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VA DISABILITY COMPENSATION: PRESUMPTIVE DISABILITY DECISION-MAKING

HEARING

BEFORE THE

COMMITTEE ON VETERANS' AFFAIRS
UNITED STATES SENATE

ONE HUNDRED ELEVENTH CONGRESS

SECOND SESSION

SEPTEMBER 23, 2010

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VA DISABILITY COMPENSATION: PRESUMPTIVE DISABILITY DECISION-MAKING

THURSDAY, SEPTEMBER 23, 2010

U.S. SENATE,
COMMITTEE ON VETERANS' AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 9:30 a.m., in room G50, Dirksen Senate Office Building, Hon. Daniel K. Akaka, Chairman of the Committee, presiding.

Present: Senators Akaka, Rockefeller, Murray, Brown of Ohio, Webb, Tester, Begich, Burris, Sanders, Isakson, Johanns, and Brown of Massachusetts.

OPENING STATEMENT OF HON. DANIEL K. AKAKA, CHAIRMAN, U.S. SENATOR FROM HAWAII

Chairman AKAKA. This hearing of the U.S. Senate Committee on Veterans' Affairs will come to order.

Welcome and aloha to today's hearing on the VA Presumptive Disability Decision-Making Process.

Today much of our focus will be on Vietnam veterans and Agent Orange. However, this discussion also extends the presumptions from the first Gulf War. We are just beginning to hear about exposures to potential toxins connected to the wars in Iraq and Afghanistan. This Committee is also addressing exposures at military installations. This is why it is so important that the presumptions created are appropriate and transparent for past and future wars.

One issue we will look at this morning is the VA Secretary's role in creating presumptions under the Agent Orange Act. The Secretary is called on to determine, on the basis of sound medical and scientific evidence, whether there is a positive association between exposure for all herbicides and occurrence of a disease. The law sets up a balancing test between exposure and disease. A positive association exists when the evidence or an association is equal to or greater than evidence against association.

In making the determination, the Secretary has to take into account reports from IOM and all other sound medical and scientific information. As we look at the recent Agent Orange decision, we must be satisfied that all scientific evidence was made available to the Secretary and we must understand how it was weighed and considered. For my part, I must be satisfied that the law enacted almost 20 years ago now, is working today.

While it is clear that there are real and substantial costs associated with this new presumption, that is not the motivation for this hearing or for our larger work of evaluating the process put in

place pursuant to the Agent Orange Act. We made a promise to care for and compensate veterans for service-connected injuries. I will never stop fighting for veterans, especially when the issue is directly related to the consequences of service.

Keeping our promise to veterans will cause us to look closely at the current presumption process. We must be sure the process gives VA appropriate authority to consider all relevant factors in order to determine whether a service-connected presumption is warranted. I hope that our witnesses will shed some light on these issues. The current Secretary and a former Secretary will testify about their experiences with presumptive decisionmaking, and experts from the scientific community will testify on dioxin and what science exists for determining an association between Agent Orange and heart disease and other diseases common to aging.

I thank our witnesses for being here today and helping us in this effort. I look forward to your testimony.

At this time I would like to call on our Ranking Member, Senator Isakson, for his opening statement.

STATEMENT OF HON. JOHNNY ISAKSON, U.S. SENATOR FROM GEORGIA

Senator ISAKSON. Thank you very much, Mr. Chairman. I want to welcome all our panelists, in particular Secretary Shinseki and former Secretary Principi. Thank you for your time today.

I also want to apologize. I am in charge of the floor from 10:30 to 12:30 in a debate and will have to leave, but Senator Johanns will take my place as ranking member, and I thank him for that.

Mr. Chairman, unfortunately many military personnel and their families have been put at risk over the years by dangerous exposure where they are living, working, or serving our Nation. Last year this Committee held a hearing to discuss some of those exposures, including the contaminated drinking water at Camp LeJeune and smoke from burn pits in Afghanistan and Iraq.

Today we will hear about defoliants with toxic contaminants that were widely used in Vietnam to destroy jungles, kill crops, and clear perimeters. For all who have been put at risk by these and other exposures, it is extremely important to have a process in place to identify how their health may be affected and make sure they receive, in a fair, hassle-free, and timely manner the benefits and services they need and they deserve.

As we will discuss today presumptions can play a critical role in that process. Those presumptions can relieve individual veterans of the burden of providing scientifically the potential health effects of dangerous exposures. This in turn can create a quicker, easier path to benefits and services.

But the current framework for creating presumptions may have flaws. In fact, the Institute of Medicine recommended a whole new approach, one that is more transparent, allows stakeholders greater input, and proactively identifies exposures and conditions that may warrant presumptions.

Given the profound impact the presumptions can have, I hope to have a productive session today about the current process where improvements may be needed, and more importantly, how any changes would impact our Nation's veterans and their families.

On top of that, I am interested in learning the extent to which medical treatment is being emphasized for those who may have been exposed. Take, for example, coronary heart disease, which we will hear today, may be very common among Vietnam veterans. Treating the risk factors associated with the disease has proven effective in keeping folks healthy.

VA's overreaching goal is to restore the capability of disabled veterans to the greatest extent possible. That goal cannot be achieved if we only focus on a disability process and neglect treatment and prevention.

Mr. Chairman, I am grateful for the opportunity to participate today, and I thank again all our panelists for being here.

Chairman AKAKA. Thank you very much Senator Isakson. Senator Rockefeller.

STATEMENT OF HON. JOHN D. ROCKEFELLER IV, U.S. SENATOR FROM WEST VIRGINIA

Senator ROCKEFELLER. Thank you, Mr. Chairman. I appreciate your commitment to oversight, I welcome our panelists, and I apologize that I also have to leave because we are having a hearing in the Commerce Committee which I need to chair about making sure that full spectrum is available exclusively for our public defenders. You know, fire, police, EMS, EMT, all the rest of them right now do not have enough. Some wireless companies want to get it for themselves. I say that we have to give it to those people who are our first responders. But I apologize for that.

First, I want to say I am very proud to be a co-sponsor of the 1991 Agent Orange Law and I still am. That law directed the Secretary of the Department of Veterans Affairs to rely on the Institute of Medicine Studies and other science to determine presumptive coverage based on exposure to Agent Orange. The standard is a positive association. And if the majority of the evidence makes such an association, the Secretary shall provide the coverage.

I have met extensively with the Secretary, who I greatly respect, and I believe he followed the standard set by the law. I believe that some will suggest that a new standard of causation, rather than positive association, is more appropriate. I do not have to agree with that, partly because I come from a coal **State where we have something called black lung. And I know perfectly well, having been in West Virginia for 46 years, that if you worked underground for 10 years, by definition you have black lung. By definition. But the presumption does not give you that diagnosis as a result. Very few of our miners in southwestern Virginia and West Virginia are getting the black lung medical care that they deserve and they die horrible deaths.

So, I am concerned that the standard is very inadequate. I am more concerned that sick veterans not be left out. Let me be clear. I believe the underlying unspoken issue here today that some will talk about and some may not want to is cost. People are going to say in muted ways, it costs too much. We cannot afford to do that. So it comes down to what are the spending priorities for our country? The Vietnam War cost $740 billion, and caring for the veterans drafted to fight that war is a fraction of that $740 billion. We did not question then. We do not question now.

Some will face enormous deficits; some say we are going to face enormous deficits, and of course that is the case. I will not get into that. They are correct. But when we are talking about deficits, we also have to present the full picture. I was here when people claimed that we had such surpluses that we had to cut taxes, including those for the very wealthy.

The Bush tax cuts enacted in 2001–2003, converted our national surplus into enormous deficits. I did not vote for that but people did and it passed and everybody said OK. The tax cuts expire at the end of this year; hence, the moral choice facing the Veterans' Affairs Committee and the U.S. Congress.

There is debate about extending these tax cuts. If we do not extend the tax cuts to the wealthiest 2 percent, we will save $700 billion in revenues over the next 10 years. Frankly, that is so much more than enough to take care of what it is the Secretary is required under law to do and needs to do and wants to do. I have never believed tax cuts for the wealthiest among us is fiscally responsible. I also do not think it stimulates the economy. I believe that is proven fact; others will disagree.

But even more than that, if given the choice between tax cuts for the rich and paying for care for our veterans, we on this Committee have a fairly clear choice about priorities, which will test who we are morally. I think the choice is clear; we spend it on veterans. We must serve our veterans. We have the resources and the ability to fulfill our obligations to care for them and we have to do that. We owe them that. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Rockefeller. Senator Johanns.

STATEMENT BY HON. MIKE JOHANNS,
U.S. SENATOR FROM NEVADA

Senator JOHANNS. Mr. Chairman, thank you very, very much. I intend to be quite brief today but I do have a few thoughts I want to offer.

First and foremost, I want to say thank you to the Chairman. I appreciate him holding this hearing. I might add, Mr. Chairman, I have appreciated being on this Committee. For me it is an honor to serve on a Senate Committee that focuses on the needs of the veterans. I just cannot tell you how much I have appreciated serving with the Chairman and our Ranking Member while trying to figure out really tough issues which help the families that are impacted here.

Sometimes the impacts are very direct, as you know, Mr. Secretary. We can identify somebody who has been physically injured in war who maybe have lost a limb or whatever. You could look at that and come to grips with what their disability is or try to help them come to grips with that. Sometimes it is much more indirect than that. But there are unintended consequences that we as a Committee and as a Congress have to deal with. That is just the reality of this situation.

I would classify Agent Orange in that category. Millions and millions of gallons of Agent Orange were used to conduct a war. I suspect at the time those who made that decision thought they were

making the right choice for a variety of reasons, but we have seen the consequences of its use are just horrendous.

Now, Mr. Secretary, I have been somewhat in your position as a former cabinet member, and I remember the hearings when I would get called up for some discussion of some action I was taking and I thought I was discharging the responsibility given to me by Congress, only to be caught in a debate.

I would imagine today you might not have thought that you would get in a debate over the 2001–2003 tax cuts. The reality of that though, I might add, is that the largest revenue in our Nation's history occurred in 2007 when they were fully in effect. You can grow the base. But let me stop there because quite honestly what I want to focus on is what you have done.

I think you have looked at this in every way we have asked you to. I think you dug deep. You did the analysis that we expected you would do. As Chairman Rockefeller points out, once you get to that conclusion your discussion ends. Once you reach the point where there is evidence that leads you to that, then you shall provide the benefits. It is not something where you say, well, I cannot do that.

So, I think as we go through this hearing we have got to focus on that and the responsibility we gave you in your attempt to discharge that responsibility.

I will offer this final thought. I come from the State of Nebraska where as Governor for 6 years I did not have the option of borrowing money. Our State does not owe any money. Why? Because our constitution prohibited borrowing; so I could never balance the budget by borrowing money. There were not many choices available to me.

Now, some might argue that is not a good way of doing things. I would argue that what it forced us to do is to make important decisions about priorities. I think this is what this hearing is about. For me, our veterans are a priority. We put them in harm's way; we asked them to risk their lives and oftentimes they give their lives. I just think in the end we have got to protect them from the direct and unintended consequences of those decisions.

I come here today with an attitude of wanting to dig deep, I want to understand what you saw; I want to feel the justification that you felt. At the end if that is there, we stand here with our veterans. So Secretary Shinseki, thank you so much for your being here, for your work in this area. I know you are trying to get to a decent and honorable result for the veterans. Thanks. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Johanns.

Senator Murray.

STATEMENT BY HON. PATTY MURRAY, U.S. SENATOR FROM WASHINGTON

Senator MURRAY. Thank you very much, Mr. Chairman, for holding this hearing.

You know, as everybody on this Committee knows, while the costs of war are never able to be predicted, it is always higher than we ever imagined. It includes lives that are lost, billions in funding to keep our troops safe and investments that are made in faraway lands. It always, always includes the many years of care seen and

unforeseen that our veterans will need. It includes what is often expensive but absolutely sacred. And that is a promise we made to our veterans: that we will care for them when they return.

Mr. Chairman, the veterans that have come forward with these new presumptive diseases are among those that we made that promise to. This is a promise I remember well when I interned at the Seattle VA medical center while I was in college during the Vietnam War. We made this promise decades ago without the thought of budget deficits or Agent Orange exposure or politics. We made it because their sacrifice warranted it, but for years now they have had to fight to see it fulfilled. They have had to fight the VA, they have had to fight with doctors, and they have had to fight with Members of Congress. That is unacceptable.

I understand the need to tighten our fiscal belt, but we cannot do it at the expense of squeezing our veterans. Mr. Chairman, as you know, in the aftermath of widespread Agent Orange exposure in Vietnam, the Department of Defense did not offer early intervention, track servicemembers who were exposed, or create a registry for affected veterans. Then as veterans became sick, they had to fight to have their diseases recognized by the VA.

Ultimately, the unacceptable challenges faced by veterans exposed to Agent Orange led Congress to pass the Agent Orange Act of 1991. That legislation established a presumptive process to lower the burden of proof for veterans in determining whether a disability or illness is service-connected. Make no mistake; I believe that veterans who have sacrificed so much deserve the benefit of the doubt. That is why it appears to me that the Secretary made the best decision possible given the limitations on the findings and the limitations of his role under that law. Given the lack of tracking data on who was exposed and to what extent, I know we must provide for our veterans if an association can be made.

With all that being said, this Committee does need to know how this process works and how it can be improved. Going forward there is no question we need to make a better effort to identify exposures that could lead to illnesses and diseases, and the Pentagon and VA need to work together to make sure that we care for these individuals.

DOD must provide treatment immediately after the exposure. I believe DOD and VA should work to create a registry to track the servicemembers and veterans and their levels of exposure, so that over time we have a better understanding of how these exposures impact veterans.

So, Mr. Chairman, I thank you for this hearing and I look forward to the testimony from our witnesses.

Chairman AKAKA. Thank you very much, Senator Murray.

Senator Brown of Massachusetts.

STATEMENT OF HON. SCOTT BROWN,
U.S. SENATOR FROM MASSACHUSETTS

Senator BROWN OF MASSACHUSETTS. Thank you, Mr. Chairman. Congratulations again on that nice award you received the other night. It is well deserved.

Mr. Secretary, thank you for your leadership and devoted service to our Nation's veterans. We had an opportunity to speak in my of-

fice about some of the issues we are discussing today. I enjoyed that meeting very much and I appreciate you taking—making the effort to reach out and talk to me. Unfortunately, I will be bouncing back and forth as well due to some other issues that I am working on as well.

As you all know, we have a solemn duty and moral obligation to our veterans. I have been fortunate enough to serve for almost 31 years now, and am still serving in the Army National Guard where I have witnessed firsthand the sacrifices made by the men and women who have decided to volunteer and serve, often at a great expense not only to them but their families. Making good on our promise to repay those sacrifices is one that will never change.

The Veterans Administration and Institute of Medicine have a steep climb here but I, along with my colleagues, want to work with you every step of the way. At the same time, the process of creating presumptive conditions for deserving veterans is one that should be examined closely with all the facts.

There exist certain realities beyond the Institute of Medicine, findings that are in my view a very critical component of the VA's decisionmaking process to assess presumptive treatment. Nonetheless, the key stakeholders involved in the process are highly qualified, and I am interested in learning more about the VA process and about determining what conditions are referred to the Institute for study and how the VA reviews the Institute of Medicine report to make presumptive determinations.

I would ask that this group of distinguished stakeholders continue to review current policies and decisionmaking processes for determining presumptive conditions and implement efficiencies where possible.

So, Mr. Chairman, I want to thank you again for all your work on this and other issues. And although I have some concerns, I think there is an opportunity to improve the process to ensure we provide our veterans with the necessary compensation they deserve while also taking into consideration the financial obligations of these decisions. As you and others should know, you are more than welcomed to provide any and all information to bring me up to speed being the new person here to give me the tools and resources I need to make better decisions.

So thank you, Mr. Chairman.

Senator AKAKA. Thank you very much, Senator Brown from Massachusetts.

Senator Sanders.

STATEMENT FROM HON. BERNARD SANDERS, U.S. SENATOR FROM VERMONT

Senator SANDERS. Thank you, Mr. Chairman. I want to thank Secretary Shinseki and the other witnesses for their participation in today's very important hearing. I also want to applaud Secretary Shinseki not only on this issue but on a number of issues; stepping up to the plate and his bold leadership in terms of addressing some very long-standing problems facing the veterans' community.

Today I want to express my support for his decision based on existing law. That is the main point to be made today based on existing law: to add three new presumptive medical conditions as serv-

ice-connected for Vietnam Veterans. I just want to say to my colleagues what I know they already know, that what we are talking about today is the ongoing cost of war. This is what war is about. War is more than bullets and guns and airplanes. War is about making sure that we take care of the last veteran who served in that war and we do that person justice. If we do not want to do that, do not send them off to war. But if you make that decision, that is the moral responsibility that we have, which I think is what we are talking about today.

We have witnessed over and over again wartime decisions that were tools of war but had an adverse impact on the health of the very young men and women this Nation has placed in harm's way. I think we are all familiar with that. We all remember the rather shameful experience that took place after World War II when many of our soldiers were exposed to atomic radiation, yet the DOD and other officials were saying, what are you talking about. Yes, you are coming down with cancer. Do not blame us. We had nothing to do with it.

Well, obviously history has proved that very, very wrong. I think all of us know the shameful history of Agent Orange. We know that it was the service organizations themselves that had to step up to the plate and sue their own government to say our people are getting sick. No, no, no. It is not us. And we have made real progress since then. But that is something we should never, ever forget. Men and women who put their lives on the line should not have to sue their own government for the benefits that they are entitled to and that they earned.

The Agent Orange Act of 1991, which is the fundamental topic of this hearing, enabled the VA to begin treating and compensating the veterans exposed in Vietnam because of positive association.

Mr. Chairman, it has been my experience in dealing with veterans, especially those with serious medical conditions, that all they really want is timely access to quality health care. When this Nation needed these young men and women to go into harm's way, they went. However, when those same veterans came back knocking on the doors of DOD or VA medical centers seeking health care, they too often found themselves turned away or denied health care because of rules and regulations that would rather split hairs than provide health care.

I was in the House for many years on the Government Operations Committee, and I will never forget as long as I live the hearings that Chris Shays, who was then chairman of the committee, and I held on Gulf War illness. We had veterans coming in whose bodies were falling apart and we had the VA at that time saying you are not sick. You are not sick. It was a very distressing experience.

The debate—this debate is about a presumption decisionmaking process rather than meeting the health care needs of veterans. It is about presumption decisionmaking. Agent Orange was a kick the can down the road issue which is too common inside the beltway but does not make a bit of sense to the men and women who truly believe VA is their health care system, which I hope all of them do believe.

Secretary Shinseki, you have been placed in a very, very difficult position. In a sense I think we owe you an apology and your predecessors an apology as to: on one hand give you the authority and responsibility to make this decision; and then perhaps turn around only to question and second guess your decisionmaking process. I am confident that you labored over this decision and sought wise counsel. I know that you did. The presumption process dates back long before Agent Orange and has repeatedly accomplished one objective that I think we can all agree on—truly demonstrated the thanks of a grateful nation by aggressively addressing health care needs and if necessary, providing veterans with their earned benefits.

My colleagues: on the issue of cost, none of us are willing to put a price tag on good health. If cost is a concern, then cost should be discussed before sending servicemembers into harm's way.

Clearly, this is about the ongoing cost of war. The cost of our efforts in Iraq and Afghanistan will be paid by not only this generation but generations to come. Personally, I believe no veteran should ever, ever be denied timely access to the VA health care system, especially if they truly believe their medical condition was due to their service in the Armed Forces. How can we call these brave servicemembers heroes in one breath and question their integrity and intentions when they come to the VA for assistance.

I would ask my colleagues how many Vietnam veterans do you think this Nation failed due to inaction between 1975 and 1991? I am afraid there are many, many thousands of them.

So Mr. Chairman, I just want to congratulate you for your efforts; and Secretary Shinseki, I hope we can proceed in addressing this issue.

Chairman AKAKA. Thank you very much, Senator Sanders.

Senator Brown of Ohio.

STATEMENT OF HON. SHERROD BROWN, U.S. SENATOR FROM OHIO

Senator BROWN OF OHIO. I thank you, Mr. Chairman. And aloha. Thanks also to General Shinseki for your many years of service prior to the Secretary's job at the VA and especially what you are doing now.

We know it has been 40 years since the last use of the dioxin Agent Orange in Vietnam. It has been a long, sad 40-year history for our servicemembers who have suffered because of exposure to Agent Orange. For decades, as other have said, veterans suffered from the effects of Agent Orange, but also were plagued by foot-dragging in Congress, at the VA, and at the Department of Defense. They and their families encountered bureaucratic mazes, ignorance, and indifference that are frankly a national disgrace.

Clearly complicated science is involved in determining presumption of illness due to Agent Orange. Exposures, close reconstructions, and ever-changing technological developments have made determining straight-line presumptions very difficult. Waiting for a causal link after 40 years is just another way of telling veterans no. Complexity is not an excuse for years of inaction. It is not an excuse for veterans nor their families like the widow from Pike County, Ohio, who for more than a year tried to get dependency

and indemnity compensation. Her husband who served in Vietnam died 5 years ago from ischemic heart disease. Her claim was originally denied. The appeal was held up, as are all the appeals in claims for that condition, because the regulations had not been approved. The widow of a Vietnam veteran wrote to me, "My late husband did not hesitate to go to Vietnam when he got his orders. He was gone and I waited for a year for him to come home. When my husband came home he was never the same and his life was cut short by the aftereffects of Agent Orange."

I recently had a long discussion with Secretary Shinseki about the most recent presumptive editions, one of which would help this widow. I am convinced he made the right decision in adding these diseases to the presumptive list. I understand we are talking about billions of dollars, but the cost of caring for the veteran is a nonnegotiable cost of war, as Senator Sanders said. If it is a question of choosing between tax cuts for the wealthiest Americans and spending money on our veterans, the clear moral answer is you take care of veterans first. Utilizing an eligibility system that can take years to produce an answer overlooks the fact that there are lives at stake; lives of men and women who served their country because we asked them to.

Under the Chairman's leadership, this Committee has been working on a host of exposure issues. Together we are trying to find the right balance between evidence in level of exposure and causation. Agent Orange was sprayed during the Vietnam War. Our troops—and I would add many citizens still today of Vietnam—suffered and are suffering still. This is beyond scientific doubt. This is about where do we draw the line. How did VA get to the decision to add three new presumptions? What lessons does this provide for us as we talk about Agent Orange and other current and future exposures? It is not easy. There are legitimate questions about the process of determining new presumptions, but I believe the Secretary of the Veterans Administration is correct.

For more than 40 years, Vietnam veterans have waited. That is simply too long. We must work together to correct this injustice. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Brown.

Senator Webb.

STATEMENT OF HON. JIM WEBB,
U.S. SENATOR FROM VIRGINIA

Senator WEBB. Thank you, Mr. Chairman and General Shinseki. Welcome. Also, I would like to welcome and thank Secretary Principi, who is going to testify later, for a great job as a counsel on this Committee and then later served as Secretary of the Department of Veterans Affairs.

I would like to thank you, Mr. Chairman, for holding this hearing. We sometimes have an uncomfortable duty to ask the hard questions, and given the questions that have come about as a result of the decision that has been made, we really need to have this hearing so people can understand the process that was put into place.

I would like to first of all say that I have pretty extensive experience with this issue, beginning as a Marine rifle platoon and com-

pany commander in one of the more war-torn areas of Vietnam. For those of you who are veterans in the audience, the Arizona Valley, An Hoa Basin, Khe Sanh Mountains, Go Noi Island. Very ravaged places with very devastated villages and populations.

I also had the privilege of serving as committee counsel on the House Veterans' Affairs Committee for 4 years, 1977 to 1981. On that committee during that period, we had a number of hearings about Agent Orange. I counseled several of them. I believe four, in my recollection, as we were attempting to come to grips with how to examine where Agent Orange was used, who actually was exposed. Then, what conditions might have resulted from this exposure, and what we should do about it as a government, as the stewards of the people who served, and as the stewards of our country at large.

Those issues have never been clearly and fully resolved. So what we are looking at today—if I could ask Juliet Beyler, also a former Marine by the way, one of my staff members, to put that chart up. Here is what we have to look at. We have a duty up here on this Committee to examine these issues.

First, the implementation of the law. This regards the Secretary's decision. I have no question that the Secretary's decision was within the ambit of the law. But we may want to ask ourselves whether this is the right way for these decisions to be made in the future with issues of this magnitude. I want to say very clearly, this is not simply a cost item. For me, as someone who has worked on veterans' issues my entire adult life, this is not a cost item at all. This is an issue about the credibility of our programs. I think Secretary Principi pointed this out in his statement very eloquently, though I do not want to get ahead of his testimony.

It is also about the accuracy of the scientific process as it pertains to Agent Orange and service in Vietnam. We have struggled with this now for more than 30 years—how we intersect scientific analysis with actual service inside Vietnam. It is about the use of presumptions. The reason I put the chart up and the reason I asked for this chart to be shared with my fellow senators here is that we really need to think about what was in the minds of the lawmakers when this law was originally passed. So, if you look at the first three items here—chlorachne, soft tissue sarcoma, and non-Hodgkin's lymphoma—those were the three conditions that actually were written into the 1991 law.

We asked the VA to give us the number of people who were receiving disability benefits as a result of those conditions today and they come up with a total of a little more than 5,000 people. The law then began, in accordance with scientific evidence, to be examined in a broader context—in the context of dual presumptions. Presumptions are a major part of what we are going to look at today.

First, that everyone in Vietnam presumptively was exposed to Agent Orange. We could not break it down so we said every single person who served in Vietnam was exposed to Agent Orange. Second, we have said that any Vietnam veteran who ends up with a systemic disease based on this process that was written into law, has, as a result, a service-connected condition with respect to Agent Orange. If you look at the last three items on this chart, you see

what has happened in terms of the number of people receiving compensation.

So we have dual presumptions, both based on very broad categorizations that we are having to struggle with, not only now, and most importantly not only now, but in the future, as we examine a whole host of issues of exposure, which were mentioned earlier in testimony.

So this hearing is vitally important for us to examine where we are now and where we need to go in the future. Mr. Chairman, I thank you again for having had the courage to hold this hearing and I very much appreciate Secretary Shinseki's appearance and the people we are going to see on the second panel.

Chairman AKAKA. Thank you very much, Senator Webb.

Senator Tester.

STATEMENT FROM HON. JON TESTER, U.S. SENATOR FROM MONTANA

Senator TESTER. I, too, want to thank you, Mr. Chairman, for holding this hearing. This is a topic that is not an easy one for anybody here. I also want to commend Senator Webb for asking some very tough questions about Agent Orange exposure and about exposure issues generally.

I also want to thank you, Secretary Shinseki for coming here today to talk about the steps that the VA has taken to do right by Vietnam veterans who were exposed to Agent Orange and now are suffering the consequences.

I do not think anyone here expects the rules expanding presumptive eligibility for Agent Orange veterans that the VA issued earlier to be changed. The rules are in place; the funding is in place. We are not going backwards, and I do not think we should. But I have been to a few Democratic Policy Committee meetings chaired by Senator Dorgan on things like burn pits in Iraq. We have heard Senator Burr's passionate pleas for help for the Camp LeJeune veterans. We obviously still need to sort out whether the VA or the DOD needs to pay for those exposure claims. However, the bottom-line is there are going to be many, many more concerns raised about exposure to toxins and toxic substances in the years to come.

In the case of granting presumptive eligibility for Parkinson's and ischemic heart disease, we need to be sure that exposure compensation is based on sound science and the right interpretation of the 1991 Agent Orange law. I am not a doctor. I am not a lawyer. But I believe that the one most basic responsibility of our government and this Committee in particular is to care for the veterans' for the injuries that they have suffered in the defense of this country. That includes services members who are exposed to toxic substances and who become ill as a result of it. At the same time, we also want to be sure that in this budget environment we are certain that we are careful stewards of the taxpayer dollars.

I look forward to hearing more about the Department's decision-making process and balancing the conclusions reached by the several different studies on Agent Orange exposure. It is not going to be easy which is why I am so very happy we are having this hearing.

I want to thank you again, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Tester.

Senator Burris.

STATEMENT OF HON. ROLAND W. BURRIS, U.S. SENATOR FROM ILLINOIS

Senator BURRIS. Thank you, Mr. Chairman. I would like to certainly thank you, Mr. Chairman, for holding this very important hearing. I would also like to extend my warm welcome to Secretary Shinseki and the other distinguished members of the panel. I also want to mention that I am glad to see on the second panel that there will be two witnesses from the great University of Illinois. So if I am not here you certainly will understand that your senator recognized you.

I am also pleased that all of you have come here to give us your assessment of the current and possible—on the possible future presumptive disability decisionmaking process. So your experience and expertise should prove to be invaluable in providing information on this important topic.

I know I have witnessed several situations in regard to our Vietnam veterans. I remember being at the parade in Chicago when they were finally welcomed home. That was a very, very heartwrenching, moving situation to see General Wes Moreland stand on that platform and watch those veterans come up and give their respect to the general. There was not a dry eye on the reviewing stand. Now we know that some of those have come home with no type of parade, no type of motorcade, no type of flags flying. They were not really given what they deserve. So, I am just hoping and praying that we do not do something that is going to cause continued misery for these men and women who gave all and were fortunate enough to come back. If they are suffering from some disease, as the Secretary has determined under law that there is presumptive support for, then we should find a way to make sure that those individuals are given the best care that we can possibly give them. They have suffered enough and do not need to be going through the wringer.

I agree with Senator Sanders, who indicated that the cost of war is costly. It is more than guns and planes and bullets and tanks. It is the aftermath of those who donned the uniform and dared to go out and face bullets and all the other trials, tribulations, and hardships to defend this country. So it is certainly my belief that we must take care of the veterans, and I would not—I am sorry the Secretary had to come and go through this type of review but I guess that is our job. It is oversight. If it costs us additional funds then there is no price that we can put on what we can do if those veterans suffer from those chemicals that were sprayed throughout that country. We do not even know what the outcome is for those individuals who are in war, and we certainly cannot use finances and budget shortfalls and other excuses to not support our veterans. So I am anxious to hear the Secretary's testimony and the other witnesses. Rest assured that we are going to be in the process of taking care of veterans who have taken care of us.

I have told everyone who donned a service uniform, the only way America is and can be great—the land of the free—is because those individuals were awfully brave. There is no reason for us, Mr.

Chairman, to give any more agony to those people who are finally coming into the VA system. Some of them stayed away. They are finally coming back in because they are now really in desperate need, illness is upon them, and they need our help. Let us not abandon those men and women. I look forward to the testimony. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Burris.

Senator Begich.

STATEMENT OF HON. MARK BEGICH, U.S. SENATOR FROM ALASKA

Senator BEGICH. Thank you, Mr. Chairman, and thank you for holding this hearing. Secretary Shinseki, thank you for the meeting we had briefly to talk about some of the issues. I appreciate that. I apologize, Mr. Chairman. I have to go to a Commerce Committee. When I saw Chairman Rockefeller here I thought I had more time but then he left, so I have to go where he is in a few minutes.

First, I want to echo some of the prior comments. One of the challenges we have as we engage in conflict, maybe they be small or large, is we fail collectively—Democrats, Republicans, former administrations, current administrations—we fail to really outline what the total cost will be. It is not just fighting the war; it is what happens after. What we have in front of us is one of those issues that was not calculated from a monetary point of when we fight wars and what we do.

Next, I want to say I support what you have done. You know, I have served in legislative bodies on the city council for 10 years when I was in Anchorage and I served in the executive branch as mayor for 5 years. There are times when you have to make decisions based on a policy set by the legislative body, which this body did. They set a policy. You did the work; actually, your predecessors did the work. Years went by; here we are. You have made a decision. I can tell you in Alaska I hear from many Vietnam veterans about the issue of Agent Orange and the work and trouble involved, the paperwork they have to go through just to prove what their ailment is and what caused it.

We can argue over, you know, certain quantities of individuals, but for the simple reason we called them up to serve our country in a war, we have an obligation to provide them with the benefits they have earned and they deserve.

I am not a doctor. I am not here to tell you what the science is. That is what you do. That is why you are the Secretary of the Veterans Affairs office. You were able to reach out over the last several months, and in this case many years of work, to determine what is the right approach to deal with Agent Orange. My issue is going to be longer term. We had the Gulf War. Then we have Iraq and Afghanistan. More than likely we have some other issues that we are not fully addressing that we are going to have to deal with the full cost of those. We have to recognize that we are going to have a bill due that is more significant than we can ever imagine from these conflicts that we have been engaged in. So, that is the cost of going to war.

After our discussion and my review of the efforts you have made, I am not going to sit here and try to second guess doctors and sci-

entists and others that have gone through this. You had an obligation to follow the law. You did. I will tell you many Vietnam veterans in my State are appreciative of the steps you have taken for the illnesses that they have and how they can be covered, as well as the disability components.

So again, I want to just thank you for the work you have done. We can argue, and we will. Oversight is good. That is part of the process of the Committee. You have a better understanding. But I hope the oversight leads us to understanding what the next issues are going to be—the next generation of veterans and the costs that are going to be associated with it, which I know will be staggering. We think this is an increasing cost in the sense of what it will be, but all you have to do is look at the wars we are engaged in today. There are going to be staggering costs that we cannot even measure today.

So again, I just want to reiterate my review that, at least from my perspective, I think the steps you have taken are positive steps for our Vietnam veterans. I think the process you went through, at least from my review, was tedious, in-depth, and came to a resolution that we have heard for so many years. I have only been here less than 2 years but I can tell you it took no longer than a few months serving in this office for people to find out I served on this Committee. They were very quick to tell me and talk about this issue very aggressively. So, again, thank you for being here today. Now you finally get to say a few words.

I will end there and say, Mr. Chairman, thank you very much for the opportunity.

Chairman AKAKA. Thank you very much, Senator Begich. I want to thank the Members of this Committee for their opening statements.

I want to welcome our lead witness, Secretary Eric K. Shinseki. Secretary Shinseki is accompanied by Dr. Robert Jesse, who is the Principal Deputy Under Secretary for Health; Dr. Victoria Cassano, the Director of the Radiation and Physical Exposure Service. The Secretary is also accompanied by Thomas J. Pamperin, Associate Deputy Under Secretary for Policy and Program Management; and Jack Thompson, the Deputy General Counsel.

Secretary Shinseki, I want to again thank you very much for joining us today to give your perspective on the Department's presumptive disability and decisionmaking process. We are looking forward to understanding the process better after this hearing and deal with it legislatively to try to improve it for the future.

So, I look forward to your testimony, Mr. Secretary. Your prepared statements will, of course, appear in the record of the Committee. Please proceed.

STATEMENT OF HON. ERIC K. SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS; ACCOMPANIED BY ROBERT L. JESSE, M.D., Ph.D., PRINCIPAL DEPUTY UNDER SECRETARY FOR HEALTH; VICTORIA CASSANO, M.D., M.P.H., F.A.C.P.M., DIRECTOR, RADIATION AND PHYSICAL EXPOSURES SERVICE; THOMAS J. PAMPERIN, ASSOCIATE DEPUTY UNDER SECRETARY FOR POLICY AND PROGRAM MANAGEMENT; AND JOHN H. THOMPSON, DEPUTY GENERAL COUNSEL

Secretary SHINSEKI. Chairman Akaka, Senator Isakson who has departed, and other distinguished Members of the Committee, thank you for the invitation to appear here today to discuss my decision to establish presumptions of service connection for three new diseases in accordance with the Agent Orange Act of 1991. Some of what I say will be somewhat repetitive of all the opening comments provided by Members of the Committee. And Mr. Chairman, thank you for including my written statement for the record.

I appreciate the generosity of time shared by Members of this Committee prior to testimony. I also want to acknowledge the representatives of our veterans' service organizations who are in attendance today. Their insights are important and have been helpful to me.

Mr. Chairman, you have already introduced the members of the panel. Let me make sure that I position who they are. On the far left is Tom Pamperin, who is the Associate Deputy Under Secretary for Policy and Program Management of the Veterans Benefits Administration.

As you indicated, to my immediate left is Jack Thompson, our Deputy General Counsel. To my immediate right is Dr. Bob Jesse, Principal Deputy Under Secretary for Health in the Veterans Health Administration. And to the far right, Dr. Victoria Cassano, from our Office of Public Health and Environmental Hazards.

Congress established many significant presumptions for service connection since creating them as part of the veterans' benefit system in 1921 following World War I. The Department of Veterans Affairs has also used its statutory authority to establish fact-based presumptions of service connection in several notable cases. Congress passed the Agent Orange Act of 1991, which prescribed a more focused and proactive policy for addressing veterans' concerns. The Act is explicit both in the information the Secretary must consider and the standard the Secretary must apply in the determinations. The Act directs VA to establish a presumption for any disease where the evidence shows a "positive association" between herbicide exposure and the development of disease in humans. By law, a positive association exists whenever the credible evidence for an association is equal to or outweighs the credible evidence against an association.

The Act further specifies that in determining whether a positive association exists, VA must consider a biannual report by the Institute of Medicine that evaluates the evidence regarding the health effects of exposure to herbicides and all other sound medical and scientific evidence available to VA. Once the IOM report is released, the law allows VA only 60 days to determine whether new presumptions are warranted. VA is mindful of its duty to faithfully

execute the requirements of the Agent Orange Act and to ensure that its determinations are made in a manner consistent with the standards Congress established. Each report from the IOM is reviewed by a working group of VA employees with medical, legal, and program expertise, and by a task force of senior VA leaders. The Secretary benefits from the advice and analyses of these groups and others in VA. But the Secretary is responsible for determining whether the evidence regarding any diseases satisfies the statutory standard.

In July 2009, VA received the most recent IOM report known as Update 2008. The most significant changes from the 2006 IOM report are: the findings of sufficient evidence of a positive association between herbicide exposure and chronic b-cell leukemias; and of limited suggestive evidence of an association between herbicide exposure and Parkinson's disease and ischemic heart disease. After reviewing the IOM's analyses and relevant scientific studies and then consulting with medical and legal experts in VA, I determined that the evidence concerning b-cell leukemias, Parkinson's disease, and ischemic heart disease met the positive association standard of the Agent Orange Act. Accordingly, VA proposed regulations to establish presumptions of service connection for those diseases.

The evidence regarding hypertension, which was placed in the limited suggestive category in 2006, was less compelling in my view and still did not meet—did not establish a positive association. I believe that these decisions in all four cases were consistent within the law. In conducting my review and making my decision under the Agent Orange Act, I was aware of the prevalence of ischemic heart disease within the general population and the fact that it is associated with a number of factors other than herbicide exposure. I carefully considered whether and to what extent those factors may be considered in applying the statutory standard. My determination that there is a positive association between herbicide exposure and ischemic heart disease was based solely upon the evaluation of the scientific and medical evidence according to the statutory standard prescribed by the Agent Orange Act.

The IOM's 2008 report identified nine studies that were rigorously conducted, some containing reliable measures of exposure that permitted evaluation of dose response relationships which are particularly compelling in determining whether or not an association exists. Of the nine primary studies, six showed strong statistically significant associations between herbicide exposure and ischemic heart disease. Five of the studies detected a dose response relationship. The studies with the best dose information all showed increased risk at the highest categories of exposure. Additionally, there is sound medical evidence of a biological mechanism of disease causation. I took particular note that all nine studies had controlled for age. Age is the primary determinant of ischemic heart disease. It is the one determinant that cannot be moderated.

Some of the studies showed the association persisting after adjustment for numerous other potentially confounding factors. The IOM study further noted that although some of the studies did not adequately control for certain risk factors, those risk factors were unlikely to explain the significant increased risks detected.

The VA's review brought to my attention an additional recent study which was particularly helpful, useful because it analyzed numerous prior studies and concluded that those with the best data and comparisons were consistent in finding a significant dose relationship between dioxin exposure and increased risk of ischemic heart disease. In my judgment, taking into account the number of statistically significant findings, the strong evidence of dose response relationship, and the extent to which the studies control for risk factors including age, the evidence for an association between herbicide exposure and ischemic heart disease more than satisfies the positive association standard of the Agent Orange Act.

The statute therefore directed that I establish a presumption of service connection without regard to the projected costs or the existence of independent risk factors. My determination regarding ischemic heart disease, Parkinson's disease, and b-cell leukemias was not made lightly. It was made in accordance with the legal responsibilities assigned to me in the Agent Orange Act and my duty as Secretary of Veterans Affairs to faithfully execute the letter and the purpose of that statute. No other course of action would have met the intent of the law.

Veterans and their families have waited decades while the sciences incrementally revealed more about the impact of Agent Orange on Vietnam veterans. Not only did our actions follow the statute, but I believe our actions on Agent Orange will be viewed as an indicator of our seriousness and commitment in addressing veterans' needs, not only for Vietnam veterans but for veterans of every generation.

Presumptions will continue to be an important part of the veterans' benefit system for the foreseeable future. They are powerful tools for promoting efficiency, fairness, and justice. These features of presumptions are particularly significant for the efforts of VA and Congress to ensure the fair and expeditious adjudication of benefits claims at a time when claims are increasing in number, scope, and complexity.

The most important lesson I have learned from this process is the one that Senator Murray and others pointed out, and that is we must track the exposures of our servicemembers to toxic chemicals and environments earlier. Such tracking does not get easier or less complicated as time passes. Early registration and surveillance of those exposed enables better treatment and rehabilitation and allows us to make proactive decisions in mitigating future exposures. Early tracking, intervention, treatment, rehabilitation, equals better health for America's veterans. We must do better and we will.

Mr. Chairman, thank you again for this opportunity to appear before this Committee, and thank you for your continued unwavering support of our veterans. I look forward to your questions.

[The prepared statement of Secretary Shinseki follows:]

PREPARED STATEMENT OF HON. ERIC K. SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Chairman Akaka, Ranking Member Burr, Distinguished Members of the Committee, I am pleased to be here today to discuss the role of presumptions of service connection in claims for Veterans' benefits and, in particular, to discuss presumptions established pursuant to the Agent Orange Act of 1991.

