) and IRB professionals. Establishment of nationally recognized standards for certification, in combination with enhanced public education and awareness, will strongly encourage all participants to achieve a high level of competence in their respective areas of endeavor. This will improve both the quality of their research and protection for human subjects.

6. OHRP will establish an on-line library of educational resources that will be publicly available to promote and augment private educational programs for investigators, institutions, review boards, research subjects and the general public. We hope to develop this as a shared resource

- **Steps should be taken to moderate the workload of institutional review boards and to ensure adequate resources for their activities**

1. Many institutions and IRBs are attempting to meet their responsibilities, but may lack necessary resources. NIH has already taken steps to avoid unnecessary review of proposals that are unlikely to be funded, thereby reducing workload. While there may be additional steps that can be taken to reduce administrative burdens and improve efficiency, these steps can do little for those IRBs that either are not given sufficient resources by their institutions, or for institutions that lack a sufficient base of research funding to build the necessary infrastructure to support an effective and efficient IRB process. OHRP, through its technical assistance programs, will work with institutions and IRBs to identify efficient ways to optimize utilization of resources.

   The system for protection of research subjects should not be viewed as a costly but necessary inconvenience associated with doing human research. Rather, it should be recognized as an important cornerstone upon which public trust in biomedical research is founded, and it should be supported appropriately. Unfortunately, the true costs of the human subjects protection process are not known, and what constitutes appropriate funding is not well-defined. OHRP will encourage funding agencies and institutions to continue to work together to identify appropriate mechanisms for funding that ensure an effective system of protection of human research subjects, and if necessary, include specific provisions in new research awards to support this critical infrastructure.

2. We will work to develop guidelines for appropriate staffing and workload levels for IRBs. These benchmarks will give institutions and research review boards a clear sense of the level of resources required for an effective process for review, approval and continuing oversight of clinical research.

3. As part of the re-engineering process recommended by the OIG report and are under consideration by NBAC, structural changes in the human research review and oversight process should be carefully considered. Concerns about conflicts of interest and

autonomy of *institutionally-based* review boards deserve careful attention. Further, the current system necessitates redundant and often conflicting reviews of an individual study by multiple IRBs, resulting in considerable inefficiency and dilution of effectiveness. This situation gives rise as well to the practice of "IRB shopping". In our present system, research that is approved by *any IRB* can be done, regardless of disapproval by several other IRBs. The resultant "sinking to the lowest standard", as some have described the process, is not in the interest of effective human subjects protection or good research practice and should be corrected.

- A system of human research review boards that is not based at the level of single institutions, one that would encourage more effective utilization of resources and that would concurrently enable a more robust, autonomous and effective process, while preserving sensitivity to important local considerations, is worthy of consideration as a long-term goal. A nationally (or even internationally) recognized system for accreditation of human research review boards will be a strong step toward resolution of this dilemma. Toward this end, OHRP will frame this question for consideration by the NHRPAC following release of NBAC's final report and a period of public comment.

Greater cooperation among the federal departments subscribing to the Common Rule is a desirable and achievable goal, and the creation of OHRP affords an opportunity to provide leadership in this area. The full potential of the Common Rule for unifying our national system for protection of human research subjects has never been realized. In fact, the Common Rule has been cited by the OIG and others as an *impediment* to creating a more uniform and effective system, because of the time and effort required to effect changes among the 17 agencies that are signatories.

We have before us an opportunity to improve this situation. Now is the time to strengthen the bonds among the federal departments who collectively share the important responsibility for protection of human subjects in research, to work together more closely to integrate our activities with an eye toward greater uniformity, simplicity and effectiveness. Already , we have extended our hand to the VA and other Executive Branch agencies, and our overtures have been welcomed.

We are working closely with ORCA to build a strong relationship with the VA, and I believe that this relationship may become an example of how the Common Rule agencies can work together more effectively. In truth, the need for a unified system for protection of human subjects in research is sufficiently great that if we are unable to foster such an approach voluntarily, calls for new legislation to require it will likely intensify.

And so to conclude my remarks, I will say once again that the time has come to translate vision to action. The program before us is admittedly ambitious; it will require both collaboration and compromise, but these objectives can be realized in a surprisingly short time-frame if we can simply work together. Indeed, many of the initiatives described here today are already underway or are in various stages of planning, although many details remain to be worked out. We hope to initiate as many of these actions as we can during the next several weeks, recognizing that sufficient time must be allowed to follow appropriate procedures for issuing guidance, etc., and to ensure proper discussion and coordination among the participating agencies and offices.

Protection of human subjects in research is everyone's responsibility. I continue to be impressed that the spirit of determination and cooperation is very much alive and is stronger right now for this cause than it is ever likely to be again. As we move forward, we will work continually to strengthen our interactions with other agencies and departments that share our common goals. Our challenge is to take full advantage of the very significant opportunity before us, and to do so now.

United States General Accounting Office

GAO

Testimony

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

For Release on Delivery
Expected at 10:00 a.m.
Thursday, September 28, 2000

VA RESEARCH

System for Protecting Human Subjects Needs Improvement

Statement of Victor S. Rezendes, Assistant Comptroller General
Health, Education, and Human Services Division

GAO/T-HEHS-00-203

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here to discuss the report we are issuing today to you and other requesters on the Department of Veterans Affairs (VA) system for protecting the rights and welfare of veterans who volunteer to participate in research at VA medical centers.[1] It has been 18 months since research was suspended at the West Los Angeles VA Medical Center[2] because officials failed to correct longstanding problems in its human subject protection system. Since that suspension, four additional VA medical centers have felt the repercussions of sanctions by regulatory agencies against their affiliated universities. My testimony summarizes our assessment of VA's implementation of human subject protections, highlights systemwide weaknesses we identified in those protections, and evaluates VA's actions to better protect human subjects at medical centers that have been affected by sanctions and throughout VA's healthcare system.

Based on our review of eight medical centers, we concluded that VA needs to take action to strengthen the protection of human research subjects. Although the extent of the problems was uneven, we documented a disturbing pattern of noncompliance across the centers we visited. The cumulative weight of the evidence indicated failures to consistently safeguard the rights and welfare of research subjects. We also identified three specific weaknesses that have compromised VA's ability to protect human subjects—lack of adequate guidance to medical centers about human subject protections, insufficient monitoring of local protections, and inadequate attention to ensuring that funds needed for human subject protection activities are allocated and available for those purposes. To VA's credit, at three other medical centers we visited, substantial corrective actions have been implemented in response to sanctions by regulatory agencies taken against their human research programs. In contrast, VA's systemwide efforts at improving protections have been slow to develop.

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[1] VA Research: Protections for Human Subjects Need to Be Strengthened (GAO/HEHS-00-155, Sept. 28, 2000).
[2] The West Los Angeles VA Medical Center is now part of the VA Greater Los Angeles Healthcare System.