Presumptions of service connection have been an important part of the Veterans benefits system since Congress established presumptions for tuberculosis and neuropsychiatric diseases following World War I. Over this period, Congress has established many significant presumptions, including those for diseases of former prisoners of war, diseases associated with ionizing radiation, and undiagnosed illnesses and chronic multisymptom illnesses in Gulf War Veterans. The Department of Veterans Affairs (VA) also plays a vital role in this process. VA's statutory authority to issue regulations governing benefit claims includes the ability to establish fact-based presumptions of service connection. VA has exercised this authority judiciously to establish several significant presumptions to complement and supplement those created by Congress, including presumptions relating to mustard gas exposure and the presumption of service connection for amyotrophic lateral sclerosis (ALS) in Veterans of all periods of service.

The Agent Orange Act of 1991 created an innovative process for establishing presumptions of service connection, one that combines the efforts of Congress and VA, while delineating their respective roles in the process. Under this act, VA is responsible for determining which diseases will be accorded a presumption of service connection, but its determination is guided by evidentiary criteria and decisional standards prescribed by Congress. Specifically, VA is charged with evaluating medical and scientific evidence and analyses from the National Academy of Sciences and other sources in order to determine whether such evidence satisfies the "positive association" standard defined in the Agent Orange Act.

VA takes seriously its responsibilities under the Agent Orange Act. I know that concerns have been expressed regarding the potential impact of my determination under this statute to establish presumptions of service connection for ischemic heart disease, Parkinson's disease, and chronic b-cell leukemias. I can assure you that my determination was made upon careful consideration of the scientific and medical evidence and the governing legal standards, was informed by consultation with medical and legal experts in VA, and reflects the best efforts of all within VA to carry out the requirements of the Agent Orange Act. I welcome this opportunity to explain the determinations VA has made in applying the Agent Orange Act and to discuss the important issue of how best to utilize presumptions to ensure that Veterans are properly compensated for their disabilities related to herbicide exposure or other factors.

Presumptions in the adjudication process eliminate the need to obtain certain evidence and decide complex issues. They permit VA to accept as established certain facts that would otherwise have to be the subject of extensive development and evidentiary analysis. They also assist Veterans in establishing service connection in cases where the slow development of disability makes direct proof of service connection difficult. For example, there is a longstanding statutory presumption that a Veteran who develops multiple sclerosis to a compensable degree within seven years after leaving service will be presumed to have incurred the disease in service. Congress established that presumption based on scientific evidence that it may take up to seven years from the date of onset for multiple sclerosis to progress to the point of a diagnosable disability. Like most presumptions of service connection, this presumption serves a number of important functions. First, it relieves claimants of the burden of submitting medical evidence directly linking the onset of their condition to service, a burden that would be difficult to meet where the condition manifests at a time remote from service and the relevant medical principles may not be widely known. Second, it ensures that similar claims are given similar treatment. Third, it enables VA to process claims more quickly by relying upon medical principles that need not be independently established in each case. Fourth, it helps Veterans, who may not have been otherwise eligible, to obtain prompt medical assistance for their service-connected conditions .

Finally, presumptions are used to implement policy when scientific certainty cannot be achieved in a timeframe necessary to address Veterans healthcare issues. This is an important aspect of the presumption process in a benefits system designed to meet the needs of our Veterans.

It has long been known that dioxin, a contaminant of Agent Orange, is a potent carcinogen. As our troops returned from Vietnam, many expressed concerns that the health problems they were experiencing had been caused by their exposure to Agent Orange. However, they found it difficult to establish service connection, because the evidence at that time did not clearly link Agent Orange to any specific illness other than a skin condition, chlorachne. In a 1984 report, Congress noted that, although VA had granted service connection based on herbicide exposure in more than 1400 cases, fewer than one hundred grants were for conditions other than chlorachne or similar skin conditions. Consequently, some Veterans grew to feel that VA was not

giving serious consideration to their legitimate concerns regarding the harmful exposures incurred in their service.

In 1984, Congress enacted the Dioxin and Radiation Exposure Compensation Standards Act in an effort to improve this process. The statute included findings that there was scientific uncertainty regarding the health effects of dioxin exposure and that claims based on such exposure present uniquely challenging issues of proof. The statute directed VA to establish standards and guidelines for deciding those claims and to identify the diseases that VA would recognize as being associated with herbicide exposure. It also established an advisory committee to review available research and make recommendations to VA. The statute did not prescribe specific criteria to govern VA's decisions, but included a more general statement of the statute's purpose. As passed by the House, the bill's stated purpose was to provide benefits for diseases that "may be attributable" to Agent Orange exposure "notwithstanding that there is insufficient medical evidence to conclude that such diseases are service-connected." As enacted, however, the statute's stated purpose was to provide benefits for diseases "that are connected, based on sound scientific and medical evidence," to Agent Orange exposure. To implement the statute, VA issued a regulation providing that chlorachne was the only disease shown by sound scientific and medical evidence to be associated with Agent Orange exposure and was thus the only disease VA would presume to be service-connected.

In 1991, Congress enacted the Agent Orange Act of 1991, which prescribed a more focused and proactive policy for addressing these Veterans' concerns. The Act directed VA to seek to contract with the National Academy of Sciences, a respected independent expert scientific body, to evaluate the evidence regarding the health effects of exposure to herbicides. Under that requirement, VA receives reports every two years from the National Academy's Institute of Medicine (IOM). The act further directed VA to establish presumptions of service connection for any disease discussed in the IOM's reports for which the evidence showed a "positive association" between herbicide exposure and the development of the disease in humans. The statute specifies that a "positive association" exists whenever the Secretary determines that the credible evidence for an association is equal to or outweighs the credible evidence against an association. The language and legislative history of this act made clear that it did not require evidence of a causal association, but only credible evidence that herbicide exposure was statistically associated with increased incurrence of the disease. The Act further specified that, in determining whether a positive association exists, VA must consider the IOM's report and any other sound scientific and medical evidence available to VA.

The Agent Orange Act was a compromise between the desire for scientific certainty and the need to address the legitimate health concerns of Veterans exposed to herbicides in service. By establishing an evidentiary threshold lower than certainty and lower than actual causation, Congress required that presumptions will be established when there is sound scientific evidence, though not conclusive, establishing a positive association between a disease and herbicide exposure. Based on the numerous reports received from IOM since 1991, VA has established presumptions of service connection for 12 categories of disease associated with herbicide exposure. While there is always room to review decisions with respect to specific diseases, there is no question that the actions of Congress and VA related to the Agent Orange Act demonstrate the Government's commitment to provide Vietnam Veterans with treatment and compensation for the health effects of herbicide exposure.

In view of this history, VA is mindful of its duty to faithfully execute the requirements of the Agent Orange Act and to ensure that its determinations are made in a manner consistent with the standards Congress has established. Each report from the IOM is reviewed by a working group of VA employees with medical, legal, and program expertise, and by a task force of senior VA leaders. I benefit from the advice and analyses of these groups and others in VA; but as Secretary, I am responsible for determining whether the evidence regarding any disease satisfies the statutory standard.

In July 2009, VA received the most recent IOM report, known as "Update 2008." The most significant findings in this report are the findings of "sufficient" evidence of a positive association between herbicide exposure and chronic b-cell leukemias and of "limited/suggestive" evidence of an association between herbicide exposure and Parkinson's disease, ischemic heart disease, and hypertension. After reviewing the IOM's analyses and relevant scientific studies, and consulting with medical and legal experts in VA, I determined that the evidence concerning b-cell leukemias, Parkinson's disease, and ischemic heart disease met the "positive association" standard of the Agent Orange Act. Accordingly, VA proposed regulations to establish presumptions of service connection for those diseases. The evidence regarding hyper-

tension was less compelling and, in my view, did not establish a positive association under the statute.

I would like to address the concerns that have been expressed regarding my determination with respect to ischemic heart disease. These concerns relate to the economic impact of the presumption, due to the high prevalence rate of ischemic heart disease, and the fact that ischemic heart disease is associated with a number of factors other than herbicide exposure, including age, smoking, serum cholesterol, body mass index, and diabetes. In conducting its review under the Agent Orange Act, VA was cognizant of the prevalence of ischemic heart disease and its known risk factors, and we carefully considered whether and to what extent those factors may be considered in applying the statutory standard.

VA's Office of General Counsel has advised that the Agent Orange Act does not permit me to weigh the potential economic impact of my decision to establish a presumption under that statute. The statute requires that I establish a presumption if the "positive association" standard is met, and it provides that the standard will be met if the credible scientific and medical evidence for an association is equal to or outweighs the credible scientific evidence against an association. Additionally, the statute does not permit VA to exclude a disease from consideration on the basis that it is a common disease. Rather, it directs VA to determine whether a positive association exists for each disease discussed in the IOM reports it receives. VA's Office of General Counsel advised me that consideration of the prevalence of ischemic heart disease and the potential economic impact of a presumption would violate the clear requirements of the Agent Orange Act. Accordingly, those factors did not enter into my decision under the positive association standard.

The impact of other known causes and risk factors for ischemic heart disease is relevant in interpreting the results of scientific studies concerning that disease. In determining whether a study provides evidence for an association between herbicide exposure and a particular disease, IOM routinely evaluates the extent to which the study controlled for other known risk factors for that disease in order to minimize or rule out the possibility that an increased prevalence in the study population may be due to factors other than herbicide exposure. By considering this factor, IOM is able to draw conclusions regarding how strongly the evidence shows that an association between herbicide exposure and a disease exists, independent of other known risk factors. In reviewing the IOM reports, VA also takes this factor into account in determining whether, and to what extent, a study provides evidence for an association between herbicide exposure and the disease independent of other risk factors. Studies that do not adequately control for other risk factors are generally less reliable than those that do.

After taking these considerations into account, if VA determines that the evidence demonstrates a positive association between herbicide exposure and a specific disease, then VA has no discretion under the Agent Orange Act to decline to establish a presumption solely on the basis that the disease is independently associated with other known risk factors. Rather, the Act requires that VA establish a presumption and provides that the presumption may be rebutted in individual cases if the evidence shows that the Veteran's disease was due to a factor other than herbicide exposure.

For these reasons, my determination that there is a positive association between herbicide exposure and ischemic heart disease was based solely upon evaluation of the scientific and medical evidence and application of the statutory standard prescribed by the Agent Orange Act. The IOM's Update 2008 report identified nine studies that were considered to be highly informative with respect to this disease. Those studies were rigorously conducted and contained reliable measures of exposure that permitted evaluation of dose-response relationships, which are particularly helpful in determining whether an association exists. Of the nine primary studies, six showed strong and statistically significant associations between herbicide exposure and ischemic heart disease. Several of the studies detected a dose-response relationship and the studies with the best dose information all showed increased risk in the highest categories of exposure. IOM noted that most of the studies had controlled for age, which is the primary risk factor for ischemic heart disease. Some of the studies showed the association persisting after adjustment for numerous other potentially confounding factors. IOM further noted that, although some of the studies did not adequately control for certain risk factors, those risk factors were unlikely to explain the significant increased risks detected in the studies. VA identified an additional recent study by Humblet and Birnbaum, 2008, which analyzed numerous prior studies and concluded that the studies with the best exposure data and comparisons were consistent in finding an association between dioxin exposure and increased risk of ischemic heart disease.

In my judgment, taking into account the number of statistically significant findings, the strong evidence of dose-response relationship, and the extent to which the studies controlled for risk factors including age, the evidence for an association between herbicide exposure and ischemic heart disease satisfies the "positive association" standard of the Agent Orange Act. The statute therefore directed that I establish a presumption of service connection, without regard to other independent risk factors.

My determinations regarding ischemic heart disease, Parkinson's disease, and b-cell leukemias were not made lightly. They were made in accordance with the responsibilities entrusted to me in the Agent Orange Act and my duty as Secretary of Veterans Affairs to faithfully execute the letter and the purpose of that statute.

A significant portion of the costs associated with the new presumptions is the result of a series of Federal court decisions in the *Nehmer* class-action litigation. In that case, the United States Court of Appeals for the Ninth Circuit has held that, each time VA establishes a new presumption under the Agent Orange Act, it must make retroactive payments based on claims filed as early as 1985. This ruling overrides statutes expressly prohibiting retroactive payments based on such new presumptions, and it thus substantially increases the costs associated with presumptions under the Agent Orange Act. Under the *Nehmer* decisions, this requirement for retroactive payment will continue to apply to any future presumptions established before the Agent Orange Act's 2015 sunset date or any later date that may be established by future extensions of the act.

The presumptions established by Congress and VA have been invaluable in addressing the challenges of claims involving unique circumstances, such as prisoner-of-war captivity and toxic exposures, and claims involving devastating diseases such as amyotrophic lateral sclerosis (ALS). Based on reports from IOM regarding Gulf War Veterans' health, VA recently proposed to establish presumptions for nine infectious diseases endemic to the Gulf War theater, and we are preparing to revise the existing presumption for medically unexplained chronic multisymptom illnesses to clarify that functional gastrointestinal disorders are covered by that presumption. Presumptions will continue to be an important part of the Veterans' benefits system for the foreseeable future. I look forward to working with Congress to ensure that the process for establishing presumptions of service connection is one that properly meets the needs of our Veterans and our Nation.

This concludes my statement, Mr. Chairman. I would be happy to entertain any questions you or the other Members of the Committee may have.

RESPONSE TO PRE-HEARING QUESTIONS SUBMITTED BY HON. JIM WEBB TO HON. ERIC SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Question 1. With regard to the decision to create a presumption for ischemic heart disease, you stated in your June 29 response to me that the VA "Task Force reviewed and summarized the IOM Report material to facilitate [your] decision." Please describe the recommendations that the VA Task Force and any other working group provided to you with regard to establishing a presumption for ischemic heart disease. Did either VHA or VBA leadership express any concerns with regard to establishing a presumption for ischemic heart disease?

Response. In an effort to expeditiously address the IOM Report in accordance with applicable statutory deadlines, a VA Task Force, which included VHA and VBA leadership, received the report of a staff level work group's comprehensive review of the IOM Report, and provided me with a summary of the IOM Report's findings, and offered perspectives for my review. The pre-decisional material developed as part of the intradepartmental deliberation process helped frame my perspective on the scientific evidence regarding the association between herbicide exposure and ischemic heart disease. Given the pre-decisional nature of the Task Force input as well as to avoid second-guessing those who participated in this review, I prefer to avoid details on this topic.

I would note the Task Force was encouraged to be candid and thorough in their work. I benefited from their advice and analysis as I made my decision. I can tell you that with respect to ischemic heart disease, the vast majority of VA medical professionals who analyzed the IOM Report and advised me agreed that the "positive association" standard in the law had been met.

Question 2. Please identify and describe the credible evidence against the association between dioxin and ischemic heart disease that the Task Force reviewed in considering this presumption. Did the Task Force review the evidence for and against the association provided in the Institute of Medicine's Agent Orange Update 2006?

Did the Task Force review the Environmental Protection Agency's Dioxin Reassessment as part of its work?

Response. In IOM Update 2008, the Committee revisited all of the studies that were reviewed in Update 2006. It expressed the fact that the 2006 committee could not reach consensus on the weight of the various studies and therefore deferred decisions on elevating ischemic heart disease to the Limited/Suggestive Evidence category. All of the credible evidence, both for and against a positive association from the 2006 report, was also available in the 2008 report.

The studies reviewed by the 2006 Committee were: Kang 2006; AFHS 2005; Vena 1998; Flesch-Janys 1995; Hooiveld 1998; and Steeland 1999. The IOM's synthesis of these studies in 2006 reads as follows: "Members of the Committee were divided in their judgments as to whether the evidence related to ischemic heart disease and exposure to the compounds of interest were adequately informative to advance this health outcome from the inadequate or insufficient category to the limited or suggestive evidence category." In the 2008 Update, the credible evidence of these studies was presented in its entirety. Additionally, in light of the inability of the 2006 Update committee to reach consensus on the information, more confidence was given to studies that had been more rigorously conducted, focused on the chemicals of concern, compared Vietnam Veterans to non-deployed era Veterans and had reliable measures of the important dose response relationships. This approach was combined with two studies published subsequent to the 2006 Report (HA 2007 and Consonni 2008) which provided the 2008 Committee with enough credible evidence to elevate ischemic heart disease to the level of Limited/Suggestive Evidence of association. Additionally, the Task Force reviewed the study by Humblet, Birnbaum, et al., 2008. The Task Force did not review the Environmental Protection Agency's Dioxin Reassessment as part of its work, because it did not address ischemic heart disease, but addressed primarily the effect of low-dose exposures present in the general environment to which many ordinary citizens are exposed.

Question 3. You stated in your June 29 response to me that "it is important to note that most of the scientific studies on which the IOM assessment relied controlled for other known or suspected risk factors." With the exception of the age risk factor, what other major risk factors for ischemic heart disease were controlled for in the mortality studies relied upon by VA?

Response. Of the nine studies given greatest weight by the IOM Committee, five were mortality-based studies. Risk factors that were controlled for included duration of exposure, gender, age, and socioeconomic status. In addition, several of the studies used an internal comparison group to eliminate the healthy worker effect and other confounders. The chart below delineates by study which risk factors were controlled for and which used an internal comparison.

Mortality Study	Internal Comparison? (Controls for healthy worker effect and other confounders)	Confounders controlled for:
Hooiveld (1998); Dutch Herbicide factory workers	YES	age, timing of exposure
Flesch-Janys (1995); FRG herbicide factory workers	YES	socioeconomic status, gender, Healthy Worker Effect (workers in a different industry)
Steenland (1999); NIOSH Cohort Study	YES	adjusted for age
Consonni (2008); Seveso Italy—mortality after 25 years	N/A Environmental Study	age, gender, exposure period
Vena (1998); IARC Cohort of phenoxy herbicide workers	YES	gender, age, duration of exposure

Question 4. In your view, is the current presumptive disability decisionmaking process established by the Agent Orange Act of 1991 the most efficient process for making presumption determinations? Is this process the appropriate mechanism to address gaps in exposure and association for diseases common to aging or other highly prevalent risk factors?

Response. The 1991 Act was a solution to address the lack of progress in addressing the concerns of the potential health effects of herbicide exposure. This was a controversy that had defied resolution for over 20 years. The resulting law created a process that replaced a causality standard with the more attainable standard of

"positive association." This standard, while in no means perfect, has resulted in more Vietnam veterans obtaining health care as a result of herbicide exposure. I am not aware of alternative approaches that address the current scientific uncertainty, regarding how we treat our Nation's Veterans with environmental hazard exposure resulting from service to their country.

Question 5. What specific guidance has VA adopted from IOM's 2008 report titled "Improving the Presumptive Disability Decision-Making Process for Veterans?" What is your view on that IOM committee's recommendation to develop and publish a formal process for considering disability presumptions that is uniform and transparent and clearly sets forth all evidence considered and the reasons for the decisions made?

Response. The 2008 IOM report titled "Improving the Presumptive Disability Decision-Making Process for Veterans" contained the following recommendation:

> The Committee suggests the following six principles as a foundation for its proposed framework: (1) stakeholder inclusiveness; (2) evidence-based decisions; (3) transparent process; (4) flexibility; (5) consistency; and (6) using causation, not just association, as the basis for decisionmaking. Flexibility and consistency are not contradictory constructs here. Flexibility refers to the ability to be adaptable through time in evaluating scientific evidence, and consistency refers to being consistent in the process of evaluating evidence and making consistent decisions based on a comparable level of certainty based on the scientific evidence.

Pages 18–19.

This IOM report was commissioned by the Veterans Disability Benefits Commission rather than by VA. Some of these recommendations already are part of VA's regulatory process. However, the ultimate recommendation to use causation as a basis for decisionmaking, rather than positive association, is contrary to the law enacted by Congress and was not endorsed by the Commission (which stated at page 157 of its report that it was "concerned over the use of causal effect rather than association as the criteria [sic] for decision and encourages further exploration"). The law requires that the Secretary determine whether there is a positive association between exposure to a herbicide agent and the occurrence of a disease in humans. It also provides that an association "shall be considered to be positive [ ] if the credible evidence for the association is equal to or outweighs the credible evidence against the association."

VA is mindful of its duty to faithfully execute the requirements of the Agent Orange Act and to ensure that its determinations are made in a manner consistent with the standards Congress established. By establishing an evidentiary threshold lower than certainty and actual causation, Congress ensured that presumptions would be established when there is sound evidence, although not conclusive, establishing a positive association between a disease and herbicide exposure. The positive association standard is evidence-based.

VA's process for establishing service-connection presumptions by regulation is uniform and transparent. Once the Secretary makes a positive association determination based upon evaluation of the IOM report and all other available sound medical and scientific information and analysis, Congress is informed and VA initiates the Federal rulemaking process. VA publishes a proposed rule in the *Federal Register* explaining the medical and scientific bases for the determination and invites public comments. In this particular case, VA received over 600 public comments on its proposed rule during the 30 day comment period. By comparison, VA seldom receives more than a dozen public comments on most proposed rules. VA responded to all of the comments and published a final rule establishing the new presumptions. As required by law, VA will also publish a notice in the *Federal Register* explaining why other diseases were not determined to have met the positive association standard.

The short timelines prescribed in the statute for making the positive association determination and publishing the required proposed rule, final rule, and public notice in the *Federal Register* generally preclude stakeholder involvement prior to the public comment period. As you know, VA has proposed legislation to establish more realistic timeframes for these steps. If VA's proposal were enacted, and additional time were made available, the Department would be better able to accommodate the IOM recommendation for greater "stakeholder inclusiveness." This might be accomplished in various ways, including publication of Advance Notice of Proposed Rulemaking (ANPRM), which is a regulatory vehicle for obtaining additional information from interested parties, prior to the actual proposal of agency rules.

RESPONSE TO POST-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO HON. ERIC K. SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Question 1. VA's response to a pre-hearing question on evidence utilized in making the presumption decision on ischemic heart disease (IHD) listed studies discussed in the IOM Update 2006 that were suggestive of an association between dioxin exposure and IHD as having been presented in the IOM Update 2008. I recognize that those studies were important in VA's decisionmaking, but the response did not mention studies discussed in the IOM Update 2006 that provided evidence against an association between dioxin exposure and IHD.

Question 1a. Was evidence against the association included in VA's decisionmaking process? If so, how was it weighed against the evidence suggestive of an association? If not, was there a reason for not including it?

Response. IOM Update 2008 reviewed all of the materials from IOM Update 2006 as well as any new materials relevant to the issue of herbicide exposure and disease. In its decisionmaking process, VA used all of the studies the IOM considered both relevant and statistically valid. A study's outcome with regard to the association between exposure to Agent Orange and development of IHD was not considered during selection. The selected epidemiologic studies demonstrated a positive association that was statistically significant, an association that was positive but could not reach statistically significance, or failed to show a positive association. Evidence against an association would have included studies that showed a statistically significant negative association. There were no studies that demonstrated a negative association.

Question 1b. Were there any other sources that VA relied upon to examine the strength of the evidence against the association since discussion of such evidence was not included in the IOM Update 2008?

Response. The Working Group searched for all peer review literature on Agent Orange published since the IOM report. No studies were found that demonstrated a negative association between exposure to Agent Orange and IHD. Similarly the IOM Update 2008 found no studies that showed a negative association between Agent Orange exposure and IHD.

Question 2. EPA examined the rigor of three of the studies—Steenland, et al; Flesch-Janys, et al; and Consonni, et al—relied upon by IOM Update 2008 to support the association between dioxin exposure and IHD. During the decisionmaking process, did anyone from the Working Group or the Task Force note that the EPA had determined that those studies were not suitable for examining an association due to inadequate exposure data and uncontrolled risk factors preventing reliable dose-response measurements?

Response. The Working Group reviewed the EPA's Reassessment but did not use it in their deliberations. The Working Group found the findings not valid pertaining to determining an association. It is significant to note that the EPA could not have considered the Consonni study referenced by the IOM Update 2008 because the study was published after the 2003 EPA review. Regarding the Steenland study, EPA stated: "Steenland et al. (1999) found mortality from ischemic heart disease moderately increased with increasing exposure score, with an SMR [(standard mortality ratio)] = 93 in the lowest septile to an SMR = 123 for workers in the highest septile ($P_{\text{test for trend}} = 0.14$)." This is a very positive statement regarding a dose—response relationship. We could not identify in the 2003 EPA assessment where it is stated that either the Flesch-Janys or Steenland studies were not suitable for examining an association. There is a difference between a statistical association and a dose-response relationship. Studies can show both or either one independent of the other. The fact that there is no dose-response relationship demonstrated does not nullify a statistically significant relative risk or odds ratio.

Question 3. In response to a pre-hearing question, VA indicated that the IOM Update 2008 reviewed two additional studies—Consonni and the Ha, et al., study—that provided enough credible evidence to elevate IHD to the level of a limited/suggestive association.

I understand that the IOM Update 2008 describes the Consonni study as not showing a dose-response pattern to support an association, and that Dr. Linda Birnbaum, a reviewer of the IOM Update 2008, describes in correspondence with the Veterans' Affairs Committee the Ha study as having "little relevance to the role of dioxin-like chemicals in the development of IHD or CVC."

Did the Working Group or Task Force note either or both of these caveats about the two studies?

Response. Not all studies contribute the same information in regard to determining a positive association. The Consonni study did show a statistically signifi-

cant positive association between exposure and disease. The dose-estimate was based on distance from the explosion. Earlier studies on this cohort did show a dose-response relationship in that the mortality for IHD was highest in the most exposed group (Zone 1—closest to the explosion) therefore those that had the highest exposure by this estimate had already died from ischemic heart disease and were therefore removed from the populations at risk. This is hypothesized as the reason that those in the zone farthest away from the explosion and with lower exposure now have a higher mortality from IHD.

We agree that the Ha study provides less useful information than the other studies. The working group's perspective of the Ha study, which provided less compelling but certainly supportive evidence, is discussed in the response to question 4 below. This study was included in our review as it had met the IOM criteria for inclusion.

Question 4. VA's June 29th letter provided a list of the five most reliable studies that informed VA's decision to establish the IHD presumption. This list did not include the Ha study. However, VA's response to pre-hearing questions noted that the Ha study was one of the two new studies providing enough credible evidence to elevate IHD to the level of a limited/suggestive association. To what extent did VA rely on the Ha study while establishing the IHD presumption?

Response. The list provided in the June 29th letter included the five mortality studies requested in the pre-hearing questions. The Ha study was not one of the six studies IOM determined to have a strong statistical association (what is stated above as the most reliable), so its contribution was limited by both IOM and the VA working group. Despite its limits, the Ha study did provide valuable information to the decisionmaking process in that it showed a statistically significant finding in women though not in men. This study also controlled well for risk factors including body mass index (BMI), smoking, family history, cholesterol and socio-economic status.

Question 5. The six studies referenced on page 630 of the IOM Update 2008 as showing "strong and statistically significant associations with ischemic heart disease" did not include either the Consonni or Ha studies. Did either the Working Group or Task Force note this during the decisionmaking process?

Response. Yes, the working group paid great attention to which studies showed statistically significant associations.

The Consonni study was included in these six studies. The three studies that were not included were Ha, Calvert and the Air Force Health Study (Ranch Hand). However, IOM also made the following statement: "Because of small numbers, the studies that did not report statistically significant associations, did not rule out modest increases in ischemic heart disease risk in those with the strongest evidence of exposure" (p. 630). These studies, in the IOM committee's conclusions, added weight to the credible evidence for an association.

Question 6. Dr. Birnbaum stated in correspondence with the Veterans' Affairs Committee that the Ha study did not correctly apply the toxic equivalency methodology for examining dioxin-like chemicals and did not measure TCDD specifically.

Response. TCDD is the most toxic of all dioxins and dioxin-like compounds. If studies show that IHD is related to exposure to less toxic dioxins and dioxin-like compounds than TCDD, this would strengthen the association between TCDD and IHD.

Question 6a. Did either the Working Group or the Task Force provide an independent review of the Ha study to determine the extent to which it provides credible evidence to elevate the level of association?

Response. The Working Group reviewed and assessed the strength of each study the IOM indicated was important in their decision. The VA Working Group also reviewed each study for its rigor and contribution to the credible evidence of association. The Working Group review included the Ha study because it provided additional useful information. The Ha study showed a statistically significant finding in women though not in men. This study also controlled for risk factors including body mass index (BMI), smoking, family history, cholesterol and socio-economic status. While the limits of the Ha study were recognized, the study was also found to contain valid and valuable information that contributed to the total body of information that led to the presumption decision.

Question 7. In response to pre-hearing questions, VA noted that the IOM 2008 Update lists among its most important study selection criteria those studies that examined the exposure risk of Vietnam veterans compared with non-deployed Vietnam-era veterans.

Only two of the nine studies discussed by the IOM Update 2008 Committee examined Vietnam veterans, and one of the two was not identified by IOM as one of the six strongest studies that supported its determination.

Did either the Working Group or the Task Force discuss the extent to which IOM's determination of a suggestive/limited association, based largely on studies examining non-veteran populations with known levels of exposure, can be extrapolated to a veteran population with unknown levels of exposure?

Response. There are measured levels of dioxin in Vietnam Veteran populations such as in the Ranch Hand and Army Chemical Corps studies. Using data from other exposed populations strengthens the argument for similar health effects found in Vietnam Veterans. Chemical toxicants do not affect different populations in grossly different ways except in cases of rare genetic susceptibility or protection. The pathophysiologic mechanisms by which TCDD causes cell damage and subsequent disease are basic and apply to human populations in general. Accordingly, the IOM and the VA Working Group and Task Force considered studies of non-Veteran populations relevant in assessing the risks in Veteran populations. This is consistent with the statutory standard in the Agent Orange Act requiring the Secretary to determine whether herbicide exposure is associated with health effects in humans generally, rather than only in Veteran populations.

Question 8. I understand that EPA's Dioxin Reassessment (available at http://www.epa.gov/ncea/pdfs/dioxin/nas-review) addresses IHD specifically, and the health effects of low-to-high dose exposures of many of the same populations examined in the studies relied upon by IOM Update 2008 [see Part II, Chapter 7B (pp. 60–66) of the EPA Dioxin Reassessment (2003)].

Dr. Linda Birnbaum cites this EPA source as the most reliable and comprehensive source for current data on the health risks of dioxin exposure.

• Did the Working Group or the Task Force provide information on the EPA reassessment during the decisionmaking process?

Response. We did not use the EPA risk assessment for a number of reasons. While it did discuss ischemic heart disease, that was not the major focus of the EPA reassessment. Also, the EPA study was completed in 2003 and many of the studies were older and superseded by more recent studies that were reviewed in the IOM report. Dr. Birnbaum also stated that: "In addition, the Institute of Medicine's report, entitled Veterans and Agent Orange: Update 2008, also provides a comprehensive and reliable source for the most current data on the health risks of dioxin exposure."

Question 9. In response to pre-hearing questions, VA seemed to suggest that a source examining the effect of low-dose exposures present in the general population would not be relevant to an examination of dioxin exposures experienced by Vietnam veterans. What evidence is available to VA that demonstrates the dioxin exposure level experienced by a majority of Vietnam veterans?

Response. In both the Ranch Hand study and the Army Chemical Corps studies, the levels of dioxin in the general population are considered the "background" levels to which levels in Vietnam Veterans were compared. In those Vietnam Veterans in which TCDD levels were measured, the levels in those who had increased relative risks had levels much higher than these "background" levels.

Question 10. VA's response to a pre-hearing question on the IOM Update 2008 committee's five most reliable mortality studies provided a list of risk factors that these studies took into account. However, none of the additional risk factors listed in VA's response are associated with developing IHD.

• How did the Working Group and the Task Force describe the strength of this evidence?

Response. The five studies listed in response to the pre-hearing questions were the five mortality studies that were utilized in the deliberative process. This information was in response to a question asked specifically about mortality studies. Because they are based on death certificates, mortality studies do not contain information regarding confounders other than age (the primary determinant of development of IHD) and gender. This is a limitation of all mortality studies, not just those related to Agent Orange.

Question 11. In the March 25, 2010, proposed rule, VA assumed a 60 percent disability rating for IHD based on the assumption that the level of disability of Vietnam veterans with IHD "would mirror the degree of disability for the current Vietnam veteran population on VA's rolls." Please clarify whether VA selected the mean, mode, or median value of the degree of disability of the current Vietnam veteran population for the proposed cost estimate of the IHD presumption, along with the basis for this choice.

Response. The 60 percent disability rating for Vietnam era Veterans with IHD that VA selected was the mean evaluation (rounded up) based on data available when the initial cost estimate was prepared for the proposed rulemaking in November 2009. VA elected to use the mean evaluation based on program judgment. As

noted in the response to the next question, when the costing was revised for the final rulemaking, more complete data was available.

Question 12. VA's August 31, 2010, final rule cost analysis included a modified assumption of a 50 percent degree of disability for IHD, as opposed to the 60 percent degree of disability assumed in the March 25, 2010 proposed rule. How does this assumed degree of disability relate to the ratings for Vietnam veterans currently service-connected for an IHD-specific disability?

Response. The modified assumption of a 50 percent degree of disability for IHD was based on actual data for 54,576 known in-country Vietnam Veterans with service-connected IHD (diagnostic codes 7005, 7006, 7017, 7018, 7019, 7020). Of the 54,574 Veterans, 1,514 were rated at 0 percent and were excluded from the analysis because a minimum of a 10 percent rating is required for a presumptive condition. Of the remaining 53,062 Veterans, the mean degree of disability was 49 percent.

Question 13. The cost analysis for the August 31, 2010, final rule contained a modified assumption that 60 percent of new IHD enrollees will be designated as Priority Group 1 veterans and 40 percent will be designated as Priority Group 2 veterans, as opposed to the designation contained in the March 25, 2010, proposed rule, which assumed a designation of Priority Group 1 patient, aged 45–64, for all new IHD enrollees. Please provide an explanation of this difference between VA's assumptions in the two cost analyses.

Response. The cost analysis for the final rule was revised based upon the new estimate, which reduced the projected average disability rating from 60% to 50%. VA reviewed the new service-connected rating distribution and determined that it was no longer appropriate to assign a single priority group for these enrollees given the substantial difference in annual health care costs associated with various priority groups ($14,608 for Priority Group 1 (PG1) versus $6,064 for Priority Group 2 (PG2)). We believe the revised estimate provides a better approximation of the health care costs that VA will incur for these Veterans.

Question 14. VA's June 29th letter provided the cost information for IHD-specific diagnostic tests and procedures used in the estimate of the overall care cost of adding IHD to the list of presumptions. Were costs for these tests and procedures factored into the final cost estimate that is described as being based on the average health care costs of Vietnam veterans in Priority Groups 1 and 2?

Response. VA considered the average costs for compensation examinations understanding that required testing is reflected in these costs when required. We believe this is an accurate methodology for estimating exam costs considering that VA can utilize previously performed test results (both from within VA and from private sector sources) to support the disability determination process. The actual health care costs by priority group provides an appropriate representation of the diagnostic testing that may be required to specifically support ongoing diagnosis and treatment of this Veteran population.

Question 15. Dr. Jonathan Samet, Chair of the IOM Committee that reviewed the presumptions process, suggests that openness and transparency in the process are important. Allowing those outside of VA to better understand how this decision is made may increase their support for the result. Are there ways to create opportunities to inform the public's opinion on the advice that the Secretary receives and how the Secretary responds to such information, while still promoting a robust internal discussion at VA?

Response. While VA believes the current process provides a great deal of transparency and opportunity for public input, we are also committed to pursuing appropriate new ways to enhance transparency for Veterans and the public concerning the determination of presumptions of service connection. Some ways VA is now working to improve transparency include Veterans' newsletters and information provided on VA's Web sites.

While we are committed to an open and transparent process, VA has concluded that VA-internal discussions are also needed to maintain an open and candid exchange of views during the decisionmaking process. In addition to VA's internal discussions, there are opportunities for the public to participate in the process. For example, when committees of the IOM are engaged in their scientific reviews for VA, they routinely hold open meetings during which the public is invited to comment. This includes when VA makes its charge to each IOM Committee before they undertake their reviews. Also, the public has an opportunity to provide comment during the rulemaking process when notices are posted in the *Federal Register*. VA's responses to these comments are provided after careful consideration by the Department.

Question 16. VA's written testimony noted that major risk factors and the prevalence of heart disease were considered during the decisionmaking process. How and

to what extent did VA consider other known risk factors for developing IHD that were not taken into account in the studies relied upon for establishing the IHD presumption?

Response. The relative contribution of different risk factors to the development of IHD was beyond the scope of the legislative mandate or the available studies. VA's charge under the Agent Orange Act was to determine if herbicide exposure was also a risk factor for IHD. The available evidence met the standard of association established by the legislation. This standard was met despite the multifactorial nature of IHD risk facts. With this in mind, the VA did not consider risk factors other than those that are most closely associated with IHD, such as family history, hypertension, and obesity. Other risk factors would be so insignificant as to render their consideration meaningless.

Question 17. Section 1116(f) of title 38, as added by the Agent Orange Act, provides that a Vietnam veteran shall be presumed to have been exposed to an herbicide agent during service in Vietnam, "unless there is affirmative evidence to establish that the veteran was not exposed to any such agent during that service." What type of evidence does VA regard as affirmative evidence in this context, how does VA determine that such evidence exists, and how many times has VA precluded a presumption for individual veterans on the basis of such affirmative evidence?

Response. The statutory mandate at 38 U.S.C. § 1116(f) provides for the presumption of exposure to certain herbicide agents for any Veteran who, "served in the Republic of Vietnam during the period beginning on January 9, 1962, and ending on May 7, 1975." VA regulations at 38 CFR § 3.307(a)(6)(iii) interpret the term "service in the Republic of Vietnam" to include service involving, "duty or visitation in the Republic of Vietnam" during the specified date range.

Examples of duty in Vietnam would include service with combat or support units operating on the ground in Vietnam and service with riverine units operating on Vietnam's inland waterways. Examples of visitation in Vietnam would include attendance at strategic command meetings held in Vietnam by military personnel stationed outside the country, shore leave in Vietnam for Navy personnel serving aboard offshore vessels, and temporary aircraft landings at airfields in Vietnam for personnel in route to other locations.

The presumption of herbicide exposure is broadly applied to all Veterans who were present in Vietnam because there generally is not sufficient information to correlate movement of troops, let alone individuals, with herbicide application in a manner sufficient to rule in or to rule out the possibility of such exposure. This fact makes it very difficult for VA to determine there is "affirmative evidence" that a Veteran was not exposed to herbicides during his or her time in Vietnam. Further, VA generally does not seek to develop evidence for the purpose of disproving a Veteran's otherwise valid claim for benefits. Accordingly, "affirmative evidence" to rebut the presumption of herbicide exposure generally could be found only if the evidence of record showed that, although the Veteran was physically present in the Republic of Vietnam, the circumstances of his or her presence were incompatible with the reasonable possibility of herbicide exposure. VA does not track claims that are denied based solely on affirmative evidence for non-exposure to herbicide agents.

Question 18. VA's written testimony states that IOM noted in its Update 2008 that "although some of the studies did not adequately control for certain risk factors, those risk factors were unlikely to explain the significant increased risks detected in the studies." I understand that IOM discussed the effects of only two uncontrolled IHD risk factors—BMI and smoking—and discussed them in the context of cardiovascular disease, as opposed to ischemic heart disease. IOM stated that "confounding by smoking could not explain RRs [relative risks] above 1.4," implying that a study that does not control for smoking must consider that smoking is potentially responsible for an RR up to 1.4. I understand that IOM did not discuss effects occurring when several major risk factors for a disease are uncontrolled in a study, further complicating examination of any association between IHD and dioxin exposure.

Did the Working Group or the Task Force discuss the multiple complicating effects of uncontrolled risk factors in efforts to weigh the credible evidence for and against the association?

Response. The Working Group and Task Force discussed the impact (confounding effect) of risk factors extensively during its deliberations. Controlling for confounding is difficult to impossible in mortality studies (five of the nine studies were mortality studies). Each of the studies considered as credible by IOM has strengths and weaknesses. When considered together, a consistent pattern emerges that exposure to dioxins, such as TCDD, increases the chances of developing ischemic heart disease. The most persuasive evidence is found in those studies in which increasing

levels of TCDD measured in serum are associated with increased risk of developing disease. These cohorts with measured TCDD levels, particularly in the Air Force Ranch Hand study, were well controlled for some important confounders and conclusively showed that risk for ischemic heart disease increased with increasing tissue levels of TCDD. Biologic plausibility demonstrated with animal models on a repeatable experimental basis adds additional important evidence that exposure to dioxins is a cause of accelerated atherosclerosis leading to ischemic heart disease.

Question 19. VA's written testimony stated that "[t]he language and legislative history of this act made clear that it did not require evidence of a causal association, but only credible evidence that herbicide exposure was statistically associated with increased incurrence of the disease. The Act further specified that, in determining whether a positive association exists, VA must consider the IOM's report and any other sound scientific and medical evidence available to VA."

Did the Working Group or the Task Force review additional health studies, disease registries, or other public health data containing reliable health information on Vietnam veterans to determine whether Vietnam veterans have an increased occurrence of IHD compared to the general population?

Response. The Working Group and Task Force consulted a cardiologist and other VA subject matter experts experienced with the health effects associated with exposure to Agent Orange. The Work Group and Task Force also considered information that was published after the IOM cutoff date for articles. One of these articles was *Dioxins and Cardiovascular Disease Mortality* authored by Olivier Humblet, Linda Birnbaum, Eric Rimm, Murray A. Mittleman, and Russ Hauser and published in the November 2008 Environmental Health Perspectives. Recent National Health and Nutrition Examination Survey (NHANES) data on the prevalence of IHD in various age categories were also reviewed.

Question 20. VA's written testimony noted that there is a possibility that decisions on presumptions for specific diseases can be reviewed. Have any previously established presumptions been subsequently reviewed by VA to determine whether scientific and medical evidence continues to suggest a positive association with dioxin exposure?

Response. The Agent Orange Act of 1991, and the statutory directives at 38 U.S.C. § 1116, grant the Secretary of VA discretion to determine whether or not there is a positive association between the occurrence of a disease in humans and exposure to certain herbicide agents. The National Academy of Sciences' Institute of Medicine (IOM) reports, Veterans and Agent Orange, issued every two years, are specified by law as an important source to be considered when making such determinations. The Agent Orange Act contemplates that the Secretary will review the evidence concerning each disease discussed in the IOM reports and remove presumptions that are no longer supported by the available medical and scientific evidence.

This review process occurs regularly with the publication of each new Veterans and Agent Orange report update released by IOM. These reports are closely followed by VA. Each new report describes relevant studies done since publication of the previous report and, based on these, provides either a continuing confirmation of a disease's prior herbicide association status or changes a disease's association status. As a result of this process, a number of diseases, such as IHD, have received an upgraded association status. Through these reports, VA is able to monitor and review the status of diseases already presumptively associated with herbicide exposure and evaluate whether a disease should remain on, be deleted from, or be added to, the presumptive list. To date, reviews of these reports have provided no basis for removing a presumptive disease from the list.

Question 21. Would there be value to VA pursuing the approach taken by the Australian Government of seeking to address scientific uncertainties regarding the health of Vietnam veterans by carrying out health studies that might identify diseases occurring at a higher prevalence in that population than in the general population that might be associated with the Vietnam experience, in general, rather than with a specific causative agent?

Response. Differences in prevalence of disease between Vietnam Veterans and the general population can be derived through well-designed studies that make comparisons in health outcomes and mortality experience between these groups. Studies of this type are important and VA is able to derive answers at this level of inquiry through several study designs. Mortality studies can be used to compare the experience of deployed Veterans with age and gender matched civilian populations or non-deployed Veteran populations. In the past year, VA has worked with the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics to enhance the questions used in CDC population based studies (e.g.

NHANES) of the general U.S. population to help identify with greater precision those survey participants who served in the military. This will help, over time, to allow comparisons between Veterans and the general population on national health related surveys. Additionally, VA has implemented rigorous studies (such as the Army Chemical Corps Study) which allow for comparisons between Vietnam Veterans and non-deployed Veterans. These types of studies have provided valuable information on health related issues of Vietnam Veterans over time.

Question 22. I was encouraged by VA's emphasis on both the importance of tracking exposures and surveillance of those exposed. Such measures hold the promise of impacting the need for future presumptions. Please describe VA's current efforts toward this goal and any progress VA has made toward collecting exposure data from DOD and establishing surveillance programs to monitor the health of veterans known to have been exposed during past and current wars.

Response. The DOD/VA Deployment Health Working Group (DHWG) is composed of environmental health experts from both VA and DOD who collaborate in establishing surveillance programs to monitor the health of Veterans exposed to potential toxicants. This group reports to the VA/DOD Health Executive Council (HEC) and has a specific mandate to coordinate efforts to increase health surveillance information sharing, track research initiatives on deployment health issues, and create annual joint health risk communication products.

One example of such a program is the medical surveillance program for those possibly exposed to sodium dichromate in Iraq at Qarmat Ali. VA has already contacted Veterans known to have been at Qarmat Ali by phone and offered them participation in the program. Veterans, active duty personnel and DOD civilians will also be contacted by mail. They will receive specific instructions on how to enroll in the Qarmat Ali medical surveillance program. This program includes both initial and follow-up examinations. If any abnormalities are found, the Veteran will be referred to the proper specialty service. The intent of this program is to closely monitor the health of Veterans and prevent the development of diseases known to be caused by sodium dichromate.

Question 23. In response to a question from Senator Sanders with respect to your knowledge of any health studies of individuals exposed to herbicides in Vietnam, you stated that "[VA has] just restarted a long term study of Vietnam veterans and Agent Orange. It is a study that continued up until about 2000, and then for lack of emphasis, it lost priority. [VA has] just restarted [its] effort to begin that study again. It is looking at the long term effects of Agent Orange on Vietnam veterans."

I am interested in learning more about this study, and request the following information:

- Date study initially began
- Date study was suspended and reason(s) for suspension
- Date VA resumed study
- Data elements being collected
- Data sources
- Vietnam veteran populations being examined (e.g., specific units, locations, etc.)
- Number of participants in each group being examined, including control groups
- Characteristics of study participants, including control groups
- Selection methodology of study participants, including control groups
- Previously published or unpublished preliminary and/or final study results
- Public and private entities partnering with VA to carry out study
- Date that VA anticipates using any of the study findings
- Study costs and funding amounts and source(s)

In addition to the above information, I request that VA provide the Committee with quarterly updates on the status and findings of this study.

Response. This study is related to Post Traumatic Stress Disorder (PTSD). In 1988, the National Vietnam Veterans Readjustment Study (NVVRS) provided an extensive report of disabilities including PTSD in Vietnam Veterans. The researchers at the Research Triangle Institute published a book titled "Trauma and the Vietnam War Generation: Report of Findings From The National Vietnam Veterans Readjustment Study" (the authors are Richard A. Kulka, William E. Schlenger, John A Fairbanks, Richard L. Hough, B. Kathleen Jordan, Charles R. Marmar, Daniel S. Weiss, and David A. Grady). An unpublished report of findings was provided to VA in two volumes, titled "Contractual Report of Findings from the National Vietnam Veterans Readjustment Study" in November 1988. Volume I contains an executive summary, description of findings and technical appendices. Volume II contains tables of findings.

In 2000, Congress required VA to use an external vendor to conduct a longitudinal follow-up study of NVVRS, and call it the National Vietnam Veterans Longitudinal

Study (NVVLS). VA contracted in 2001 to conduct NVVLS. However, delays, escalating costs, and concerns about contracting practices prompted suspension of the study and a VA Office of Inspector General (OIG) audit in 2003.

To address Congressional concerns and respond to increasing interest in understanding the long-term effects of PTSD, in September 2009, VA reinstituted the process to contract for the completion of NVVLS. The contract was awarded to Abt Associates on September 30, 2010, and the study began immediately. The contract amount is $ 6,637,089 (firm-fixed price), funded directly from the Office of Research and Development budget appropriations.

Between 2011 and 2013, the awarded contractor will obtain Institutional Review Board (IRB) and Office of Management and Budget (OMB) approvals for the project and initiate the study under VA monitoring. By 2014, the data should be available for analysis and we anticipate the results will be available shortly thereafter for publication in a scientific journal.

The goal is that NVVLS will result in a credible, comprehensive report on the long-term effects of Vietnam military service including:

(1) What is the long-term course of PTSD in Vietnam Veterans?

(2) What is the relationship between PTSD and other psychiatric disorders and physical health in Vietnam Veterans?

(3) Are particular subgroups of Vietnam Veterans at greater risk of chronic, more severe problems with such psychiatric disorders, including later life onset of PTSD?

(4) What services are used by Vietnam Veterans who have or have had PTSD, and what is the relationship between those services (VA and other) on the course of the PTSD?

The new National Vietnam Veterans Longitudinal Study (NVVLS) will consist of the following four main phases:

- *Feasibility Phase:* To establish how many individuals from the original NVVRS cohort are available to participate in the NVVLS.
- *Start Up Phase:* To prepare the assessment and data collection materials, finalize protocol and obtain IRB approval.
- *Implementation Phase:* Recruit and enroll participants and conduct assessment by phone and by mail. A limited number of in-person interviews may be required to validate assessment tools and to increase the participation rate.
- *Close Out Phase:* Analyze data, prepare final reports, and deliver data to VA.

There were 2,348 Veterans from original NVVRS (1988), including both theater and era Veterans. The contractor is tasked with trying to contact, obtain consent from and survey as many of the original cohort as possible to determine willingness and availability to participate in NVVLS. The entities involved in completing the study are OMB and Abt Associates.

TIMELINE:

FY 2010

Contract Awarded	September 29, 2010
Study begins, feasibility phase	September 30, 2010

FY 2011

October:

Data transfer agreement to be completed	
Kick off meeting with Abt Associates	October 14, 2010

April: Feasibility phase to be completed

May: Start-up phase begins

FY 2012

October: Implementation phase begins

FY 2012–2013

Conduct study; monitor ongoing performance

FY 2014

Analyze data; submit final report to VA, publish results in scientific journal

The Office of Research and Development does provide quarterly updates on the status of the NVVLS to the Committees on Veterans Affairs. The timeline above provides the most up to date information on award of the contract and projected course of action that is contained in the most recent quarterly report.

Question 24. In response to a question from Senator Tester, you stated that a 10-year administrative cost estimate of $1.66 billion for the IHD presumption that was provided to you on a document at the hearing appeared to reflect a calculation error. I understand that the $1.66 billion estimate for the IHD portion of the administra-

tive costs was based on a table on page 22 of VA's August 31, 2010, final rule cost impact analysis. Please clarify the administrative costs and provide the underlying basis for each line item listed in that table.

Response. We are not certain of the origin of the $1.66 billion estimate to which you make reference. However, the table shown below expands upon the table from page 22 of VA's Impact Analysis. Please note that administrative costs are determined by the level of FTE, which is calculated based on expected workload for claims receipts. The total estimated 10-year administrative cost is $894 million.

Diseases Associated With Exposure to Certain Herbicide Agents
Administrative Costs ($000s)

Cost Element	1st Year (FY 2010)	5 year	10 year
Personal Services	*4,554	665,621	753,904
Training	-	16,856	16,856
Rent	-	99,724	108,582
Supplies & Materials	-	15,272	15,272
Total	$4,554	$797,473	$894,614

*FTE costs in FY 2010 represented a level of effort of current FTE that would be used to work claims received in FY 2010. New hiring would begin in 2011.

Question 25. In response to a question that I asked with respect to concerns that may have been raised while you were deliberating on establishing the IHD presumption, you noted that you sought open dialog and advice from several sources and that some of the information was more helpful than others, but that the process for creating presumptions is not perfect. What improvements might be made to the current process?

Response. Enactment of legislation to extend VA's timeframe to review IOM evidence would better accommodate the comprehensive review that must be conducted prior to making critical policy decisions relating to presumption of service connection.

Question 26. In response to a question that I asked with respect to any challenges faced in making the IHD determination, you indicated time constraints were a substantial challenge. I support your effort to establish a timeframe that will permit VA to conduct a thorough and independent review of the IOM report, all underlying studies considered by IOM in its review of the evidence for and against an association, as well as all other sound medical and scientific information available. What specific changes do you recommend?

Response. In May 2010, VA submitted to Congress a draft bill, "The Veterans Benefit Programs Improvement Act of 2010," section 103 of which would extend the time limits for VA's action under the Agent Orange Act to better accommodate the need for thorough analysis of the numerous complex medical and scientific issues presented in the IOM's reports and to permit effective coordination within the executive branch. Section 103 would provide that (1) within 120 days after receiving the IOM report, the Secretary would determine whether a presumption of service connection is warranted for any disease; (2) within 170 days from the Secretary's determination, VA would publish proposed rules to establish any warranted presumptions; (3) within 200 days after the Secretary's determination, VA would publish a notice explaining why presumptions are not warranted for other diseases; and (4) within 230 days after publication of the proposed rules, VA would issue final rules establishing any warranted presumptions. Further, to minimize the impact of these extended time periods on Veterans' benefits, section 103 would also provide that presumptions established under this process would take effect retroactive to the date on which the Secretary's determination was required to be made (i.e. 120 days after receipt of the IOM report).

Further, VA fully supports enhancement of exposure-tracking mechanisms within the military services so that reliable data is available for future scientific studies and reviews. The availability of this exposure data will serve as the foundation for high quality studies that will lead to sound presumptive decisionmaking. If this data, along with other scientific data, is available for review, then the current presumptive framework appears to be sufficient to render equitable decisions. VA will continue to analyze various options provided by IOM and other experts regarding the presumptive decisionmaking process.

Question 27. Treatments for heart disease range from medications and lifestyle counseling up to high-tech surgeries. What steps is VHA taking to be prepared to absorb the increased workload that will result from the IHD regulation?

Response. Informed by a national advisory workgroup of VA cardiologists, an algorithmic approach to confirm and /or diagnose IHD and assess disability has been developed. The goal of this algorithm was efficiency both in terms of providing the Compensation and Pension (C&P) data for Veterans, but also to optimally utilize VA resources. More specifically, the algorithm takes maximum advantage of medical information in the Veterans' Electronic Medical Record. This information would include diagnostic tests, medications, procedures and health care provided in outpatient visits and inpatient admissions that the Veterans have already had. The algorithm also suggests less resource-intensive methods for obtaining ratings information (e.g. patient interviews to assess metabolic equivalents, chest X-rays and EKGs to assess for cardiac enlargement and hypertrophy). When combined with information provided by the Veteran for care and testing outside of VA, the resulting data available to providers will help avoid any unnecessary or duplicative testing. Despite these measures, it is expected that Veterans will require additional testing, but this will largely consist of noninvasive testing such as echocardiography or treadmill tests. Moreover, the increase in testing requests is likely to rise for some period of time, but then decrease toward prior levels. However, there may be some facilities where capacity could be an issue, and these facilities may need to request additional resources from the Veterans Integrated Service Network (VISN) to ensure timely response to requests for tests. If the VISN cannot provide these resources, a request will be made to VA Central Office. It is our intention to closely monitor workload and intervene to provide additional resources as needed.

Question 28. I am pleased to note that the final regulation corrected the draft regulation with respect to the numbers of those potentially affected by heart disease and the resulting cost. Are you satisfied that the cost estimate is now accurate?

Response. The Final Regulation Preamble contains a discussion of a revised cost forecast that is discussed in detail in the Impact Analysis. Since, as discussed in the Preamble, cost forecasts are based upon data that is available at the time the forecast is prepared, we are confident that VA has identified the appropriate forecasted funding levels needed at this time.

Question 29. I understand that VA will rely, in part, on examinations by non-VA health care providers in order to conduct some of the examinations that will be necessary to establish that a veteran has heart disease. Are there any concerns about either the reliability of these outside exams or about VA's ability to secure and utilize the results of those exams?

Response. VBA's goal is to have Disability Benefit Questionnaires (DBQs) replace the current 67 C&P Examination worksheets. Upon completion of the approval process, the DBQs will be available on VA's internet site and accessible for use by private physicians. VBA will not be requesting examinations from non-VA healthcare providers. The use of DBQs by non-VA clinicians is merely another option available for Veterans to submit medical evidence in support of a claim.

VA's DBQ Project Management Plan requires that all DBQs be made available to VA or non-VA clinicians of the Veteran's choosing, with the exception of initial evaluations of Post Traumatic Stress Disorder. A properly completed DBQ will reflect the clinician's examination and evaluation of the Veteran's disability and should provide the information VA needs to evaluate the claim. Accordingly, a DBQ from a private clinician that is sufficient for VA rating purposes may obviate the need for an examination conducted by VA or VA-contractor personnel.

The use of DBQs, as opposed to C&P Examination worksheets, offers several advantages. First, DBQs collect only essential rating criteria related medical information that a Rating Veterans Service Representative (RVSR) would need to render benefit claim decisions. The expected results are more timely and standardized benefit claim decisions. Second, the use of the DBQs by private physicians is expected to reduce the number of VA exams needed, which will improve processing timeliness. Finally, the use of DBQs will allow for a more focused examination. In cases of IHD, performing an examination using a DBQ, as opposed to a current C&P heart examination worksheet, is expected to be at least 50 percent more efficient.

In sum, DBQs provide additional medical evidence from a Veteran's VA or non-VA physician that RVSRs may use in rendering decisions on benefit claims. DBQs are not the sole piece of evidence used in rendering benefit claim decisions. Rather, DBQs are considered with the totality of other evidence contained in the Veteran's claims file. In cases where DBQs received are of questionable reliability or are otherwise insufficient for rating purposes, VBA will request a VA examination under the provisions of 38 CFR § 3.326 and the Veterans Claims Assistance Act.

Question 30. If credible evidence relating to a disease is made available to VA that is not in the IOM report, does VA discuss the credibility of such evidence with IOM prior to making a presumption determination?

Response. The Agent Orange Act of 1991 and the statutory directives at 38 U.S.C. § 1116 grant the Secretary of VA discretion to determine whether or not there is a positive association between the occurrence of a disease in humans and exposure to certain herbicide agents. The IOM periodic reports, Veterans and Agent Orange, play a significant role in making such determinations.

By law, "all other sound medical and scientific information and analyses" that are available to the Secretary are also considered. However, because IOM is a reputable and reliable scientific organization and because its mission in this case is to review and evaluate all studies on the health effects of herbicide exposure, it would be unusual that "credible evidence" relating to a disease and herbicide exposure would be unknown to IOM or excluded from its reports. However, new evidence may be developed subsequent to issuance of an IOM report.

In the event that such credible evidence not considered by IOM is made available to VA, VA is not required to discuss its credibility with IOM, but may seek to do so if warranted. For example, following receipt of IOM's Agent Orange 1998 Update (released in February 1999), VA asked IOM to evaluate two new studies concerning type II diabetes that had been released too late for consideration in the 1988 update. IOM provided its analysis of the new reports in October 2000, ultimately leading to VA's issuance of a presumption of service connection for type II diabetes. Accordingly, while IOM's insights may be helpful, its processes for formulating and providing views may interpose substantial delays incompatible with statutory time limits for VA determinations.

Question 31. When IOM modifies the categorization of a disease based on newly published evidence, does VA conduct an independent review of such evidence or rely solely upon IOM's analysis?

Response. VA carefully reviews all evidence considered when IOM modifies the categorization of a disease. VA assembles a team of medical and legal experts to review not only the IOM findings, but also the actual scientific evidence, (i.e., studies, reviews, statistics, etc.) which IOM considered in making its conclusions.

Question 32. In an article in the July 2010 edition of the Agent Orange Review, you are quoted as saying: "We must do better reviews of illnesses that may be connected to service, and we will." Do you have any specific suggestions or ideas in mind to accomplish this?

Response. VA plans to pursue several avenues of inquiry to better understand what illnesses affect Veterans and to what extent these are related to their military service. By conducting detailed long term follow-up studies, we can understand specific impacts, as we are doing with Vietnam Veterans of the U.S. Army Chemical Corps. A study of Army Chemical Corps Veterans is under development. Part of the study will carefully review a sample of medical records to establish whether specific diagnoses were recorded by health care providers. In addition, this same group of Veterans will be asked to participate in physical exams to measure cardiovascular and respiratory health outcomes. Another approach that VA has taken, and continues to pursue, is the identification of a large group of Veterans known to have served in a conflict and a similar group of Veterans without the same deployment experience. The groups are surveyed to assess health and illness outcomes, health care utilization, and other indicators of well-being. A sample of 60,000 Veterans, half of whom returned from Afghanistan and Iraq, were enrolled in a health study that used survey methodology to learn about their health experience and concerns. Data collection for this study, The National Study of a New Generation of U.S. Veterans, was recently completed and preliminary results are expected in 2011. VA has also partnered with the CDC to collect information through broad based population surveys that will allow for better comparisons between the health outcomes of Veterans and general population groups.

RESPONSE TO POST-HEARING QUESTIONS SUBMITTED BY HON. JIM WEBB TO HON. ERIC K. SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Question 1. Secretary Shinseki, when adjusted for age, smoking, cholesterol, body mass index, and other major contributing factors, what is the increased rate of ischemic heart disease (IHD) in Vietnam veterans when compared to the general population?

Response. Currently, there are no studies in the literature that compare estimates of the prevalence of IHD among Vietnam Veterans to the general population. The studies cited by the Institute of Medicine (IOM) reflect the evidence of a statistical

association of IHD and Agent Orange and support the presumption for ischemic heart disease. The study designs demonstrate limited or suggestive increased risk associated with Agent Orange. These studies neither provide, nor rely on, other risk factors in the population impact of disease. They do not allow for comparisons to other risk factors in the general population.

Question 2. Secretary Shinseki, in response to pre-hearing questions you stated that the positive association standard is not perfect, but that it has resulted in more Vietnam veterans obtaining health care as a result of herbicide exposure. Understanding that health care benefits yielded by the presumption process are important, and that 30 percent of service-connected veterans rely on DVA health care, the question arises regarding levels of disability compensation for systemic illnesses whose onset is affected by other factors and typically occurs with a latency period of thirty to forty years. Please provide the Committee your view on the issue of how best to determine the level of such compensation, separate from the issue of access to medical care.

Response. Under the provisions of title 38, U.S.C. § 1155, disability compensation is to be based on the average impairment in earning capacity due to injury or disease incurred in or aggravated by active military service. VA maintains a Schedule for Rating Disabilities consisting of disabilities in 15 body systems with associated levels of severity from zero to 100 percent that represent the average impairment in earning capacity for any listed condition.

There is no basis in law for compensating Veterans for disabilities in a bifurcated system that would be based on relative risk for developing any particular disease. Such a system, if able to be developed, would be fraught with inconsistency and add substantial time to the already lengthy claims process.

Question 3. Secretary Shinseki, in correspondence with the Senate Committee on Veterans Affairs (SVAC), Dr. Mary Paxton, Study Director, Institute of Medicine (IOM) Update 2008 said that the three additional studies (Ha, et al.; Consonni, et al.; and Calvert, et al.) included in the 2008 report "did not show strong and statistically significant associations with IHD" and, in fact, provided weaker evidence than the six studies relied upon and determined as inadequate evidence by the IOM Update 2006 Committee. Given the weak nature of these new studies, did the Department ask the Update 2008 Committee specifically how and why it reached a different determination on the strength of the association between herbicides and IHD than the Update 2006 Committee?

Response. There were two, not three, additional studies: Ha and Consonni. Calvert was published in 1998 and also was considered by the 2006 committee. The Calvert and Ha studies, while not providing a statistically significant association, still had results and conclusions that supported the determination of a positive association when taken into consideration with all of the other studies. This includes a very substantial body of toxicologic literature which elucidated the pathophysiologic mechanism by which 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) damages arteries and leads to ischemic heart disease.

The three studies referred to by Dr. Paxton (see quote below) were the Air Force Health Study (AFHS), Calvert and Ha.

> "* * * The three studies having individual measurements of serum dioxin levels that did not show "strong and statistically significant associations with ischemic heart disease" were AFHS (2005), Calvert et al. (2008 [should be 1998]), and Ha et al. (2007)."

Except for the Ha study, which VA agrees provides only supporting evidence, the other two studies referred to by Dr. Paxton were reviewed by the 2006 committee. (The quote above incorrectly states the date of publication for the Calvert study. It was 1998, rather than 2008).

IOM gives the explanation for why a different decision was made by the 2008 committee on pages 628–630 of the published report. VA referenced this explanation in testimony before the Committee on September 23, 2010. VA was well aware of and understood the legitimate scientific reasons for a different decision:

1. Two new epidemiologic studies (Consonni and Ha) provided additional evidence in support of a positive statistical association; and
2. Several toxicological and animal studies since Update 2006 have provided clear evidence of biological plausibility and a pathophysiologic mechanism for the development of ischemic heart disease secondary to exposure to Agent Orange.

The Committee was impressed by the fact that those studies with the best dose information all showed evidence for risk elevations in the highest exposure categories.

Chairman AKAKA. Thank you very much, Mr. Secretary. I know we all appreciate understanding more about your decision.

Will you please tell me about any concerns within VA that were raised while you were deliberating on the issue—on your decision?

Secretary SHINSEKI. By concerns do you mean about the dialog that went on inside of our process?

Chairman AKAKA. Within VA.

Secretary SHINSEKI. Well, I can say, as I indicated, we had a work group and a task force and then there were other independent views I sought. I would say it was an open dialog. You know, people were encouraged to participate fully. So in that kind of an environment you are going to have give and take on the discussions. I listened to all of it and all of it was helpful. Some of it was more key in focusing my final decision. I would say perhaps the most robust of the debate centered on ischemic heart disease for much of the same discussion that has already prevailed. I would also say that the vast majority of the medical experts who engaged in that dialog with me were solidly in support of the positive associations. So that is as much as I can describe for you about the internal process.

I will add that when I say 60 days is what the law stipulates, I would say it was a time-constrained process. The dialog was important, and I had to find a way to make sure that all views, including minority views, were shared. But the 60-day time limit was a bit constraining. One of my suggestions is that we look at a way to expand the window that the VA has to do its part of this. After all, the study that is provided to VA is a 2-year process out of the IOM. Of all the studies they looked at, we receive a report about 650 pages in length. Sixty days is a little challenging.

Chairman AKAKA. According to responses to pre-hearing questions from a witness on the next panel, 80 to 90 percent of patients suffering from heart disease have lifestyle factors such as smoking, lack of exercise, and a diet high in cholesterol. How did this affect your decision?

Secretary SHINSEKI. Well, Mr. Chairman, I do not have any data that would refute that. I think it is fair to say that for folks my age in this country, the 60-year group folks, heart disease of some kind is a fact of life for all. Eighty percent may be the right number, and I will accept that, but we are not talking about asymptomatic heart disease. The 80 percent of people who have this condition, whether it is having to control lipids through medication or the buildup of plaque in blood vessels, that 80 percent is for the most part asymptomatic.

What we are concerned about in ischemic heart disease, the 17 percent who are estimated to have symptomatic ischemic heart disease—symptomatic in the sense that there is pain associated with it or that in doing a routine activity like climbing a flight of stairs, they are exhausted and cannot do it. This is what we are talking about. It is this lesser subset that we are focused on with the ischemic presumption that we are dealing with.

Chairman AKAKA. Thank you. We will have 5-minute rounds of questions here. Let me call on Senator Johanns for your questions.

Senator JOHANNS. Thank you, Mr. Chairman.

Mr. Secretary, let me, if I might, go back a ways and just lay some groundwork here. Back when Agent Orange was so routinely used, how much of it was ultimately used in Vietnam?

Secretary SHINSEKI. Senator, this is a great question. I would say our best review of the records says that 19 million gallons of Agent Orange was dispersed over Vietnam. I accept Senator Webb's description of his area. But the records show that Agent Orange was dispersed along the DMZ and all four major military regions along the tri-border areas between Cambodia, Laos, and Vietnam, areas in the central highlands, northwest of Saigon, southeast of Saigon, along those canals and down in the delta. So it was dispersed throughout the country.

Senator JOHANNS. And typically how would it be dispersed?

Secretary SHINSEKI. Aerosol sprayed by planes. And so asking a veteran to prove that he was sprayed—many of them may not know.

Senator JOHANNS. Yeah.

Secretary SHINSEKI. I mean, it is distributed by aerosol. And unless you happen to be there when it is sprayed, you probably did not know you were in the midst of it. So it was throughout the country.

Senator JOHANNS. So if you happened to be out on patrol or you went into an area where that disbursement was made and walked through the brush and the trees and whatever else, you probably got soaked to the skin I would imagine.

Secretary SHINSEKI. I guess if you were there when the spraying went on you would probably know it if you could see through the canopies.

Senator JOHANNS. Yeah.

Secretary SHINSEKI. In some areas the canopies were 200 to 300 feet in the air and you might not see the aircraft. But I think if you moved through an area where it was used, very clearly the foliation will tell you you are in a different ground. But again, in those days I do not think most youngsters understood or realized what that meant. With the deployment of fires, artillery fires and bombing, you have in effect a landscape and sort of a moonscape. Landscape to look like the moonscape because it is devoid of trees and foliation. I am not sure youngsters could distinguish between what caused it but the facts show 19 million gallons. If you think of the big 50,000 gallon tankers that pull up at Exxon to download into the tanks underground as being a significant fuel supply or a supply of liquids, we are talking 19 million gallons, which is significant.

Senator JOHANNS. That is significant.

Now, moving ahead to this presumption and how you will handle it, the last piece of your testimony in response to the Chairman's question raises a question or two for me. What I understand you to be saying, and correct me if I am wrong, is that if I walk in and I say, I have got some elevated cholesterol, how are you going to handle that versus somebody who says, look, I have not been able to work for a number of years. Walking to the bathroom I am short of breath. I have pain in my chest. Tell me the degrees here. Kind of walk us through how you are going to handle managing this presumption.

Secretary SHINSEKI. That is a fair question. Clearly, again, we are talking about symptomatic ischemic heart disease which would be the latter condition you described. But in fairness to the first veteran who walked in, what we should be doing is accepting the fact that there is some signature here with cholesterol and at least begin the process of monitoring the health condition so that over time, if it does become of the ischemic symptomatic order, we can make decisions about whether and what kind of disabilities are involved. But if it is asymptomatic, there is no disability and until you reach a 10 percent level of disability, we are not into that discussion.

Let me just turn to the one cardiologist on the panel and see if there is more to be added here. Dr. Jesse?

Dr. JESSE. Yes. Thank you, sir. A couple of comments. While the statement was made that 80 percent of the people will have risk factors, which is inherently true, roughly one-third will have hypertension and two-thirds will not. Almost 50 percent will have a total cholesterol over 200 and about one-third will have an LDL, bad cholesterol, beyond what is acceptable. But two-thirds will not. A third will be but these two-thirds will not. So the risk factors are important but they are not able to be parsed out in this presumption of Agent Orange. But what is important, and it comes back to comments made by several of the senators, is that in the treatment of those risk factors, high quality care is imperative. Whether a veteran was in Vietnam and exposed to Agent Orange or was in World War II or is in a current conflict, we take the mitigation of risk for cardiac disease very seriously. We have performance measures in place that are at par or better in most cases than any other health care system in this country for the treatment of hypertension, the treatment of lipids, the treatment of diabetes. Mitigating the risk is the best that we can do.

We have a program called MOVE, which is focused at getting the veterans to increase their physical activity. So all of these are taken very seriously and the VA does it very well. Can we do better? Yes. We are trying to do even more but we clearly are at attention for these.

Senator JOHANNS. Thank you. That is helpful. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Johanns.

Senator Murray.

Senator MURRAY. Thank you very much, Mr. Chairman. Mr. Secretary, in his statement, the former Secretary Principi made some suggestions: to improve the Agent Orange Act of 1991, including some new studies in dioxin level blood testing; to direct the IOM to provide VA with an estimate for latency period for Agent Orange-related illnesses; and finally, asking IOM to estimate the number of Vietnam veterans who might be affected by an illness linked to herbicide exposure. I wanted to ask you what your thoughts are on those recommendations, and how do you think we ought to move forward from here?

Secretary SHINSEKI. Let me call on Dr. Jesse to talk about the specific technical aspects of those recommendations and then let me conclude.

Dr. JESSE. If we move to the issue of attributable risk it becomes very difficult to do that. In the charge of the Institute of Medicine, they have been since the inception of their engagement—it has been asked to answer that question. They very specifically, in each of their biannual reports, have said we cannot do that. If we go back to causation, which inherently makes sense, it is actually the wisdom of Congress in the 1991 Act that moved beyond making that decision. Then finally, in terms of trying to assign how many veterans might or might not be affected because of this, if you cannot do attributable risk and we cannot do causation, it makes that very difficult to do. We are back in the same position of even trying to define the highest exposed populations.

Senator MURRAY. Mr. Secretary, how do we move forward?

Secretary SHINSEKI. Dr. Cassano.

Dr. CASSANO. Senator, the question is on measuring levels of TCDD. Unfortunately as time goes by these levels drop. You have some very good determined levels from 1980 and 1987 in some of the studies. But at this point the residual from those exposures in Vietnam are now approaching the level of the residual exposure in the general population because TCDD was used in this country.

The other important point regarding that is that we do not know when the damage to the cells actually occurred that eventually develops into clinically significant disease. It could have happened in the 1960s. It could have happened in the 1970s. And the Air Force Health Study shows that in showing that increased disease risk correlates with 1980 and 1987 levels.

Senator MURRAY. OK. Which goes to——

Secretary SHINSEKI. Let me just wrap here. There is one issue you asked about also which was latency.

Senator MURRAY. Yes.

Secretary SHINSEKI. I would just offer that there has been some engagement on latency in the past, and I forget the disease—30 years—what was it?

Dr. JESSE. In the original presumption, pulmonary cancers were given a latency period of 30 years. That latency period was actually withdrawn by Congress. When the Institute of Medicine was again asked to address that they said there was no sound basis for it continuing. Now, some of the presumptions, like chlorachne would be expected to be present at the time of high exposure and not appear many years later. So there is certainly a rationale for doing that. But broadly, for ischemic heart disease in particular, you cannot put a time period on this.

Secretary SHINSEKI. I just wanted to get that discussion out.

Senator MURRAY. Good, thank you.

Secretary SHINSEKI. Senator, I think this is a tough question. This is what we are wrestling with. I would say that our best opportunity to set up an outcome different than the one we are dealing with today is sort of what you suggest, and that is when an exposure occurs we ought to be looking for it, first of all. When an exposure occurs we ought to acknowledge it. It does not mean that we are into the discussion of disabilities. It means that we have acknowledged that an exposure occurred. What we want to do next is much like what Senator Webb described, and that is identify the units who were exposed, get a registry of everyone who was in that

unit, begin a surveillance over time that will help us provide better treatment for veterans, and in the long run you address the outcome issue that has a cost associated with it.

As I am fond of saying, you either believe in the efficacy of medicine or you do not. I happen to be one who believes in the efficacy of medicine which is, if you diagnose and treat, you influence the outcomes of those patients. That is what we in VA are very much into here, the prevention model: early diagnosis and treatment. And as these diseases reveal themselves, we treat them and then begin to modify the severity and the incidents. I think that in the long run will address the other question about cost.

Senator MURRAY. Right. I think that it is something you and I have talked about before, too. Denial of something at the time never gets us to a good place later. We sort of have a history of that when it comes to warning this country. I think that—I hope that is a lesson we all learn and are thinking about now as we have troops overseas in Afghanistan and Iraq.

My time is——

Secretary SHINSEKI. May I follow up, Senator?

Senator MURRAY. Yes, please.

Secretary SHINSEKI. I guess this is the next comment. That is to look around and see where we have the opportunity to change the outcome and not have the Agent Orange example repeated.

We do know about burn pits in Iraq.

Senator MURRAY. Right.

Secretary SHINSEKI. Operationally we have departed Iraq. Opportunities to figure out where and what was the exposure, and to which units; we are losing the opportunity to do that.

Senator MURRAY. Every day.

Secretary SHINSEKI. Each passing day. Qarmat Ali, same thing. So this is the tough part of the business: identifying that exposure and then being willing to do something about it early on.

Senator MURRAY. Well, good. I want to keep working on that and I appreciate that. My time is up. Mr. Secretary, while I have you, real quickly, we have a severe problem in my State in a very rural area on the Olympic Peninsula with access for our veterans. A high number of veterans coming home live there miles and miles and miles from care with very jammed facilities, and I want to talk to you later about perhaps getting a full service CBOC or a Vet Center there to begin to deal with some of those folks who are home and have—are not getting the care that they need. So I will contact you.

Secretary SHINSEKI. Happy to have that discussion.

Senator MURRAY. Thank you.

Chairman AKAKA. Thank you very much, Senator Murray.

Senator Sanders.

Senator SANDERS. Thank you, Mr. Chairman. This is a very difficult discussion because we are asking the Secretary to play God. I happen to think you are doing a great job but you are not God. None of us are.

And the difficulty is that in the old days, before we knew what we knew today, everybody recognizes that if a soldier was wounded, lost a leg, lost an arm, there was no debate. That was a cost of war and that soldier gets all the care he or she needs plus all

the benefits. The difficulty is that the world has changed very significantly as a result of chemical exposure. Let us not forget that when Agent Orange was first used, our friends at Dow, Monsanto, and all of those companies, they said this was benign; there is not a problem.

Am I correct on that, Mr. Secretary?

Secretary SHINSEKI. My recollection also.

Senator SANDERS. I am certainly sure the military would not have used this chemical if they thought otherwise. By the end of the day we used a poison and we poisoned our own people. Who is smart enough to know exactly what the impact—would somebody have come down with a heart disease or other illnesses if they had never been to Vietnam? The answer is of course they would have. On the other hand, because somebody was in Vietnam and exposed to Agent Orange to some degree, combine the exposure to genetic predisposition, for example, could that have led to one or another illness? Of course it could have. Who is smart enough to make the determination as to exactly what the balance is? I am not. I do not think you are. Nobody is.

What presumption is about is to say you, soldier, put your life on the line. We are going to give you the benefit of the doubt. We are going to assume that if you come down with an illness that we can relate to exposure—in this case to Agent Orange—we are going to make the presumption that was the cause. Maybe it was not but that is the presumption we are going to make. And I think that is the right presumption.

In terms of Agent Orange—now is not the time to go into a lengthy discourse on it. Our history on the subject as a government has not been particularly good. There has been a lot of denial, as I mentioned earlier, on the part of the government against Vietnam vets who originally came back. I was in Vietnam a few months ago. We were in Da Nang, which was one of the hotspots. To the best of my knowledge, interestingly enough, Mr. Chairman, I believe—and somebody correct me if I am wrong—that we have really not done a thorough study of the impact of Agent Orange on the Vietnamese people. Not necessarily because, you know, we are concerned about everybody in the world, but to learn from their exposure what it means to Americans.

I do not think that was an accident. I think originally, especially in the years after the war, the attitude was the less we know, the better we will be. Because the less we know means that when people come forward and say I am sick because of exposure, we can say, well, we really do not know. But I am kind of curious, so the Secretary or anybody on the panel, does not it seem strange that the people who were most exposed—people who were dumped on who were eating food, drinking water in Vietnam, in addition to our own soldiers—that we have never done a thorough study about the impact of Agent Orange on the people of Vietnam.

Am I wrong on that or am I right about it? Does somebody want to comment on that?

Secretary SHINSEKI. Senator, I am not familiar with studies on the people of Vietnam. There may have been studies. I am just not personally aware of them, but I will have a look at that and provide you with an answer. I would also say that we have just re-

started a long-term study of Vietnam veterans and Agent Orange. It is a study that continued up until about the year 2000, and then due to lack of emphasis it was a lost priority. We have just restarted our efforts to begin that study again which is looking at the long-term effects of Agent Orange on Vietnam.

[Response was not received within the Committee's timeframe for publication.]

Senator SANDERS. If somebody on the panel could answer my question. Would not one think that if we were worried about American soldiers and their exposure you would take a look at the impact of where Agent Orange was dropped on the Vietnamese people to learn their suffering or non-suffering. Am I missing something there or would that be a legitimate scientific quest?

Dr. JESSE. I will try to answer that. Would it be a legitimate scientific quest? Obviously, yes. Could it be done, I think, is another challenge. And just as we are not able to precisely identify the veterans who were maximally exposed, it would be equally and probably more difficult to actually identify which of those folks in Vietnam were also——

Senator SANDERS. Actually, Doctor, I think not because our soldiers came and went, were dispersed. There are people who live in given communities and so forth. But does anybody—alright. OK.

That was the point I wanted to make. I think we have put the Secretary in a very difficult position and I think he has done the right thing. So I think we have got to give the benefit of the doubt to the people who served.

Thank you very much, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Sanders.

Senator Webb.

Senator WEBB. Thank you, Mr. Chairman. Mr. Secretary, I have three or four questions and we have a very short time period here. I am going to try to get them all in but they are, again, an attempt to clarify the decisional process and also to clarify for people who may be paying attention to this hearing what set of unknowns that we have been working on in order to try to bring some validity to this process.

I looked at these nine studies that you mentioned in your testimony. You are correct that all of them did adjust for age but there was a great variance in the other control factors, risk factors. Only two studies actually dealt with Vietnam veterans. One of them as I recall was Army chemical veterans; another was, I assume, Ranch Hand because it was Air Force. And I am struck by the fact that I do not know of any extensive study that actually has looked at Vietnam veterans as a whole. What you just said a minute ago about a study that was begun and then interrupted in the year 2000—are you aware of any other studies that have examined Vietnam veterans as a whole?

Secretary SHINSEKI. I am not. This is the long-term study of Vietnam veterans that to my understanding, sometime around 2000 or shortly thereafter, began to lose momentum. But we have, in an effort to answer some of the questions you have raised, recently reinitiated an effort to create that long-term look.

Senator WEBB. Right. I appreciate that there are questions about the half life of dioxin in the environment, which goes to one of the

areas that Senator Sanders was sort of hinting at with respect to Vietnam but also from what I am hearing in terms of being able to trace the dioxin or other chemicals in one's blood. Wouldn't there be a way to still examine, say, tissue damage and these sorts of things where you could determine exposure among a control group? Doctor?

Dr. CASSANO. Senator, it is very attractive to look at that type of delineation but it is not possible. There are many different numbers out there regarding what the half life of TCDD is. Actually, it is very variable from individual to individual. When you look at actual tissue damage there is no way to really say that this damage was due to TCDD and this damage was due to smoking, for instance. There is no way to tease that out. Once a cell is damaged, it is damaged.

Senator WEBB. So one of the——

Dr. JESSE. Senator——

Senator WEBB. I take your point. I am on a very short period of time here. Let me suggest something else because as Secretary Shinseki and I were discussing in the office, when we were first looking at this issue back in 1978, one of the discussions that we were having with committee staff on the House side with the Army Historical Center was to take veterans from specific units that we know had been in areas where dioxin had been sprayed and do a comparable study of them as opposed to other Vietnam veteran groups and non-veterans groups in the age group. I do not know if that is what they had begun and interrupted in 2000 or is that something you are thinking about doing?

Secretary SHINSEKI. Fair question. I will get more into this and provide you a better answer of exactly what had transpired in that previous study. I think you and I are in agreement. We need for the long term an effort to create better data than what we are working with today. But it does not change the conditions today. We have veterans who are suffering from these diseases, and the presumption allows us to accept them into our programs for treatment.

RESPONSE TO REQUEST ARISING DURING THE HEARING BY HON. JIM WEBB TO HON. ERIC K. SHINSEKI, SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

VA plans to pursue several avenues of inquiry to better understand what illnesses affect Veterans and to what extent these are related to their military service. By conducting detailed long term follow-up studies, we can understand specific impacts, as we are doing with Vietnam Veterans of the U.S. Army Chemical Corps. A study of Army Chemical Corps Veterans is under development. Part of the study will carefully review a sample of medical records to establish whether specific diagnoses were recorded by health care providers. In addition, this same group of Veterans will be asked to participate in physical exams to measure cardiovascular and respiratory health outcomes. Another approach that VA has taken, and continues to pursue, is the identification of a large group of Veterans known to have served in a conflict and a similar group of Veterans without the same deployment experience. The groups are surveyed to assess health and illness outcomes, health care utilization, and other indicators of well-being. A sample of 60,000 Veterans, half of whom returned from Afghanistan and Iraq, were enrolled in a health study that used survey methodology to learn about their health experience and concerns. Data collection for this study, The National Study of a New Generation of U.S. Veterans, was recently completed and preliminary results are expected in 2011. VA has also partnered with the CDC to collect information through broad based population surveys that will allow for better comparisons between the health outcomes of Veterans and general population groups.

Senator WEBB. I understand that. In that regard, when you are looking at disability compensation on this issue, has there been any discussion about these other risk factors as a component of evaluating one's disability? Or do you just measure the overall disability of the individual despite smoking or all the other conditions that were mentioned?