BACKGROUND

Conducting medical research is one of VA's core missions. 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. Funds from the appropriations for VA medical research and VA medical care support VA researchers and the indirect costs of research, which includes support for the human subject protection system. VA researchers receive additional grants and contracts from other federal agencies such as the National Institutes of Health (NIH), research foundations, and private industry sponsors including pharmaceutical companies. In fiscal year 2000, biomedical or behavioral research involving human subjects is being conducted at about 70 percent of VA medical centers.

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 subjects are veterans, or the studies are conducted on VA grounds. Responsibility for administration and oversight of the research program has rested primarily with the Office of Research and Development (ORD). Recently, VA created the Office of Research Compliance and Assurance (ORCA) to advise the Under Secretary for Health on matters affecting the integrity of research protections, to promote the ethical conduct of research, and to investigate allegations of research impropriety. In addition, some VA research is subject to oversight by two components of the Department of Health and Human Services (HHS). 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).[3]

[3]The Office for Human Research Protections (OHRP) is in the Office of the Assistant Secretary for Health. HHS established OHRP in June 2000 to assume the human subject protection functions of the former Office for Protection from Research Risks (OPRR), which was part of NIH. We refer to both organizations as OHRP. Actions taken before June 18, 2000, were taken by OPRR.

Research offers the possibility of benefits to individuals or to society, but it is not without risk to research subjects. To protect the rights and welfare of human research subjects, 17 federal departments and agencies, including VA, adopted regulations designed to safeguard the rights of subjects and promote ethical research. These regulations establish minimum standards for the conduct and review of research to ensure that studies are conducted in accordance with the ethical principles outlined in the Belmont Report, issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. These principles require that subjects voluntarily give informed consent to participate in research and that the expected benefits of research to the individual or to society outweigh its anticipated risks.

Federal regulations create 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 local committees known as institutional review boards (IRB) that are responsible for reviewing both research proposals and ongoing research. 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. VA requires that each of its medical centers engaged in research with human subjects establish its own IRB or secure the services of an IRB at an affiliated university. As of August 2000, approximately 40 percent of the VA medical centers conducting research with human subjects relied on an IRB at an affiliated university.

IMPLEMENTATION OF HUMAN SUBJECT PROTECTIONS UNEVEN

We found various degrees of noncompliance with VA regulations and policies involving protections for human subjects at the eight medical centers we visited. Although we recognize that the results of our visits cannot be projected to VA as a whole, we found sufficient patterns of noncompliance to be concerned. We saw multiple problems at some sites, but relatively fewer problems at others. The five sites we visited that relied

on VA-run IRBs had the most extensive problems. The three university-run IRBs we visited, however, were not without problems.

We found that medical centers and their affiliated universities did not comply with all the regulations designed to protect the rights and welfare of research participants in four areas: (1) informed consent; (2) IRB review; (3) IRB membership, staff, and space; and (4) IRB documentation. OHRP noted similar compliance problems in letters to universities and hospitals it has found to be out of compliance with federal regulations. As shown in fig. 1, some sites we visited had more problems than others.

Figure 1: Noncompliance with VA Regulations at Eight Sites

		Informed Consent			IRB Review				IRB Membership, Staff, and Space			IRB Documentation			
		Percentage													
		IRB-Approved Consent Forms That Provided Incomplete or Unclear Information [a]	Studies In Which the Investigator Used a Nonapproved Consent Form [b]	Research Conducted Without Consent	Initial Review—IRB Held Meetings Without a Quorum	Initial Review—High-Risk Study Improperly Approved by IRB Chair	Continuing Review—Not Conducted on Time	Continuing Review—Analysis Based on Insufficient Information	Potential Conflict of Interest in IRB Membership	Insufficient IRB Staff	Insufficient Space for IRB Operations	Inadequate Documentation in IRB Project Files	Written IRB Procedures Did Not Meet Standards	Incomplete Documentation in Minutes of IRB Discussions	IRB Votes Not Recorded as Required
VA-Run IRBs	A	100	■				■	●		●	●		●		
	B	88	■	●			■		●	●	●	●	●		
	C	25	■				●	●		●		●	●		●
	D	78	28				●	●	●	●		●	●	●	●
	E	87	■		●		●	●				●	●	●	●
University-Run IRBs	F	59	25									●			●
	G	44	33			●									
	H	26	12								●				

■ We did not compare consent forms signed by subjects with IRB-approved consent forms at these sites.
■ We did not assess the timeliness of continuing review at these sites.
● We observed noncompliance at these sites.

[a]We reviewed from 14 to 20 IRB-approved consent forms at each site, for a total of 138 forms.

[b]We compared consent forms signed by subjects to IRB-approved consent forms for 17 to 20 studies at each of 4 sites. We compared forms for a total of 73 studies.

We found problems with the content or use of informed consent forms at all of the medical centers we visited. We found that some informed consent documents that had been approved for use by IRBs provided incomplete or unclear information. For example, we found that a consent form given to subjects did not mention possible risks of a biopsy in a study designed to test a treatment for esophageal cancer. We found

another that did not indicate who would have access to data obtained during a study on treatment for cirrhosis of the liver. We found a third that did not describe alternative treatment options in a study comparing two drug treatments for schizophrenia. Obtaining informed consent is a primary ethical requirement of research with human subjects. The ability of competent subjects to make their own informed decisions about whether to participate in research and the ability of legally authorized representatives to protect those unable to provide consent because they are incapacitated are undermined when IRBs fail to ensure that all required information is included in consent forms or when investigators fail to obtain consent using approved procedures.

We also found that five of the sites we visited did not implement certain required procedures for IRB review of research. For example, one IRB held meetings without having all required members in attendance. Studies, such as those on new drug treatments for unstable coronary symptoms and pneumonia, were thus initiated without legitimate approval. In addition, three review boards did not meet the requirement that each study be re-reviewed at least once a year. At one of these, a VA-run IRB, re-review delays of up to 14 months occurred in one-half of the projects we sampled. Regular re-review allows reassessment of a study's ratio of risks to benefits in light of data obtained since a study was begun, such as data about adverse events.

We found problems with IRB membership, staff, and space. Two IRBs we visited did not ensure that their members had no potential conflict of interest, four IRBs did not have adequate staff to support review activities, and IRB staff at three sites did not have sufficient space to conduct their work or store all necessary documents. IRBs must have secure, private areas for the review, discussion, and storage of confidential materials. But we observed IRB file folders stacked loosely on top of filing cabinets and on floors at one of these sites.

In addition, six of the eight IRBs we visited did not maintain all the records required by VA regulations. We found incomplete documentation of IRB activities, such as local written IRB procedures that were inadequate, IRB meeting minutes that did not

document substantive discussions, and votes that were improperly recorded. One medical center we visited had been cited by the FDA in June 1999 for failure to have adequate written procedures. The center agreed to have them in place by August 1999 but did not do so until December 1999. The written procedures we reviewed from three other VA-run IRBs did not include required descriptions of procedures for conducting project review, determining when additional project monitoring is necessary, or responding to investigator noncompliance. Although inadequate documentation does not alone place subjects at risk, documentary failures prevent appropriate monitoring and oversight activities. For example, records of actions, deliberations, and procedures can help identify problems and corrective actions.

SPECIFIC WEAKNESSES COMPROMISE VA'S PROTECTION OF HUMAN SUBJECTS

We identified three specific weaknesses in VA's system for protecting human subjects: not ensuring that research staff have appropriate guidance, insufficient monitoring and oversight activity, and not ensuring that the necessary funds for human subject protection activities are provided. These weaknesses indicate that human subject protection issues have not historically received adequate attention from VA headquarters.

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 need to protect the rights and welfare of human subjects. We found that VA had not developed a systemwide educational program or ensured that each of its facilities had an appropriate training program in place. A need for increased educational guidance from headquarters was one of the most commonly identified issues regarding human subject protections in a VA-sponsored survey of network managers. Educational programs are critical to ensuring that IRBs and investigators can implement appropriate protection for human research subjects.

The second weakness we identified is that VA did not have an effective system for monitoring protections of subjects, thus allowing noncompliance with regulations to go undetected and uncorrected. For example, we found that VA headquarters and affected medical centers were generally unaware of regulatory investigations and impending actions by OHRP and FDA against university-run IRBs until after the regulatory sanctions were applied. Also, VA headquarters has not provided medical centers with guidance on ensuring access to minutes or other key information when they arrange for the services of a university-run IRB. As a result, one medical center we visited did not have access to the minutes of its university-run IRB, and two medical centers affected by regulatory sanctions against their affiliated universities had not monitored IRB minutes to assess compliance with regulations. Seven of the eight medical centers we visited did not routinely check whether investigators provided subjects with the correct IRB-approved consent form.

The third weakness we identified is that VA has not ensured that funds needed for human subject protections are allocated for that purpose at the medical centers. Officials at some medical centers told us that they did not have sufficient resources to accomplish their mandated responsibilities. We found that responsibility for funding human subject protections is diffused across several decisionmakers: the medical center's associate chief of staff for research and development, the medical center's director, and the board of directors of the medical center's nonprofit research foundation, which has discretion over the use of funds from non-VA research sponsors. Each of these may also have competing priorities for the same funds. The result is that no one official is responsible for ensuring that medical center research programs have the resources they need to support IRB operations and provide training in human subject protections. Research officials at five of the eight medical centers we visited reported that they had insufficient funds to ensure adequate operation of their human subject protection systems. Moreover, headquarters research officials told us that VA has not determined the funding needed for human subject protection activities at the medical centers.

LOCAL ACTIONS ADDRESS PROBLEMS IDENTIFIED BY REGULATORS BUT SYSTEMWIDE FOCUS SLOW TO DEVELOP

To VA's credit, substantial corrective actions have been implemented at three medical centers we visited in response to regulatory sanctions taken against their human research programs. However, VA's systemwide efforts to improve protections have been slow to develop.

Medical centers and affiliated universities affected by sanctions have taken numerous steps to improve human subject protections. They have, for example, hired and trained IRB staff and developed written procedures for their IRB operations. These medical centers and affiliated universities have made progress, and each has resumed human research activities.

We identified several issues of concern at some of these medical centers, however. For example, VA's authorization of a resumption of IRB operations at the West Los Angeles VA Medical Center on April 19, 1999—less than 1 month after OHRP's sanctions against the medical center—was premature. At that time, the medical center still lacked approved, written procedures for operation, relied on untrained administrative staff to assist newly formed IRBs, and had not provided investigators with training in human subject protection issues. We are also concerned that officials at the medical center were particularly slow to respond to the issues OHRP identified over a 5-year period, including the requirement to establish a data and safety monitoring board to oversee studies involving subjects with severe psychiatric disorders.

VA also has been slow to identify systemwide deficiencies and obtain necessary information about the human subject protection systems at its medical centers. Although OHRP identified problems with human subject protections at the West Los Angeles VA Medical Center in 1994, VA did not have a plan to address systemwide concerns involving research until July 1998. VA did not begin to implement systemwide

Only recently has VA headquarters begun to implement systemwide changes to improve its human subject protections. Its steps have included providing information to investigators and research staff and obtaining information about medical centers' research programs, such as identifying medical centers that use their own IRBs and those that use university-run IRBS, which will allow headquarters officials to determine the additional steps that may be needed locally or systemwide to ensure compliance with regulations and protection of human subjects.

In addition, VA is making two organizational changes to enhance monitoring and oversight of human research. The changes are designed to allow routine onsite monitoring of medial centers' research programs, thereby helping medical centers identify weaknesses and develop strategies to improve compliance with human subject protection regulations. Although promising in concept, it is too soon to determine whether these initiatives will fulfill their objectives. The first, the creation of ORCA, was announced in April 1999, but VA did not appoint the chief officer until December 1999. As of September 2000, staffing of ORCA, which includes four regional offices, was incomplete. Although ORCA's specific plans for monitoring medical center research activities are still under development, ORCA officials told us they planned to conduct a site visit to each medical center on a rotating basis. In its second initiative, VA has awarded a contract for external accreditation of its IRBs. The contractor is expected to conduct a site visit to each medical center conducting research with human subjects every 3 years to review IRB performance and assess compliance with regulations. VA officials told us VA expects that the university-run IRBs it uses will grant access to the accreditation team. VA is the first research organization to seek external accreditation of its human research programs.

VA needs to do more systemwide to protect the rights and welfare of human subjects who participate in research at VA medical centers. In the report we issue today, we make recommendations to the Acting Secretary of Veterans Affairs to take immediate steps to provide staff training and resources and to take other measures to ensure that

VA medical centers, their IRBs—whether operated by VA or not—and VA investigators comply with all applicable regulations for the protection of human subjects.

In concurring with the recommendations, VA identified the steps it has taken and its planned initiatives. Critical to timely and effective implementation will be sustained commitment to a program of heightened vigilance regarding the protection of human subjects. Without this, the rights and welfare of veterans who participate in VA research remain vulnerable.

Mr. Chairman, this concludes my prepared statement. I will be happy to answer any questions that you or Members of the Subcommittee may have.

GAO CONTACT AND STAFF ACKNOWLEDGEMENTS

For more information regarding this testimony, please contact Cynthia A. Bascetta, Associate Director, Veterans' Affairs and Military Health Care Issues, at (202) 512-7101. Key contributors to this testimony include Bruce D. Layton, Cheryl Brand, and Kristen Joan Anderson.

(406206)

Statement

of

Thomas L. Garthwaite, M.D.