Secretary SHINSEKI. At this point, Senator, I think Dr. Cassano's insights are helpful. It is difficult to tease the level of contribution of these various confounding factors. All we know is from the studies presented, scientific and medical evidence, that TCDD attacks the vasculature of animals. That is the biological mechanism, and it exists in this case. So we know there is a contribution here. What we cannot tease out is to what degree that contribution is more significant than others. I would venture to say that——

Senator WEBB. So you are basically just taking the medical condition at the time and assigning a disability rating to it?

Secretary SHINSEKI. Assigning a disability to the conditions overall.

Senator WEBB. Right, overall, rather than breaking out one component having been TCDD.

Secretary SHINSEKI. That is correct.

Senator WEBB. I would like to get an understanding of your motivations moving toward your decision based on the 2008 report in this area. The 2006 report had stated that an association between herbicides and ischemic heart disease was unwarranted. The 2008 report concluded there was limited but suggestive evidence. Were there new studies that came into effect or what was the reason that the recommendation changed?

Secretary SHINSEKI. Let me call on Dr. Jesse.

Senator WEBB. OK.

Dr. JESSE. The 2006 report was split. They could not come to an agreement. There were two new studies between 2006 and 2008 that drove that preponderance of association much stronger to the point that the committee then agreed to elevate it to the suggestive category. So there was new information.

Senator WEBB. Was there new research or new evaluation of old research?

Dr. JESSE. No, it was new studies.

Senator WEBB. New research?

Dr. CASSANO. The 2008 Committee, Senator, looked at all of the available literature that was there for 2006, as well as 2008. There were two additional studies, *Ha* and *Consonni* that were published after 2006 which we looked at. In addition, most of the animal studies on the toxicological data that was available was published after—most of it was published after the 2006 Committee had their deliberations. So when you look at all of the evidence for a positive association you have these consistent studies. You have animal experimentation. You have a known biological mechanism and a dose dependent response.

Senator WEBB. So between the two studies you are saying that there was actually new research that had been conducted. It was not simply an evaluation of old material?

Dr. CASSANO. Yes, sir.

Senator WEBB. OK. One final question. The clock is beating me here.

Secretary Shinseki, do you believe that this authority should remain with the Secretary of Veterans Affairs to make these decisions or do you believe that it should be given to the Congress in the future?

Secretary SHINSEKI. The last part of the question as whether it should be left to Congress?

Senator WEBB. The decisional authority as it now exists in the statute. Is that something that you believe should remain with the Secretary of Veterans Affairs or should it be a recommendation from the Secretary of Veterans Affairs to be made by the Congress in the same way as say cost of living or, you know, weapon systems in the Pentagon or whatever.

Secretary SHINSEKI. Senator, I never presume to suggest to Congress how to do its work. I just would reply that it says Congress' intent in the 1991 law, if we understand the history that led up to it and then see what transpired—no presumptions to treat Vietnam veterans up until 1991 and then following 1991, 12 presumptions; the last three being my decision of a year ago to bring it to 15. If the intent of Congress was to move from where we were and causation was not working, and we needed some other mechanism, I think the will of Congress was met. Congress achieved what it wanted.

Now, we can discuss how to modify that process to include if Congress would like to retain to itself the decision authority on determining whether or not a presumption is warranted. It will require the kind of work that I have been through for the past nearly a year now. But, you know, I think in that 1991 legislation, besides being very prescriptive on what Congress expected the Secretary of Veterans Affairs to do, unstated in that legislation is any reference to cost. As I have been advised by general counsel, that was not oversight. That was clearly the intent of Congress that the Secretary's decision would be based on sound medical scientific evidence.

What I also interpret from that is that Congress reserved to itself the decisional authority on whether, how, and when to pay for that decision. So I do think there is significant involvement on the part of Congress and oversight. If that needs to be adjusted, I am more than happy to have that discussion as we look for a better outcome. I would also add this, that Congress has decided to fund these three determinations through the appropriations process. So I think, again, Congress had an opportunity to review my decision and decide to do its part.

Senator WEBB. Well, with respect to funding, as you know, if a disability is service-connected, it will be funded. This is the United States of America. So, whether Congress would fund this or not was never really a question.

Thank you, Mr. Chairman.

Chairman AKAKA. Thank you. Thank you, Senator Webb.

Senator Tester.

Senator TESTER. Thank you, Mr. Chairman. Secretary Shinseki, I also want to thank you for being in my office last Tuesday to help me understand the process on presumptive disability decision-

making. I think you have been very conscientious in making some, as is apparent today, some tough decisions.

I, as well as everybody else I think in this room, stand firmly behind veterans getting the benefits that they have earned and that they deserve. I also believe it is important that the process for determining service connections prevents or limits at a minimum fraudulent claims from being made.

In the meeting that we had on Tuesday, you mentioned the fact that claims for ischemic heart disease are rebuttable in certain cases. This is—I have been broached with several different questions since I have been sitting here and I want you to walk through, if you could, the kind of latitude that you envision the VBA has in determining ischemic heart disease and its—and who is responsible for what. Let me give you an example.

You got somebody who pounds a couple of packs of cigarettes a day and a like amount of alcohol that comes to you with a problem. Is that rebuttable or is it a situation where—and they have the heart disease—is it a situation where you just say they are in. You cannot——

Secretary SHINSEKI. Let me take the question on in two pieces. Let me just ask Dr. Jesse to talk about how we distinguish ischemic heart disease and——

Senator TESTER. Yes.

Secretary SHINSEKI [continued]. All other asymptomatic. Then I will turn to Mr. Pamperin to talk about the benefits decision.

Senator TESTER. OK.

Dr. JESSE. Thank you, sir. Ischemic heart disease is by definition where the heart does not get enough oxygen to meet its needs. Generally, that is symptomatic. People have chest pain or shortness of breath or lack of exercise activity, and that would essentially constitute the disability. We, as clinicians, we confirm that that shortness of breath, say, or chest pain is due to ischemic heart disease from a number of mechanisms—stress testing, necro imaging associated with stress testing, and some other methodologies, and/or the presence of having had a heart attack or having had a diagnosis of stable or unstable angina—would automatically meet the level of testing for that. If somebody came in and said I am having chest pain; well, a lot of things can cause chest pain if they have a normal stress test, and we determine this is not ischemic heart disease.

Senator TESTER. But cannot overuse of tobacco and alcohol create ischemic heart disease?

Dr. JESSE. Well, they do not cause ischemic heart disease. The risk factors, particularly when you get multiple risk factors, can contribute to its progress.

Senator TESTER. OK. So let us back up. So if they served in Vietnam and they got it, regardless of their lifestyle, it is an Agent Orange problem?

Dr. JESSE. Yes. Because we cannot parse that out perfectly.

Senator TESTER. You had somebody else who wanted to comment?

Mr. PAMPERIN. Yes, sir. With respect to a rebuttal of presumption, again, the claims examiners in the regional offices are not making a medical opinion. If there is clear evidence in the file of

risk factors for heart disease, when they request the examination it is appropriate for them to ask the clinician in light of this risk factor, this risk factor, and this risk factor, is it as likely as not that the veteran's current disability is due to herbicide exposure? We will then award benefits based upon what the clinician says.

Senator TESTER. All right. Based on what Dr. Jesse just said though, it would be very difficult for a doctor to say it is not herbicide exposure. Or is there some marker within a test that would indicate this is herbicide exposure?

Mr. PAMPERIN. I do not believe so, sir.

Senator TESTER. OK. Secretary Shinseki——

Secretary SHINSEKI. Senator, just to add——

Senator TESTER. Yes?

Secretary SHINSEKI. At this point of the Vietnam veteran age group, age 60, because of the confounding aspects of age, lifestyle, and the exposure, it is difficult to parse out.

Senator TESTER. Yes.

Secretary SHINSEKI. But we do know from the studies, those nine studies I referred to and that the IOM considered rigorous enough for us to give weight for them, six of the studies were strong and statistically significant in making the tie between herbicide exposure and ischemic heart disease. For Vietnam veterans, what this means is anywhere from 1.4 to 2.8 times the risk of others for developing this ischemic heart disease. So, we have to make this connection and say that the exposure occurred.

Senator TESTER. I understand, General. And I understand this is a very difficult topic. I also understand that there are a number of veterans out there that have tried to get through the door and could not for whatever reason—not on this issue but others. I know you have worked on it. Your predecessors worked on it to make sure that veterans are treated fairly. I think that is the whole point here. I think everybody that earned a benefit should get it, they should get it ASAP.

I guess the question is as we try to limit potential fraud, is there a rebuttal process if somebody comes in that served in Vietnam—and maybe everybody was exposed to Agent Orange who served in Vietnam; I do not know that but it appears to me that if they come in with ischemic heart disease and they served in Vietnam, they are going to get it. Is that a fair statement?

Secretary SHINSEKI. That is correct, absent a rebuttable condition. I am told that there is one individual who recently made a comment that he is receiving Agent Orange benefits, yet he only paused in the airport in Saigon for 8 hours. I do not know if this is true, but it is reported. I say that when someone self-identifies like this, we are going to go take a look. And if there is rebuttable——

Senator TESTER. OK. My time is long past. Thank you, Mr. Chairman, and thank you, General.

Chairman AKAKA. Thank you very much for this round. Are there any further questions for the Secretary?

Senator TESTER. I have one. It is a real quick one if he can do it. I did not ask it because I ran out of time.

Chairman AKAKA. Then ask it.

Senator TESTER. It deals with administrative costs. One estimate says presumptive eligibility for ischemic heart disease would cost about $1.6 billion over the next decade. Implementing Type 2 diabetes was about $250 million. Do you agree with those estimates?

Secretary SHINSEKI. Senator, I think you are referring to a 10-year cost estimate.

Senator TESTER. Yes.

Secretary SHINSEKI. I am just reading the notes on the sheet and the note that applies to the ischemic heart disease administrative cost estimate of $1.6 billion. The note reads that multiply the total admin costs of $1,888,574 at 31 August 2010, by 88 percent for IHD administrative costs. I think we have got a calculation error here. I do not know how 88 percent of one million becomes one billion.

Senator TESTER. 1.6 billion.

Secretary SHINSEKI. I think we——

Senator TESTER. Well, I would just say that if these figures are correct, as I would expect, I believe you would do your best to try to reduce that administrative overhead to get those benefits for the soldiers.

Secretary SHINSEKI. Absolutely.

Senator TESTER. Thank you. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you very much, Senator Tester.

Mr. Secretary, I really appreciate your being here today and this panel as well. I believe there is much value added through transparent discourse. I will have follow-up questions for you that will be included in the record. I want to thank this panel very much for your responses. Thank you.

Secretary SHINSEKI. Thank you, Mr. Chairman.

Chairman AKAKA. Now I welcome the second panel.

Our first witness is former VA Secretary Anthony Principi, who served as the head of the Department from 2001 to 2005. He is the one who will focus on the challenges he faced with the presumption process and the primary factors that influenced his decision to establish a presumption for Type 2 diabetes. Mr. Principi is also a former staff director of this Committee.

I understand Mr. Principi that you will need to leave soon for a flight. There may be questions that will be sent to you for the record.

STATEMENT OF HON. ANTHONY J. PRINCIPI, FORMER SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Mr. PRINCIPI. Thank you, Mr. Chairman. I certainly will try to stay as long as possible. I do regret I have a flight out west to give a speech this evening, but I certainly will stay as long as I can.

Mr. Chairman, Members of the Committee, thank you for allowing me to submit my written testimony for the record. I am pleased to testify this morning on an issue of great importance to our Nation's veterans, their families, and to the American people. We know that neither individual veterans, nor the VA, can show that an individual veteran's post-service illness is or is not the result of in-service exposure to a harmful substance. That is why the Congress established a process for determining presumptive service connection and that is why I endorse the concept of presumptive service connection.

In the real world, the Secretary of Veterans Affairs must decide, based on imperfect knowledge and substantial uncertainty, whether or not to presumptively service-connect a disease and to do so within 60 days after receiving the IOM report. The 1991 decision of Congress to have the Institute of Medicine review this scientific literature and report its findings casts some light into the starkness of unprovability. The state-of-the-art is such that decisions must still be made despite ambiguity and uncertainty. My decision to establish a presumptive service connection for Vietnam veterans with Type 2 diabetes illustrates the point.

While IOM's report pointed out significant uncertainties and possible confounding factors, other risk factors with Type 2 diabetes, IOM's findings on the relationship of herbicide exposure and Type 2 diabetes reported positive associations in most of the morbidity studies they evaluated. These included the Air Force Ranch Hand study, a National Institute of Occupational Safety and Health of U.S. Chemical Workers, and studies of male and female veterans from Australia. Only the survey of female Australian veterans did not show a positive association. Five self-reported cases of diabetes were found when 10 were expected. However, the study of male Australian Vietnam veterans found 2,391 cases reported when only 1,780 were expected.

So at the time I believed that only one small dataset kept IOM from declaring a positive association instead of a limited or suggestive one between Type 2 diabetes and exposure to Agent Orange. I also considered the recommendation of my Under Secretary for Health, whose staff thoroughly reviewed the entire report and recommended a presumption. Finally, my belief that America's veterans earned the benefit of the doubt led me to decide in favor of presumptively service-connecting Type 2 diabetes.

I was very aware that the American people were watching my decision closely, both to ensure that I would treat those who defended our Nation fairly and to ensure that I was a good steward of the resources entrusted to me. This was a very, very difficult decision and one I labored over, and even at one point called in an IOM representative to see if I could get more definitive information and help make a better decision. Because I believe if the American people lose faith in the integrity of the VA's disability compensation system—and that is not just about cost—veterans and their families will most certainly suffer. And the surest way for that to happen is for the American people to believe that large numbers of veterans are being compensated for illnesses that may not be the result of their military service. I think that is the crux of the issue we are all grappling with, how to make the right decision.

A herbicide-based presumption for a Vietnam veteran rests on the foundation of three degrees of possibility. First, the possibility that the veteran was exposed to dangerous herbicides; second, the possibility that such exposure leads in at least some cases to illness; and third, the possibility that the individual veteran's illness was caused by that exposure. Presumptions are premised on the transformation of those three possibilities into certainties, and that transformation has significant consequences for veterans and for the American people. It is unquestionably a very difficult question.

I have a few suggestions I believe will reduce the uncertainty surrounding these decisions and improve the process. Senator Murray asked Senator Shinseki about them and he responded accordingly. The first is about new studies. Medicine and medical research have made tremendous strides in the 20 years since the Agent Orange Act of 1991 was enacted. At the time the 1991 Act was enacted we were dealing with rare diseases—non-Hodgkin's lymphoma and soft tissue sarcoma. Today we are dealing with diseases of ordinary life. Do new studies now exist or could they be commissioned that might improve our ability to base future presumptive service connection decisions on stronger scientific evidence? Perhaps we could consider replicating the Center for Disease Control's Vietnam Experience Study of the 1990s.

Second, I would suggest that Congress or the Secretary of Veterans Affairs direct IOM to provide VA with an estimate of a latency period for the illness. That is a point after which it is no longer likely that the illness onset is a result of exposure but rather of other factors. This has been done twice in the past to my knowledge. Certainly, a presumptive service connection for peripheral, I am sure I know the name of the disease, has to be manifested within 1 year of exposure to herbicides. I believe in 1994 the Institute of Medicine indicated that respiratory cancer could last a couple of decades after exposure.

So, for example, there are certain diseases that are prevalent in older people and not in younger ones. Is it a better policy to establish a presumptive service connection for veterans who develop those diseases for a period of time after disservice, whether that is 10 years, 20 years, or 50 years, depending upon what science might conclude.

Then third, I believe that IOM should be asked to estimate the additional number of Vietnam veterans who might be affected by an illness as a result of herbicide exposure. In other words, if 100,000 veterans and an age cohort of Vietnam veterans could be expected in the normal course of life to develop a disease, approximately how many more veterans would develop that disease as a result of their exposure to herbicides? If the number is very small, then perhaps other steps can be taken to ensure that they receive proper medical care—all 100,000 or whatever that number might be—and to hold off on disability compensation until there is further evidence that takes it out of the limited suggestive category and puts it into the positive association category.

Mr. Chairman, in conclusion I am very proud of the role I played in my career of service to veterans. I make no apology for ensuring Vietnam veterans receive the benefits they earn, including diabetes. They earn those benefits in response to our Nation's gratitude in the heat of battle during a very long, difficult, and unpopular war. But I am also aware that the American people are the source of those benefits and I believe all Americans are entitled to know that the veterans' benefits are rooted in sound science. VA's benefit system must be beyond reproach and decisions must be based on the best facts available. I hope you and the VA will consider my suggestions to help us make better informed decisions.

Thank you for this opportunity to testify, Mr. Chairman and Members of the Committee.

[The prepared statement of Mr. Principi follows:]

PREPARED STATEMENT OF HON. ANTHONY J. PRINCIPI, FORMER SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Mr. Chairman and Members of the Committee, good morning. Thank you for this opportunity to testify on decisions to presumptively service connect diseases related to the use of herbicides (dioxin in Agent Orange) in Vietnam.

This is not a new question. The Congress held its first hearing related to the possible effects of herbicide exposure in Vietnam on April 7 and 15, 1970—forty years ago. The most contentious issue has long been the criteria for providing service connections for veterans for health problems that might have resulted from their presumed exposure to herbicides.

In 1984, the Congress provided Vietnam veterans with automatic disability benefits for chlorachne and porphyria cutanea tarda. Congress also directed VA to establish the Veterans Advisory Committee on Environmental Hazards, and asked VA to determine new standards for evaluating disability claims based on herbicide exposure.

At the time, Mr. Chairman, I was on the staff of this Committee, and I was very proud to have been part of this important step forward for my fellow Vietnam veterans.

When I became Deputy Secretary for Veterans Affairs in 1989, I took up this issue from "the other side," as it were—working closely with this Committee to create the landmark legislation that became Public Law 102–4: the Agent Orange Act of 1991. The provisions of that Act have served our Nation well for twenty years, but I believe it is time to look at some of the Act's unintended consequences—and to make a few changes that will allow the Act to remain useful in the future.

In Pub. L. 102–4, Congress permanently granted presumptive service connection for chlorachne, non-Hodgkin's lymphoma, and soft-tissue sarcoma: all diseases associated with exposure to dioxin in Agent Orange. The law also transferred the responsibility of reviewing scientific literature on the association between herbicide exposure and health outcomes suspected to be associated with that exposure from the Advisory Committee on Environmental Hazards to the National Academy of Sciences. Congress left the ultimate decision to presumptively service connect additional diseases in the hands of the Secretary of Veterans Affairs.

In response, VA developed a policy that if a positive association exists between the exposure of humans to a herbicide agent and the occurrence of a disease in humans, the Secretary would, by regulation, establish a presumption of service connection for that disease.

In theory, this is an even-handed, fair, and scientifically based method of making decisions on which illnesses should be presumptively service-connected. As a former Secretary of Veterans Affairs, however, I can tell you that such decisions are much more difficult than they would seem.

First of all, it has always been difficult, if not impossible, to determine the level of exposure to herbicides, if any, experienced by troops in Vietnam. While some of the evidence reviewed by IOM comes from evaluations of Air Force and Army troops who worked with herbicides, most of the documentation they use is from studies of people who were exposed to herbicides in civilian life or in industrial accidents.

It is also true that while levels of herbicide contaminants can still be detected in the blood of Vietnam veterans, those levels vary. All Americans are exposed to herbicides in their daily lives, and there is no way to tell where or when any individual with dioxin in his or her blood was exposed to the chemical

IOM has soldiered on, however. Their biennial reports evaluate illnesses to determine whether an association with herbicide exposure exists, and whether there is a plausible biologic mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

They categorize their findings in four ways: illnesses that have sufficient evidence of an association with herbicide exposure; illnesses that have limited or suggestive evidence of an association; illnesses with limited or suggestive evidence of no association; and illnesses with inadequate or insufficient evidence to determine whether an association exists.

Cases in which IOM believes sufficient evidence of an association exists, or in which they do not believe such evidence exists, are easy to decide. Where we can say for certain, with scientific evidence, that there is a direct link between a veteran's service and illness, it is clear that veterans should be service-connected for that illness. On battlefields, not all injuries are caused by shrapnel and bullets.

But those illnesses in which IOM has found only limited or suggestive evidence of an association are much more difficult to decide. Today, fourteen diseases are pre-

sumed to be connected to exposure to herbicide use in Vietnam. Some are rare; others, like diabetes, prostate and lung cancer, and leukemia, are much more common.

In making this kind of decision, we are taking degrees of possibility; the possibility that veterans were exposed to dangerous herbicides; the possibility that such exposure might lead to illness; and the possibility that the illness in any individual veteran was caused by that exposure—and turning them into certainties with significant consequences for veterans and the American people. It is, unquestionably, a difficult process.

My decision to establish a presumptive service-connection for Vietnam veterans with type II diabetes illustrates this point. While IOM's report pointed out significant uncertainties and possible confounding factors, IOM's findings on the relationship of herbicide (dioxin) exposure and type II diabetes reported positive associations in most of the morbidity studies they evaluated.

These included the Air Force's Ranch Hand study; a National Institute for Occupational Safety and Health study of U.S. Chemical Workers; and studies of male and female veterans from Australia. Only the survey of female Australian veterans did not show a positive association: 5 self-reported cases of diabetes were found while 10 were expected. However, the study of male Australian Vietnam veterans did find a statistically significant excess of self-reported diabetes (2,391 cases were reported when 1,780 were expected.)

To me, this was an indication that only one data set kept IOM from declaring a "positive association" instead of a "limited/suggestive" one between Type II diabetes and exposure to Agent Orange. In addition, I received a report from the Under Secretary for Health, whose staff thoroughly reviewed the entire report from a scientific viewpoint. The recommendation was to presumptively service connect for diabetes. And finally, my belief that America's veterans have earned the benefit of any doubt led me to decide in favor of presumptively service connecting type II diabetes for Vietnam veterans.

Make no mistake: these decisions do not merely affect those who may or may not receive presumptive service connections and their families. The American people watch these decisions closely, both to ensure that those who have defended our Nation while in uniform are treated fairly, and to ensure that those who have been given the responsibility to administer the program are good stewards of the resources with which they have been entrusted. If the American people lose faith in the integrity of our disability benefits system, veterans and their families will be the ones who will suffer. The surest way for that to happen is for the public to be convinced that presumptive service connection decisions are based on anything other than sound scientific advice.

Accordingly, I have three suggestions I believe will improve the process. First, medicine and medical research have made tremendous strides in the twenty years since the Agent Orange Act of 1991 was enacted. In those twenty years, has anyone found a better way to measure dioxin levels in blood for Vietnam veterans and a control group? Is there now a way to differentiate between those servicemembers who received repeated and prolonged exposure to dioxin in Vietnam and those whose exposure was brief or nonexistent? And are there new studies that now exist, or can be commissioned, that might improve our ability to base future presumptive service connection decisions on strong scientific evidence? One such study might be a replication of the Centers for Disease Control's Vietnam Experience Study of the 1980s. IOM, or some other scientific organization, should look into these issues and report back to VA and Congress.

Second, I would suggest that Congress, or the Secretary of Veterans Affairs, direct the IOM to provide VA with an estimate of a latency period for the illness; that is, a point after which it is no longer likely that the illness' onset is a result of exposure, but rather of other factors. For example, heart disease is prevalent in older people and not in younger ones. It may be that the best policy here is to establish a presumptive service connection for veterans who develop that disease for a fixed post-service period of time, but not the rest of their lives.

This has already been done twice: first, presumptive service connection for peripheral neuropathy was limited to those cases that manifested themselves within one year of herbicide exposure; and second, IOM in 2004 decided that the effects of herbicides on respiratory cancer "could last many decades." IOM's best estimate for each new disease, and perhaps a review of previous decisions, would be helpful for the public record and to any Secretary in his or her decisionmaking.

And third, IOM should be asked to estimate the number of Vietnam veterans who might be affected by an illness with limited or suggestive linkage to herbicide exposure. In other words, if 100,000 veterans in the age cohort of Vietnam veterans could be expected to develop a disease, approximately how many more veterans will develop that disease as a result of exposure to herbicides. Secretaries must weigh

that information too before making a final decision on presumptive service connection.

Mr. Chairman, I am proud of the role I played during my long career of service in getting my fellow Vietnam veterans the benefits they have earned for their service and sacrifices on behalf of our Nation. The benefits Vietnam veterans now have were earned in the heat of battle during a difficult and often unpopular war. But I am also aware that the American public is the source of those benefits, and I believe all Americans are entitled to know veteran benefits are rooted in the reality of science and good public policy.

I hope that you, and VA, will consider my suggestions to help us make better and more informed decisions of this nature in the future.

Thank you again for this opportunity to testify. I look forward to your questions.

RESPONSE TO PRE-HEARING QUESTIONS SUBMITTED BY HON. JIM WEBB TO HON. ANTHONY J. PRINCIPI, FORMER SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Question 1. Please describe the process in place when you were Secretary for reviewing the scientific evidence provided by IOM and other sources to determine whether to establish a presumption for type II diabetes. How did VA translate IOM's categorization of "limited/suggestive" evidence of an association into meeting the legal standard of a "positive association" standard for establishing a presumption? What sources, other than the specially commissioned IOM report on diabetes, did VA review in making its presumption determination for type II diabetes?

Response. IOM's study stated that "positive associations are reported in most of the (type II diabetes) morbidity studies" they identified, including the Air Force's Ranch Hand study; a National Institute for Occupational Safety and Health study of U.S. Chemical Workers; and studies of male and female veterans from Australia. Only the survey of female Australian veterans did not show a positive association: 5 self-reported cases of diabetes were found while 10 were expected. However, the study of male Australian Vietnam veterans did find a statistically significant excess of self-reported diabetes (2,391 cases were reported when 1,780 were expected.)

To me, this was a clear indication that only one small data set kept IOM from declaring a "positive association" instead of a "limited/suggestive" one between Type II diabetes and exposure to Agent Orange. Still, I was concerned by the uncertain findings, and I met personally with an IOM representative to discuss their report before making a decision. I left that meeting with great uncertainty that IOM had developed the kind of strong scientific evidence I believed I needed to make a significant policy decision, as their recommendations were almost entirely based on literature reviews of those morbidity studies. However, their findings, a recommendation from the Under Secretary for Health, whose staff thoroughly reviewed the entire report from a scientific viewpoint, and my lifelong belief that America's veterans have earned the benefit of any doubt, led me to decide in favor of presumptively service connecting type II diabetes for Vietnam veterans.

Question 2. Please describe the challenges that you faced and the primary factors that influenced your decision to establish a presumption for type II diabetes.

Response. The challenges I faced in the Type II diabetes decision were significant, and the decision I made came only after significant deliberation. Before I made the decision to presumptively service-connect type II diabetes, I called in an IOM representative to my office. I spoke with him at length about their work and the methodology behind it. I came away with the realization that I would have to make an extremely consequential decision with profound implications for individual veterans and the Nation as a whole with great uncertainty.

Because IOM's study came very close to declaring a positive association between Agent Orange exposure and Type II diabetes; because I believe strongly that on modern battlefields, not all injuries are caused by bullets and shrapnel; and because I believe that veterans, through their honorable service to our Nation, have earned the benefit of any doubt, I accepted the recommendation of my Under Secretary for Health that type II diabetes should be presumptively service-connected.

Question 3. Please describe any benefits you believe could be gained from the recommendation made by the IOM's Committee on Evaluation of the Presumptive Disability Decision-Making Process for Veterans that Congress create a formal Advisory Committee and a Science Review Board to advise and assist the Secretary with reviewing scientific research and considering conditions for presumptions.

Response. I am not convinced that additional layers of review will improve the decisionmaking process. What will improve the process is better information. I would like to know, from IOM or some other scientific source, whether or not there

is now a better way to measure dioxin levels in blood, and their source, than there was twenty years ago. I would also ask IOM, in any future study, to estimate a latency period for illnesses in which they have found a limited or suggestive linkage with dioxin: that is, a point after which it is no longer likely that the onset of the illness is a result of Agent Orange exposure. We might consider replicating the Centers for Disease Control's Vietnam Experience study of the 1980s. And finally, where IOM has found a limited or suggestive linkage, I would like them to estimate for me the number of Vietnam veterans who might have developed the illness as a result of their exposure, compared to the total number of Vietnam veterans who might be expected to develop that illness.

With that information, it would be easier to make a decision that takes into account all facets of the issue, and additional levels of oversight would be less necessary.

Question 4. Please describe the challenges that common diseases of aging or other highly prevalent risk factors generated for you in your attempt to make a presumption decision based on sound medical and scientific evidence, and whether these challenges are adequately addressed by the language in the Agent Orange Act of 1991.

Response. These are significant challenges, especially as they relate to illnesses with limited but suggestive evidence of linkage to Agent Orange exposure. The decision to presumptively service connect an illness is a long-term decision, obligating our Nation to veterans, their families and descendants for many years, even centuries, to come. The American people watch these decisions closely, both to ensure that those who defended our Nation while in uniform are treated fairly, and to ensure that those who have been given the responsibility to administer the program are good stewards of the resources with which they have been entrusted.

If the American people lose faith in the integrity of our disability system, veterans and their families will suffer. The surest way for that to happen is for the public to be convinced that presumptive service connection decisions are based on anything other than sound scientific advice. Based on my discussions with IOM I was quite concerned that I was about to make an extremely consequential decision with profound implication for veterans and the Nation with great uncertainty. The language of the 1991 Act, in my opinion, did not fully anticipate this problem.

Question 5. Do you believe that the Secretary is able to determine, on the basis of sound medical and scientific evidence, whether a positive association exists between exposure to an herbicide and the occurrence of a disease that is common to aging or results from other highly prevalent risk factors?

Response. No Secretary is able to make such a determination; however, the law does not ask Secretaries to determine whether or not positive associations exist. That is IOM's responsibility. Secretaries are required to act on IOM's findings to make public policy decisions based on those findings, and that is an appropriate division of responsibilities.

Question 6. Do you believe that the presumption process is the appropriate mechanism to address gaps in exposure and association for diseases common to aging or other highly prevalent risk factors?

Response. VA's disability compensation system is the manner in which Americans compensate our veterans for injuries or diseases that happen while on active duty, or are made worse by active military service. I supported the concept of presumptive service-connection because I believe strongly that on the modern battlefield, not all injuries are caused by shrapnel and bullets; and that veterans must be compensated for those injuries they incur while on active duty. In addition, the burden of providing a nexus between exposure and disease cannot be placed on individual veterans. Implementation of the process, however, has to take into account all factors relating to the veteran and his or her overall health, including the length of time the veteran is removed from active service.

It should be noted, however, that we are taking degrees of possibility: the possibility that veterans were exposed to dangerous herbicides; the possibility that such exposure might lead to illness; and the possibility that the illness in any individual veteran was caused by that exposure—and turning them into certainties with significant consequences for veterans and the American people. It is, unquestionably, a difficult process. While I personally do not know of a better way to address illnesses incurred as a result of environmental factors, I would be open to reviewing others' suggestions.

Question 7. In your view, what is the value of science in the process for evaluating the merits of a presumption for a disease that is common in an aging population or that is highly related to other prevalent risk factors? Is this a question more appropriately addressed by Congress or the Secretary?

Response. The responsibility of reviewing scientific literature on the association between herbicide exposure in Vietnam and health outcomes suspected to be associated with that exposure has been in the hands of scientists since 1984: first the Advisory Committee on Environmental Hazards, and, since 1991, the National Academy of Sciences. The decisionmaking responsibility, however, is in the hands of the Secretary of Veterans Affairs. I believe this is an appropriate division of responsibility between scientists and Presidential appointees.

However, I believe that Secretaries have a responsibility to ask for additional information when what scientists provide them is insufficient to make a sound, reasoned decision—and to override the recommendations of scientists without fear of criticism, especially when uncertainty levels are as high as they are in this issue. Science is an appropriate tool for political appointees, and Congress, to use as a public policy guide; but other factors come into play as well, and ultimate decisions will have to be made by those with a view of the entire picture, not only its scientific aspects.

RESPONSE TO POST-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO HON. ANTHONY J. PRINCIPI, FORMER SECRETARY, U.S. DEPARTMENT OF VETERANS AFFAIRS

Question 1. In response to a pre-hearing question on your establishment of the presumption for type 2 diabetes, you described your reliance on a study of male Australian Vietnam veterans among the studies examined by the IOM Update Committee as suggestive of an association between type 2 diabetes and dioxin exposure. You stated that "[s]till, [you] were concerned by the uncertain findings, and [you] met personally with an IOM representative to discuss their report before making a decision. [You] left that meeting with great uncertainty that IOM had developed the kind of strong scientific evidence [you] believed [you] needed to make a significant policy decision * * *"

I understand that this study conducted by the Australian Government examined the health effects of the Vietnam experience in general, rather than herbicide exposure.

I admire the great effort you made to come to an informed decision. When you met with the representative from the IOM Committee to discuss your reservations about the uncertain findings, did that representative advise you that the Australian study upon which the IOM Committee relied for its determination of a suggestive association between type 2 diabetes and dioxin exposure did not actually examine dioxin exposure, rather the study examined the health effects of the Vietnam experience in general? If not, do you believe that information would have been valuable for your decisionmaking?

Response. Unfortunately, I do not remember many of the specifics of my meeting, and cannot say for certain whether I was informed that the Australian study examined the health effects of the Vietnam experience, not dioxin exposure. I am certain, however, that I would have found any information IOM could have provided me to be useful, as the entire purpose of my meeting was to learn more than I had already learned from reading their report before making my decision. I cannot say whether such information would have changed that decision in any way—but it would have been useful for me to have known more about the Australia study, if I did not know it at the time.

Question 2. In your view, does IOM's reliance on the Australian study suggest value in examining the health effects of the Vietnam experience in general, in place of examining the health effects of herbicides used in Vietnam in the absence of sound exposure data? Do you believe that Vietnam cohort health studies might yield more reliable information about those Vietnam veterans who may be suffering adverse health effects from their service in Vietnam, than the current attempts to directly examine an association with herbicides in the absence of sound exposure data and controlled risk factors?

Response. In my testimony to the Committee, I suggested that the Vietnam Experience Study, which was completed by the Centers for Disease Control in 1989, should be brought up to date in order to provide additional information to future decisionmakers. (The Vietnam Experience Study was a multidimensional assessment of the health of Vietnam veterans in the 1980's, compared to the health of non-Vietnam veterans who served in the same era.) I do not see, however, why a study of this data should be used in place of the current system or that the information it would provide would be more reliable than current data, as your question suggests. Instead, I think both sets of information would be valuable. The updated Vietnam Experience Study, in particular, would allow Secretaries of Veterans Af-

fairs to better answer the questions I posed in my testimony about estimating latency periods for illnesses, and about estimating the number of veterans who might be affected by an illness with limited or suggestive linkage to herbicide exposure.

Question 3. In response to a question from Senator Johanns with respect to identifying things you wish you could have had at your disposal to help your decisionmaking, you stated:

> "Certainly, a more definitive recommendation from IOM. I felt like I was getting conflicting data. On the one hand, honestly telling me about all of the confounding factors—about diet, about lifestyle, about heredity. And then on other hand, pointing out that I had three studies that showed a positive association, which really made it very difficult for a Secretary to take all that information, absorb it, assimilate it, and then come up with a decision. So I think better information is needed, a more definitive recommendation from the scientists, whether it's done by IOM, or a scientific review board, to help the Secretary make the right decision, especially as it relates to common diseases. It's a greater challenge for Secretaries when you're dealing with diabetes, prostate cancer—because we know if we live long enough we're going to die of prostate cancer, as well as heart disease. Those confounding factors really make it very, very difficult for us. So I think better information would be very useful."

a. Would you characterize the challenge you faced when establishing the type 2 diabetes presumption as being how to interpret scientific findings that appeared credible but not entirely on point for addressing the unique policy matter before you?

b. Do you envision the role of a scientific review board to extend beyond merely a scientific review of the evidence, but also to assist the Secretary with interpreting the scientific evidence within the context of the Secretary's policy decisionmaking, to ensure that any limitations of the scientific findings are given proper weight?

c. Should such a scientific review board be independent from VA, as recommended by the IOM Committee that reviewed the presumptions process?

Response. a. I am not certain that the problem with the scientific findings was that they were not entirely "on point." IOM's reports were, and continue to be, accomplished fully in accordance with the expectations of Public Law 102–4 and VA policy. Rather, my problem with the reports were in the degrees of possibility that the reports leave unanswered: the possibility that veterans were exposed to dangerous herbicides; the possibility that such exposure might lead to illness; and the possibility that the illness in any individual veteran was caused by that exposure. Decision makers are required to turn these possibilities into certainties with significant consequences for veterans and for all Americans. In my opinion, they are required to do so without sufficient information.

b. Should a scientific review board be established, I would expect it to do more than just review the evidence IOM presents—VA's Under Secretary for Health can accomplish that task and has historically done so. I would hope that a board would suggest to the Secretary any additional areas where possible evidence may be found that IOM did not consider, and synopsize the information to be found; that the board would provide its thoughts and estimates on possible latency periods based on any information it believes to be relevant; and that the board would also provide its thoughts and estimates on the number of veterans whose illnesses might be attributed to herbicide exposure as opposed to aging for the illness under review.

c. As long as the Secretary remains the final decisionmaker, I would have no problem if any scientific review board that is established were independent from VA in its deliberative processes.

Question 4. During the hearing, you described the uncertainties of the presumption process for conditions that IOM has found to have only limited or suggestive evidence of an association with herbicide exposure in the following manner:

> "The herbicide-based presumption for a Vietnam veteran rests on the foundation of three degrees of possibility:
>
> • First, the possibility that the veteran was exposed to dangerous herbicides;
> • Second, the possibility that such exposure leads, in at least some cases, to illness; and
> • Third, the possibility that the individual veteran's illness was caused by that exposure.
>
> Presumptions are premised on the transformation of those three possibilities into certainties. And that transformation has significant consequences

for veterans and the American people. It is an unquestionably a very difficult question."

You then provided the following three suggestions for improving the process:

- Commission studies that might differentiate between servicemembers who received significant exposure to dioxin in Vietnam and those whose exposure was insignificant or nonexistent in order to base presumptive service connection decisions on stronger scientific evidence. You suggested that such studies might replicate the Centers for Disease Control's Vietnam Experience Study.
- Commission IOM to provide VA with an estimate of a latency period for illness; that is, a point after which it is no longer likely that the illness' onset is a result of exposure, but rather other factors.
- Commission IOM to estimate the number of Vietnam veterans who might be affected by an illness found by IOM to have only limited or suggestive evidence of an association with herbicide exposure.

a. Would a Vietnam veteran health study, such as the CDC's Vietnam Experience Study, address some or all of the three degrees of possibilities you described? Do you envision such a study or studies being ongoing throughout a veteran's lifetime?

b. What role would a scientific review board play in assisting the Secretary and implementing the suggestions you have offered?

Response. a. I believe a Vietnam Veterans Health study would help improve our ability to determine latency periods for individual illnesses, and to make more realistic assessments of whether an individual veteran's illness was caused by exposure to herbicides. Better knowledge of the overall health of Vietnam veterans in comparison to a control group, and to the study done twenty years ago (which used Vietnam-era veterans who had not served in Vietnam as a control) would give us improved information on the latency periods for illnesses. This would be true both for illnesses that only appear after many years have passed, and those that disappear with time, depending on whether the difference in percentages of Vietnam veterans contracting an illness compared to non-Vietnam veterans has increased, decreased, or remained the same over time.

The percentage of any observed increases would also offer us additional data to help determine whether individual illnesses were more likely to be caused by exposure to herbicides or by aging. If the number of Vietnam veterans who become ill from a disease was significantly larger than that for those who did not serve in-country, we would have an indication that a significant number of veterans with the disease contracted it as a result of their Vietnam service. If there was little difference between Vietnam veterans and the control group, we would be much more likely to conclude that there was little, if any, association between the illness and Vietnam service.

It should be understood however, that in a cohort study such as this, results are expressed at a 95% level of confidence. Such a study is likely to find false positives. Given the 95% confidence level, about 5% of the positive correlations should be incorrect, and therefore any positive correlations the study uncovers should be considered as a basis for further studies such as IOM's, but not as proof that a correlation—or the lack of a correlation—exists for any illness. In addition, statisticians are aware that correlation does not imply causation, which means that any correlations that are uncovered will not automatically imply that one causes the other. Other sound studies will therefore always be needed for a Secretary to be confident in his or her decisionmaking.

Although this information will not provide decisionmakers with certainty, it should significantly improve a Secretary's ability to estimate the effects of Vietnam service on individual illnesses. I would envision that these studies should be repeated every ten years for the next two or three decades if resources are available.

b. The scientific review board I envision would use the Vietnam Experience studies and any other data they think relevant to help the Secretary better quantify the possibilities I listed in my testimony for illnesses which IOM believes may be linked to herbicide exposure. Their review, along with IOM's original report and the review of VA's Under Secretary for Health, would be part of the Secretary's decisionmaking process and would assist Congress in their oversight responsibilities.

Chairman AKAKA. Thank you very much, Mr. Principi. And thank you for your suggestions.

One question before you leave and then I will continue with the rest of the panel. Mr. Principi, you have suggested that the language of the Agent Orange Act did not fully anticipate the chal-

lenge of determining presumptions based on limited or suggestive evidence with respect to diabetes. Did you believe that it was clear under the law how you were to weigh evidence that was suggestive in association but where there were uncontrolled risk factors?

Mr. PRINCIPI. Mr. Chairman, that was clearly the most difficult part of the decision I had to make, whether the evidence was clear. Again, I felt, based upon the fact that three of the four studies that I reviewed that IOM submitted to me showed a positive association and my Under Secretary's recommendation. Then, of course, balancing the evidence for and against and the fact that it was relatively close, I erred on the side of giving the benefit of the doubt to the veteran.

But clearly, I think we need to look at the '91 Act. We need to make whatever changes are appropriate. Certainly, the 60-day time limit that Secretary Shinseki also eluded to is too short a period of time. So it does, indeed, create certain difficulties for us.

Chairman AKAKA. Let me ask the other senators whether they have specific questions for Mr. Principi.

Senator JOHANNS. I will just ask one.

Chairman AKAKA. Senator Johanns.