Under Secretary for Health

Department of Veterans Affairs

on

Protection of Human Subjects of Research in the

Veterans Health Administration

before the

Subcommittee on Oversight and Investigations

of the

Committee on Veterans' Affairs

U.S. House of Representatives

September 28, 2000

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Mr. Chairman and Members of the Subcommittee:

Thank you for the opportunity to appear before you to discuss the VA Medical and Prosthetic Research and Development program and, in particular, protection of human subjects of research in the Veterans Health Administration (VHA).

VHA's Research and Development program is focused upon the high priority health care needs of veterans. A special advantage of the VA research program is that it is nested within a health care system that serves more than 3 million veterans, creating a unique national laboratory for the discovery and application of new medical knowledge. VA research is conducted by VA scientists and clinicians who also have responsibility for providing care for our patients and for training future health care providers for the nation. Unlike NIH, VA does not make research grants to colleges and universities, cities or states, or any other non-VA entity. Many advances in health care that benefit veterans and the nation have emerged from VA research – from the first treatments for tuberculosis and some of the first successful organ transplants, to the discovery of a gene for schizophrenia and improved treatments for Post-Traumatic Stress Disorder.

Given the importance of clinical research in VA, it is essential that our research program be committed to protect the safety of patients and research subjects. VA is one of the 17 federal agencies that are signatories to the Common Rule for the Protection of Human Subjects of Research (38 CFR 16) and also has a separate regulation (38CFR 17.85) that guarantees needed medical care for any patient injured in a VA research project. All VA scientists are expected to abide by stringent ethical principles and rigorous regulatory requirements to ensure the protection of their research subjects.

VA considers all research conducted at a VA facility to be VA research, even if direct funding costs do not derive from federal funds. Therefore, the provisions of the Common Rule and the requirements of VA regulations apply equally to all VA research, regardless of sponsor or funding source. Much of the research conducted in VA facilities is also subject to the regulations of other federal agencies. For example, human studies funded by pharmaceutical companies and conducted at VA facilities in support of a new drug or device application are subject to FDA as well as VA regulations and oversight. Similarly, studies funded by NIH and conducted in VA facilities are subject to Department of Health and Human Services as well as VA regulations and oversight. Thus the framework for a strong human subjects protection program has long been in place in the VA.

During the past two or more years, VHA has taken several aggressive steps to further enhance and strengthen protections for human subjects of research. In April 1999, the former Under Secretary for Health announced that VHA would establish a separate Office of Research Compliance and Assurance (ORCA) to assure compliance with VA and other federal research policies and regulations and, in addition, would engage an external contractor to inspect and certify the human subjects protection program of every VA facility conducting research involving human subjects. Within weeks of that announcement, VHA had initiated a search for a Chief Officer to direct ORCA and had issued an RFP for an external contractor to certify VA research programs. Both of these initiatives have now come to fruition:

- ORCA has been assigned a full scope of assurance and compliance responsibilities and is currently recruiting to a level of 8 staff in headquarters and is staffing four

regional offices in Washington, DC, Atlanta, Chicago, and West Los Angeles for an initial staff of 24 persons.

- VHA has issued a contract for external accreditation of human subjects programs to the National Committee for Quality Assurance (NCQA), an independent, not-for-profit accrediting organization that is nationally renowned for its objective evaluations of health care organizations, and the pilot phase of that program has been initiated. NCQA will soon commence a series of on-site inspections of human subjects programs at VAMCs and will be accompanied by observers from ORCA. VA is the first and, so far, the only public or private organization in the nation to mandate external certification of its human subjects protection programs.

VHA has implemented many other initiatives to further enhance human subjects protections. Let me highlight a few examples for you:

- In the summer of 1999, a VA Multiple Project Assurance Contract (VA MPA Contract) was issued to require each VA facility conducting research involving human subjects to provide documentation of its human subjects protection program and assurances that it would abide by all VA regulations and federal policies governing such research. (See Attachment 1) Issuance of VA MPA Contracts to more than 100 VA facilities was completed late last winter.
- ORCA has continuing responsibility for the MPA contracts and will be completing a comprehensive validation of all of these contracts at 120 VAMCs this fall.
- Last spring, ORCA launched the Training, Education, and Development (TED) Initiative, a program designed to develop and disseminate information on a wide spectrum of training and education activities, including those offered by public and private agencies, for investigators and research administrators. ORCA is currently developing a strategic plan for education and training for all VHA personnel involved in the protection of human subjects in research.
- Earlier this year VHA established a requirement that all VA investigators must provide documentation that they have participated in educational programs on human subjects protections before their research projects can be approved, and I am announcing today that, effective January 1, 2001, VA investigators will be required to

be certified on human subjects protection regulations in order to be eligible for VA research funding.

- A complete revision of the Research and Development Policy Manual is currently underway to ensure that VHA's research policies are as complete and up-to-date as possible. The first drafts of the revised policy directive and research handbooks are currently under review within VHA. Copies of the draft directive and the draft handbook on protection of human subjects in research were provided to the committee earlier this week. We intend to finalize and publish these documents, which include informed consent requirements, before the end of this calendar year.
- Compliance with research requirements is included in VISN Director performance agreements for 2001.

ORCA and the VHA Office of Research and Development (ORD) have, over the past year and a half, provided extensive guidance and information to field facilities in the form of satellite conferences, monthly Hotline conference calls, surveys, information letters, formal conferences, site visits, self-study materials, and many, many ad hoc informal consultations.

ORCA has recently assumed responsibility for two additional oversight functions. ORCA is now the headquarters component that receives reports of adverse events involving research protocols from VA field facilities. The development of an improved process for the submission of these reports and the systematic collection of data has been initiated in coordination with VHA's National Center for Patient Safety. ORCA is also responsible for liaison and coordination of enforcement activities with other federal research regulatory agencies, including the Food and Drug Administration (FDA) and the Department of Health and Human Services' Office of Human Research Protections (OHRP). As an example of this collaboration, the FDA has recognized the need to revise its reporting procedures for serious adverse events and has involved ORCA in the development of a clearer set of procedures and guidelines. Also, ORCA officials have met with their counterparts in these other agencies and are working collaboratively to develop educational initiatives for investigators and research administrators in the field.

GAO's recent report acknowledges that VHA has in place strong policies for the protection of human subjects who volunteer to participate in VA research projects. The report also recognizes that VA has taken many steps to strengthen human subjects protections. GAO's review of research that was being conducted in the 1997-1999 timeframe documents variability across the VA system in the implementation of VA's policies for the protection of human subjects. VHA concurs with GAO's recommendations and believes that the initiatives currently underway will significantly strengthen processes for the protection of human research participants. We view GAO's report as validating the need for the strong actions that we are taking. We intend to continue these oversight efforts so that our patients who participate in research projects will have confidence that their rights, dignity and safety are of paramount importance to VA. Attachment 2 provides a more detailed description of the steps VA has already taken or will initiate that will implement GAO's recommendations.

CONCLUSION

The Department of Veterans Affairs intends to be leader in the nation in assuring that its scientists follow the highest standards for assuring respect of the rights, dignity, and safety of research participants. We believe the approach VA is taking, with its continued emphasis on training and education, independent oversight and external accreditation will result in a system-wide human subjects protections program that will place VA at the forefront of protecting human research subjects. I appreciate your invitation to discuss these important issues with you, and my colleagues and I will be pleased to try to answer any questions you may have.

ATTACHMENT 1

VA Multiple Project Assurance Contract

Assurance of Compliance
For Protection of Human Research Subjects

The _____, hereinafter known as the "institution" (see Appendix A), hereby gives assurance, as specified below, that it will comply with the Department of Veterans Affairs (VA) regulations for the protection of human research subjects, 38 CFR Part 16 and Part 17, as amended to include provisions of the Federal Policy for the Protection of Human Subjects (56FR28003), also known as the Common Rule, and as described in VA Manual M3, Part I, Chapter 9 and as may be further amended during the approval period for this Assurance. Where applicable it will also comply with FDA regulations 21 CFR 50 and 56.

PART 1 -PRINCIPLES, POLICIES, AND APPLICABILITY

I. Ethical Principles

A. This institution is guided by the ethical principles regarding all research involving humans as subjects, as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (entitled: Ethical Principles and Guidelines for the Protection of Human Subjects of Research [the "Belmont Report"]), regardless of whether the research is subject to Federal regulation or with whom conducted or source of support (i.e., sponsorship).

B. All institutional and non-institutional performance sites for this institution, domestic or foreign, will be obligated by this institution to conform to ethical principles which are at least equivalent to those of this institution, as cited in the previous paragraph or as may be determined by the Department of Veterans Affairs Undersecretary for Health.

II. Institutional Policy

A. All requirements of Title 38, Part 16 and Part 17, of the Code of Federal Regulations (38 CFR 16) will be met for all *federally-sponsored* research, and all other human subject research regardless of sponsorship, except as otherwise noted in this Assurance. Federal (all departments and agencies bound by the Federal Policy) funds for which this Assurance applies may not be expended for research involving human subjects unless the requirements of this Assurance have been satisfied.

B. Except for those categories specifically exempted or waived under 38 CFR 16 Section 101(b) (1-6) or 101(i), all research covered by this Assurance will be

reviewed and approved by an Institutional Review Board (IRB) which has been established under this Multiple Project Assurance Contract (MPA Contract) with VA Headquarters (VAHQ), or as may otherwise be agreed to by VAHQ (see Part I, II, G). The involvement of human subjects in research covered by this Assurance will not be permitted until an appropriate IRB has reviewed and approved the research protocol and informed consent has been obtained from the subject or the subject's legal representative (see M3 Part I Chapter 9, Sections 9.09, 9.10, 9.119.12 and appendix 9c), unless properly waived by the IRB under Section 9.11 b (3) or by any applicable waiver under 38 CFR 16 Section 101(i). The referenced VA manual sections include and amplify on 38 CFR 16 Sections 111, 116 and 117.

C. This institution assures that before human subjects are involved in nonexempt research covered by this Assurance, the IRB(s) will give proper consideration to:

1. The risks to the subjects
2. The anticipated benefits to the subjects and others,
3. The importance of the knowledge that may reasonably expected to result, and
4. The informed consent process to be employed.

D. Certification of IRB review and approval for all non-HHS sponsored research involving human subjects will be submitted to the Office of Research Administration (ORA) for forwarding to the appropriate Federal department or agency or other funding source. Compliance will occur within the time and in the manner prescribed for forwarding certifications of IRB review to VAHQ or other Federal departments or agencies for which this Assurance applies.

As provided for under 38 CFR 16 Section 118, applications and proposals lacking definite plans for involvement of human subjects will not require IRB review and approval prior to award. However, except for research exempted or waived under section 3 8 CFR 16 Section 101 (b) or (i), no human subjects may be involved in any project supported by such awards until IRB review and approval has been certified to the appropriate Federal Department or agency.

As required under 38 CFR 16 Section 119, the IRB will review proposed involvement of human subjects in Federal research activities undertaken without prior intent for such involvement, but will not permit such involvement until certification of IRBs review and approval is received by the appropriate Federal department or agency

E. Institutions that are not signatories to this Assurance are not authorized to cite this Assurance. This institution will ensure that such other institutions and investigators not bound by the provisions of this Assurance will satisfactorily assure compliance with 38 CFR 16, as required (see Part 2, 1, D and II, K), as a prior condition for involvement in any human subject research which is under the auspices of this institution (see part 1, IIIA). Institutions that have entered into an

Inter-Institutional Amendment (IIA) to this Assurance must submit a Single Project Assurance (SPA) to the Office for Protection from Research Risks (OPRR) for DHHS-sponsored research, or to VAHQ for other research when that research is not conducted under the auspices of a signatory institution to this Assurance.

F. This institution will ensure that any collaborating entities (i.e., those entities engaged in human subject research by virtue of subject accrual, transfer of identifiable information, and/or in exchange of something of value, such as material support (e.g., money, drugs, or identifiable specimens), co-authorship, intellectual property, or credits) materially engaged in the conduct of non-federal sponsored research involving human subjects will possess mechanisms to protect human research subjects that are at least equivalent to those procedures provided for in the ethical principles to which this institution is committed (see Part 1, 1).

G. This institution will exercise administrative overview to ensure that the institution's policies and procedures designed for protecting the rights and welfare of human subjects are being effectively applied in compliance with this Assurance.

H. Descriptions of this institution's policy for the protection of human subjects is contained in its internal written procedures which are available to VAHQ and other Federal departments or agencies, upon request.

III. Applicability

A. Except for research in which the only involvement of humans is in one or more of the categories exempted or waived under 38 CFR 16, Sections 101 (b) (1 -6) or 101 (i) and M3 Part 1, Section 9, appendix A, this Assurance applies to all research involving human subjects, and all other activities which even in part involve such research, regardless of sponsorship, if one or more of the following apply:

1. The research is sponsored by this institution, or
2. The research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities, or
3. The research is conducted by or under the direction of any employee or agent of this institution, or
4. The research involves the use of this institution's non-public information to identify or contact human research subjects or prospective subjects.

B. All human subject research which is exempt under M3 Part 1, Appendix 9A will be conducted in accordance with: (1) the Belmont Report, (2) this institution's administrative procedures to ensure valid claims of exemption, and (3) orderly accounting for such activities.

C. This Assurance may be accepted by other Federal departments or agencies that are bound by the Federal Policy for the Protection of Human Subjects with the exception of the Department of Health and Human Services, when appropriate for the research in question and therefore applies to all human subject research so sponsored.

PART 2 - RESPONSIBILITIES

I. Institution

A. This institution acknowledges that it bears full responsibility for the performance of all research involving human subjects, covered by this Assurance, including complying with Federal, state, or local laws as they may relate to such research.