Senator JOHANNS [continued]. That I hope will be just a brief question, which I think you have answered in part. Looking back on those days when you were going through the decisionmaking process, if you could identify one, two, three things that you wish you would have had at your disposal—because I can see even today you agonized over this. And I understand why. It is a tough call. What would those one, two, or three things be?

Mr. PRINCIPI. Well, certainly a more definitive recommendation from IOM. I felt that I was getting conflicting data on the one hand, honestly telling me about all of the confounding factors about diet, about lifestyle, about heredity. Then on the other hand pointing out that I had three studies that showed a positive association really made it very difficult for a secretary to take all of that information, absorb it, assimilate it, and then come up with a decision. So I think better information is needed. A more definitive recommendation, if you will, from the scientists, whether it is done by IOM or a scientific review board to help the Secretary make the right decision, especially as it relates to common diseases. I think that is where—it is a greater challenge for secretaries when you are dealing with the diabetes, the prostate cancer, because we know if we live long enough we are going to die of prostate cancer, as well as heart disease. Those confounding factors really make it very, very difficult for us. So I think better information would be very useful.

Senator JOHANNS. Under the law that you had to work with there is this 60-day limit. Do you have the option as secretary to say, gosh, the information is so conflicting. I want to hold this open for a year or I want to hold it open for 6 months? Or do you just simply have to yes or no at the end of that period?

Mr. PRINCIPI. Well, you certainly—good question, Senator—we try to adhere to the law. I know veterans are very anxious to get a decision. You know, if you delay the decision there is no penalty, so to speak, but you always try to be responsive to the dictates of the Congress. It should clearly be longer, perhaps no time limit. It

should be up to the secretary to make a decision based upon the IOM report. He may have to go back or she may have to go back to IOM to get further information. I think it should be a little more open-ended.

Senator JOHANNS. That is helpful. Thank you.

Chairman AKAKA. Senator Webb.

Senator WEBB. Thank you, Mr. Chairman. I would like first of all to thank Secretary Principi for coming to this hearing and for the perspectives that he brings to this issue because like myself, you know, Tony, you started as a staff person struggling to come up with answers on this issue well before you became a member of the Executive Branch, and you and I both know how well intentioned the members were all through this process. We have heard some comments about the inattentiveness, people being inattentive to the struggles of the people who served in Vietnam. I never found that. It is just an incredibly hard issue when we have, as you said in your testimony, when we are putting together a series of unknowns to try to come up with a legislative known.

There are two portions of your testimony that I hope everyone will pay attention to, particularly, those people who are working in the area of veterans' law. The first is when you said if the American people lose faith in the integrity of our disability benefits system, veterans and their families will be the ones that will suffer. There is no truer statement. We must maintain the integrity of our compensation system, even given these unknowns.

The other thing that I would like to say is I think you have given three really constructive forward-looking recommendations here, and I, for one, am going to take those and see if we cannot come up with a way to better deal with this issue. There is nothing wrong with trying to make laws better. So, the recommendation that you have, given your experiences here and over in the VA, I think are really going to help us do that. I appreciate you coming today.

Mr. PRINCIPI. Thank you, Senator Webb. Thank you, Mr. Chairman and Senator Johanns. I apologize again for an early departure, and I certainly apologize to my fellow panel members. I look forward to learning more about their testimony and hopefully working with this Committee to find a good solution that protects our Nation's veterans and, of course, preserves the integrity of the system. I think that is very, very important. Thank you very much, Sir.

Chairman AKAKA. Thank you very much for your presence and your responses. Without question it is going to be helpful to us as we try to improve the legislation. Thank you.

Our next witness is Jonathan Samet, Chair of IOM's Committee on Evaluation of the Presumptive Disability Decision-Making Process for Veterans. He is here today to share insights on what his committee has learned from evaluating the process that yielded the presumptions for prostate cancer and Type 2 diabetes. I also intend to seek his views on how we might apply those lessons for current decisionmaking, such as a presumption for IHD.

So will you please proceed with your statement?

STATEMENT OF JONATHAN M. SAMET, M.D., M.S., CHAIR, COMMITTEE ON EVALUATION OF THE PRESUMPTIVE DISABILITY DECISION-MAKING PROCESS FOR VETERANS, INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES

Dr. SAMET. Thank you, Mr. Chairman, Members of the Committee. I am Jonathan Samet from the Keck School of Medicine at the University of Southern California. I am a physician and epidemiologist and I will note that I was in the U.S. Army from 1971 to 1973 working as an anesthesiologist in Panama.

I am here representing the Committee that I chair—the Committee on Improving the Presumptive Disability Decision-making Process for Veterans. I note that with me is one of our distinguished committee members, Guy McMichael, in fact, formerly a counsel to this Committee.

Our committee had two broad assignments. One was to describe and evaluate the model in place, to recognize diseases that might be subject to service connection on a presumptive basis. I feel that remarks up to now have probably covered the same ground as our report. I will focus my remarks on our second assignment, which was to, if appropriate, propose a scientific framework that would justify recognizing or not recognizing conditions as presumptive. Our committee produced an extensive report that I think covered much of both the theoretical and practical groundwork that would be needed to put a system into place and I think address some of the methodological complexities that you have heard about today.

I will say that in our case studies that we carried out as part of the groundwork for our report, we noted some of the problems that have already been discussed—the lack of evidence on exposures, the difficulty of retrospectively identifying the effects of an exposure associated with service from those that might be sustained from lifestyle or other factors. We, in fact, in our report propose that there should be a more robust and evidence-based process for future cohorts of veterans. We, in our work, examined the data being collected and the epidemiological studies in progress and found gaps—I think gaps that are well known—the difficulties of assessing exposures and in tracking health, particularly after veterans leave service. Nonetheless, we thought that these gaps might be addressed by using our fundamental research tools of public health.

We made recommendations for a new presumptive disability decisionmaking process that would be transparent, stakeholder inclusive, and evidence-based. We recommended that VA establish an advisory committee that would provide guidance on disability matters, including presumptive disability. This advisory committee was proposed as the clearing house for new possible presumptions that might be recommended by veterans, researchers, the government, VA, DOD, and others. Also as part of this process we recommended that an independent scientific organization be identified to perform the function of the science review board just as IOM does now. This independent group would consider the relevant evidence and analyze candidate presumptive conditions given to it by VA.

We recommended a two-step process. A first step that would involve literature review and determination of the strength of evidence to assess whether a given health outcome can be caused; and

I will note that we did recommend causation as the standard by a particular exposure. We recommended that strength of evidence be graded and that if there was a tie, meaning possible causation or stronger evidence, that consideration would then be given to a presumption.

In the second step we recommend that this science review board calculate the service-attributable fraction of the disease if the needed data were available. That is, there would be an assessment of how much of the observed disease could be attributed to the exposure. We thought that this information would be important for decisionmaking and give an understanding of the scope of the population that would be covered by a presumption. We note that there would be times as evidence accumulated that it would be incomplete and action would need to be taken.

I will say that the report does address the complexities of disentangling the effects of an exposure—military exposure—from those of other factors and the need for good data. Let me move quickly to the report's bottom-line. I think the example of ischemic heart disease shows why a new approach would be of benefit to the veterans. We found limitations in the current process, one, the focus on association and not causation. In looking at the VA process, our committee at least did not understand with clarity what the internal process was and how the VA moves from evidence on limited suggestive association—evidence of association to presumption. The problem of insufficient exposure and risk data is clear.

Our new approach includes these two committees and a process that we view as evidence-based and transparent. We recommended that the evidence be looked at for its support of causation and the calculation of the service attributable burden of disease to provide a better indication of the magnitude of the support that would be given to the veterans. Again, the details are provided here in our report which was published 3 years ago.

Thank you for the opportunity to address the Committee.

[The prepared statement of Dr. Samet follows:]

PREPARED STATEMENT OF JONATHAN M. SAMET, M.D., M.S., CHAIR, COMMITTEE ON EVALUATION OF THE PRESUMPTIVE DISABILITY DECISION-MAKING PROCESS FOR VETERANS, INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES

Mr. Chairman and Members of the Committee: My name is Jonathan M. Samet. I am Professor and Chair of the Department of Preventive Medicine, Keck School of Medicine, University of Southern California, and I direct the Institute for Global Health at the University of Southern California.

I have been invited to this hearing today because of my previous role as chairman of an Institute of Medicine (IOM) Committee which examined the presumptive disability decisionmaking (PDDM) process. By way of introduction, IOM is the health policy arm of the National Academy of Sciences, which was created by a Congressional charter signed by President Abraham Lincoln in 1863 as a private honorary society dedicated to the furtherance of science and its use for the general welfare. The IOM was chartered in 1970 to enlist distinguished members of the appropriate professions in the examination of policy matters pertaining to the health of the public. Under the terms of this charter, the IOM is called upon to act as an official, yet independent, advisor to the Federal Government in matters of science.

The IOM, like other Academy units, is uniquely situated to provide assessments in areas of science, health care, and public policy. Studies are undertaken by distinguished panels of individuals selected for their expertise and experience in the topic under study. To a degree unmatched elsewhere, the IOM can secure the participation of virtually any expert whom it invites to serve. Members on IOM study committees serve without compensation.

IOM has a longstanding interest in veterans' health issues and has conducted several studies that touch on ways to improve disability processing performed by the Department of Veterans Affairs.

The study committee that I chaired produced a report titled, "*Improving the Presumptive Disability Decision-Making Process for Veterans*" (hereafter the PDDM committee). This Committee complemented a second IOM study committee which produced a report titled "*A 21st Century System for Evaluating Veterans for Disability Benefits*". Both of these VA-funded studies were requested by the Veteran Benefits Disability Commission (VBDC), begun in 2006, and completed in 2007.

I am submitting the full summary of the report of the PDDM committee as an attachment to my testimony. [Attachment follows.] Here, I will attempt to provide a brief overview. The VBDC asked the PDDM committee to:

- Describe and evaluate the current model used to recognize diseases that are subject to service connection on a presumptive basis.
- If appropriate, propose a scientific framework that would justify recognizing or not recognizing conditions as presumptive.

In tackling the first task—to review the current presumptive decisionmaking process—the Committee reviewed statutes, received input from the VA, spoke with former congressional staff and reviewed the IOM's methodology in support of this process. I will offer a brief synopsis here.

In 1921, Congress empowered the VA Administrator (now Secretary) to establish presumptions of service connection for veterans. Only Congress and the VA Secretary had the authority to establish presumptions. Over time, presumptions have been made to relieve veterans of the burden to prove that disability or illness was caused by a specific exposure which occurred during military service (e.g., Prisoners of War). Since 1921, nearly 150 health outcomes have been service-connected on a presumptive basis.

The current presumptive disability decisionmaking process for veterans involves several steps and several organizations. The process involves input from many parties—Congress, VA, the National Academies, Veteran Service Organizations, advisory committees, and individual veterans. Congress has on it own authority made presumptions in the past. In the current model, which evolved from the Agent Orange Act, Congress may call on VA to assess whether a presumption is needed. The VA turns to the IOM for completion of a review of the scientific evidence and a determination as to the strength of evidence linking military service, or some specific element of military service, to risk for some health outcome. Our committee examined several decisions made in the past regarding presumptions, treating them as case studies in order to identify "lessons learned" of potential value for improving the process. In examining these case studies, our committee found variable approaches to synthesizing evidence on the health consequences of military service. The target of scientific evidence reviews had not been consistent and varied between causation (e.g., mustard gas and lewisite, Gulf War) and association alone (e.g., Agent Orange). Starting in 1991 the basis for the scientific review in regard to Agent Orange was specified in the statute (Public Law 102–4). This statute says, "the Academy shall review and summarize the scientific evidence and assess the strength thereof, concerning the association between exposure to an herbicide * * * and each disease suspected to be associated with such exposure." Specifically:

(1) whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association;

(2) the increased risk of the disease among those exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and

(3) whether there exists a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

This guidance from the VA has not substantively changed since the beginning of the Agent Orange series of studies, which are now carried out biannually. Each IOM committee in the Veterans Agent and Orange (VAO) Update series is selected as a different and new committee. Each committee has the prerogative to decide how it will review the published literature and to assign categories of strength on assessing association. The several IOM committees since 1991 have been quite consistent in their categorization schemes for strength of evidence, typically assigning four categories:

- Sufficient evidence of an association
- Limited/suggestive evidence of an association
- Inadequate/insufficient evidence to determine whether an association exists
- Limited/suggestive evidence of no association

Once the IOM committee completes its task, it provides its report to the VA. The VA staff described its internal decisionmaking processes to our committee in a general fashion, and the Committee reviewed the VA's *Federal Register* notices and documents to gain further insights. However, it was unclear to our committee how the VA makes particular determinations once the IOM report is received and how information beyond the IOM's findings figure into decisionmaking by the VA, such as the size of the affected population of veterans and the potential costs of a presumption. Generally the VA staff makes recommendations to the Secretary and the Secretary decides whether to assign a presumption of service connection to any new condition. That decision is then documented in the *Federal Register*.

Our committee determined that a more robust and evidence-based process could be envisioned for future cohorts of veterans. We reviewed the current approach to characterizing exposures of veterans to toxins and other stressors that might adversely affect their health. We also considered the scope of epidemiological research undertaken by the DOD and the VA. Our review found gaps in the assessment of exposures of military personnel and in the tracking of their health that could be addressed through a more systematic approach.

We also made recommendations for a future presumptive decisionmaking process that would build on accumulating evidence on exposure and risk. We recommended that the VA establish an Advisory Committee to provide guidance on disability matters including presumptive disability (if allowed by Congress). That Advisory Committee would serve as a clearing house for new presumptions recommended by veterans, veteran service organizations (VSOs), veterans' families, VA, DOD, other governmental bodies, researchers, or the general public. We also recommended that Congress allow the VA to contract with an independent scientific organization to perform the function of a Science Review Board. This independent scientific entity would consider the relevant evidence and analyze candidate presumptive conditions given to it by the VA through VA's Advisory Committee.

We also recommended the establishment of an independent Science Review Board. This Science Review Board would use a two-step process. In step one, the scientific literature would be reviewed to determine the strength of the evidence to assess whether a given health outcome can be caused by a given exposure. This scientific review process is very much like that currently followed by IOM. The Committee recommended that the target of the review should be to determine likelihood of causation and not simply the existence of statistical association. The Committee developed a system to grade the strength of the scientific evidence for causation using four levels in ascending order of certainty (highest at top). The upper two levels were set to correspond to 50% or more certainty of causation. If the strength of the scientific evidence reached either of these upper two levels, the process would move on to step two. In step two, the Science Review Board would calculate the service-attributable fraction of disease, if the required data and information were available. This second step assesses how much of the observed disease both in absolute and relative terms can be attributed to the exposure. The calculation is independent of the classification of the strength of evidence for causation, and the magnitude of the service-attributable fraction is not considered in categorizing evidence. Rather, the service-attributable fraction would be of value for decisionmaking, giving an understanding of the scope of the population to be covered by a presumption. In step two, the Science Review Board would consider the extent of exposure among veterans and subgroups of veterans, as well as dose-response relationships. A critical element in the deliberations of the Science Review Board would be evidence available from studies on exposures and health risks to the veterans. When such information is available, the board would estimate the service-attributable fraction and the related uncertainty. The purpose of step two is to convey the impact of the exposure on veterans as a whole for the purpose of decisionmaking and planning, but not to serve, inappropriately, as an estimate of probability of causation for individuals. Some exposures may contribute greatly to the disease burden of veterans, while other exposures (even with a known causal effect) may have a small impact overall. This additional information would be useful to the VA in its decisionmaking as to whether a presumption should be made for the veteran population in general, for subgroups, or not at all. In the absence of service-attributable fraction data, as will likely occur for many exposures over the short-term, we assumed that the VA would consider presumptions on the basis of information considered in step one.

Under this model, the VA Advisory Committee would be more effective, visible, and stakeholder-inclusive in establishing candidate conditions for presumptive determinations. In addition the Science Review Board would permit the VA to receive outside, independent, evidence-based advice that would not be perceived as politically driven or influenced. This model would also identify important research gaps to which the VA could give special emphasis to reduce uncertainty.

I have been asked to comment on how the PDDM committee would evaluate the three new presumptions, ischemic heart disease (IHD), Parkinson's Disease (PD), and B-cell leukemias in a manner similar to our committee's assessment of previously established Agent Orange presumptions such as prostate cancer and diabetes. Our PDDM committee finished its work and has been inactivated, so my comments are my own and cannot be construed as coming from the PDDM committee or the IOM.

Keep in mind that our PDDM committee performed our case studies well after the presumptions had been established whereas these three new presumptions have not gone into effect, so it is too soon to tell what experiences will result and what lessons will be learned.

Nevertheless I will try to draw from some of the relevant observations we made from our prior case study analysis as they relate to the three new presumptions. I will start with the presumption that is likely to affect the most veterans, that for ischemic heart disease (IHD).

The PDDM committee noted that association and not causation was the target for the IOM reviews on Agent Orange and remarked that causation would be a preferable choice. In addition our committee concluded that it would have been desirable to better integrate information concerning "plausible biologic mechanism or other evidence of a causal relationship" into the interpretation of the evidence. Consideration of mechanistic and other biological evidence is a standard element of causal inference.

Our critique was done with recognition that all of the IOM committees evaluating the effects of Agent Orange were operating under the statutory guidance, incorporating judicial rulings, that were passed from Congress to the VA and then from the VA to IOM. When evaluating any possible medical condition that might be associated with Agent Orange exposure, the VAO update committees were required to perform the three tasks delineated above.

The PDDM report pointed out the imprecise wording included in the explanation of criteria for the "limited/suggestive" category that had been carried along since the first Agent Orange report. Literally interpreted, this implies that a single positive "high-quality" study would permanently keep a health outcome in the "limited/suggestive" category of association no matter how many negative "high-quality" studies were published later. Such a standard did not appear to be reasonable to our committee. It has been brought to my attention that VAO update committees for *Update 2006* and *Update 2008* have revised this statement to better characterize this particular category of evidence.

Criteria for the strength of evidence can be established, but that evidence exits along a continuum, extending from no evidence at all to full certainty. An element of subjectivity always remains in synthesizing evidence into a particular category of strength of evidence. It requires "expert scientific judgment" to conduct these reviews. IOM has a very systematic process and uses acknowledged experts who have volunteered their time pro bono to arrive at consensus findings and recommendations.

For both prostate cancer and Type II diabetes our PDDM case studies pointed out the difficult challenges of establishing a service connection for a common chronic condition when exposure data are unavailable and evidence of association is limited. There was no additional exposure data available relating to Vietnam veterans when considering an association with IHD.

For prostate cancer and Type II diabetes mellitus, the PDDM committee was unable to judge the rationale for the VA's translation of IOM's VAO update committee's category of "limited/suggestive" association to a presumptive decision, considering that the congressionally stipulated standard requires evidence to be "equal to or outweighs" lack of such evidence. This basis for this decision on VA's part remains unclear. The designation of the evidence for IHD as limited-suggestive appears reasonable in light of the evidence reviewed. But, the scientific rationale for a presumptive determination is still unclear.

One of the key lessons learned from the PDDM case studies and particularly those related to Agent Orange exposure was a need for high-quality data on cohorts of veterans; ideally such data would include more accurate assessments of exposure during service, evaluation of other risk factors that may have been present during service or have developed after service before the onset of disease, and longitudinal assessments for evaluation of diseases that may have long latency periods. IOM VAO update committees have made this same suggestion since 1994. Such cohort information remains an unquestionably desirable resource for future presumptive decisionmaking. It is not generally feasible to obtain accurate exposure data many years after the fact.

I will make just a few comments about the other two presumptions, Parkinson's Disease and B-cell malignancies. The VAO committee (*Update 2008*) observed that data were accumulating with regard to Parkinson's disease. They upgraded the evidence of association to limited/suggestive based on several recent published studies supporting evidence of an association not just with herbicide exposure, but specifically, exposure to the phenoxyherbicides that were the intended components of Agent Orange.

Regarding B-Cell leukemias, the VAO (*Update 2008*) determined that B-cell leukemia should be regarded as a form of chronic lymphocytic leukemia (CLL). A previous VAO committee (*Update 2002*) had already concluded that there was sufficient evidence for CLL being associated with herbicide exposures. Investigation of the biological nature of the cells progressing to B-cell leukemia confirmed that this malignancy is a form of CLL. CLL itself has now been classified as form of non-Hodgkin's lymphoma, which has long been recognized as a presumptive illness. Consequently, the VAO committee (*Update 2008*) placed this in the "sufficient" association category.

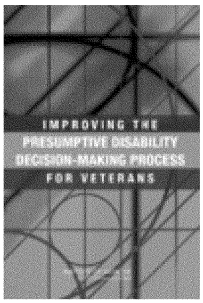
A major theme that emerged from the case reviews was the difficulty of disentangling the potential role of service-related factors in diseases that have multiple causes, particularly as disease rates rise with age through the actions of these causes. Additionally, there is the possibility that the effects of exposures in the military, e.g., Agent Orange, might be synergistically enhanced by other factors. There are multiple causes for all the presumptive conditions mentioned above. Beyond assessing whether these conditions are associated with exposure to Agent Orange and other herbicides, it would be useful to determine to what extent these exposures are contributing to disease burden among our servicemen and women. In the absence of accurate exposure data this estimation would be difficult for Vietnam veterans, but the PDDM committee concluded that future presumptive decisions would be made more useful if the attributable fraction of the disease burden caused by a military service-related exposure were determined.

I have also been asked to comment on the degree of clarity that the VA has provided to various IOM committees for determining how to weigh conflicting evidence related to possible presumptions. I have not been privy to the contractual discussions that the VA has held with IOM as IOM convened committees to conduct scientific review on potential health effects of military-relevant exposures. Nevertheless, in my opinion, the VA understands the role of IOM as an independent advisory organization and it allows IOM committees to determine how to best search for, weigh, and synthesize the scientific evidence on health effects relating to military-relevant exposures. In recent years congressional legislation has stipulated what should be considered in the scientific reviews conducted for Agent Orange and Gulf War presumptions. The VA has ensured that this congressional guidance is made evident to IOM before IOM conducts its scientific reviews.

Finally, I have been asked to provide my views on the extent to which the PDDM committee's recommendations were followed by the Secretary in his most recent presumptive decisions, especially with respect to ischemic heart disease. The specific basis for this decision is not apparent. As far I am aware, the VA is operating under the established statutory guidelines and procedures used in prior presumptive reviews. The PDDM committee proposed a model that would make the basis for decisionmaking fully transparent so that, for the future, this type of question could be answered.

This concludes my remarks. Thank you for the opportunity to speak with the Committee. I will be pleased to address questions from the Senate Committee Members.

ATTACHMENT



Improving the Presumptive Disability Decision-Making Process for Veterans

Committee on Evaluation of the Presumptive Disability Decision-Making Process for Veterans, Jonathan M. Samet and Catherine C. Bodurow, Editors

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Summary

INTRODUCTION

The United States has long recognized and honored military veterans' service and sacrifices. Veterans injured by their service, becoming ill while in service, or having an illness after discharge as a long-term consequence of their service have been given healthcare coverage and disability compensation. As the complexity of exposures during combat has increased, the list of service-connected illnesses has grown. The Department of Veterans Affairs (VA) now provides disability compensation to approximately 2.6 million veterans for 7.7 million disabilities annually, expending approximately $24 billion for this purpose (VBA, 2006, pp. 19, 24, 27).

Disability compensation for military veterans requires that there be a service connection. A medical illness or injury that occurred while a member was in military service is considered service connected whether caused by or aggravated by an exposure or event during service *or simply occurring coincidentally* with military service. However, if a medical condition appears after the period of military service and it is presumed to be caused by or aggravated by an exposure or an event that occurred during military service, then veterans may receive compensation based on that presumption (Pamperin, 2006).

In making a decision to provide compensation, VA needs to determine whether the illness of concern can generally be caused by exposures received during service and whether the illness in a specific claimant was caused by the exposure. The answer to the general question of causality comes from a careful review of all available scientific information, while the answer

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to the question of causation in a specific person hinges on knowledge of the exposure received by that individual and of other factors that may be relevant. If the scientific evidence is incomplete, there may be uncertainty on the question of causation generally; if there is limited or no information on exposure of individual claimants or if other factors also contribute to disease causation, there may be uncertainty on the question of individual causation.

To provide benefits to veterans in the face of these two broad types of uncertainty, Congress and VA make presumptive decisions that bridge gaps in the evidence related to causation and to exposure. Presumptions may relieve the veteran of persuading VA that the exposure produced the adverse health outcome and of proving that an exposure occurred during military service (Pamperin, 2006). Once a medical condition is service connected through presumptions, and the veteran can document military service consistent with having received the given exposure, the veteran only has to show the basic fact that he or she suffers from the condition in order to receive a disability payment and eligibility for medical care (Zeglin, 2006).

In 2004, Congress established the Veterans' Disability Benefits Commission (the Commission), which was charged with "studying the benefits provided to compensate and assist veterans for disabilities attributable to military service" (VDBC, 2006, p. 1; as found in Appendix A). The Commission identified the presumptive disability decision-making process as a topic needing assessment and asked the Institute of Medicine (IOM) to establish a committee for this purpose that would be funded by VA. The resulting committee, the Committee on Evaluation of the Presumptive Disability Decision-Making Process for Veterans (the Committee), was given the following charge by VA:

- Describe and evaluate the current model used to recognize diseases that are subject to service connection on a presumptive basis.
- If appropriate, propose a scientific framework that would justify recognizing or not recognizing conditions as presumptive.

The Commission further elaborated the charge, asking the Committee to "help ensure that future veterans are granted service connection under a presumptive basis based on the best scientific evidence available" (VDBC, 2006, p. 4; as found in Appendix A). The Commission asked the Committee to "evaluate the current model used to determine diseases that qualify for service connection on a presumptive basis, and if appropriate, propose improvements in the model" (VDBC, 2006, p. 1; as found in Appendix A). The Commission emphasized that "having a method of granting service connection quickly and fairly based on a presumption is

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of critical importance to our disabled veterans and their surviving spouses" and that "ensuring that future presumption processes reflect the then current medical knowledge about the causal relationship would benefit the entire veteran community" (VDBC, 2006, p. 4; as found in Appendix A). The Commission's summary statement further commented that "[t]o the extent possible, suggestions that will avoid the necessity for many future presumptions by ensuring that exposure of service members is documented and scientific evidence is made available would be important" (VDBC, 2006, p. 4; as found in Appendix A).

IOM appointed a 14-member committee that covered the broad scientific and medical areas of general, occupational, and psychiatric medicine; biostatistics; epidemiology; toxicology; industrial hygiene; and exposure and risk assessment. The Committee's members also brought expertise in law, philosophy, causal decision making, and policy as well as knowledge of the Department of Defense (DoD) and VA's approach to disability compensation.

THE COMMITTEE'S APPROACH TO ITS CHARGE

In fulfilling its charge, the Committee first investigated and attempted to characterize Congress' and VA's recent approach to presumptive disability decision making, and then developed a conceptual framework for a new, more evidence-based process. It then constructed a way to move forward that builds on the framework and addresses deficiencies of the current process.

The Committee held three open meetings to gather information on the current presumptive disability decision-making process. The Committee heard from past and present congressional staff members, representatives of VA, DoD, IOM, various stakeholder groups (e.g., veteran service organizations [VSOs]) and the general public. Committee members also participated in conference calls with DoD experts on medical surveillance and exposure data collection and exposure assessment systems.

The Committee reviewed extensive background information including: documents provided by the Commission, public laws and supporting House and Senate reports, *Federal Register* notices, VA documents (e.g., cost estimates, a white paper on VA's decision-making processes [found in Appendix G], and responses by VA to written questions from the Committee), DoD documents, and past IOM reports commissioned by DoD and VA. The Committee conducted 10 case study reviews—Mental Disorders' Presumptions, Multiple Sclerosis Presumption, Prisoners of War Presumptions, Amputees and Cardiovascular Disease Presumption, Radiation Presumptions, Mustard Gas and Lewisite Presumptions, Gulf War Presumptions, Agent Orange and Prostate Cancer Presumption, Agent Orange and Type 2

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Diabetes Presumption, and Spina Bifida Program (not a presumption but a VA program area)—that cover a wide variety of circumstances for which presumptions have been established by Congress and VA since 1921. The case studies were a foundation for the Committee's efforts in understanding past practices of all participants in the presumptive disability decision-making process (see Appendix I).

The Committee also researched and considered capabilities and limitations of the exposure data and health outcome information available to DoD and VA for exposure assessment, surveillance, and research purposes. The Committee examined whether DoD and VA have a strategic research plan and vision for the necessary interface between the agencies, as well as with other, relevant research organizations.

The Committee considered the use of scientific evidence in guiding the process for making presumptive decisions that affect the compensation of veterans. Drawing upon the Committee members' expertise in epidemiology, medicine, toxicology, biostatistics, and causal decision making, the Committee covered the evaluation of evidence for inferring association and causation as well as methods for quantifying the contribution of an agent to disease causation in populations and extending this quantification to individuals. Using this framework, the Committee developed an evidence-based approach for making future decisions with regard to presumptions.

THE PRESUMPTIVE DISABILITY DECISION-MAKING PROCESS FOR VETERANS

In 1921 Congress empowered the VA Administrator (now Secretary) to establish presumptions of service connection for veterans. Only Congress and the VA Secretary have the authority to establish presumptions. Over time, presumptions have been made to relieve veterans of the burden to prove that disability or illness was caused by a specific exposure that occurred during military service (e.g., Prisoners of War). Since 1921, nearly 150 health outcomes have been service connected on a presumptive basis (see Appendix F). In February 2006, Congress codified all regulatory presumptions that VA had put in place to that time.

The current presumptive disability decision-making process for veterans involves several steps and several organizations. The process involves input from many parties—Congress, VA, the National Academies, and stakeholders (e.g., VSOs, advisory committees, and individual veterans) (Figure S-1). Congress has made presumptions itself. In the current model, Congress or stakeholders acting through Congress may call on VA to assess whether a presumption is needed. The VA turns to IOM for completion of a review of the scientific evidence. The findings of that evaluation are consid-

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FIGURE S-1 Roles of the participants involved in the presumptive disability decision-making process for veterans.
[a] Stakeholders include (but are not limited to) veterans service organizations (VSOs), veterans, advisory groups, federal agencies, and the general public; these stakeholders provide input into the presumptive process by communicating with Congress, VA, and independent organizations (*e.g.*, the National Academies).
[b] Congress has created many presumptions itself; in 1921, Congress also empowered the VA Secretary to create regulatory presumptions; on several occasions in the past, Congress has directed VA to contract with an independent organization (e.g., the National Academies) to conduct studies and then use the organization's report in its deliberations of granting or not granting regulatory presumptions.
[c] VA can establish regulatory presumptions; VA sometimes contracts with the National Academies to conduct studies and uses the organization's report in its deliberations of granting or not granting regulatory presumptions.
[d] The National Academies (Institute of Medicine and National Research Council) submit reports to VA based on requests and study charges from VA.

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ered by VA in its presumptive disability decision-making process. Decisions made in the courts have also influenced the current presumptive process.

Three major legislative actions by Congress have influenced the recent presumptive decisions—the Radiation Exposed Veterans Compensation Act of 1988 (Public Law 100-321. 100th Cong., 2d Sess.), the Agent Orange Act of 1991 (Public Law 102-4. 102d Cong., 1st Sess.), and the Persian Gulf War Acts of 1995 (Veterans' Benefits Improvement Act of 1994. Public Law 103-446. 103rd Cong., 2d Sess.) and 1998 (Making Omnibus Consolidated and Emergency Appropriations for the Fiscal Year Ending September 30, 1999, and for Other Purposes. Public Law 105-277. 105th Cong., 2d Sess.). The concept of "at least as likely as not" with regard to exposure potential was introduced for radiation exposures and its use has since been continued. The Agent Orange Act (Public Law 102-4. 102d Cong., 1st Sess.) grew out of events following the Vietnam War, and its language expresses substantial and significant elements of the presumptive story. The presumptions put in place by Congress for Gulf War illnesses represent the first time that Congress produced a list of health outcomes that it defined as "undiagnosed illnesses" (Veterans Education and Benefits Expansion Act of 2001. Public Law 107-103. 107th Cong., 1st Sess.).

When Congress enacted the Agent Orange Act of 1991 (Public Law 102-4. 102d Cong., 1st Sess.), it started a model for a decision-making process that is still in place. Congress asked VA to contract with an independent organization—VA contracted with IOM—to review the scientific evidence for Agent Orange. Since 1994, IOM has produced biennial reports on Agent Orange for VA to use as it considers making presumptive decisions (IOM, 1994, 1996, 1999, 2001, 2003b, 2005b). IOM has also delivered five volumes on the Gulf War (IOM, 2000a, 2003a, 2005a, 2006, 2007). Congress requires VA to respond after receiving an IOM report with a determination as to whether VA will make a service connection for particular health outcomes on a presumptive basis. VA has described its internal decision-making processes to the Committee in a general fashion, and the Committee has reviewed VA's *Federal Register* notices and documents (see Chapter 3). However, it remains unclear to the Committee how VA makes particular determinations with regard to weighing strength of evidence for causation and exposure potential in making its presumptive decisions.

Analysis of the Agent Orange and Gulf War case studies (see Appendix I) shows important similarities and differences relevant to the overall presumptive process. One difference is that Agent Orange is a single product (actually a mixture of compounds that contains the contaminant dioxin), extensively researched for associated health outcomes, whereas the health consequences of the Gulf War are unlikely to be the result of any single agent. Military service men and women may have received a number of health-relevant exposures during service in the Persian Gulf, complicating the development of evidence reviews. For Agent Orange, there is one

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exposure of concern and a more constrained set of health indicators. There have been some differences in approaches of Agent Orange and Gulf War committees. The IOM Agent Orange reports (IOM, 1994, 1996, 1999, 2001, 2003b, 2005b) did not explicitly include a causal category in their evaluations whereas recent Gulf War reports (IOM, 2000a, 2003a, 2005a, 2006, 2007) did include a category for evidence sufficient to infer causation when characterizing the strength of evidence for agents evaluated. For neither set of reports does VA describe in its *Federal Register* notices how it accounted for exposure potential or magnitude in making its presumptive decisions.

FINDINGS OF CASE STUDIES

The case studies offered a diverse set of lessons learned and indicated elements of the current process that need to be addressed. In carrying out the case studies, this Committee had the opportunity to retrospectively examine the work of IOM committees as they grappled with the challenge of using uncertain evidence and of VA staff as they used the findings of IOM committees to make decisions about presumptions. The case studies demonstrate that the process has acted to serve the interests of veterans in many instances. Congress and VA have repeatedly acted to maximize the sensitivity of presumptive decisions so as to assure that no veteran who might have been affected is denied compensation. On the other hand, in maximizing sensitivity of presumptive disability decision making, substantial numbers of veterans whose illnesses may or may not have been actually service related are nonetheless compensated. There are both financial and nonfinancial costs to such decisions.

The case studies illustrate the use of presumptions to cover gaps in evidence, gaps that exist in part because of lack of information on exposures received by military personnel and inadequate surveillance of veterans for service-related illnesses. Secrecy is a particularly troubling source of incomplete information, as illustrated by the veterans who participated in studies of mustard gas and lewisite. Research carried out directly on the health of veterans has proved useful in some instances, leading to a decision, for example, on granting disability compensation for cardiovascular disease in amputees. But the research has not been systematic, and in the example of cardiovascular disease in amputees no further evidence relevant to a presumption made in 1979 has been collected. Research on radiation risks in veterans has been severely constrained by a lack of dose information, and the studies on radiation-exposed veterans have not been highly informative.

Across the case studies, the Committee found variable approaches to synthesizing evidence on the health consequences of military service. The inferential target of scientific evidence reviews has not been consistent

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and varied between causation (e.g., mustard gas and lewisite, Gulf War) and association alone (e.g., Agent Orange). The more recent IOM Agent Orange reports have emphasized findings of observational studies on association and interpretation that might have been enhanced by placing the findings within a biological framework strengthened by greater attention to other lines of evidence. In the Agent Orange case studies, the category "limited/suggestive" for classifying evidence for association has been used for a broad range of evidence from indicating the mere possibility of an association to showing that an association is possibly causal. The "limited/suggestive" evidence of association—on which the VA's presumptive decisions to compensate type 2 diabetes and prostate cancer were made—may be below the level of certainty needed to support causation absent strong mechanistic understanding or to meet the congressional language of "if the credible evidence for the association is equal to or outweighs the credible evidence against the association," which the Committee refers to "at least as likely as not."

Both prostate cancer and type 2 diabetes illustrate situations in which the contribution of military exposures should be assessed against a background of disease risk that has other strong determinants: age in the case of prostate cancer and family history and obesity in the case of type 2 diabetes, as indicated by the IOM committee in its report (IOM, 2000b). For both type 2 diabetes and prostate cancer, the magnitude of the relative risks observed for pesticide exposure implies that the contribution of military exposures is likely to be small in comparison to those of the other contributing factors. In such circumstances, an estimation of the proportion of cases attributable to military exposures could be helpful to the VA in considering whether or not to presumptively service-connect disabilities. The Committee recognizes that development of such estimations is a complicated process dependent on acquiring better exposure data, which may not be available for some period of time.

In the case studies, the Committee's analyses were based on the very general information provided by VA about its internal decision-making processes. The case studies and VA's decision to withhold documents related to specific decisions from the Committee did make clear, however, that these processes are not fully transparent. VA believes that access to predecisional documents by outside sources could stifle candid staff discussions on issues. Once IOM carries out its reviews and provides VA with reports documenting the extent of evidence available on associations, the internal processes of VA that follow are not fully open to scrutiny. This closed process could reduce trust of veterans in the presumptive disability decision-making process and may hinder efforts to optimize the use of scientific evidence. The Committee also found inconsistency in the decision-making process.

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SCIENTIFIC FOUNDATION FOR PRESUMPTIVE DISABILITY DECISION MAKING

In developing a future approach for presumptive disability decision making, the Committee first gave extensive consideration to causal inference and the processes used to make causal judgments. In other words, the Committee considered how scientific evidence is used to determine *if* exposure causes some disease. These determinations are generally made by expert committees that examine all relevant evidence for strengths and weaknesses and then synthesize the evidence to make a summary judgment. The Committee defines "exposure" in a broad manner to include chemical, biological, infectious, physical, and psychological stressors. The Committee recognizes that psychological stressors may be particularly difficult to describe, let alone measure and quantify.

The Committee then considered the quantification of the contribution of a particular exposure to disease causation. This second issue addresses the question of *how much* of the observed disease in a group, in both absolute and relative terms, is caused by the exposure.

Provision of compensation to veterans on a presumptive basis, or to any other group that has been injured, requires a *general* decision as to whether the agent or exposure of concern has the potential to cause the condition or disease for which compensation is to be provided in at least some individuals, and a *specific* decision as to whether the agent or exposure has caused the condition or disease in a particular individual. The determination of causation in general is based in a review and evaluation of all relevant evidence including (1) data on exposures of military personnel during service; (2) evidence on risks for disease coming from observational (epidemiologic) studies of military personnel; (3) other relevant epidemiologic evidence, including findings from studies of nonmilitary populations exposed to the agent of interest or similar agents; and (4) findings relevant to plausibility from experimental and laboratory research. The determination of causation in a particular case is based first on the general determination as to whether the exposure can cause disease, then on information about the exposures of the individual being evaluated for compensation, and on any other relevant information about the individual.

The Committee considered the properties of a decision-making process, recognizing the possibility of two types of systematic errors: making a decision to compensate when the exposure has not caused the illness (false positive) and to not compensate when the exposure has actually caused the illness (false negative). The Committee recommends that any decision process consider the trade-off between these two errors and attempt to optimize both the sensitivity (i.e., minimize the false negatives) and the specificity (i.e., minimize the false positives). Generally, higher sensitivity

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cannot be achieved without lower specificity. These errors have costs. False positive errors result in the expenditure of funds for cases of disease not caused by military service while false negative errors leave deserving veterans uncompensated. The appropriate balancing of these costs also needs consideration.

The Committee considered ways to classify evidence, reaching the conclusion that a broader and more inclusive evidence review process is needed. It found that IOM reviews could be enhanced if a broader array of epidemiologic and other evidence (e.g., animal and mechanistic data) was considered. The Committee also found that the target of inference had varied from causation (e.g., mustard gas and lewisite, Gulf War) to association (e.g., Agent Orange). Consequently, the Committee recommends that categories of evidence for reviews be established to make clear those relationships that are at least as likely as not to be causal. The Committee has concluded that a categorization of evidence is needed that gives a scientifically coherent rendering of the language employed by Congress in calling for review of available scientific evidence. The Committee proposes a four-level hierarchy that classifies the strength of evidence for *causation, not just association,* and that incorporates the concept of equipoise: that is, whether the weight of scientific evidence makes causation at least as likely as not in the judgment of the reviewing group.

The Committee also gave consideration to the quantification of the burden of disease attributable to an exposure. This quantification would be made to provide an evaluation of the numbers of veterans to be compensated, but it would not be a component of the evidence evaluation for causation. For the purpose of quantification, the attributable risk, termed the *service-attributable fraction*, can be calculated if the needed information is available on the relative risk of disease among exposed individuals. For those exposures meeting the necessary level of evidence for compensation, the Committee recommends that the service-attributable fraction should be estimated overall and for subgroups of veterans, perhaps grouped by level of exposure, if the requisite data are available. Until more complete exposure information becomes available in the future, such calculations may not be possible for all conditions for which presumptions are made.