B. This institution will require appropriate safeguards in research that involves the cognitively impaired or other potentially vulnerable groups as provided in M3, Part 1, Section 9.12.

C. This institution acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects in research covered by this Assurance.

D. This institution is responsible for ensuring that no performance site cooperating in the conduct of federally sponsored research for which this Assurance applies does so without Federal department or agency approval of an appropriate assurance of compliance, in whatever appropriate form, and satisfaction of IRB certification requirements.

E. In accordance with the compositional requirements of M3, Part 1, Sections 9.08, and 38 CFR 16 Section 107, this institution has established the IRB(s) listed in the attached roster(s) (See Appendix A). Certain research supported by the U.S. Department of Education will be reviewed in accordance with the requirements of Title 34 CFR Parts 350 and 356 which require that the IRB(s) include at least one person who is primarily concerned with the welfare of handicapped children or mentally disabled persons.

F. This institution will provide both meeting space and sufficient staff to support the IRB's review and record-keeping duties.

G. This institution is responsible for ensuring that it and all its affiliates comply fully with all applicable Federal policies and guidelines, including those concerning notification of seropositivity, counseling, and safeguarding confidentiality where research activities directly or indirectly involve the study of human immunodeficiency virus (HIV).

H. The Institution shall provide appropriate medical care to a subject injured in connection with participation in VA research under provisions of 38 CFR 17.

II. Office of Research Administration (ORA) Responsibilities

A. The institution's ORA will receive from investigators, through their supervisors, all research protocols that involve human subjects, keep investigators informed of

decisions and administrative processing, and return all disapproved protocols to them.

B. The ORA is responsible for reviewing the preliminary determination of exemption by investigators and supervisors and for making the final determination based on 38 CFR 16 Section 101 and M3, Part 1, 9.06 and 9A of the regulations. Notice of concurrence for all exempt research will be promptly conveyed in writing to the investigator; such research may not commence until written concurrence is issued. All nonexempt research will be forwarded to the appropriate IRB.

C. The ORA will make the preliminary determination of eligibility of expedited review procedures (see 38 CFR 16 Section 110, and 63FR60364). Expedited review of research activities will not be permitted where full board review is required.

D. The Research and Development Committee (R&D) assisted by the ORA will review all research (whether exempt or not) and recommend to the CEO whether the institution will permit the research. If approved by the IRB, but not permitted by the CEO, the ORA will promptly convey notice to the investigator and the IRB Chair. Neither the ORA nor any other office or official of the institution may approve a research activity that has been disapproved by the appropriate IRB.

E. The ORA will forward certification of IRB approval of proposed research to the appropriate Federal department or agency only after all IRB-required modifications have been incorporated to the satisfaction of the IRB.

F. The ORA will designate procedures for the retention of signed consent documents for at least three years past completion of the research activity.

G. The ORA will maintain and arrange access for inspection of IRB records as provided for in 38 CFR 16 Section 115 and VA M3, Part I section 9.14.

H. The ORA is responsible for ensuring constructive communication among the research administrators, department heads, research investigators, clinical care staff, human subjects, and institutional officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of the subjects.

I. The ORA will arrange for and document in its records that each individual who conducts or reviews human subject research has first been provided with a copy of this Assurance, as well as with ready access to copies of 38 CFR 16, regulations of other federal departments or agencies as may apply, the Belmont Report, and all other pertinent federal policies and guidelines related to the involvement of human subjects in research.

J. The ORA will report promptly to the IRB(s), appropriate institutional officials, the VAHQ, and any other sponsoring federal department or agency head:

1. Any injuries to human subjects or other unanticipated problems involving risks to subjects or others,
2. Any serious or continuing noncompliance with the regulations or requirements of the IRB, and
3. Any suspension or termination of IRB approval for research.

K. The ORA will ensure (a) solicitation (or confirmation where applicable assurances to comply already exist), receipt, and management of all assurances of compliance (whatever the appropriate format), and (b) certifications of IRB review (where appropriate) for all performance sites to this institution (including those listed in Appendix B) and subsequent submission of new documents to the proper federal department of agency authorities (e.g., VAHQ for VA) or any other Federal department or agency for which this Assurance applies.

L. The ORA will ensure that all affiliated performance sites that are not otherwise required to submit assurances of compliance with Federal regulations for the protection of research subjects at least document mechanisms to implement the equivalent of ethical principles to which this institution is committed (see Part I,I). The ORA is responsible for assuring adequate numbers and training of staff to support IRB functions.

M. The ORA will be responsible for procedural and record-keeping audits not less than once every year for the purpose of detecting, correcting, and reporting (as required) administrative and/or material breaches in uniformly protecting the rights and welfare of human subjects as required at least by the regulations and as may otherwise be additionally required by this institution(s)

III. Institutional Review Board (IRB)

A The IRB(s) will review, and have the authority to approve, require modification in, or disapprove all research activities, including proposed changes in previously approved human subject research. For approved research, the IRB will determine which activities require continuing review more frequently than every twelve months or need verification that no changes have occurred if there was a previous IRB review and approval.

B. IRB decisions and requirements for modifications will be promptly conveyed to investigators and the ORA, in writing. Written notification of decisions to disapprove will be accompanied by reasons for the decision with provision of an opportunity for reply by the investigator, in person or writing.

C. Initial and continuing convened IRB reviews and approvals will occur in compliance with 38 CFR 16 and provisions of this Assurance for each project

unless properly found to be exempt (Section 101(b) or (i) and M3 Part 1, Sections 9.06 and Appendix 9A by the Office of Research Administration. Continuing reviews will be preceded by IRB receipt of appropriate progress reports from the investigator, including any available study-wide findings.

D. The IRB(s) will observe the quorum requirements of 38 CFR 16 Section 108(b). This institution's IRB(s) must have effective knowledge of subject populations, institutional constraints, differing legal requirements, and other factors which can foreseeably contribute to a determination of risks and benefits to subjects and subjects' informed consent and can properly judge the adequacy of information to be presented to subjects in accordance with requirements of 38 CFR 16 Sections 103(d), 107(a), 111, and 116.

E. The IRB(s) will determine, in accordance with the criteria found at 38 CFR 16 Section 111 and Federal policies and guidelines for involvement of human subjects in HIV research, that protections for human research subjects are adequate.

F. The IRB(s) will ensure that legally effective informed consent will be obtained and documented in a manner that meets the requirements of 38 CFR 16 Sections 116 and 117. The IRB will have the authority to observe or have a third party observe the consent process.

G. Scheduled meetings of the IRB(s) for review of each research activity will occur not less than every 12 months and may be more frequent, if required by the IRB on the basis of degree of risk to subjects. The IRB may be called into an interim review session by the Chairperson at the request of any IRB member or institutional official to consider any matter concerned with the rights and welfare of any subject.

H. The IRB(s) will prepare and maintain adequate documentation of its activities in accordance with 38 CFR 16 Section 115 and in conformance with ORA requirements.

I. The IRB(s) will forward to the ORA any significant or material finding or action, at least to include the following:

1. Injuries or any other unanticipated problems involving risks to subjects or others,
2. Any serious or continuing noncompliance with the regulations or requirements of the IRB, and
3. Any suspension or termination of IRB approval.

J. In accordance with 38 CFR 16 Section 113, the IRB(s) will have the direct authority to suspend or terminate previously approved research that is not being

conducted in accordance with the IRB(s) requirements or that has been associated with unexpected serious harm to subjects.

K. The IRB(s) for this institution will ensure effective input (consultants or non-voting members) for all initial and continuing reviews conducted on behalf of performance sites where there will be human research subjects. IRB minutes will document attendance of those other than regular voting members. The IRB list(s) in Appendix A includes those who are identified as knowledgeable about any affiliate institution having entered into an Inter-Institutional Amendment or other institutional performance site for which an Assurance is required when relying on one or more of the IRBs of this institution.

L. Certifications of IRB review and approval will be forwarded through the ORA to the appropriate federal department or agency for research sponsored by such departments or agencies.

IV. Research Investigator

A. Research investigators acknowledge and accept the responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provision of this Assurance.

B. Research investigators who intend to involve human research subjects will not make the final determination of exemption from applicable federal regulations or provisions of this Assurance.

C. Research investigators are responsible for providing a copy of the IRB approved and signed informed consent document to each subject at the time of consent, unless the IRB has specifically waived this requirement. All signed consent documents are to be retained in a manner approved by the ORA.

D. Research investigators will promptly report proposed changes in previously approved human subject research activities to the IRB. The proposed changes will not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subjects.

E. Research investigators are responsible for reporting progress of approved research to the ORA, as often as, and in the manner prescribed by the approving IRB on the basis of risks to subjects, but no less than once per year.

F. Research investigators will promptly report to the IRB any injuries or other unanticipated problems involving risks to subjects and others.

G. In the event of injury to a subject, the research investigator shall seek to provide any necessary emergency and continuing medical care. Such care is authorized under 38 CFR 17.

H. No research investigator who is obligated by the provisions of the Assurance, any associated Inter-institutional Amendment, or Non-institutional Investigator Agreement will seek to obtain research credit for, or use data from, patient interventions that constitute the provision of emergency medical care without prior IRB approval. A physician may provide emergency medical care to a patient without prior IRB review and approval, to the extent permitted by law (see 3 8 CFR 16 section 116(f)). However, such activities will not be counted as research nor the data used in support of research.

I. Research investigators will advise the IRB, ORA and the appropriate officials of other institutions of the intent to admit human subjects who are involved in research protocols for which this Assurance or any related Inter-institutional Amendment or Noninstitutional Investigator Agreement applies. When such admission is planned or a frequent occurrence, those institutions must possess an applicable OHRP-approved Assurance prior to involvement of such persons as human subjects in those research protocols.

Part 3 - SIGNATURES

Institutional Endorsements

The officials signing below assure that any research activity conducted, supported or otherwise subject to DVA or other Federal departments or agencies that are authorized to rely on the Assurance (Parts 1,2,3 and Appendices) or any other sources provided for in this Assurance, will be reviewed and approved by the appropriate IRBs in accordance with the requirements of all applicable subparts of Part 16 and Part 17, Title 38 Code of the Federal Regulations, with this Assurance, and the stipulations of the IRB(s).

A. Primary Signatory Institution (if any)

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____

Name: _____

Title: Chief Executive Officer

Institution and Address: _____

_____

_____

_____

Phone: _____

FAX: _____

E-mail: _____

PRIMARY CONTACT

Signature: _____

Name: _____

Title: ACOS/Research & Development

Institution and Address: _____

_____

_____

Phone: _____

FAX: _____

E-mail: _____

VHA Office of Research Compliance and Assurance

Approval A.

VHA Recommending Official

AUTHORIZED INSTITUTIONAL OFFICIAL

Signature:_____

Name: JOAN P. PORTER, DPA, MPH

Title: Associate Director, Office of Research Compliance & Assurance

Institution and Address: Veterans Health Administration
Office of Research Compliance & Assurance
811 Vermont Ave., N.W., Room 574 (10R)
Washington, D.C. 20005
Phone: (202) 565-7191
FAX: (202) 565-9194
E-mail: joan.porter@mail.va.gov

EFFECTIVE DATE OF ASSURANCE:

EXPIRATION DATE OF ASSURANCE:

B. VHA APPROVAL OFFICIAL

AUTHORIZED INSTITUTIONAL OFFICIAL

Signature:_____

Name: JOHN H. MATHER, M.D.

Title: Chief Officer, Office of Research Compliance & Assurance

Institution and Address: Veterans Health Administration
Office of Research Compliance & Assurance
811 Vermont Ave., N.W., Room 574 (10R)
Washington, D.C. 20005
Phone: (202) 565-9080
FAX: (202) 565-9194
E-mail: john.mather@hq.med.va.gov

VA Multiple Project Assurance Contract
Assurance of Compliance
For Protection of Human Research Subjects

Contract Number:

AMENDMENT 1

The purpose of this amendment is to include the VA_____ in this Assurance.
Name and Location

The first paragraph on the first page of the Assurance should be amended to include: _____

Part 3, *Signatures*, should be amended to include, after A, *Primary Signatory Institution*:

B. Secondary Signatory Institution (if any)

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____
Name:
Title:
Institution and Address:

PRIMARY CONTACT

Signature: _____
Name:
Title:
Institution and Address:

Part 3—SIGNATURES

Contract Number:

AMENDMENT 1

Institutional Endorsements
The officials signing below assure that any research activity conducted, supported, or otherwise subject to DVA or other Federal departments or agencies that are authorized to rely on the Assurance (Parts 1,2,3, and Appendices) or any other sources provided for in this Assurance, will be reviewed and approved by appropriate IRBs in accordance with the requirements of all applicable subparts of Part 16 and Part 17, Title 38 Code of the Federal Regulations, with this Assurance, and the stipulations on the IRB(s).

A. Primary Signatory Institution (if any)

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____
Name:
Title:
Institution and Address:

PRIMARY CONTACT

Signature: _____
Name:
Title:
Institution and Address:

B. Secondary Signatory Institution (if any)

1. AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____
Name:
Title:
Institution and Address:

PRIMARY CONTACT

Signature: _____
Name:
Title:
Institution and Address:

All other terms of the Assurance are hereby incorporated by reference and will apply to .

[List all institutions signing.]

Concurrence: VISN Director

Signature:_____

Name:

Address:

Date:_____

VA MPA Contract Number:

Amendment 1

VHA Office of Research Compliance and Assurance

Approval A

VHA Recommending Official

AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____

Name: JOAN P. PORTER, DPA, MPH

Title: Associate Director, ORCA

Institution and Address: 811 Vermont Ave., NW (10R) Ph.: (202) 565-7191

Room 574 Fax: (202) 565-9194

Washington, DC 20005

EFECTIVE DATE OF ASSURANCE:

EXPIRATION DATE OF ASSURANCE: February 2003

B. VHA APPROVAL OFFICIAL

AUTHORIZED INSTITUTIONAL OFFICIAL

Signature: _____

Name: JOHN H. MATHER, M.D.