COMMITTEE'S RECOMMENDED APPROACH FOR THE FUTURE

Overview

The Committee's recommended approach for the future (Figure S-2) has multiple new elements: a process for proposing exposures and illnesses for review; a systematic evidence review process incorporating a new evidence classification scheme and quantification of the extent of disease

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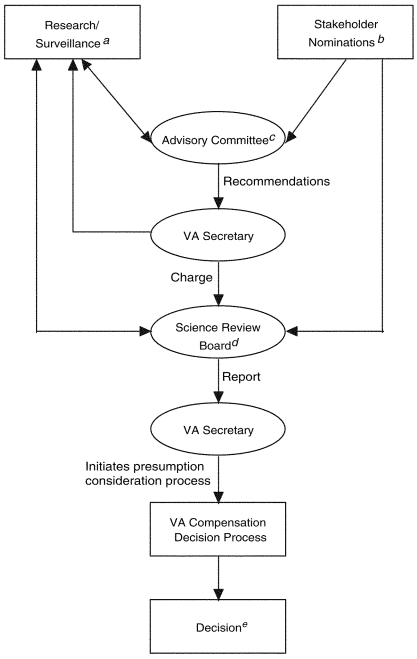

FIGURE S-2 Proposed framework for future presumptive disability decision-making process for veterans.
[a] Includes research for classified or secret activities, exposures, etc.
[b] Includes veterans, Veterans Service Organizations, federal agencies, scientists, general public, etc.
[c] This committee screens stakeholders' proposals and research in support of evaluating evidence for presumptions and makes recommendations to the VA Secretary when full evidence review or additional research is appropriate.
[d] The board conducts a two-step evidence review process (see report text for further detail).
[e] Final presumptive disability compensation decisions are made by the Secretary, Department of Veterans Affairs, unless legislated by Congress.

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attributable to an exposure; a transparent decision-making process by VA; and an organizational structure to support the process. The Committee also calls for comprehensive tracking of exposures of military personnel and monitoring of their health while in service and subsequently.

Organizational Structure

The Committee recommends the creation by Congress of two new permanent boards: the Advisory Committee, serving in an advisory capacity to VA, and the Science Review Board (independent from VA). The Advisory Committee would consider the exposures and illnesses that might be a basis for presumptions and recommend to the VA Secretary exposures and illnesses needing further consideration. It would also consider research needs and assist VA with strategic research planning. The Science Review Board would evaluate the evidence for causation and, if warranted, estimate the service-attributable fraction of disease in veterans. One critical element in the deliberations of the Science Review Board would be evidence from monitoring the exposures and health of the veterans. The Science Review Board would provide VA with input for its presumptive decisions, including a summary report of the available scientific evidence in a standardized classification scheme.

Congress and VA may find alternative processes to achieve the overall objective of the Committee's recommendations: an evidence-based approach to making presumptive disability decisions. The Committee recognizes that specific elements of its proposal (e.g., the call for carrying out exposure assessments and making exposure estimates) are not yet fully practicable and would take time to develop and implement. However, future methodologic developments should enhance the feasibility of some of the challenging elements of this proposal. The Committee believes that this proposal can significantly improve the presumptive disability decision-making process for veterans and, therefore, the process for implementing it should begin without delay.

Underlying Principles

VA's decision to make a presumption may involve weighing difficult and incomplete scientific evidence, in the context of veterans' concerns and society's obligations to the affected veterans, and potential costs. Although the potential complexity of the decision-making process may make a complete codification difficult, the underlying principles can be clearly expressed. The Committee suggests the following six principles as a foundation for its proposed framework: (1) stakeholder inclusiveness; (2) evidence-based decisions; (3) transparent process; (4) flexibility; (5) consistency; and (6) using

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causation, not just association, as the basis for decision making. Flexibility and consistency are not contradictory constructs here. Flexibility refers to the ability to be adaptable through time in evaluating scientific evidence, and consistency refers to being consistent in the process of evaluating evidence and making consistent decisions based on a comparable level of certainty based on the scientific evidence.

Proposals to Review for Potential Presumption

In this process, conditions and causative agents or circumstances would be proposed for review based on evidence of a connection between the condition and military service and evidence that a sizable or well-defined group of veterans is likely to be affected. The possibility of a need for a presumption might arise from surveillance of veterans or active military personnel, laboratory research discoveries, or findings from studies of exposed workers. The process would be open, with proposals accepted from any source (e.g., veterans, veterans' families, VSOs, VA, DoD, other governmental bodies, researchers, the general public). Proposals accepted by the VA Secretary would be sent to the Science Review Board for full, comprehensive scientific evaluation.

Science Review Board

The Committee recommends a two-step process for scientific evaluation by the Science Review Board. The first step would involve a systematic review of all relevant data to decide the strength of evidence for causation, using one of four categories:

1. *Sufficient*: The evidence is sufficient to conclude that a causal relationship exists.
2. *Equipoise and Above*: The evidence is sufficient to conclude that a causal relationship is at least as likely as not, but not sufficient to conclude that a causal relationship exists.
3. *Below Equipoise*: The evidence is not sufficient to conclude that a causal relationship is at least as likely as not, or is not sufficient to make a scientifically informed judgment.
4. *Against*: The evidence suggests the lack of a causal relationship.

If the evidence for causation were categorized as *Sufficient* or at *Equipoise and Above*, then we anticipate that VA would consider a presumptive service connection based upon causal evidence categorization and its consideration of the service-attributable fraction if available (to be estimated in the second step of the process, described below). As is current VA policy,

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if the evidence is at *Equipoise*, the benefit of the doubt would be given to the veteran. If the evidence were categorized as *Against*, then we anticipate that VA would not consider a presumptive service-connection. If, however, the evidence were categorized as *Below Equipoise*, then we anticipate that VA would, after carefully considering the prospects and recommendations for future research, decide on an appropriate time frame for the subsequent scientific review of the evidence, with the expectation that the evidence would then be sufficient to resolve matters either for or against the causal claim at that time. Such information would be considered by the Advisory Committee serving in its capacity as overseer of the overall process and advisor to the VA Secretary.

If the VA Secretary were to decide that a presumption would not be established for evidence categorized as *Below Equipoise* or, for other reasons, for evidence categorized as *Equipoise and Above*, then during the period of further evidence development and gathering and prior to the subsequent scientific review of the evidence, VA should consider providing some support to potentially affected veterans, such as providing provisional access to medical care.

As evidence accumulates, the balance might move to strengthen or to weaken the case for causality. Importantly, the Science Review Board should be free to upgrade the level of evidence, to downgrade the level of evidence, or to leave it as the same categorization. For evidence that has reached the classification of *Sufficient*, we would not anticipate a potential lowering of the classification, if the original determination was correctly made and based on sound scientific evidence.

If the strength of the evidence reaches *Sufficient* or *Equipoise and Above*, then the evaluation would move to step two, the calculation of the service-attributable fraction of disease when required data and information are available. This calculation is independent of the classification of the strength of evidence for causation, and the magnitude of the service-attributable fraction is not considered in the application of the four-level schema for categorizing evidence. Rather, the service-attributable fraction would be of value for decision making, giving an understanding of the scope of the population to be covered by a presumption.

In step two, the Science Review Board would consider the extent of exposure among veterans and subgroups of veterans, as well as dose-response relationships. When such information is available, the board would estimate the service-attributable fraction and its related uncertainty. The purpose of step two is to convey the impact of the exposure on veterans as a whole for the purpose of decision making and planning, but not to serve inappropriately as an estimate of probability of causation for individuals. Some exposures may contribute greatly to the disease burden of veterans, while other exposure (even with a known causal effect) may have

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a small impact overall. This additional information would be useful to VA in its decision making as to whether a presumption should be made for the veteran population in general, for subgroups, or not at all. In the absence of service-attributable fraction data, as will likely occur for many exposures over the short term, we assume the VA would consider presumptions on the information contained in step one.

Expanding the Evidence Base

In the Committee's view, the best scientific decisions about presumptions can be made only with comprehensive exposure and health surveillance of military personnel. Data collection should begin on entry into the military and continue through discharge, and when harmful exposures are suspected surveillance should be extended indefinitely. Surveillance refers to the ongoing collection, analysis, and use of data relevant to the health of a population. Elements of a surveillance system are already in place, but fall short of what is required. A fully functioning surveillance system would track military exposures and health outcomes, during military service and after discharge, and maintain a repository of data and biological specimens so that emerging and unanticipated questions could be retrospectively addressed. The system needs to be seamless in following military personnel, including National Guard and reservists, from active duty as they transition and become civilians.

This surveillance system should also track job and deployment history for each Service member through the period of service, with exposure assessment and monitoring for a range of job categories. Information on disease risk factors more generally could also be tracked. Use of personal biological samples for individual monitoring also holds promise.

Assessing exposures relevant to the neuropsychiatric disorders that are frequent among veterans of recent and current combats is particularly problematic. Documentation of stress is requisite to the diagnosis of post-traumatic stress disorder (PTSD), but approaches for capturing exposures to such stressors and to the circumstances of combat have not yet been developed and put into place. Research is needed for this purpose that builds on existing approaches so that data become available over the long-term.

In addition to surveillance, the Committee recommends an effort to coordinate and focus research on the health effects of military exposures. Associations identified in the surveillance data might need follow-up through more focused epidemiologic studies or exposure assessments. Toxicological research might be indicated to explore the mechanistic basis for an association between an exposure and a health condition.

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VA Procedures

Ultimately, the decision regarding which proposed topics for potential presumptions deserve full evaluation resides with VA. In the Committee's proposed process, VA also receives scientific input from the Science Review Board. We recommend that VA establish a uniform and transparent process for making decisions regarding presumptions following receipt of evidence reviews. VA should establish procedures with input from the many stakeholders, and a clear, evidence-based rationale should be offered for all decisions. The Committee's recommendations are aimed at providing a sound scientific framework for the presumptive disability decision-making process. The Committee clearly recognizes that there are social, economic, political, and legal factors beyond the scope of scientific evidence that may influence the presumptive disability decision-making process for veterans and the presumptive decisions that are established by Congress and VA.

Scientific evidence is not static, and it often is less than certain. Given that the scientific basis for presumptive decisions will change over time, the Committee recommends that VA should be able to adjust future decisions when such change is scientifically justified. This does not mean that the Committee recommends that benefits previously granted should be terminated. The Committee is aware that disabled veterans and their families are often dependent on such payments and that it could create a hardship to remove them, a matter that VA disability policy recognizes in other situations.

SPECIFIC RECOMMENDATIONS

Based on its evaluation of the current process for establishing presumptive disability decisions and its consideration of alternatives, the Committee has specific recommendations for an approach that would build stronger scientific evidence into the decision-making process and, at the same time, be even more responsive and open to veterans. We propose a transformation of the current presumptive disability decision-making process. We recognize that considerable time would be needed to implement some of these recommendations as would additional investment to create systems needed to track exposures and health status of currently serving military service personnel and veterans. Progress depends on greater research capacity and improvements in the evaluation and utilization of scientific evidence in making compensation decisions. We find that there are elements of the current process that could be changed quickly and we recommend that VA consider prompt action as it moves toward implementation of a new approach. The recommendations that follow are based around the Committee's proposed framework for making presumptive decisions. We list the recommendations in relation to the appropriate body.

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Congress

Recommendation 1. Congress should create a formal advisory committee (Advisory Committee) to VA to consider and advise the VA Secretary on disability-related questions requiring scientific research and review to assist in the consideration of possible presumptions.

Recommendation 2. Congress should authorize a permanent independent review body (Science Review Board) operating with a well-defined process that will use evaluation criteria as outlined in this Committee's recommendations to evaluate scientific evidence for VA's use in considering future service-connected presumptions.

Department of Veterans Affairs

Recommendation 3. VA should develop and publish a formal process for consideration of disability presumptions that is uniform and transparent and clearly sets forth all evidence considered and the reasons for the decisions reached.

Science Review Board

The recommendations that follow are directed towards the proposed, future Science Review Board, the entity to be established in the Committee's proposed approach.

Recommendation 4. The Committee recommends that the goal of the presumptive disability decision-making process be to ensure compensation for veterans whose diseases are *caused by* military service and that this goal must serve as the foundation for the work of the Science Review Board. The Committee recommends that the Science Review Board implement its proposed two-step process.

Recommendation 5. The Committee recommends that the Science Review Board use the proposed four-level classification scheme, as follows, in the first step of its evaluation. The Committee recommends that a standard be adopted for "causal effect" such that if there is at least as much evidence in favor of the exposure having a causal effect on the frequency or severity of disease as there is evidence against, then a service-connected presumption will be considered.

1. *Sufficient*: The evidence is sufficient to conclude that a causal relationship exists.

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2. *Equipoise and Above*: The evidence is sufficient to conclude that a causal relationship is at least as likely as not, but not sufficient to conclude that a causal relationship exists.
3. *Below Equipoise*: The evidence is not sufficient to conclude that a causal relationship is at least as likely as not, or is not sufficient to make a scientifically informed judgment.
4. *Against*: The evidence suggests the lack of a causal relationship.

Recommendation 6. The Committee recommends that a broad spectrum of evidence, including epidemiologic, animal, and mechanistic data, be considered when evaluating causation.

Recommendation 7. When the causal evidence is at Equipoise and Above or Sufficient, the Committee recommends that an estimate also be made of the size of the causal effect among those exposed.

Recommendation 8. The Committee recommends that, as the second part of the two-step evaluation, the relative risk and exposure prevalence be used to estimate an attributable fraction for the disease in the military setting (i.e., service-attributable fraction).

Department of Defense and Department of Veterans Affairs

The following recommendations are intended to improve the evidence on exposures and health status of veterans:

Recommendation 9. Inventory research related to the health of veterans, including research funded by DoD and VA, and research funded by the National Institutes of Health and other organizations.

Recommendation 10. Develop a strategic plan for research on the health of veterans, particularly those returning from conflicts in the Gulf and Afghanistan.

Recommendation 11. Develop a plan for augmenting research capability within DoD and VA to more systematically generate evidence on the health of veterans.

Recommendation 12. Assess the potential for enhancing research through record linkage using DoD and VA administrative and health record databases.

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Recommendation 13. Conduct a critical evaluation of Gulf War troop tracking and environmental exposure monitoring data so that improvements can be made in this key DoD strategy for characterizing exposures during deployment.

Recommendation 14. Establish registries of Service members and veterans based on exposure, deployment, and disease histories.

Recommendation 15. Develop a plan for an overall integrated surveillance strategy for the health of Service members and veterans.

Recommendation 16. Improve the data linkage between the electronic health record data systems used by DoD and VA—including capabilities for handling individual Service member exposure information that is included as part of the individual's health record.

Recommendation 17. Ensure implementation of the DoD strategy for improved exposure assessment and exposure data collection.

Recommendation 18. Develop a data interface that allows VA to access the electronic exposure data systems used by DoD.

Recommendation 19. DoD and VA should establish and implement mechanisms to identify, monitor, track, and medically treat individuals involved in research and other activities that have been classified and are secret.

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Improving the Presumptive Disability Decision-Making Process for Veterans
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RESPONSE TO PRE-HEARING QUESTIONS SUBMITTED BY HON. JIM WEBB TO JONATHAN M. SAMET, M.D., M.S., CHAIR, COMMITTEE ON EVALUATION OF THE PRESUMPTIVE DISABILITY DECISION-MAKING PROCESS FOR VETERANS, INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMY OF SCIENCES

Question 1. To the extent the Committee that you chaired examined this question, please describe the varying approaches IOM committees have taken since 1991 in reviewing the scientific evidence and in forming their opinions on the possibility that exposure to Agent Orange during military service contributed to causing various health conditions.

Response. Across the case studies, our Presumptive Disability Decision-Making (PDDM) committee found variable approaches for synthesizing evidence on the health consequences of military service. The inferential target of scientific evidence reviews had not been consistent and varied between causation (e.g., mustard gas and lewisite, and the Gulf War) and association alone (e.g., Agent Orange). However, since 1991, as shown by the three case studies on the association of several health outcomes prostate cancer, type 2 diabetes, and spina bifida in offspring) with Agent Orange exposure in Vietnam veterans, the IOM's Veterans and Agent Orange (VAO) committees were consistent in executing the congressional mandate set out in the Agent Orange Act of 1991 (Public Law 102–4).

When Congress enacted the Agent Orange Act, it started a model for a decision-making process that is still in place. Congress asked VA to contract with an independent organization-VA contracted with IOM-to review the scientific evidence related to exposure to the herbicides used in Vietnam. Since l994,IOM's VAO committees have produced biennial evidence-synthesis reports for VA to use in making presumptions. These reports are referred to as *Updates 1996, 1998, 2000, 2002, 2004, 2006*, and most recently *Update 2008*. The tasks given to IOM by VA were directly drawn from the criteria contained in statutory language of Public Law 102–4: When looking at a possible health outcome of concern, the requirements were to determine:

(1) whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association;

(2) the increased risk of the disease among those exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and

(3) whether there exists a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

Although VA has on occasion added requests about specific health outcomes, this general guidance has not changed since the beginning of the Agent Orange series of studies. Each IOM VAO committee is selected as a different and new committee. Each committee has the prerogative to decide how it will review the published literature and to assign categories of strength on assessing association within the constraints of the above statement of task. Each successive committee does have the precedents of prior committees as they carry out their reviews. Several VAO committees have been consistent in their categorization schemes for the strength of evidence, assigning four categories:

- Sufficient evidence of an association
- Limited/suggestive evidence of an association
- Inadequate/insufficient evidence to determine whether an association exists
- Limited/suggestive evidence of no association

After a VAO committee completes its task, it provides its report to the VA and the VA then considers the report and other information in its internal decision-making process. The VA described its internal decisionmaking processes to the PDDM Committee in a general fashion and the Committee reviewed VA's *Federal Register* notices and documents for additional insights into these processes. However, it was unclear to our committee as to how VA makes a particular determination after receiving an IOM report; specifically, we were unable to characterize how VA weighs strength of evidence for association and exposure potential in making its presumptive decisions. Generally, the VA staff makes recommendations to the Secretary and the Secretary decides whether to assign a presumption of service connection to any newly categorized condition.

Since the completion of the study by the PPDM committee, I have been advised that subsequent VAO Update committees have made some adjustments in their approach to their tasks. For example:

- In response to an observation of the PDDM committee, the VAO committees for *Update 2006* and *Update 2008* acknowledged the imprecise wording included in the explanation of criteria for the "limited/suggestive" category that had been carried

along since the first VAO report. Those earlier committees considered evidence in the category of "limited/ suggestive" if at least one high-quality study shows a positive association, but the results of other studies were inconsistent. This wording implies that a single positive "high-quality" study would permanently keep a health outcome in the "limited/suggestive" category of association no matter how many negative "high-quality" studies were subsequently published. Beginning with the VAO *Update 2006*, the designation of this category has been revised for clarity.

• With the improvement of methods and technology for assessing exposure that has occurred over the period of the VAO reviews, the Committees have become somewhat more selective about the characterizations of (possible) exposure to the five chemicals of interest (COI) (COIs: TCDD; 2,4-D; 2,4,5-T; cacodylic acid; and picloram). Recent committees have required greater exposure specificity for new studies under consideration.

• The VAO committees for *Update 2006* and *Update 2008* were uncomfortable with the assertion of the original VAO report that several outcomes should be put in the category of "limited/suggestive evidence of no association" without reliable negative findings for all five of the COIs and returned them to the category of "inadequate/insufficient" evidence.

Question 2. Please indicate whether the Committee that you chaired had any contact, and in what capacity, with IOM's VAO Update 2008 committee in reference to its determination of "limited/suggestive" evidence for an association between dioxin and ischemic heart disease.

Response. No, we did not have contact with this other committee. Our IOM committee's work was concluded long before the independent IOM committee that produced the Agent Orange *Update 2008*, which found ischemic heart disease to be associated with AO exposure.

Question 3. Similar to the case study analyses that the Committee you chaired included in your report with reference to the presumptions of prostate cancer and type 2 diabetes, please provide a brief analysis and lessons learned with reference to the Secretary's most recent presumption for ischemic heart disease.

Response. The PDDM Committee's judgments in its case studies were made after-the-fact. The three new potential presumptions from the VAO Update 2008 (ischemic heart disease (IHD), Parkinson's disease (PD), and hairy cell leukemia and other B-cell malignancies) have not yet gone into effect, so my comments will be limited accordingly.

I will attempt to answer this question by noting aspects of the PDDM committee's case studies on prostate cancer and type 2 diabetes that appear to be applicable to the new presumption for IHD.

Before turning to the case studies, I note that several general comments of the PDDM Committee are relevant to the question. First, the PDDM Committee commented in its report on the use of association rather than causation as the benchmark for its evaluations. In addition, our committee thought it would be preferable and more consistent with common practices in evidence evaluation to better integrate information concerning "plausible biologic mechanism or other evidence of a causal relationship" into the determination and interpretation of association.

Our assessments in the case studies were conducted with the understanding that the IOM VAO committees evaluating the effects of Agent Orange operated under the statutory guidance passed from Congress to the VA and then from the VA to the IOM. When evaluating any possible medical condition that might be related to Agent Orange exposure, the statutory guidance below was followed by the VAO committees:

(1) whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association;

(2) the increased risk of the disease among those exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and

(3) whether there exists a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

The PDDM report pointed out the imprecise wording included in the explanation of criteria for the "limited/suggestive" category that has been applied since the first Agent Orange report. Literally interpreted, this wording implies that a single positive "high-quality" study would permanently keep a health outcome in the "limited/ suggestive" category of association, regardless of how many negative "high-quality" studies were published later. A criterion with such consequences was not viewed as reasonable by the PDDM committee.

Criteria for the strength of evidence can be established but that evidence exits along a continuum. An element of subjectivity always remains in synthesizing evi-

dence into a strength category. It requires "expert scientific judgment" to conduct these reviews. IOM has a very systematic process and uses recognized experts who volunteer their time pro bono to arrive at consensus findings and recommendations.

For both prostate cancer and type 2 diabetes, the PDDM case studies exemplified the difficult challenges of establishing a service connection for a common chronic disease with multiple causes under circumstances of not having exposure data. Additionally, the level of association found in the studies was low. The occurrence of both prostate cancer and type 2 diabetes rises with age as age-related causal factors come into play. Consequently, the number of persons affected by presumptions for prostate cancer and type 2 diabetes becomes very large because of the age-driven increase in background rates.

For prostate cancer and type 2 diabetes, the PDDM Committee was unable to identify a specific rationale for VA's translation of IOM's Agent Orange Update committee's category of "limited/suggestive" association to a presumptive decision; the congressionally stipulated standard requires evidence to be "equal to or outweighs" lack of such evidence.

The case studies of prostate cancer and diabetes highlight the problem of characterizing the role of Agent Orange exposure for diseases with multiple causes. Absent any "signature" feature of a case in which Agent Orange played a role, epidemiological evidence can only provide evidence as to whether it is a risk factor and as to the proportion of cases that it may cause. A robust body of evidence is needed to be able to estimate the attributable burden of disease; an understanding of both the risk and the magnitude of exposure is needed for this calculation. Consequently, the PDDM committee concluded that future presumptive decisionmaking would be improved if the attributable fraction of the disease burden caused by a military service-related exposure were determined.

One of the key lessons learned from the PDDM case studies and Agent Orange exposure was a need for high-quality data on a cohort of veterans; ideally such data would include more accurate assessments of exposure during service, evaluation of other risk factors that may have been present during service or have developed after service before the onset of disease, and longitudinal assessments for evaluation of diseases that may have long latency periods. Many IOM VAO Update Committees have made this same suggestion since 1994. Such cohort information remains an unquestionably desirable resource for future presumptive decisionmaking. However, it is not feasible to obtain accurate exposure data many years after the fact.

Question 4. Please elaborate on what the Committee you chaired saw as the benefits to be gained from VA developing and publishing a formal process for consideration of disability presumption that is uniform and transparent and which clearly sets forth all evidence considered and the reasons for the decisions made.

Response. The PDDM Committee felt very strongly that a transparent process for determining presumptive disability was needed and that such a process would better serve all involved parties including veterans, VA, Congress, and the Nation as a whole. These presumptive disability decisions are often contentious and emotionally charged, and their implications may be costly. In addition, government agencies, deservedly or not, are not trusted by all citizens to make the best decisions on their behalf. Our committee's recommendations were intended to enhance openness and inclusiveness in the process. Greater transparency would lead to a higher level of confidence in the outcome and all affected parties would be able to see the evidence and the rationale that drove the decisionmaking process. Transparency is likely to lead to more acceptable, consistent, and equitable decisionmaking.

Question 5. Which of the recommendations made by the Committee you chaired for improving the presumptive disability decisionmaking process could be carried out promptly by VA?

Response. Many of our committee's recommendations would take time to implement including those requiring coordination, agreement, and joint actions with other agencies such as DOD. But some could be accomplished rather quickly.

If statutorily permitted by Congress, VA could establish an Advisory Committee to help advise them on disability matters including presumptive disability. That Advisory Committee would serve as a clearing house for new presumptions suggested by veterans, veteran service organizations (VSOs), veterans' families, VA, DOD, other governmental bodies, researchers, or the general public.

Also with agreement or directives from Congress, VA could contract with an independent scientific organization to perform the function of the Scientific Review Board to analyze candidate presumptive conditions given to it by the VA, as recommended by its Advisory Committee.

In addition, VA could inventory research related to the health of veterans, including research funded by DOD and VA, and research funded by the National Insti-

tutes of Health and other organizations; it could develop a strategic plan for research on the health of veterans, particularly those returning from conflicts in the Gulf and Afghanistan; and it could establish registries of Servicemembers and veterans based on exposure, deployment, and disease histories.

In my opinion, recommendations relating to the better surveillance and exposure data on deployed personnel (necessary for more refined estimation of service-attributable fraction in step two for the Science Review Board), will require considerably more time to be of sufficient scope, intensity, and specificity to accurately assign a level of exposure to potential toxic agents to which they may be exposed. This is particularly problematic for past wars such as Vietnam where exposure information is currently very limited and exposures cannot be accurately reconstructed.

Question 6. Which, if any, of the recommendations made by the Committee you chaired have been adopted by VA?

Response. I do not know specifically at this time. Our sponsors are not required to inform study committees about actions that they have taken or plan to take as a result of our studies.

Question 7. Please elaborate on what you believe are the benefits from the recommendation made by the Committee you chaired that Congress create a formal Advisory Committee and a Science Review Board to advise and assist the Secretary with reviewing scientific research and considering conditions for presumptions. In your response, please indicate whether this recommendation was intended as a replacement for the current function of the IOM Committees in the presumptive disability decisionmaking process and the rationale for any such intention.

Response. The design of the future presumptive decisionmaking process envisioned by our committee was to have two advisory groups, one assembled by and answering to VA and a second independent entity which would advise VA, but be independent of the government.

The Advisory Committee would consider the exposures and illnesses that might be a basis for presumptions and recommend to the VA Secretary exposures and illnesses needing further consideration. It would also consider research needs and assist VA with strategic research planning.

The Science Review Board would use a two-step process. In step one, published literature would be reviewed to determine the strength of the evidence to assess whether a given health outcome can be caused by a given exposure. This scientific review is very much like what IOM does in the current process. The Committee believes that the target here should be to determine likelihood of causation, and not simply statistical association. The Committee developed a categorization schema with four levels for grading the strength of the scientific evidence in ascending order. If the strength of the scientific evidence reached level two or one (50% or more likelihood of causation), the process would move on to step two. In step two the Science Review Board would attempt to estimate the service-attributable fraction of disease if the required data and information were available. This second step assesses how much of the observed disease both in absolute and relative terms can be attributed to the exposure. The calculation is independent of the classification of the strength of evidence for causation, and the magnitude of the service-attributable fraction is not considered in categorizing evidence. Rather, the service-attributable fraction would be of value for decisionmaking, giving an understanding of the scope of the population to be covered by a presumption. In step two, the Science Review Board would consider the extent of exposure among veterans and subgroups of veterans, as well as dose-response relationships. A critical element in the deliberations of the Science Review Board would be any evidence available on exposures and health of veterans. When such information is available, the board would estimate the service-attributable fraction and its related uncertainty. The purpose of step two is to convey the impact of the exposure on veterans as a whole for the purpose of decisionmaking and planning, but not to serve, inappropriately, as an estimate of probability of causation for individuals. Some exposures may contribute greatly to the disease burden of veterans, while other exposure (even with a known causal effect) may have a small impact overall. This additional information would be useful to VA in its decisionmaking as to whether a presumption should be made for the veteran population in general, for subgroups, or not at all. In the absence of service-attributable fraction data, we assume the VA would consider presumptions on the information contained in step one.

There are a number of potential beneficial consequences of this model. The VA Advisory Board would be effective, visible, and stakeholder-inclusive in establishing candidate conditions for presumptive determinations. The Scientific Review Board would give VA outside, independent evidence-based advice synthesizing the best

available data that could inform the relationship between exposures and outcomes in veterans.

The report does not speak to the details of the Science Review Board or imply that this body should replace the IOM. It is against IOM policy to recommend in our study reports that IOM be selected to serve future specific advisory roles.

IOM committees are currently performing step one of the roles envisioned by the Science Review Board. If this new model were to be adopted, the function of the current committees would need to be expanded to evaluate how much of the disease burden in veterans is due to these presumed exposures (the service-attributable fraction).

Question 8. Faced with the challenge of identifying a possible small increased risk of commonly occurring diseases absent accurate exposure data, how would you describe the approach that policymakers have adopted to minimize the possibility of denying service connection to a veteran whose disease may have been caused by Agent Orange?

Response. It is clear that VA has decided to set a very high level of sensitivity in making its presumptive disability decisions. Let me explain my use of the word "sensitivity." In the decisionmaking process there exist two possible types of errors: (1) to make a decision to compensate when the exposure has not caused the illness (false positive) and (2) to not compensate when the exposure has actually caused the illness (false negative). Our PDDM committee noted that any decision process cannot avoid considering the tradeoff between these two errors and that it is not possible to simultaneously maximize both the sensitivity (i.e., minimize the false negatives) and the specificity (i.e., minimize the false positives). Generally, higher sensitivity cannot be achieved without lower specificity. These errors have costs. False positive errors result in the expenditure of funds for cases of disease not caused by military service while false negative errors leave deserving veterans uncompensated. The appropriate balancing of these costs needs great consideration. Where that proper balance should be established is a social policy issue rather than a scientific one. What this scientific model does is allow one to place the fulcrum along the balance board with more precision.

Question 9. Do you believe that the current process for creating presumptions is the appropriate mechanism to address gaps resulting from the inability to measure attributable risk of dioxin exposure for diseases common to aging or other highly prevalent risk factors? Can determinations of whether common diseases of aging are positively associated with dioxin exposure be resolved by science in the absence of accurate exposure data?

Response. The current process does not specifically involve the estimation of the attributable fraction or utilization of such information. In the current process, there is not a role for using the attributable fraction. As implied by the question, the attributable fraction may be low for those diseases that become increasingly common with aging and for which there are multiple risk factors. Hence, presumptions that all cases are caused by Agent Orange are being applied to some cases caused by other factors or for which Agent Orange may make only a minor contribution to causation.

To move beyond such generic presumptions, sufficiently robust information on exposure and risks would be needed. Because so much time has elapsed since U.S. troops were in Vietnam, it is very difficult to estimate levels of exposures to dioxin or other related chemicals with needed certainty. In situations where so little is known about exposures and risks are not estimated with great certainty, it is probably not possible to calculate the service-attributable fraction. Absent sufficiently accurate exposure information, epidemiological approaches are not likely to provide more certain estimates of the risk for diseases such as prostate cancer that occur frequently in persons in the age span of Vietnam Veterans at present.

Question 10. In your opinion, do you believe that the challenges that diseases common to aging or other highly prevalent risk factors pose to the presumptive disability decisionmaking process are a question of science or law, and do you believe that such a question is most appropriately addressed by Congress or the Secretary?

Response. I believe that the model proposed by our committee allows better science to inform decisions made on behalf of our veterans. Our committee recognized and acknowledged that final decisions often must weigh many other factors such as economic, social, and legal factors. We viewed both the current and future decisionmaking models as advisory in nature only, without decisionmaking authority. The decisionmakers need to understand the nature and limitations of the scientific evidence that will be available to support their decisionmaking. Final decisions rest with government elements accountable for such decisions.

RESPONSE TO POST-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO DR. JONATHAN M. SAMET, CHAIR, COMMITTEE ON EVALUATION OF THE DISABILITY DECISION-MAKING PROCESS FOR VETERANS, INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMY OF SCIENCE

Question 1. In response to pre-hearing questions, Dr. Linda Birnbaum, Director of the National Institute of Environmental Health Sciences, described the Boehmer et al. study (the CDC Vietnam Experience Study) and The Third Australian Vietnam Veterans Mortality Study among the studies considered by IOM Update 2008 in its determination of an association between IHD and dioxin exposure. I understand that these studies examined the health effects of the Vietnam experience in general, rather than herbicide exposure.

• Does IOM's reliance on these studies suggest value in examining the health effects of the Vietnam experience in general, in place of examining the health effects of herbicides used in Vietnam in the absence of sound exposure data?

Response. In setting the context for answering this question, I offer the reminder that I was not on the IOM committee that conducted the Veterans and Agent Orange (VAO) Update 2008. Additionally, the question does not refer to a topic specifically covered by our Presumptive Disability Decision-making (PDDM) Committee. However, our committee did call for studies of military personnel in general, including sustained follow-up to track long-term consequences of exposures during military service. Our committee thought that there were opportunities to learn much about the consequences of military experience by constructing prospective cohort studies of military personnel. By carrying out such studies prospectively, exposures could be assessed in real-time, so as to avoid the difficulties of retrospective exposure assessment. The range of exposures assessed could be broad, extending from chemical and physical to psychological.

Regarding general cohort studies of veterans who served in Vietnam, such as the CDC Vietnam Experience Study, since individual exposures to Agent Orange cannot be estimated with sufficient accuracy, comparisons need to be made to external populations to detect unexpected disease occurrence. Such studies represent a useful form of surveillance but are insensitive to detecting modest excesses of disease, unless there is some link to a "signature condition" (for example, mesothelioma, a cancer caused almost exclusively by asbestos). For Agent Orange, chlorachne represents such a signature but most other diseases of concern have multiple causes. Such general studies might also provide leads for more focused follow-up studies.

Question 2. Does a recognized standard exist for determining a threshold for concern with respect to the magnitude of an increased relative risk for developing a disease in a specific cohort compared to the general population? Does such a threshold differ depending on whether the concern is for purposes of prevention versus post-injury causal investigation?

• What would be an appropriate threshold for concern with respect to the magnitude of an increased relative risk for developing a disease associated with the Vietnam experience in general, compared to the general population?

Response. There is no general standard for a specific level of excess relative risk that signals a value of concern. In interpreting a relative risk estimate, consideration needs to be given to both the magnitude of the increase and the extent to which the population is exposed to the factor of interest. A relatively "small" relative risk associated with a common exposure could lead to a substantial burden of disease in the exposed population. Additionally, while higher levels of relative risk provide greater assurance that the association is causal because bias becomes a less plausible explanation, the magnitude of the relative risk reflects underlying biological processes. For example, the relative risk for lung cancer in never smokers who live with smokers is about 1.25, compared to never smokers living with non-smokers. An increase of this magnitude is plausible in terms of the exposures to secondhand smoke received by never smokers in the home. Some have proposed that the relative risk needs to be at least 2.0 if causality is to be inferred in a particular individual; this proposition incorrectly applies a legal standard of "more likely than not" to causal inference more generally.

The question of whether there is a "threshold for concern" with regard to interpreting findings from studies related to the Vietnam experience is a complicated matter, involving not only scientific considerations but broader issues with regard to actions that will be taken based on the findings. At lower and lower relative risk values, the contribution of the exposure to the overall burden of becomes smaller and smaller. For multi-caused chronic diseases, such as diabetes or ischemic heart disease, a "small" relative risk indicates a correspondingly "small" contribution in relation to that coming from other factors.

Any further response to this question would depend on the actions taken if a "threshold of concern" were reached. If a threshold were to be established for making a presumption, given the implications for veterans, a broad discussion would be needed that would move beyond scientific issues to broader matters related to principles by which the Veterans Administration and the Congress compensate veterans for the consequences of their service.

Question 3. In Dr. Birnbaum's written testimony, she stated that "[t]he epidemiological studies that the IOM evaluated and considered in their recommendations for ischemic heart disease varied considerably in their attempts to adjust or control for all the major risk factors of ischemic heart disease, such as, age, smoking, high blood pressure, diabetes, and obesity. It should be noted that few of the studies attempted to control for all of these major risk factors. Also, the epidemiological studies have not attempted to compare the attributable risks of developing ischemic heart disease from dioxins to these other risk factors and have not reported the data in a manner that would allow the quantification of these comparisons. It may be possible to obtain some of this data and reanalyze it in order to address these questions. However, at present this analysis is not available."

• I am encouraged by the possibility Dr. Birnbaum mentioned of calculating the amount of risk contributed by dioxin exposure and comparing the amount contributed by other risk factors in developing IHD. How might such data be obtained and analyzed in order to calculate the amount of risk? What would be the level of effort and cost involved in such an undertaking?

Response. The PDDM Committee recommended that an independent Science Review Board would attempt to make such assessments of service attributable fraction. The report addresses the analytic techniques and methods used to estimate attributable risk. To calculate a service-attributable fraction and make a comparison to the contributions of other factors, data would ideally be available from a cohort of veterans on the suite of factors of interest. The level of effort and costs would depend on the approach taken and the future possibilities of carrying out cohort studies of veterans through linkages of their exposure information to health data obtained from electronic medical records. Approaches based on intensive collection of data from individuals, while likely to be more informative, would be more costly; well established cohort studies, like the Framingham study of cardiovascular disease, exemplify this approach.

Question 4. In correspondence with the Veterans' Affairs Committee, Dr. Birnbaum commented that "if there is a desire to derive a [TCDD] blood concentration that does not increase the risk of ischemic heart disease, it may be best to set up an expert panel that is designed to specifically answer this question."

• How would an expert panel derive such a value? What would be the level of effort and cost involved in such an undertaking?

Response. I have not spoken with Dr Birnbaum about the proposal for using an expert panel to "* * * derive a [TCDD] blood concentration that does not increase the risk of ischemic heart disease." Given the lack of relevant human data, the panel would need to rely on findings from animal models. However, according to VAO Update 2000, "establishing a correlation between the effects of TCDD in experimental systems and in humans, however, is particularly problematic because species differences in susceptibility to TCDD have been documented." Additionally, animal models may not accurately reflect ischemic heart disease in people. Thus, I am uncertain as to the evidence that would be considered by the panel.

Question 5. In response to a question from Senator Webb with respect to the extent to which common risk factors for developing IHD may have attributed to the elevated risk observed in the studies reviewed by the IOM Update 2008, you explained that dioxin exposure can also increase the risk for developing many of the risk factors for IHD, further complicating the examination of whether such risk factors have a stronger association than dioxin exposure.

I understand from Dr. Diane Bild's testimony that age is the strongest risk factor for developing IHD, and that other major risk factors include smoking, physical inactivity, poor diet, and family history of heart disease. While I have learned that the studies reviewed by the IOM Update 2008 controlled for the risk factor of age, these other risk factors were not controlled for in the mortality studies.

• In your view, does dioxin exposure increase the risk for these other IHD risk factors? Do these other risk factors increase the risk for developing IHD without regard to any complicating effect of dioxin exposure?

Response. Prior VAO Update reports have reviewed evidence showing associations between herbicide exposure and risk factors for IHD, specifically hypertension and DM Type II, both of which are known causal risk factors for IHD. Consequently it

would be difficult to determine whether dioxin exposure may increase risk for IHD directly or indirectly by increasing risk for these two causal factors.

Question 6. In response to a question from Senator Webb, Dr. Birnbaum discussed the value of the dose-response findings in the Air Force Health Study (AFHS), one of the studies referenced in the IOM Update 2008 as suggestive of an association between IHD and dioxin exposure.

The AFHS states that "[e]xtrapolation of the serum dioxin results to the general population of ground troops who served in Vietnam was difficult because Ranch Hand and ground troop exposure situations were very different. Based on serum dioxin testing results obtained by the CDC and others, nearly all ground troops tested had current levels of dioxin similar to background levels. Even combat troops who served in herbicide-sprayed areas of Vietnam had current level similar to those in men who never left the United States * * *. There is little scientific basis for an extrapolation of these results to the larger population of Vietnam veterans * * *. These possibilities and a multitude of factors * * * suggest that existing data do not provide an adequate basis for extrapolation." [section 1.6.8 of AFHS]

• To what extent should the findings of the AFHS be extrapolated to the general Vietnam veteran population, in light of the above caveat?

Response. The most recent AFHS (Ranch Hand) findings were reported by Ketchum and Michalek (2005). As summarized in Table 9–5 of the IOM VAO Update 2008, there was not a clear dose-response relationship of circulatory disease mortality with serum TCDD concentrations. A dose-response relationship was observed in other studies composed of non-military personnel.

It is true that the Ranch Hand cohort was thought to be among the most heavily exposed military population in Vietnam. It is a common approach in public health to evaluate health effects in the most exposed group for identifying hazards.

Whether information obtained in Ranch Handers should be extrapolated to the ground troops is an open question since their exposure levels are not known. The quotation below is relevant to the extrapolation question:

> "AFRL-HE-BR-TR-2007-0070
> Air Force Health Study—Summary of Findings in the Ranch Hand Group
>
> 3.9. EXTRAPOLATION TO ARMED FORCES GROUND TROOPS
> Extrapolation of the serum dioxin results to the general population of ground troops who served in Vietnam is problematic because Ranch Hand and ground troop exposure situations were very different from one another. Based on serum dioxin testing results obtained by the CDC (7) and others (8), nearly all ground troops tested had 1987 levels of dioxin similar to background levels. Even combat troops who served in herbicide-sprayed areas of Vietnam had 1987 dioxin levels similar to those in men who never left the United States (with average dioxin levels of 4.2 ppt and 4.1 ppt, respectively). Little scientific basis for an extrapolation of these results to the larger population of Vietnam veterans exists. The possibility that a limited number of veterans could have been exposed to levels of dioxin comparable to the Ranch Hand veterans cannot be excluded, but because blood or adipose tissue were not collected immediately after their return from Vietnam, the actual exposures of these veterans cannot be known. Others may have received long-term low-dose exposure. These possibilities and a multitude of factors, including differential elimination and exposures to other persistent organic pollutants, suggest that existing data do not provide an adequate basis for extrapolation."

Question 7. During the hearing, Former Secretary of Veterans Affairs Anthony Principi described the uncertainties of the presumption process for conditions that IOM has found to have only limited or suggestive evidence of an association with herbicide exposure. Mr. Principi provided the following three suggestions for improving the process:

• Commission studies that might differentiate between servicemembers who received significant exposure to dioxin in Vietnam and those whose exposure was insignificant or nonexistent in order to base presumptive service connection decisions on stronger scientific evidence. Mr. Principi suggested that such studies might replicate the Centers for Disease Control's Vietnam Experience Study.

• Commission IOM to provide VA with an estimate of a latency period for illness; that is, a point after which it is no longer likely that the onset of the illness is due to exposure, but instead due to other factors.

• Commission IOM to estimate the number of Vietnam veterans who might be affected by an illness found by IOM to have only limited or suggestive evidence of an association with herbicide exposure.

I would appreciate your views on Mr. Principi's suggestions.

Response. As these topics were not addressed by the PDDM Committee, the following responses reflect my own views and not those of the Institute of Medicine. With regard to Mr. Principi's first point, several IOM study committees have recommended the desirability and value of conducting longitudinal studies in military personnel to better understand long term health effects due to military service that were not evident when the servicemember left active duty. Of course, various such studies have been carried out on Vietnam veterans and further studies could be done today by enrolling surviving Vietnam veterans into a cohort study, making comparison to non-deployed Vietnam-era veterans. However, a new cohort study would be unlikely to be informative on the consequences of Agent Orange exposure, given the uncertainties associated with any attempt to estimate exposures for individual cohort members. Of note, a recent IOM report entitled "The Utility of Proximity-based Herbicide Assessment in Epidemiology Studies of Vietnam Veterans" suggested approaches to advance retrospective estimation of exposures using sophisticated reconstruction modeling of herbicide spraying operations in country.

Regarding the second recommendation, that IOM investigate the time course ("latency") of the adverse effects of herbicides, the requisite data are not available to the best of my knowledge. The data needed for this purpose would track the relative risk across the course of follow-up with sufficient precision to determine the temporal pattern of the relative risk. Whether a decline in relative risk over time would be anticipated from a biological perspective could be explored by the IOM, though the relevant evidence may be too limited to provide a sufficiently certain answer to the question posed by Mr. Principi. Certain clinical endpoints, such as selected cancers, might not become manifest until several decades elapsed following exposure.

Regarding the third recommendation, IOM could make such calculations, drawing on available literature and estimates of the size of the exposed population. While such estimates could be made, they would be subject to various sources of uncertainty. They would provide an indication of the numbers of cases attributable to Agent Orange for these disease associations. The PDDM committee recommended that an independent scientific review board also estimate to what extent that condition might be due to specific military exposure verses other non-military factors.

Question 8. If Congress called for a Vietnam veteran health study, what would be the value of such a study for addressing uncertainties of the presumption process? Should such a study continue throughout a veteran's lifetime? Should there be multiple studies uniquely designed for each wartime veteran cohort? What would be the most critical information to be sought from such a study?

Response. Our PDDM committee commented on the high importance and relevance of prospective studies among veterans. However, whether a new study initiated at present could prove informative is not clear. Any new study could not address Agent Orange directly; instead, inferences would have to be based on comparison of Vietnam veterans to non-deployed veterans of the same era. Implementing an informative study would require substantial effort and useful results might not be forthcoming for a number of years. Perhaps, an assessment could be carried out as to the feasibility and costs of mounting a new study, along with an assessment of the potential for obtaining results that would be useful.

The PDDM Committee's report provides an extensive discussion of the need for prospective cohort studies of veterans. The Committee did recommend that each wartime group of veterans should be separately studied, as each may have unique exposures and experiences. Most critically, exposures would be prospectively assessed so that the cohort studies undertaken would be informative on a broad array of questions, including concerns that may not have been anticipated when the cohort was established. The report of the PDDM Committee provides general guidance.

Question 9. I understand that the IOM Committee that you chaired recommended the establishment of an independent Science Review Board to assist the Secretary in the presumptive disability decisionmaking process. The Committee described a two-step process through which the Science Review Board would function.

• How would the two-step process of the Science Review Board address the uncertainties in the current presumption process?

Response. The Science Review Board (SRB) would use a two-step process. In step one, published literature would be reviewed to determine the strength of the evidence to assess whether a given health outcome can be caused by a given exposure. This scientific review is very much like the role of IOM in the current process. The PDDM Committee recommended, however, that the target for the review should be

the likelihood of causation, and not simply statistical association. The Committee developed a categorization schema with four levels for grading the strength of the scientific evidence in ascending order. If the strength of the scientific evidence reached level two or one (50% or more likelihood of causation), the process would move on to step two in the recommended process.

In step two, the SRB would estimate the service-attributable fraction of disease if the required data and information were available. This second step assesses how much of the observed disease, both in absolute and relative terms, can be attributed to the exposure. The calculation is independent of the classification of the strength of evidence for causation, and the magnitude of the service-attributable fraction is not considered in categorizing evidence. Rather, the service-attributable fraction would be of value for decisionmaking, giving an understanding of the scope of the population to be covered by a presumption.

In step two, the SRB would consider the extent of exposure among veterans and subgroups of veterans, as well as dose-response relationships. A critical element in the deliberations of the SRB would be any evidence available on exposures and the health of veterans. When such information is available, the board would estimate the service-attributable fraction and the related uncertainty. The purpose of step two is to convey the impact of the exposure on veterans as a whole for the purpose of decisionmaking and planning, but not to serve, inappropriately, as an estimate of probability of causation for individuals. Some exposures may contribute greatly to the disease burden of veterans, while other exposures (even with a known causal effect) may have a small impact overall. This additional information would be useful to VA in its decisionmaking as to whether a presumption should be made for the veteran population in general, for subgroups, or not at all. In the absence of service-attributable fraction data, we assume that the VA would consider presumptions based on the information contained in step one.

There are a number of potential beneficial consequences of the proposed SRB. It would give VA outside, independent evidence-based advice synthesizing the best available data that could inform the relationship between exposures and outcomes in veterans.

IOM committees are currently performing step one of the roles envisioned for the SRB. If this new model were to be adopted, the function of the current committees would need to be expanded to evaluate how much of the disease burden in veterans is due to these presumed exposures (the service-attributable fraction).

Question 10. The IOM Committee that you chaired recommended causation, not just association, as the target for determining a presumption of service-connection for health conditions.

I understand the presumptions process attempts to address two uncertainties relating to the relationship between dioxin exposure and health outcomes: the uncertainty that an exposure to an herbicide leads, in at least some cases, to illness and the uncertainty that an individual veteran's illness was caused by that exposure.

• While you stated in your testimony that the lack of exposure data seems to preclude a causal analysis for an individual veteran's illness, would a causal analysis be appropriate for purposes of examining whether an exposure to an herbicide leads, in at least some cases, to illness in the presence of reliable exposure data?

Response. Our committee concluded that the basis for decisionmaking should be causation and not just association. The proposed approach incorporates all of the relevant evidence, both from epidemiological studies and from other lines of investigation. The Committee's report provides guidance on causal inference. A commonly accepted set of criteria, sometimes referred to as the Bradford Hill criteria for causation, include a proper temporal relationship between cause and effect, strength of association, a dose-response relationship, consistency of response, plausibility, ruling out alternative possibilities, proof by controlled experiment, specificity of effect, and coherence with existing knowledge and theory.

In step one of the process—determining that an exposure can cause an effect—exposure data is needed, of course. To find an association and to infer causality, it is necessary to demonstrate that the exposure occurred before the effect (correct temporal relationship); that more exposure leads to greater effect in the number or severity of cases (dose-response); and that several different studies showed the same general finding (consistency). Such findings might be made in epidemiological analyses if exposures could be assigned to specific groups with sufficient accuracy, even if exposures could not be accurately designated for individuals.

Question 11. When examining the link between an exposure and a health outcome, does a causal analysis require a higher quality of exposure data, as compared to an analysis examining only association? Are job classifications, soil samples, and residential locations valid indicators for examining dioxin exposure for a study co-

hort? To what degree should such indicators, as opposed to human biological samples, be relied upon for examining association and causation?

Response. An analysis limited to association considers only the findings of epidemiological studies while a causal analysis considers the full range of evidence. Mechanistic evidence may give strong support to causation. The quality of exposure information is of comparable relevance and importance to assessments of either association or causation. In classifying exposures to dioxin, all relevant sources of data should be considered; each has limitations and attendant uncertainties. Biomarker data, when available, may be very useful for classifying exposure, particularly if they cover a biologically relevant interval for causation.

Question 12. In response to pre-hearing questions, Dr. Bild explained the level of increased risk for each of the major risk factors for developing IHD. If a health study examines only service-connected exposures and health status of individual veterans, without collecting data on lifestyle behaviors, what would be the potential limitations of the study's findings?

Response. As mentioned, all factors that can contribute toward an effect should be measured. If the comparison groups used in these studies had the same level of these unmeasured factors as the exposed population, then the effect of these unmeasured factors would cancel out. However one would not know this unless these important factors were measured, documented, reported and properly adjusted.

Question 13. During the hearing, I asked you if a different approach comparing disease levels among Vietnam veterans and the general population would be more likely to identify diseases that may be associated with Vietnam service. You stated:

"I would say that we have the tools to do that. It would require a large effort and measurement of many factors. And in the end, I think in the case of trying to retrospectively do this we would be left with an imperfect and uncertain answer."

• Can you elaborate on your answer regarding a retrospective study yielding imperfect and uncertain results?

Response. In responses to other questions, I have already addressed this issue. The model proposed by the PDDM Committee is to be implemented prospectively.

Question 14. In response to a question from Senator Webb on uncontrolled risk factors in the studies cited in the IOM Update 2008, Dr. Diane Bild stated:

> "Those studies [examined] the relationship of dioxin and IHD mortality. They were able to adjust for age but were not necessarily all able to take into account other so-called confounders, such as smoking. For example, if somebody was exposed to dioxin also happened to [be in a] group with a higher smoking rate, the IHD could be attributable to smoking rather dioxin and that would not be apparent from the study if you did not have the data on smoking and were unable to adjust for it in the analysis."

• If a study is unable to control for multiple risk factors for IHD, such as smoking, obesity, or physical inactivity, how might each additional uncontrolled risk factor affect the uncertainty of the relative risk calculation for the association between dioxin exposure and IHD? How would a researcher account for such uncertainty in determining whether the findings of a study are reliable?

Response. If control is not possible for other risk factors, there is concern for the possibility of confounding—that is, the effect of dioxin is incorrectly estimated because it is "contaminated" by the effects of other, uncontrolled factors. It is possible, using external information on the relative risk associated with the confounding factor, to estimate the potential magnitude of any bias. Comparability of findings across multiple studies, which may have differing potential confounding factors, weighs against confounding as the explanation for the association of the exposure of interest with the health outcome.

Chairman AKAKA. Thank you very much. Next, we have two witnesses from NIH, Dr. Diane Bild from the National Heart, Lung, and Blood Institute, and Dr. Linda Birnbaum, from the National Institute of Environmental Health Sciences. Both have been asked to provide insight on IHD and its major risk factors and to address what role science is currently capable of with respect to determining an association between dioxin exposure and IHD and other diseases common to aging.

Will you please begin, Dr. Bild and following you will be Dr. Birnbaum. Dr. Bild.

STATEMENT OF DIANE BILD, M.D., M.P.H., ASSOCIATE DIRECTOR, PREVENTION AND POPULATION SCIENCES PROGRAM, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH

Dr. BILD. Mr. Chairman and Members of the Committee, thank you for the opportunity to appear before you on behalf of the Acting Director of the National Heart, Lung, and Blood Institute of the National Institutes of Health.

I was asked to address our current understanding of ischemic heart disease, or IHD, including information on known risk factors and the extent of those risks for developing the disease, methods of diagnosis and treatment, physician qualifications for treating IHD, its prevalence among men over age 60, and the relationship between dioxin exposure and IHD.

Atherosclerotic plaque begins to develop in humans during the first two decades of life in the form of "fatty streams" inside the artery walls. I brought along this diagram to help illustrate the process. This is meant to show an artery at different stages throughout life and the "fatty streams" that I referred to that begin early in life are shown here. This is the lumen of the artery where the blood flows.

A good example of the evidence that this disease starts early in life was a landmark study published in 1953 that found visible evidence of coronary plaque in 77 percent of U.S. casualties in Korea. The average age of these young solders was 22. This study opened our eyes to the fact that coronary disease or IHD starts early and generally progresses throughout life. For most people this plaque causes no symptoms but for some people later in life it may eventually rupture, blocking the artery as shown here, leading to chest pain or angina or heart attack, also known as myocardial infarction or MI. By the eighth decade of life, almost all Americans have some plaque in their arteries.

The major causes of IHD are smoking, dyslipidemia—that is high LDL, "bad cholesterol," or low HDL, "good cholesterol"—high blood pressure, and diabetes. Sedentary lifestyle, poor diet, obesity, and psychosocial factors such as stress and depression are also believed to contribute to IHD and altogether these factors account for 80 to 90 percent of IHD.

I mentioned several forms of IHD. I will briefly mention how they are diagnosed. The diagnosis of angina is usually based on symptoms of chest pain or shortness of breath, particularly upon exertion. Because these symptoms can be nonspecific, some testing is needed to confirm the diagnosis—exercise testing with an electrocardiogram, echocardiogram, nuclear imaging, or angiography, which demonstrates the actual narrowing in the artery if present. The diagnosis of an acute MI or heart attack is made on the basis of similar symptoms but they are usually more severe and prolonged, plus a certain pattern on the electrocardiogram and elevation of cardiac enzymes in the blood.

Internal medicine, family practice, and general practice physicians in the U.S. are all trained to recognize the typical symptoms of IHD and understand the need for prompt treatment in the acute setting. Treatment guidelines from respected professional organizations are readily available and widely promulgated. Most physi-

cians who do not feel comfortable diagnosing or treating IHD will refer to a subspecialist, generally a cardiologist.

I was asked to address the prevalence of IHD. In the U.S., 17 percent of men aged 60 to 69 and 26 percent of men 70 to 79 report having IHD. In addition, a larger proportion will have atherosclerotic plaque, of which they are unaware, which brings the total of men age 60 to 79 with symptomatic or asymptomatic disease to about 80 or 90 percent.

Treatment of IHD involves aggressive modification of the risk factors mentioned earlier, such as blood pressure, lipids, with medication or lifestyle changes, daily aspirin, or more invasive interventions to treat specifically narrowed arteries with coronary bypass or angioplasty.

Dr. Birnbaum is going to address the relationship between dioxin and IHD in more detail. My only comment is to say that although the National Academy of Sciences concluded that dioxin exposure does appear to be associated with IHD mortality, the association is modest and most of the studies could not be adjusted for confounders such as smoking that might have contributed to the risk. This has been discussed in some detail earlier in these proceedings. It is also impossible to determine in a given individual if dioxin was responsible for their IHD.

Thank you again for this opportunity to provide information on this topic. I would be pleased to try to answer any questions that you have.

[The prepared statement of Dr. Bild follows:]

PREPARED STATEMENT OF DIANE BILD, M.D., M.P.H., ASSOCIATE DIRECTOR FOR PREVENTION AND POPULATION SCIENCES, DIVISION OF CARDIOVASCULAR SCIENCES, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and Members of the Committee, thank you for this opportunity to appear before you on behalf of the Acting Director of the National Heart, Lung, and Blood Institute, part of the National Institutes of Health, an agency of the Department of Health and Human Services (HHS). I was asked to address current understanding of ischemic heart disease, or IHD, including information on known risk factors and the extent of those risks for developing the disease, methods of diagnosis and treatment, physician qualifications for treating IHD, its prevalence rates among males over age 60, and the relationship between dioxin exposure and IHD.

Atherosclerotic plaque begins to develop in humans during the first two decades of life in the form of "fatty streaks" inside the artery walls. A landmark study published in 1953 found gross evidence of coronary plaque in 77.3% of U.S. fatalities in Korea. The average age of these young soldiers was 22 years. This eye-opening study taught us that coronary disease or IHD starts early and generally progresses throughout life. These findings have been repeatedly confirmed. For most people this plaque causes no symptoms, but for some persons later in life it may eventually "rupture," blocking an artery and leading to symptoms including chest pain or angina, or heart attack (myocardial infarction, known as MI). By the eighth decade of life almost all Americans have some plaque in their arteries.

The major causes of IHD are smoking, dyslipidemia (high low-density lipoprotein [LDL] cholesterol and/or low high-density lipoprotein [HDL] cholesterol levels), high blood pressure, and diabetes. Sedentary lifestyle, poor diet, obesity, and psychosocial factors such as stress and depression are also believed to contribute to IHD. Together these factors account for 80 to 90% of IHD.

The diagnosis of angina is based on symptoms of chest pain and shortness of breath, particularly upon exertion. The diagnosis of acute MI or heart attack is made on the basis of similar but usually more severe symptoms, a certain pattern on an electrocardiogram, and elevation in cardiac enzymes measured in the blood. Diagnostic testing for IHD may include exercise electrocardiogram; nuclear testing with exercise; echocardiography with exercise; computed tomography (CT), including

CT angiography; or conventional angiography. Stress testing would never be performed on someone suspected of having an acute MI.

Primary care, internal medicine, family practice, and general practice physicians in the U.S. are all trained to recognize the typical symptoms of IHD and understand the need for prompt treatment. Treatment guidelines from respected sources are readily available and widely promulgated. Most physicians who do not feel comfortable instituting or changing treatment for IHD would refer to a subspecialist.

In the US, 17% of men aged 60–69 and 26% of men aged 70–79 report having IHD. These proportions have remained stable since 1996, as indicated by the National Health Interview Survey of HHS's Centers for Disease Control and Prevention. Three of four men 60–69 years old and 80% of men 70–79 who do not report having IHD would be expected to have coronary atherosclerotic plaque. Combining these estimates, approximately 80–90% of men aged 60–79 would be expected to have either symptomatic or asymptomatic IHD.

Treatment of IHD includes aggressive treatment of the risk factors mentioned earlier with medication and lifestyle changes, daily aspirin, and more invasive interventions as indicated, including coronary artery bypass or angioplasty.

Although the National Academy of Sciences recently concluded that dioxin exposure does appear to be associated with II-ID mortality, the association is modest, and most of the studies in the NAS review could not be adjusted for the other factors I have just described, known as confounders. Men in these studies who had been exposed to dioxin also may have had other exposures that increased their risk of IHD, such as smoking. It is also impossible to determine in a given individual if dioxin caused the IHD. The specific risk factors for disease are more clearly identifiable in populations than in individuals.

Thank you again for this opportunity to provide information on this topic. I would be pleased to try to answer any questions you may have.

RESPONSE TO PRE-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO DIANE BILD, M.D., MPH, ASSOCIATE DIRECTOR, PREVENTION AND POPULATION SCIENCES PROGRAM, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH

Question 1. Please describe ischemic heart disease (IHD), including the difference between symptomatic and asymptomatic ischemic heart disease, and indicate the major causes of the disease.

Response. Ischemic heart disease (IHD) gets its name from ischemia or reduction of blood flow to the heart muscle due to blockage of the blood supply. Other terms for IHD are coronary heart disease and coronary artery disease, because the coronary arteries are the ones that supply blood to the heart muscle. Build-up of atherosclerotic "plaque" in the coronary arteries is extremely common—plaque is the complex mixture of cells, fibrous connective tissue, fatty material, and sometimes cellular debris and calcification that may eventually lead to clinical, symptomatic ischemic heart disease.

Atherosclerotic plaque is believed to begin developing in humans during the first two decades of life in the form of "fatty streaks" inside the artery walls. Plaque develops slowly over the decades and may reach a point, generally during older adulthood, when it "ruptures," tightly narrows an artery, and leads to symptoms including angina or heart attack (myocardial infarction). By the eighth decade of life almost all Americans have some plaque in their arteries, which may be identified at autopsy or by some types of imaging. However, for most people this plaque causes no symptoms.

Asymptomatic IHD may be thought of in several categories: The smallest category in terms of numbers in the general population are new myocardial infarctions (MIs) that are silent, occurring without symptoms or detection. One-quarter to one-third of new MIs are silent. In another category, roughly 2–4 percent of the general population has asymptomatic or silent IHD—artery blockages that could be detected by stress testing. Finally, a higher proportion has coronary artery disease that does not significantly block the arteries. The prevalence of both symptomatic and asymptomatic IHD is higher in older men than in the general population.

The major causes of IHD are smoking, dyslipidemia (high low-density lipoprotein (LDL) cholesterol and/or low high-density lipoprotein (HDL) cholesterol), hypertension (high blood pressure), and diabetes. Sedentary lifestyle and poor diet also contribute, in part by causing obesity, which is in turn related to IHD. Psychosocial factors such as stress and depression are also believed to contribute to IHD. Together these factors account for 80–90% of IHD in the United States.

Question 2. Approximately what percentage of the major causes of ischemic heart disease is explained by lifestyle factors, and to what extent does each major factor increase an individual's risk for developing IHD?

Response. Approximately 80–90% of IHD is explained by lifestyle factors, either directly or indirectly. For example, a factor such as a high cholesterol diet is an indirect factor because it may result in a high LDL-cholesterol level, which in turn is a direct cause of IHD.

A contemporary international study of 15,152 cases of acute myocardial infarction and 14,820 controls (called INTERHEART) provides a good estimate of the percentage contribution of different lifestyle factors in men aged 55+. In this study, smoking, low fruit and vegetable consumption, low levels of exercise (regular participation in moderate or vigorous physical activity for 4 hours or more a week), low alcohol consumption (<3–4 times per week), hypertension, diabetes, abdominal obesity, psychosocial factors (reflecting depression, stress, life events, and locus of control), and a high ApoB/ApoA1 ratio (which indicates high LDL-cholesterol and low HDL-cholesterol) accounted for 88.3% of all cases of acute myocardial infarction.

In this same group, the "attributable risk" (AR, explained below) for each of these factors was as follows:

Factor	AR
Smoking	39.0%
Lack of fruit and vegetable consumption	10.1%
Lack of exercise	12.5%
Low alcohol consumption	10.5%
Hypertension	15.7%
Diabetes	7.8%
Abdominal obesity	18.3%
Psychosocial factors	23.7%
High ApoB/ApoA1 ratio	45.3%

These attributable risk figures represent the proportions of disease in the population that might be prevented by modifying each factor. For example, in the overall INTERHEART population, elimination of smoking could eliminate 39% of the acute MI cases. It is important to note several caveats about these data:

1. The amount of the contribution of each of the factors depends on two characteristics: the prevalence of the factor in the population and the strength of the causal relationship to acute MI. Thus, if smoking rates decline, the AR due to smoking will decline.
2. The ARs do not add up to 100%, because there is overlap in behaviors. For example, people with abdominal obesity tend to have more diabetes than people without abdominal obesity, so eliminating both factors does not mean that 7.8% + 18.3% = 26.1% of disease would be prevented.
3. This type of analysis conveys the risk associated with whether a variable is present or absent, rather than considering different levels of a risk factor. For example, the risk of smoking 5 cigarettes per day is less than the risk of smoking 20 cigarettes per day, but this analysis sets smoking as any tobacco use in the previous 12 months.
4. This analysis is based on an observational study, and the interpretation depends on statistical modeling and knowledge of the impact of the risk factors on disease. In some cases (exercise, fruit and vegetable intake, alcohol consumption, diabetes, and abdominal obesity), there is no clinical trial evidence to confirm that modifying the factor will reduce risk to exactly this extent.
5. This is just one study, but it is a large one, and the relationships between these factors and IHD are generally what have been found in other studies.
6. This unique, large study used acute MI as its endpoint. It is an extrapolation, but not an unreasonable one, that similar relationships would be found for the general broader category of IHD.

Question 3. Do most primary care, internal medicine, and general practice physicians possess the necessary qualifications to competently diagnose and treat IHD?

Response. Primary care, internal medicine, and general practice physicians in the U.S. are all trained to recognize the typical symptoms of ischemic heart disease and understand the need for prompt treatment. Treatment guidelines from the American College of Cardiology and American Heart Association (ACC/AHA) are readily available and widely promulgated (e.g., Kushner, et al. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction. JACC 2009;54:2205–41). Most physicians who do not feel comfortable insti-

tuting or changing treatment would refer to a subspecialist, but there is significant regional and economic variation in subspecialty access—for example, physicians in remote or underserved areas assume a greater portion of subspecialty care.

Internal Medicine physicians receive specific training in cardiovascular disease, and in fact it accounts for 14% of the content on the internal medicine certification exam, of which about one-third of the questions are about ischemic heart disease.

The American Board of Family Medicine, which certifies Family Practitioners, includes eight modules in its examination, including ambulatory medicine, emergent/urgent care, and hospital medicine, all of which include heart disease (https://www.theabfm.org/cert/examcontent.aspx). Cardiovascular disease accounts for 12% of the in-training examination content (https://www.theabfm.org/residency/ite.aspx).

While most internists and family practitioners are capable of overseeing routine diagnosis and optimal medical management, they would not be qualified to perform coronary angiograms, read nuclear/echo/PET/CT images, implant coronary stents, or perform coronary bypass surgery. For these advanced imaging tests or invasive treatments, primary care physicians need to refer their patients to specialists.

According to the Bureau of Labor Statistics, in 2007, internists made up 20.1% of all active practicing physicians (http://www.bls.gov/oco/ocos074.htm). Cardiology is a subspecialty of internal medicine, and cardiologists comprise about 3% of all physicians (Watcher RM. NEJM 2004;350:1935–36). Family practitioners and general practitioners made up 12.4% of practicing physicians. Most are trained as family practitioners, which means that they have had 3 years of training after completing medical school, and often been certified by the American Board of Family Medicine. Few are true general practitioners who have had only one year of post-medical school clinical training. At least one year of training after medical school is required for a license to practice medicine.

Question 4. Does the prevalence rate of 17.2 percent for coronary artery disease in males ages 60–69, as reported by the Centers for Disease Control, represent the prevalence rate for IHD specifically or the broader category of all cardiovascular diseases?

Response. The prevalence rate as reported by the Centers for Disease Control and Prevention (CDC) represents IHD specifically. This rate was derived from men who participated in the 2008 National Health Interview Survey and is based on self-report, where each respondent answered questions about whether a doctor or other health professional told him that he had coronary heart disease, angina, or a heart attack. The self-report method is generally accepted for measuring prevalence and trends in the general population. It is important to recognize that this is an estimate of clinically apparent or symptomatic disease. Because such a large proportion of the adult population in the U.S. has clinically silent or asymptomatic IHD, it is neither practical nor medically necessary to identify this much larger proportion on a routine basis.

Question 5. Will the prevalence rate for IHD in males ages 60–69 increase as the average age of the group increases? If so, what is the expected magnitude of any such increase over a ten year period?

Response. The estimate of IHD for those aged 70–79 years was 26.3%, also based on the 2008 National Health Interview Survey.

The rates of IHD for the 60–69 and 70–79 year olds agree closely with those obtained from CDC's Behavioral Risk Factor Surveillance System, which further shows that the reported prevalence has remained steady in these groups since 1996. Thus, one may expect that the cohort of 60–69 year olds will experience the prevalence of IHD noted above for 70–79 year olds 10 years later.

Question 6. Do these prevalence rates include individuals who are not experiencing symptoms, but could be diagnosed with IHD based on test results alone? What do you estimate to be the prevalence rate of males ages 60–69 with either symptomatic or asymptomatic IHD?

Response. Since the prevalence rates are based on self report rather than diagnostic testing results, they likely represent only symptomatic disease. The only exception would be asymptomatic men who underwent some type of screening for coronary artery disease and were then told that they had IHD. While such screening has become increasingly popular, it is expensive, not routinely recommended, and not generally covered by insurance, and therefore unlikely to have affected this figure.

In the US, three-fourths of men 60–69 years old who do not report having IHD would be expected to have coronary atherosclerosis or plaque, based on a measure of coronary calcification, a marker of plaque. The amount of calcification, which reflects of the amount of plaque, may range from very small to substantial. (See http://www.mesa-nhlbi.org/Calcium/input.aspx)

Therefore, approximately 80% of men aged 60–69 would be expected to have either symptomatic or asymptomatic IHD.

Question 7. Is it common practice for physicians to diagnose and treat asymptomatic IHD? What are some of the dangers of treating asymptomatic IHD identified by imaging alone?

Response. While screening for asymptomatic IHD has been widely marketed since the mid-1990s, the National Heart, Lung, and Blood Institute is not aware of survey data on its use by physicians. While direct-to-consumer advertising would tend to increase its use, several other factors are likely to discourage screening. For example, informed professional groups that develop consensus practice guidelines, including the American College of Cardiology and the American Heart Association, do not support general screening, although they do suggest it as an option in selected circumstances. Screening procedures that can be performed without a physician's order tend to be expensive. For example, one company charges $395 for a coronary calcium scan, and another company that specializes in ultrasound testing charges $119 for the basic "stroke and vascular disease" screening package. These procedures are often not covered by insurance.

Over the past six decades, the scientific community and public health advocacy groups have developed guidelines for when it is appropriate to implement screening, however the benefits of screening for asymptomatic IHD have not been demonstrated. Three of the most commonly used IHD screening techniques include coronary artery calcium (CAC) detection, which uses computed tomography (CT, a type of X-ray), carotid artery ultrasound, and stress testing. Of these, CAC screening has received the most attention recently because it has several features that make it a potentially attractive screening tool.

However, the dangers of treating asymptomatic IHD identified by imaging alone are confounded by the disadvantages of implementing unproven screening strategies overall. These include:

- Turning healthy people into patients, causing worry
- Reassuring people inappropriately. The tests do not exclude the presence of plaque, and a negative test could lead persons to de-emphasize proven effective preventive measures such as control of other risk factors which may exist.
- Subjecting people to ionizing radiation
- Identifying incidental findings that are commonly found on X-ray, triggering follow-up diagnostic testing and interventions, most of which are unnecessary
- Creating the need for more testing to further elucidate IHD
- Providing medication for disease that never becomes symptomatic
- Leading a patient to undergo potentially unnecessary invasive interventions, such as angioplasty or bypass surgery, if further testing identifies blockages
- Incurring the costs of the testing

When it comes to the dangers of treating asymptomatic disease per se, it should be noted that no proven effective treatment for asymptomatic IHD is known, other than treating individuals with established risk factors, such as high blood pressure or high LDL-cholesterol, or initiating use of aspirin therapy. In rare cases, CAC testing may lead to further testing that identifies severe disease of the left main coronary artery, and physicians are likely to proceed with an intervention, such as coronary artery bypass.

Question 8. What are the most effective preventive measures for IHD, and to what extent does each of the measures lower an individual's risk for adverse outcomes associated with IHD?

Response. The most effective preventive measures for IHD are smoking avoidance and cessation, lipid-lowering, blood pressure control, weight control, and aspirin. Proper diet and exercise may achieve the goals of maintaining optimal blood pressure, lipids, and weight, but often medications are needed to lower blood pressure and LDL-cholesterol. Below is a general (and rounded) indication of the preventive potential of each of these strategies:

Intervention	Reduction in IHD	References
Smoking cessation	30–60%	1, 2
Lipid lowering (statin therapy)	30%	3
Blood pressure control	20%	4
Exercise	20%	5
Aspirin	30%	6

References

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RESPONSE TO POST-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO DIANE BILD, MD, MPH, ASSOCIATE DIRECTOR, DIVISION OF CARDIOVASCULAR SCIENCES, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH

Question 1. In response to a question from Senator Webb about the extent to which common risk factors for developing IHD may have [contributed] to the elevated risk observed in the studies reviewed by the IOM Update 2008, Dr. Linda Birnbaum testified that dioxin exposure can also increase the risk for developing many of the risk factors for IHD, further complicating the examination of whether such risk factors have a stronger association than dioxin exposure.

I understand from your correspondence with the Veterans' Affairs Committee that age is the strongest risk factor for developing IHD, and that other major risk factors include smoking, physical inactivity, poor diet, and family history of heart disease. While I have learned that the studies reviewed by the IOM Update 2008 controlled for the risk factor of age, these other risk factors were not controlled for in the mortality studies.

• In your view, does dioxin exposure increase the risk for these other IHD risk factors? Would it be correct to say that these other risk factors increase the risk for developing IHD without regard to any confounding effect of dioxin exposure?

Response. The ischemic heart disease (IHD) risk factors with which dioxin has most often been found to be associated are diabetes and hypertension. Based on my review of expert opinion, there appears to be more evidence for a relationship between dioxin and diabetes than between dioxin and hypertension, but neither relationship is strong. The October 2000 Institute of Medicine (IOM) report, Veterans and Agent Orange: Herbicide/Dioxin Exposure and Type 2 Diabetes, found "limited/suggestive evidence of an association between exposure to the herbicides used in Vietnam or the contaminant dioxin and Type 2 diabetes," but noted that "the increased risk, if any * * * appears to be small [and the] known predictors of diabetes risk—family history, physical inactivity, and obesity—continue to greatly outweigh any suggested risk from wartime exposure to herbicides." The published literature on associations between dioxin exposure and hypertension is insufficient to draw conclusions.

It is correct that diabetes and hypertension greatly increase the risk of IHD regardless of dioxin exposure.

Question 2. In response to a question that I asked with respect to men aged 60–69 who have IHD but no apparent symptoms, and the likelihood of their developing symptomatic disease, you explained that "[a]therosclerosis is a progressive disease, and by middle and late age, particularly in men in this country, there will be some plaque, early forms of coronary disease, detectable through some method. It is a relatively small proportion in the US. About 17% of men aged 60–69 will report having IHD; that is, they have symptoms, [such as] a heart attack, [or] bypass surgery, so it is clinically apparent IHD, as opposed to the much larger proportion who have silent or asymptomatic disease that may never become clinically apparent."

I understand that CDC's NHANES prevalence data show an increasing IHD prevalence rate of 17.2 percent, 26.3 percent, and 43.9 percent for men aged 60–69, aged 70–79, and aged 80 and over, respectively.

• Would it be correct to say that while only approximately 17.2 percent of men aged 60–69 exhibit symptomatic IHD, an additional 26.7 percent of asymptomatic men aged 60–69 are predicted to develop symptomatic IHD by their eighties?

Response. One would actually expect approximately one-third of men aged 60–69 who do not have IHD to develop it within 20 years.

While intuitive, one cannot simply subtract 17.2 percent from 43.9 percent to conclude that an additional 26.7 percent of men aged 60–69 would develop IHD 20 years later. Many men in their 60s will die of causes other than IHD before they reach their 80s; they never have a chance to develop symptomatic IHD. In epidemiology, we call this phenomenon "competing risks." Also, men who are now in their 60s were born 20 years later than men who are in their 80s. That means they began life and lived it in a healthier environment and therefore enjoy greater longevity; in epidemiology, we call this phenomenon a "cohort effect." The U.S. population of men aged 80–89 is only 27 percent the size of the population of men aged 60–69 (according to the U.S. Census Bureau Population Division, estimates for 2009).

According to data from three large NHLBI cohort studies that included 2,615 men aged 60–69 who did not have symptomatic IHD and who were followed for 17–21 years, 890 (34.0 percent) developed IHD during that period. Of the group that developed IHD, 251 (9.6 percent of the original 2,615) died from IHD, 382 (14.6 percent) developed IHD but were still alive at the end of the follow-up period, and 257 (9.8 percent) developed IHD but died from other causes. Note that this cohort had more survivors to age 80–89 than one might expect based on the Census data because the studies started with groups that were healthier than the general population (i.e., they were without IHD); moreover, there was no "cohort effect"—it was all one cohort of men born within the same 10-year calendar period.

Question 3. In response to pre-hearing questions, you described the level of increased risk for developing IHD due to each of the major risk factors. If a health study examines only service-connected exposures and health status of individual veterans, without collecting data on lifestyle behaviors, what would be the potential limitations of the study's findings?

Response. Failure of a study to collect data on lifestyle behaviors and analytically control for their confounding effects may lead investigators to impute false associations. An example of this comes from the recent controversy about whether postmenopausal hormone therapy reduces the risk of IHD in women. Numerous observational studies found an apparent protective effect of hormone therapy, but none of them measured socioeconomic status (SES)—a variable that ultimately proved to be quite important. Women with higher SES (i.e., more education and wealth) were more likely to take hormone therapy. They were also less likely to smoke or be overweight and more likely to have access to regular medical care and to engage in healthy lifestyle behaviors. Eventually, the Women's Health Initiative clinical trial—in which women from all walks of life were randomly assigned to take or not take hormones—definitively showed that taking hormones does not reduce the risk of heart attack and, in fact, may increase the risk.

Question 4. In response to a question from Senator Webb with respect to the uncontrolled risk factors in the studies relied upon by the IOM Update 2008, you stated:

> "Those studies [examined] the relationship of dioxin and IHD mortality. They were able to adjust for age but were not necessarily all able to take into account other so-called confounders, such as smoking. For example, if somebody exposed to dioxin also happened to [be in a] group with a higher smoking rate, the IHD could be attributable to smoking rather than to dioxin and that would not be apparent from the study if you did not have the data on smoking and were unable to adjust for it in the analysis."

If a study is unable to control for multiple risk factors for IHD, such as smoking, obesity, or physical inactivity, how would each additional uncontrolled risk factor affect the uncertainty of the relative risk calculation for the association between dioxin exposure and IHD? How would a researcher account for such uncertainty in determining whether a study's findings are reliable?

Response. The level of uncertainty that results from failure to control for a confounder is related to how closely the confounding factor is linked to both the exposure and the disease of interest. With regard to dioxin exposure in Vietnam, ideally it would be useful to have information on health habits, such as smoking, among men who were and were not exposed. If, for example, one were able to determine

that men who were exposed to dioxin had the same levels of risk factors before their dioxin exposure as men who were not exposed, one could conclude that confounding is less likely to be responsible for the findings that dioxin is associated with IHD.

Chairman AKAKA. Thank you. Thank you very much. And now we will hear from Dr. Birnbaum. Please proceed.

STATEMENT OF LINDA BIRNBAUM, Ph.D., D.A.B.T., A.T.S., DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SERVICES, NATIONAL INSTITUTES OF HEALTH, AND DIRECTOR, NATIONAL TOXICOLOGY PROGRAM, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Ms. BIRNBAUM. Mr. Chairman and Mr. Webb, I am pleased to appear before you today to present testimony on the relationship between dioxin exposure and the risk of ischemic heart disease. I am Linda Birnbaum and I am the director of the National Institute of Environmental Health Sciences of the National Institutes of Health, an Agency of the Department of Health and Human Services. I am also the director of the National Toxicology Program, an interagency program housed at NIEHS whose mission is to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology.

Understanding the role that environmental and occupational exposures play in the development of chronic diseases can be challenging, particularly for diseases that have significant risk factors in addition to the chemical exposure. Thus, the task of estimating the quantitative role of Agent Orange and dioxin exposure in the development of ischemic heart disease in Vietnam veterans is clouded by the contributions of other risk factors, such as age, smoking, family history, body mass index, serum lipid concentrations, and other factors.

In 2008, my colleagues and I published a systematic review that evaluated the evidence of an association between dioxin exposure and cardiovascular disease mortality in humans. We found that the group of highest quality studies reported consistent and significant dose-related increases in ischemic heart disease mortality and concluded that there is an association between dioxin exposure and mortality from ischemic heart disease and cardiovascular disease.

Similarly, the Institute of Medicine concluded in 2008 that there is limited or suggestive evidence of an association between Agent Orange or dioxin exposure and ischemic heart disease. The IOM based this decision on an approach that used all the available data from epidemiological, toxicological, and mechanistic studies. There are several challenges and limitations of the toxicological and epidemiological studies. In experimental animals dioxin increases the severity and the incidence of cardiomyopathy that is already present in aging rats. Similarly, in humans dioxin is not causing a unique cardiovascular disease but is increasing the risk of developing ischemic heart disease which has significant background incidence.

Thus, there are a number of other risk factors that can also influence the development of this disease. The epidemiological studies that the IOM evaluated and considered in their recommendations varied considerably in their attempts to address, adjust, or control for all the major risk factors of ischemic heart disease, such

as age and smoking, high blood pressure, diabetes, and obesity. It should be noted that few of the studies attempted to control for all of the major risk factors.

Also, the epidemiological studies have not attempted to compare the attributable risks of developing ischemic heart disease from dioxins to these other risk factors and have not reported the data in a manner that would allow the quantization of these comparisons. It may be possible to obtain some of these data and reanalyze them in order to address these questions. However, at present this analysis is not available.

The timing of exposure is another question that arises in evaluating risk. The window of possible exposure during service in Vietnam adds a level of uncertainty to the actual exposure estimates that are based on blood levels measured much later on.

It is also unclear from the studies available to us how much risk remains many years after exposure. Research in Seveso, Italy, showed an increase in the incidence of cardiovascular disease among people living in the most highly exposed areas after the 1976 accident that resulted in widespread dioxin exposure. But over time this effect dissipated.

In contrast, a recent study from the Australian Department of Veterans' Affairs of their Vietnam War veterans observed a pattern of increased risk for ischemic heart disease with increase in time. A number of review activities in this area by different agencies of the U.S. Government, as well as the National Academy of Sciences and the IOM, have generated comprehensive reviews of the risk of dioxin exposure.

For instance, in 2008, EPA released a literature search entitled "TCDD Dose Response Studies: Preliminary Literature Search Results and Request for Additional Studies" as part of an ongoing update of their dioxin reassessment. This literature search was reviewed by an outside panel of experts to ensure that all appropriate studies were identified with special emphasis on the latest literature.

The summary from this workshop, which was held in February in Ohio, was released in June 2009. In addition, the IOM's report entitled "Veterans and Agent Orange: Update 2008" also provides a comprehensive and reliable source for the most current data on the health risks of dioxin exposure.

Thank you again for this opportunity to testify on this important and difficult issue. I would be happy to answer any questions.

[The prepared statement of Ms. Birnbaum follows:]

PREPARED STATEMENT OF LINDA BIRNBAUM, PH.D., D.A.B.T., A.T.S., DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH, AND DIRECTOR, NATIONAL TOXICOLOGY PROGRAM U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and distinguished Members of the Committee: I am pleased to appear before you today to present testimony on the relationship between dioxin exposure and the risk of ischemic heart disease. My name is Linda Birnbaum; I am the Director of the National Institute of Environmental Health Sciences (NIEHS), of the National Institutes of Health, an agency of the Department of Health and Human Services, and Director of the National Toxicology Program (NTP), an interagency program, housed at NIEHS, whose mission is to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology. The program maintains an objective, science-based approach in dealing with

critical issues in toxicology and is committed to using the best science available to prioritize, design, conduct, and interpret its studies.