Title: Chief Officer, ORCA

Institution and Address: 811 Vermont Ave., NW (10R) Ph.: (202) 565-9080

Room 574 Fax: (202) 565-9194

Washington, DC 20005

ATTACHMENT 2

VHA Actions to Respond to GAO Recommendations
To Strengthen Human Research Protections

GAO Recommendation 1: Provide research staff with current, comprehensive, and clear guidance regarding protections for the rights and welfare of human research subjects.

Response 1:
The statement mentions the policy update being undertaken by the Office of Research and Development and the TED initiative launched earlier this year by ORCA. ORCA has also established a Field Advisory Committee to assure broad input from – and broad outreach to – our field facilities on how to make protection of human research subjects increasingly evident in the VA system. Additional guidance has been provided by both ORCA and ORD in the form of information letters, satellite conferences, presentations at our National Leadership Board meetings, monthly national Hotline conference calls, surveys, and distribution of self-study materials. These efforts will continue.

GAO Recommendation 2: Provide periodic training to investigators, IRB (Institutional Review Board) members, and IRB staff about research ethics and standards for protecting human subjects.

Response 2:
ORD has established a training requirement for investigators, similar to the educational requirements recently announced by NIH. Beginning in January, we will require investigators to be certified in human subjects protections to be eligible for VA research funding. The primary responsibility to ensure adequate training of investigators and IRB members rests with the management of local facilities. ORD provides self-study materials to every research office in the field and posts research policies, guidance, and training opportunities on its web site. National opportunities for training are provided by

ORD through the Society of Research Administrators annual meeting, the annual meetings of each of the divisions of the VA Research Service, and the Office of Research and Development biennial national meeting. ORD is also planning a State of the Art conference on informed consent, in collaboration with the VA National Ethics Center and the Hastings Center.

ORCA is proceeding, in conjunction with the Employee Education System and other VA offices and with organizations with like responsibilities outside of VA, to develop and promote training, education, and development activities in conjunction with the Veterans Integrated Systems Networks (VISNs) and other internal and external stakeholders. ORCA is accomplishing this, in part, through coordination with its VA-wide TED Focus Group. ORCA now participates as a full partner with the Department of Health and Human Services' Office of Human Subjects Protections and the Food and Drug Administration in sponsoring several regional workshops on human subject protections annually. ORCA will also sponsor a one-day symposium on VA-specific issues at the Public Responsibility in Medicine and Research annual meeting in October 2000.

ORCA's new web site will provide a comprehensive information resource for VA's research community by providing policies and procedures, regulatory requirements, Frequently Asked Questions, formats for documents, VA MPA contract listings, announcements of educational opportunities, links to other helpful sites and many other features.

ORCA plans additional activities to help investigators, other research staff, institutional review board (IRB) members and administrators, and other VISN and Veterans' Affairs Medical Center management understand and carry out their responsibilities in the human subjects protection system. These activities will include a series of information letters, teleconferences, on-line training modules, face to face workshops and presentations, satellite coverage of major related meetings, and on site advisory consultations. ORCA will complete the preparation of a comprehensive strategic plan for all these training and education activities for all personnel involved in human subjects research this year.

GAO Recommendation 3: Develop a mechanism for handling adverse event reports that ensures that IRBs have the information they need to safeguard the rights and welfare of human research participants.

Response 3:

This is currently an area of concern throughout the broader research and regulatory community and will require careful attention. VA will participate actively in ongoing Federal government-wide efforts to develop a more useful and coordinated system to manage adverse event reporting. As an initial step the Office of Research and Development has expanded the distribution of reports from its Data Safety Monitoring Boards to include all appropriate IRBs. As I indicated earlier, ORCA is now the headquarters component that receives from VA medical centers adverse event reports and serious adverse event (SAEs) reports involving research protocols. The development of an improved process for the submission of these reports and the systematic collection of data has been initiated in coordination with VHA's National Center for Patient Safety.

GAO Recommendation 4: Expedite development of information needed to monitor local protection systems, investigators, and studies and ensure that oversight activities are implemented.

Response 4:

VHA has initiated the contract with NCQA for mandatory external accreditation of IRBs, the first such initiative in the country. Performance measures have been put in place for VISN Directors regarding research assurance processes and external accreditation. ORD initiated a performance plan for Associate Chiefs of Staff for Research and Development at field facilities that includes responsibility for risk management, including monitoring local human subjects protection systems, investigators, and studies. ORD has established a site monitoring and review unit to conduct on-site visits at local facilities, during the conduct of clinical trials. ORD established, and ORCA is maintaining, VA Multiple

Project Assurances Contracts with all local facilities that conduct research involving human subjects. .

ORCA has developed and will continue to refine an oversight program that will involve regular routine visits and for cause visits, known as Special Inquiry Force Team (SIFT) reviews, with scheduled and unscheduled on-site visits to VA sites carrying out research. ORCA staff has already conducted five of these SIFT visits to address specific concerns at several sites and to determine where systemic problems may need to be addressed. ORCA is urging sites to contact staff for help and advice and to self-report problems identified in protection of human subjects at their sites so that those problems can be rapidly and fairly addressed and ethical research can go forward. ORCA's new Mini-Assessment Program (MAP) review Focus Group has met and is advising on the development of a Self-Assessment process for Research Services and defining the most effective procedures for conduct of on-site MAP reviews. In addition, ORCA staff will serve as participant/observers at the external accreditation site visits for human subjects to be conducted by NCQA and will also collaborate with ORD's project manager in advising on the accreditation mechanism; ORCA will provide a comprehensive overview of the findings from the accreditation visits in order to ascertain systemic problems for correction through regulatory or educational activity.

GAO recommendation 5: Determine the funding levels needed to support human subject protection activities at medical centers and ensure an appropriate allocation of funds to support these activities.

Response 5:

VHA has established a mechanism to account for allocation of VERA funds in support of the indirect costs of research, including support for assurance processes at the facility level. The Office of Research and Development already provides financial support to partially fund the assurances process, and has provided guidance to the field on the VERA allocation mechanism and on accessing additional funding streams from research that is supported by non-VA sources to fund the assurances process. VHA has asked the

Director of the National Institutes of Health to add an indirect cost allocation to NIH grants for research carried out at VA facilities to partially compensate those institutions for the supplemental costs of supporting NIH research, including the costs of regulatory compliance. ORD has also provided preliminary guidance to the VISN Directors on the needed IRB staffing levels and has commissioned a formal Health Systems Research and Development study to gather real data to direct our resource allocation decisions.