Understanding the role that environmental and occupational exposures play in the development of chronic diseases can be challenging, particularly for diseases that have significant risk factors in addition to the chemical exposure. Thus, the task of estimating the quantitative role of Agent Orange and dioxin exposure in the development of ischemic heart disease in Vietnam Veterans is clouded by the contributions of other risk factors such as age, smoking, family history, body mass index, serum lipid concentrations, and other factors. In 2008, my colleagues and I published a systematic review that evaluated the evidence of an association between dioxin exposure and cardiovascular disease mortality in humans.[1] We found that the studies in the highest-quality group found consistent and significant dose-related increases in ischemic heart disease mortality and concluded that there is an association between dioxin exposure and mortality from ischemic heart disease and cardiovascular disease.

Similarly, the Institute of Medicine (IOM) concluded in 2008 that there is limited or suggestive evidence of an association between Agent Orange or dioxin exposure and ischemic heart disease. The IOM based this decision on an approach that used all the available data from epidemiological, toxicological, and mechanistic studies. There are several challenges and limitations of the toxicological and epidemiological studies. In experimental animals, dioxin increases the severity and incidence of cardiomyopathy that is already present in aging rats. Similarly in humans, dioxin is not causing a unique cardiovascular disease, but increases the risk of developing ischemic heart disease, which has a significant background incidence. Thus there are a number of other risk factors that can influence the development of this disease. The epidemiological studies that the IOM evaluated and considered in their recommendations for ischemic heart disease varied considerably in their attempts to adjust or control for all the major risk factors of ischemic heart disease, such as, age, smoking, high blood pressure, diabetes and obesity. It should be noted that few of the studies attempted to control for all of these major risk factors. Also, the epidemiological studies have not attempted to compare the attributable risks of developing ischemic heart disease from dioxins to these other risk factors and have not reported the data in a manner that would allow the quantification of these comparisons. It may be possible to obtain some of this data and reanalyze it in order to address these questions. However, at present this analysis is not available.

The timing of exposure is another question that arises in evaluating risk. The window of possible exposure during service in Vietnam adds a level of uncertainty to the actual exposure estimates that are based on blood levels measured much later on. It is also unclear from the studies available to us how much risk remains many years after exposure. At least one study, the Australian Department of Veterans Affairs study of Vietnam War Veterans in that country, observed a pattern of increased risk for ischemic heart disease with time.[2] In contrast, while there was an increase in the incidence of cardiovascular disease in Seveso, Italy, shortly after the 1976 accident there that resulted in widespread dioxin exposure, this effect dissipated over time.[3]

A number of review activities in this area, by different agencies of the U.S. Government as well as the National Academy of Sciences (NAS) and the IOM, have generated comprehensive reviews of the risks of dioxin exposure. For instance, In 2008, the EPA released a literature search entitled "*2,3,7,8-Tetrachlorodibenzo-P-Dioxin (TCDD) Dose-Response Studies: Preliminary Literature Search Results and Request for Additional Studies*," as part of an ongoing update of the Dioxin Reassessment. This literature search was reviewed by an outside panel of experts at a workshop to ensure that the all appropriate studies were identified, with special emphasis on the latest literature. The summary from this workshop, held on February 18–20, 2009, in Cincinnati, Ohio, was released by the EPA in June 2009. In addition, the IOM's report entitled *Veterans and Agent Orange: Update 2008* also provides a comprehensive and reliable source for the most current data on the health risks of dioxin exposure.

Thank you for inviting me to testify. I would be happy to answer any questions.

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[2] ADVA (Australian Department of Veterans Affairs). 2005b. *The Third Australian Vietnam Veterans Mortality Study 2005*. Canberra, Australia: Department of Veterans' Affairs.

[3] Consonni D, Pesatori AC, Zocchetti C, Sindaco R, D'Oro LC, Rubagotti M, Bertazzi PA. 2008. Mortality in a population exposed to dioxin after the Seveso, Italy, accident of 1976: 25 years of follow-up. *American Journal of Epidemiology* 167(7):847–858.

RESPONSE TO PRE-HEARING QUESTIONS SUBMITTED BY HON. DANIEL K. AKAKA TO LINDA BIRNBAUM, PH.D., DABT, ATS, DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, NATIONAL INSTITUTES OF HEALTH AND DIRECTOR, NATIONAL TOXICOLOGY PROGRAM, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Question 1. What is the most reliable and comprehensive source for the most current data on the health risks of dioxin exposure?

Response. The series of documents included in the United States Environmental Protection Agency's (USEPA) Dioxin Reassessment are the most reliable and comprehensive sources for the most current data on the risks of dioxin exposure. The latest full version of the reassessment is the draft that was sent to the National Academy of Sciences (NAS) for review in 2004 entitled the "*NAS External Review Draft of the Dioxin Assessment*". However, since the 2004 document, the USEPA has released several other documents as part of the reassessment. In 2008 the USEPA released a literature search entitled "*2,3,7,8-Tetrachlorodibenzo-P-Dioxin (TCDD) Dose-Response Studies: Preliminary Literature Search Results and Request for Additional Studies*" as part of an update of the reassessment. This report was reviewed by an outside panel of experts at a workshop to ensure that the all appropriate studies were identified, with special emphasis on the latest literature. The summary (*Dioxin Workshop Summary report containing discussions and conclusions*) from this workshop held on Feb 18–20, 2009, in Cincinnati, Ohio was released by the USEPA in June 2009. The most recent addition to the Dioxin Reassessment entitled "*EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments (External Review Draft)*" was released on May 2010. This is a response to the NAS review of the 2004 draft dioxin reassessment. The draft response to the NAS review provides dose response analysis for low dose effects of dioxins in animals and humans. In summary, the above-cited documents provide the most recent and comprehensive review of the literature evaluating the risks associated with dioxin exposure. In addition, the Institute of Medicine's report entitled *Veterans and Agent Orange: Update 2008* also provides a comprehensive and reliable source for the most current data on the health risks of dioxin exposure.

Question 2. Given the currently available data for Viet Nam veterans, is it possible to calculate a quantitative estimate for the attributable and relative risks of developing ischemic heart disease from exposure to dioxin for males over the age of 60? If not, please describe the data limitations.

Response. Complex chronic diseases are difficult to attribute to a single factor due to the challenges and limitations of toxicological and epidemiological studies. The strength of the relationship between TCDD exposure and ischemic heart disease is based on epidemiological, toxicological and mechanistic arguments, and this strength evidence approach makes it difficult to quantify attributable and relative risk. In addition, the epidemiological studies have not attempted to address this issue; thus, the data is not reported in a manner that would allow the quantification of these comparisons. It may be possible to obtain some of this data and reanalyze it in order to address these questions.

Question 3. As a reviewer of the Institute of Medicine's Agent Orange Update 2008, please describe which, if any, of the studies relied upon by the IOM committee in reaching its determination reported a suggestive association between dioxin and ischemic heart disease after controlling for all of the major risk factors of ischemic heart disease, such as age, smoking, high blood pressure, diabetes and obesity.

Response. The epidemiological studies that the IOM evaluated and considered in their recommendations for ischemic heart disease varied considerably in their attempts to adjust or control for all the major risk factors of ischemic heart disease, such as age, smoking, high blood pressure, diabetes and obesity. Below is a list of those studies that considered other risk factors and which of the risk factors they considered:

- Kang HK, Dalager NA, Needham LL, Patterson DG, Lees PSJ, Yates K, Matanoski G.M. 2006. Health status of Army Chemical Corps Vietnam veterans who sprayed defoliant in Vietnam. *American Journal of Industrial Medicine* 49(11):875–884. Adjusted for age, race, rank, body mass index (BMI) and smoking. Kang et al also compared risks in diabetics and non-diabetics but did not adjust for high blood pressure or family history.
- AFHS. 2005. *An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides. 1997 Follow-up Examination and Results.* Brooks AFB, TX: Epidemiologic Research Division, Armstrong Laboratory. AFRL-HE-BR-SR–2005–0003. Adjusted for age, rank, race, smoking and drinking history,

high-density lipoproteins (HDL), cholesterol, HDL/cholesterol ratio, uric acid, diabetes, BMI or percent body fat, waist-hip ratio, family history of heart disease.

• Boehmer TK, Flanders WD, McGeehin MA, Boyle C, Barrett DH. 2004. Postservice mortality in Vietnam veterans: 30-year follow-up. Archives of Internal Medicine 164(17):1908–1916. Adjusted for age, race and military occupation.

• Vena J, Boffeta P, Becher H, Benn T, Bueno de Mesquita HB, Coggon D, Colin D, Flesch-Janys D, Green L, Kauppinen T, Littorin M, Lynge E, Mathews JD, Neuberger M, Pearce N, Pesatori AC, Saracci R, Steenland K, Kogevinas M. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. Environmental Health Perspectives 106 (Supplement 2):645–653. Adjusted for age and timing of exposure.

• Hooiveld M, Heederik DJ, Kogevinas M, Boffetta P, Needham LL, Patterson DG Jr, Bueno de Mesquita HB. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. American Journal of Epidemiology 147(9):891–901. Adjusted for age and timing of exposure.

• Calvert GM, Wall DK, Sweeney MH, Fingerhut MA. 1998. Evaluation of cardiovascular outcomes among US workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Environmental Health Perspectives 106 (Supplement 2):635–643. Adjusted for age, sex, BMI, smoking, drinking, diabetes, triglycerides, total cholesterol, HDL, family history of heart disease, chemical plant.

• Kitamura K, Kikuchi Y, Watanabe S, Waechter G, Sakurai H, Takada T. 2000. Health effects of chronic exposure to polychlorinated dibenzo-p-dioxins (PCDD), dibenzofurans (PCDF) and coplanar PCB (Co-PCB) of municipal waste incinerator workers. Journal of Epidemiology 10(4):262–270. Adjusted for age, BMI, smoking.

• Consonni D, Pesatori AC, Zocchetti C, Sindaco R, D'Oro LC, Rubagotti M, Bertazzi PA. 2008. Mortality in a population exposed to dioxin after the Seveso, Italy, accident in 1976: 25 years of follow-up. American Journal of Epidemiology 167(7):847–858. Adjusted for age, gender, period.

Question 4. As a reviewer of the Institute of Medicine's Agent Orange Update 2008, please describe which, if any, of the studies relied upon by the IOM committee in reaching its determination of a limited or suggestive association reported elevated risks for ischemic heart disease associated with dioxin exposure beyond 20 years after suspected dioxin exposure.

Response. Ketchum and Michalek (2005) examined the relationship between dioxin exposure and circulatory system disease in Vietnam War veterans in 1999. They concluded from this study that, "The risk of death attributable to circulatory system diseases continues to be increased, especially for enlisted ground crew, a subgroup with relatively high skin exposure to herbicides." Since this is a study of Vietnam War veterans, these veterans were exposed between 1961, when spraying started, to 1974, when the last of the US troops left Vietnam. The mortality study collected data up to December 31, 1999. This study suggests that some of these veterans were exposed for at least 20 years when the study was completed. However, the study does not specifically examine onset of the disease post exposure.

In addition, the IOM concluded that the ADVA (2005) study of Australian Vietnam War veterans displayed a pattern of increased risk for ischemic heart disease with time. The latter time period in this study was 1991–2001 which would suggest increasing risk 20 years after the initial exposure.

In contrast, the incidence of cardiovascular disease in Seveso Italy was increased by dioxin exposure shortly after the accident and this effect dissipated over time (Consonni et al 2008).

• ADVA (Australian Department of Veterans Affairs). 2005b. *The Third Australian Vietnam Veterans Mortality Study 2005*. Canberra, Australia: Department of Veterans' Affairs.

• Consonni D, Pesatori AC, Zocchetti C, Sindaco R, D'Oro LC, Rubagotti M, Bertazzi PA. 2008. Mortality in a population exposed to dioxin after the Seveso, Italy, accident in 1976: 25 years of follow-up. *American Journal of Epidemiology* 167(7):847–858.

• Ketchum NS, Michalek JE. 2005. Postservice mortality of Air Force veterans occupationally exposed to herbicides during the Vietnam War: 20-year follow-up results. *Military Medicine* 170(5):406–413.

Question 5. Does the scientific evidence indicate that an individual who has been medically determined to have developed ischemic heart disease more than 20 years after suspected exposure to dioxin is more likely than not to have developed ischemic heart disease as a result of a factor other than dioxin exposure?

Response. No epidemiological studies have directly addressed this issue, thus there is no direct evidence to support or refute this statement.

Chairman AKAKA. Thank you very much, Dr. Birnbaum.

Dr. Samet, in response to pre-hearing questions you noted that the lack of exposure data for Vietnam veterans precludes a determination of any increased risk of disease that might be caused by a specific exposure. The question is would an alternative approach comparing disease prevalence among Vietnam veterans and the general population more accurately identify diseases that are likely to be associated with Vietnam service?

Dr. SAMET. So without going into all the complexities of epidemiological research, I think the comparison that one would like to make is the risks of ischemic heart diseases or other diseases in those who were in Vietnam exposed to Agent Orange compared to a group of similar military personnel in Vietnam and not exposed, then absent that you look for alternatives that may be suitable to varying degrees depending on how similar or alike Vietnam veterans are, let us say, to the general population or any other group. If we try to make that comparison, let us say for ischemic heart disease, where we know there are many lifestyle factors, our ability to make that comparison with validity really hinges on how well we can measure all those relevant factors in the Vietnam veterans group and then equally make and compare to the general population, in essence trying to compare like to like, except for the Vietnam experience.

I would say that we have the tools to do that. It would require a large effort and measurement of many factors. In the end I think, in the case of trying to retrospectively do this, we would be left with an imperfect and uncertain answer. I will in part use your question to say that the difficulty of retrospect reconstruction speaks to the need to really be thinking prospectively for those troops who are now receiving exposures, how not to be in this position 20, 30, or 40 years from now with collection of exposure data and prospective follow up.

Chairman AKAKA. Thank you. Dr. Birnbaum, your responses to pre-hearing questions suggest that the EPA's dioxin reassessment is the most reliable source on the health risks related to dioxin. What is EPA's most recent analysis on the association between dioxin and IHD?

Ms. BIRNBAUM. The EPA's document is still undergoing final review by their science advisory board. The final meeting of that board will be the end of next month. But in the draft that has been released and is available for public comment there is a great deal of analysis of many of the different health impacts and review of the literature. It is clear from the wealth of animal studies in multiple animal species. It is clear from data from mechanistic studies, both in animals and cells in culture, including human cells, that dioxin can cause heart disease as a consequence. They have not directly quantitated the association between dioxin and ischemic heart disease in people.

There does appear to be an association with cardiovascular disease more broadly defined in some of the studies. I think it is important that we mention the Ranch Hand Study, which was the long-term study conducted by the Air Force, the Air Force Health Study, which unfortunately ended in 2006. But in that study, in one of the last reports from it which has been published since then,

there was a dose-related increase in the Ranch Handers with the highest measurable dioxins in their blood as compared to other veterans who had not served in southeast Asia but had served at the same time window. I think they did not explicitly look for ischemic heart disease in that study, which is one issue of many in the epidemiology studies, which makes them difficult to compare because not all of them looked for the same measures of effects on the cardiovascular system.

Chairman AKAKA. Dr. Bild, in your response to pre-hearing questions, you stated that approximately 80 or 90 percent of IHD is explained by lifestyle factors. You have explained the major factors that cause the disease. What can you share about what role, if any, scientists believe dioxin exposure plays in connection with the lifestyle factors?

Dr. BILD. Are you asking what role dioxin plays in connection with the lifestyle factors to produce IHD?

Chairman AKAKA. Yes.

Dr. BILD. Well, there are decades of very good evidence that link the lifestyle or risk factors that I discussed earlier with ischemic heart disease. Dr. Birnbaum and others are more expert than I am on the specific relationship between dioxin and IHD, but in general the 80 to 90 percent figure that I quoted was looking at all IHD and from models estimating that proportion attributable to the lifestyle factors in the population. Theoretically, if one were able to eliminate or modify all those factors, one would eliminate that amount of disease in the population.

Now, in order to understand how dioxin might contribute to that you have to know the strength of its association with IHD, and we know some of that from the studies that Dr. Birnbaum has quoted. We have to also know the extent of exposure in the population at risk, which is a big unknown. So if you assume that the proportion of people exposed was low, then that attributable risk becomes very low. That is not really a question that I can answer.

Chairman AKAKA. Thank you. Senator Webb, you have questions.

Senator WEBB. Thank you, Mr. Chairman. I believe Mr. Samet, did you have a follow-on to that? You had your hand up.

Dr. SAMET. I wanted to comment, just because I think there may be a misimpression that if other lifestyle—if lifestyle factors cause 80 or 90 percent of coronary heart disease there is only 10 or 20 percent left over to be caused by other things. That is really not correct. If, let us say, dioxin or any other exposure amplifies the effects of these common lifestyle exposures which might be the case, then that is important to know and understand and best addressable by research. So the problem, in fact, is that these diseases are common because these risk factors are common. Then we have on top of that the question of how additional Agent Orange or other exposures might amplify this background.

Chairman AKAKA. Dr. Birnbaum.

Ms. BIRNBAUM. I would also like to add to that. There is lots of evidence that indicates, certainly from, again, all the mechanistic studies, the animal studies, and from of the epidemiological studies, that dioxin can contribute to all of these common risk factors that we talked about. So for example, dioxin alters the triglyceride content. Dioxin is associated or can be associated with Type 2 dia-

betes which is a risk factor. Dioxin can be associated with elevated blood pressure, again, both in animal studies and in some human studies. And we know that dioxin can alter the vasculature as well. So I think the point that Dr. Samet made that you have interacting factors here that all may be involved is a very important one.

Senator WEBB. Thank you. Mr. Chairman, I would like to ask a couple questions. First of all, thank all of you for the details that you provided in your written statements and the follow-on questions. We have gone through those. There is a tremendous amount of valuable material here that will be useful to this Committee.

Dr. Birnbaum, on your July 15 response, on the second page you were referring to the Steenland and Vena studies. Basically it says, based solely on those studies it would appear less likely that incidences of ischemic heart disease that occurred 20 years after exposure are related to dioxin exposure. Your point was that if the condition had been manifested before the 20th year that it would be more likely to be dioxin-related but if a person was later determined to have ischemic heart disease or in the 30th year after their suspected dioxin exposure, the credible evidence or an association between dioxin exposure and ischemic heart disease would be outweighed by the credible evidence against.

Ms. BIRNBAUM. I may want to eat those words a little bit because I do not think we really understand. Some of the things that dioxin can do, it can permanently alter how our body functions. And once you permanently change the expression, for example, of certain genes, you cannot reverse those changes. And there may be critical windows of exposure. I think when we think especially about our veterans, especially in Vietnam, many of them were young men. And the additional stress that the early dioxin exposure, which may have in some ways set them up for all the additional risk factors that would occur later on, I think we have to think about that.

I think there are different studies. There is a recent study which clearly shows—the Australian Veterans Study—clearly shows that risk appears to increase with time since the Vietnam experience; and there is actually a suggestion of that again from the Ranch Hand Study. But the last Ranch Hand analysis was terminated before we could really find out whether it would continue to show the same.

Senator WEBB. I recall going through the original Ranch Hand Studies in great detail back in the late 1970s, looking at the mortality rates and the incidence, particularly the liver—conditions of the liver were prominent back then.

I am still curious to get your comments, collectively or whoever would like to comment, on the reason that the recommendation on ischemic heart disease was changed between 2006 and 2008. Was this actual new scientific studies or was this as a result of further evaluation of studies that had already been done?

Ms. BIRNBAUM. Science continues to advance. There is always new information which is incremental to what was known before and there are new approaches to the data so that there were several new epidemiological studies that were published in that time window. There were also additional mechanistic and animal studies that were published in that timeframe, all which added to the evi-

dence that supported the limited association between ischemic heart disease and exposure to dioxin.

I think the biggest problem that we face which has been referred to by many of the panelists is the fact that we really do not—frequently do not have good measures of what exposure was and continues to be in the affected people.

Senator WEBB. Dr. Bild, you mentioned in your oral statement—I think I wrote this down right—the studies cannot be adjusted for risk factors and that it is impossible to know if dioxin was instrumental. Would you like to comment further on that?

Dr. BILD. Yes. I was reiterating statements that were made earlier and in part the scientific review that Dr. Birnbaum's group published which examined a set of studies on the relationship between dioxin and IHD mortality which were able to adjust for age but were not necessarily all able to take into account other so-called confounders such as smoking.

So, for example, if those exposed to dioxin also happened to be part of a group that had a higher smoking rate, the IHD could be attributable to smoking rather than dioxin. But that would not be apparent from the study if you did not have the data on smoking and were not able to adjust for it in the analysis.

Senator WEBB. Well, Secretary Shinseki made a comment toward the end of his testimony; he had actually made a similar comment when I met with him, though I am not sure where this data comes from or what exactly he meant. But he said something to the effect that Vietnam veterans have a three times greater probability of contracting ischemic heart disease. Does staff have a better understanding of what he said? 1.4 to 2.8?

Dr. JESSE. Yes. 1.4 to 2.8. That is the relative risk of ischemic heart disease in the veteran population cited across the six different studies.

Senator WEBB. Based on which studies?

Dr. JESSE. The six studies that the Institute of Medicine put forward. The fact that there were six, which Dr. Birnbaum in her meta-analysis looked at as well. So those studies, they ranged from 1.4 to 2.8 as increased relative risk in the exposed population.

Senator WEBB. Were these studies among the nine that were reported out?

Dr. JESSE. Yes. Yes.

Senator WEBB. And only two of those studies even related to Vietnam veterans.

Dr. JESSE. Well, the exposure—I am sorry.

Senator WEBB. None of them related to Vietnam veterans at large. So basically, what you are saying—what the point is so that I can understand it—let me say it and tell me if I am wrong, is that looking at the analytical data from these studies based on dioxin exposure or TCDD exposure, you can then summarize that the probability or the risk factors were 1.4 to 2.8.

Dr. JESSE. Yes.

Senator WEBB. We do not have actual determinant of information on that. Do we? We do not have a Vietnam veteran control group——

Dr. JESSE. Not for being on veteran controls.

Senator WEBB. So we cannot say a Vietnam veteran is 1.4 to 2.8 more times likely to come down with ischemic heart disease than a non-veteran?

Dr. JESSE. Well, what we can say is that those exposed to Agent Orange—and we have a presumption that a Vietnam veteran was exposed—so we can say that those exposed to Agent Orange have a 1.4——

Senator WEBB. Well, first of all, I do not think anyone will, in fact would agree that all people that went to Vietnam were exposed to Agent Orange. Those who were presumptively exposed——

Dr. JESSE. Presumptively exposed. Right.

Senator WEBB. Right?

Dr. JESSE. Yes.

Ms. BIRNBAUM. In the Air Force Health Study by Ketchum and Michalek, which was published in 2005, they reported that for the ground crew, if you compared the ground crew on the sprayers to all Southeast Asia veterans not including those in Vietnam, they had an estimated relative risk of 1.7.

Senator WEBB. Right. Well, that would——

Ms. BIRNBAUM. But that was of heart disease.

Senator WEBB [continued]. Also seem to be logical and understandable because of the functions that they performed.

Ms. BIRNBAUM. Right.

Senator WEBB. Compared to a lot of other people. Thank you, Mr. Chairman.

Chairman AKAKA. Thank you. We still have a second round here. Dr. Samet, you note that it is unclear how VA makes a particular determination once the IOM report is received and how information beyond the IOM's findings figure into VA's decision. What specific changes in that process do you recommend? And what do you see as a value of greater openness and transparency in that process?

Dr. SAMET. This was one of the tasks of our committee, to describe the VA process in place. We interacted with VA extensively trying to understand in general what their processes were, and in particular what their processes were and how they responded to particular findings by IOM. As we talk to stakeholder groups, we found I think frustration with understanding how VA made decisions once the IOM reported in terms of its predecisional internal processes. They were described to us in general as involving a consideration of IOM and additional evidence, and we understood that some burden and cost estimates were made. And I think the Secretary provided some insights into that around the IHD decision.

We felt and proposed in our process for decisionmaking for improving the process, that there be full transparency. That would show how the scientific evidence and all the nonscientific considerations, particularly related to handling of uncertainty, would be played out. When the decision was made, whether for a presumption or not, it would be very clear what the underlying internal logic was. So we think that process should be transparent.

Chairman AKAKA. Thank you. Dr. Birnbaum, does IOM's conclusion that there is a limited or suggestive evidence of an association between IHD and dioxin serve as proof that Vietnam veterans have a higher risk for prevalence of the disease than the general population?

Ms. BIRNBAUM. I think the science supports the conclusion of the IOM, that there is an association between an exposure to dioxins and ischemic heart disease. Whether that means that all veterans have an increased risk or not I cannot say.

Chairman AKAKA. Dr. Bild, in your pre-hearing questions you stated that approximately 80 percent of men aged 60 through 69 could be expected to have some symptoms of IHD or have IHD but no apparent symptoms. Can you explain why? And how many of them will develop symptoms?

Dr. BILD. Yes. Well, as I explained earlier, atherosclerosis is a progressive disease and by middle and late age, particularly in men in this country, there will be some plaque, early forms of coronary disease detectible through some method. A relatively small proportion in the U.S., about 17 percent of men age 60 to 69, will report having IHD—that is they had symptoms, they had a heart attack, or they have had bypass surgery. This is clinically apparent IHD as opposed to the much larger proportion who have silent or asymptomatic disease that may never become clinically apparent.

Chairman AKAKA. I want to thank you very much. In closing, I again say thank you for your responses and for appearing here today. You have been very helpful in what we want to do in the future and for work on a process that would be legislatively helpful.

As chairman, it is my responsibility to make certain that this Committee fulfills its obligation to conduct the oversight of the Department of Veterans Affairs. Issues raised at today's hearing affect not only Vietnam veterans but Persian Gulf, Iraq, and Afghanistan veterans, as well as those who were exposed on military installations. My hope is that we can move forward from today's hearing with a better understanding of how the current process is working and what improvements need to be made. I, again, thank all of you for your participation.

This hearing is now adjourned.

[Whereupon, at 12:19 p.m., the hearing concluded.]

A P P E N D I X

PREPARED STATEMENT OF THE RESERVE OFFICERS ASSOCIATION OF THE UNITED STATES AND RESERVE ENLISTED ASSOCIATION OF THE UNITED STATES

Mr. Chairman and Members of the Committee, the Reserve Officers Association (ROA) and the Reserve Enlisted Association (REA) thank the Committee for the opportunity to submit testimony. Many Soldiers, Sailors, Marines, and Airmen from both the Active and Reserve Components were exposed to Agent Orange and other toxic herbicides in Vietnam. While many ailments may appear to be that of an aging population, statistically the incidents of these ailments are much more prevalent than the general populations. In addition to those veterans whose illnesses have been exacerbated by exposure, there are other veterans who remain ineligible that suffer from ailments that are recognized by the Department of Veterans Affairs (VA).

Both ROA and REA believe that blue-water sailors, and blue-sky airmen need to be included under the eligibility for VA treatment of ailments relating to exposure to toxic herbicides. The current litmus test of "boots on the ground" is inadequate when the effects of exposure extended beyond the boundaries of Vietnam.

Decisions being made by this Committee will affect not only veterans of the Southeast Asia conflict, but also later generations, such as veterans who have fought in the Southwest Asia during Desert Storm, and the Iraq and Afghanistan contingency operations. Precedents will be set, for not only contemporary conflicts but for the next generations' wars as well.

ROA has a resolution, number 11, that passed in 2008 (see page 7) that talks to "Preserving Veteran Status and Benefits for Those Who Have Served in Theaters of Operations" that originates from the lack of available treatment for certain Vietnam veterans.

ROA and REA recognizes that exposures to chemicals, toxins and heavy metals can occur in any war and that these can be spread more widely by airborne drift or water-borne runoff than calculated computer models. It remains vitally important in any theater of contingency operations that individuals are recognized for their service and remain eligible for health benefits regardless of the manner of exposure whether on land, sea, or in the air. Medical treatment of serving members as well as veterans needs to take precedence over determining statistical correlations.

BACKGROUND

As the Committee is aware, American forces sprayed millions of gallons of Agent Orange and other defoliants over parts of Vietnam from 1961 to 1971. During "Operation Ranch Hand," US forces sprayed about 20 million gallons of Agent Orange and other herbicides ion southern and central Vietnam to deprive enemies of jungle cover.

Veterans who served "in country" in Vietnam may be eligible for disability compensation and health care benefits for diseases that VA has recognized as associated with exposure to Agent Orange and other herbicides. These are the diseases which VA currently presumes resulted from exposure to herbicides like Agent Orange.

- Acute and Subacute Peripheral Neuropathy

A nervous system condition that causes numbness, tingling, and motor weakness.

- AL Amyloidosis

A rare disease caused when an abnormal protein, amyloid, enters tissues or organs.

- Chloracne (or Similar Acneform Disease)

A skin condition that occurs soon after exposure to chemicals and looks like common forms of acne seen in teenagers.

- Chronic Lymphocytic Leukemia and Other Chronic B Cell Leukemias

A type of cancer which affects white blood cells. Currently, only chronic lymphocytic leukemia is recognized as associated with Agent Orange exposure.

• Diabetes Mellitus (Type 2)

A disease characterized by high blood sugar levels resulting from the body's inability to respond properly to the hormone insulin.

• Hodgkin's Disease

A malignant lymphoma (cancer) characterized by progressive enlargement of the lymph nodes, liver, and spleen, and by progressive anemia.

• Ischemic Heart Disease

A disease characterized by a reduced supply of blood to the heart that leads to chest pain.

• Multiple Myeloma

A disorder which causes an overproduction of certain proteins from white blood cells.

• Non-Hodgkin's Lymphoma

A group of cancers that affect the lymph glands and other lymphatic tissue.

• Parkinson's Disease

A motor system condition with symptoms that include a trembling of the hands, imbalance, and loss of facial expression.

• Porphyria Cutanea Tarda

A disorder characterized by liver dysfunction and by thinning and blistering of the skin in sun-exposed areas.

• Prostate Cancer

Cancer of the prostate; one of the most common cancers among men.

• Respiratory Cancers

Cancers of the lung, larynx, trachea, and bronchus.

• Soft Tissue Sarcoma (other than Osteosarcoma, Chondrosarcoma, Kaposi's sarcoma, or Mesothelioma)

A group of different types of cancers in body tissues such as muscle, fat, blood and lymph vessels, and connective tissues.

Under current law, only veterans who served in the Republic of Vietnam during the war are entitled to a presumption of exposure to Agent Orange and other toxic herbicides when seeking compensation for conditions linked to herbicide exposure. Excluded are sailors from ships who sailed in littoral waters of Vietnam and airmen who may have been exposed to toxins at storage and load out locations

The "boots on the ground" policy was unsuccessfully challenged in *Haas* vs. Nicholson. In January 2009, the Supreme Court let stand an earlier court ruling that requires a veteran to have served on land or on the inland waterways of Vietnam in order to be presumed exposed to Agent Orange.

ROA and REA thank the Committee for earlier letters sent by the Chairman to expand the presumption, and the associations believe that there is justification to introduce legislation that will extend eligibility to those who were exposed to toxic herbicides outside of Vietnam.

Blue Water Exposure

In addition to the Navy's reverie "brown water" missions in Vietnam, the U.S. Navy controlled the coastal waters off of Vietnam, provided power projection along the shore, and provided logistic support both afloat and ashore by having a sizable portion of its fleet in Vietnam waters. This blue water Navy supplemented the Republic of Vietnam navy to deny access along the coastal waterways for infiltration of men and supplies from the North.

One tactic used by the Navy was to use shipboard guns as artillery along the coast to support military operations, and destroy military targets. Working from four corps areas, a destroyer (and cruiser) gunline of U.S. and Australian ships furnished shore bombardment and naval gunfire support. Located between one to two miles off the coast, they accurately fired 5 inch shells at a rate of 40 rounds per minute on targets at ranges beyond 14 nautical miles inland. This bombardment would go 24 hours a day, with ships firing thousands of rounds. These ships were close enough ashore that during the war, twenty-nine gunline ships were hit by enemy shore artillery.

Operation Sea Dragon provided coast destroyer and cruiser patrols that searched for water borne logistic craft head to the South. Destroyers and frigates also gave search and rescue support along the coast for downed pilots.

Navy supplies ships cruised along the coast resupplying these littoral vessels allowing them to stay on station.

Many blue water ships were exposed to herbicide runoff from Vietnam river basins. With 13 large river systems, Vietnam is considered to have a complex and dense river network with most of the large river systems linked. The Mekong River,

alone, splits into nine arms, with all flowing down and emptying into the sea. Agent Orange is insoluble. It was carried whole into the swamps, down creeks into the rivers and down the rivers into the South China Sea.

It can also be noted in Figure One (see page 6) that herbicides were heavily sprayed along the coast. The Navy ships stationed off the coast were adrift in an herbicide soup, with runoff continuing to occur even after spraying ended in 1971. Even today, certain areas off the Vietnam coast are off limits to fishing, remaining as toxic hot spots.

Aboard Navy ships, potable water is produced by evaporative distillation of seawater. In distillation plants on ships seawater was usually fed into an evaporator where the water was boiled by a combination of heating and reduced pressure (vacuum). The vapor was condensed in the condenser from where it was pumped into the feed tanks.

As a result insoluble agents remained in the potable water. An Australian study focused on the evaporative distillation process that was used to produce potable water by Navy ships from surrounding estuarine waters. It was entitled Co-Distillation of Agent Orange and other Persistent Organic Pollutants in Evaporative Water Distillation, and found that "the main contaminant in Agent Orange was found at about 85 percent of the quantity observed in the control samples and co-distilled to a greater extent than any other PCDD/F investigated here." Sailors were being exposed to herbicides through their drinking water.

A question needs to be asked as to what happened to the remaining 15 percent? As kitchen chemistry demonstrates to anyone who cooks, an agent in the water when it is boiled migrates to the sides of a container. Boil insoluble salt in a coffeepot, soon that insoluble salt coats the inside of the coffeepot. Through the distilling process, Agent Orange continued to percolate within the evaporators even after external exposure ceased because it coated the system. Every additional load of seawater taken into a Navy ship and then boiled added to the concentration of Agent Orange on the inside of the evaporators and condensers—continuing to contaminate potable water used on the ship.

The Australian study was motivated by an Australian Veterans Administration report noted that veterans of the Royal Australian Navy (RAN) experienced higher mortality than other Australian Vietnam Veterans. Australia's largest naval commitment to the Vietnam War was the provision of destroyers, on rotation, to serve on the gunline, along side American ships—delivering naval gunfire support for allied ground forces.

Blue Sky Airmen Exposure

In 1996, Dr. Michael Gough, the chairman of the Federal panel charged with investigating the potential health impacts of Agent Orange use, "[The Centers for Disease Control and Prevention] found that while the Air Force's Operation Ranch Hand sprayed 90 percent of the Agent Orange used in Vietnam, there is no difference in the health of the Ranch Hands, the only veterans known to have been exposed, and that of other veterans who served in Southeast Asia at the same time and flew the same kinds of airplanes but were not exposed to Agent Orange."

Yet, the Air Force studies of the Operation Ranch Hand personnel showed that the exception was an increased mortality rate for circulatory diseases seen in enlisted ground crew personnel, a group at higher risk for skin exposure to herbicides. In 2005, an AFHS update reviewing 20 years of Epidemiologic data on mortality rates reported a small, but significant, increase in all cause death rates for Ranch Hand veterans.

Research has determined that there was significant use of herbicides on the fenced in perimeters of military bases in Thailand intended to eliminate vegetation and ground cover for base security purposes. Security policemen, security patrol dog handlers, members of a security police squadron, or others that served near the air base perimeter during the Vietnam Era were exposed to toxins.

A U.S. Court of Appeals for Veterans' ruling in 2005, concluded that an air force veteran contracted a disease as a result of his exposure to Agent Orange while stationed on Guam in the late 1960s. During the Vietnam War era, Guam was used as storage facility for Agent Orange.

Johnston Island is less than 2 miles long and less than a half mile wide. Approximately 113,400 kg of Agent Orange accidentally spilled in 1972 during redrumming after the Air Force brought approximately 5.18 million liters of unused Agent Orange from Vietnam to Johnston Island. In addition, 49,000 gallons per year of Agent Orange are estimated to have leaked from drums at the Johnston Island storage site.

The above examples are but a few cases where airmen were exposed to Agent Orange and other herbicides. During the Vietnam War, there is reported use of herbi-

cides in Thailand, Okinawa, Guam, Philippines, and many other locations on the Pacific rim, mainly at Air Force bases. Additionally the Department of Defense has published a list of locations even in the U.S.s where these toxins were used.

Congress needs to continue to explore cases where the health of veterans has been compromised by Agent Orange and other toxic herbicides.

CONCLUSION

The majority of studies have focused on morbidity and mortality of Vietnam veterans. Studies on Agent Orange are historically burdened by the lack of reliable exposure data. For veterans who have been exposed to Agent Orange and other toxic herbicides, the burden of proof is placed on the veteran to demonstrate a causal link between ailments and exposure.

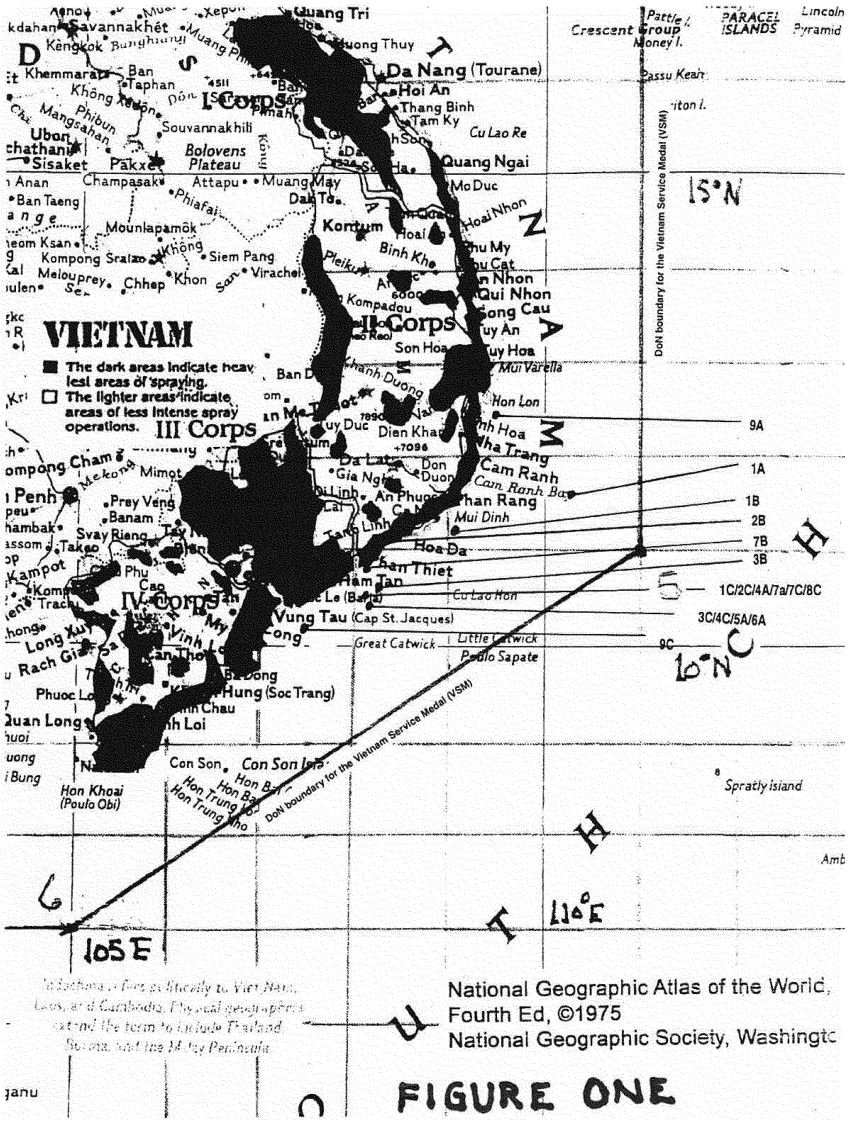
Thousands of Sailors served providing gunfire support aboard destroyers along the coast and on Yankee Station aircraft carriers providing air cover and bomb support over Vietnam. Navy veterans who were awarded the Vietnam Service Medal as a result of service in the waters offshore Vietnam (blue water vets) should be entitled to the same presumption of exposure to Agent Orange as veterans who set "foot on land" in Vietnam or did duty in brown water missions. As a result, many Navy veterans who served offshore and their survivors were granted disability or DIC benefits based on an Agent Orange-related disease.

Also overlooked are Air Force Airmen who were exposed to herbicides stored at staging airbases, and storage sites outside of Vietnam and in the airspace above. Many of these same bases used herbicides to control vegetation along the perimeters of the bases and airfields for security reasons. Numerous mechanics, supply clerks, and air patrolman are suffering the same diseases as a result of exposure to the herbicide Agent Orange, and deserve Veteran health care, and disability benefits for their ailments, or care for survivors.

The Reserve Officers Association and the Reserve Enlisted Association representing over 63 thousand members support expanding the presumptive coverage by the Department of Veterans Affairs.

Please see the following pages for Figure One: Spray Patterns of Herbicides in Vietnam, and Attachment One: ROA Resolution 08–11, "Preserving Veteran Status and Benefits for Those Who Have Served in Theaters of Operations."

FIGURE 1.—SPRAY PATTERNS OF HERBICIDES IN VIETNAM.



ATTACHMENT ONE.—ROA RESOLUTION 08–11.

PRESERVING VETERAN STATUS AND BENEFITS FOR THOSE WHO HAVE SERVED IN THEATERS OF OPERATIONS.

RESOLUTION 08–11

WHEREAS, the Department of Veterans Affairs (VA) has proposed to amend its adjudication regulations regarding the definition of service in the Republic of Vietnam in regard to exposure to Agent Orange;

WHEREAS, the current definition of service in Vietnam includes service in the waters offshore and service in other locations if "conditions of service involved duty or visitation in the Republic of Vietnam"; and

WHEREAS, the VA wishes the definition "to include only service on land and on inland waterways" of the Republic of Vietnam; and WHEREAS, thousands of Sailors served providing gunfire support aboard destroyers along the coast and on Yankee Station aircraft carriers providing air cover and bomb support over Vietnam; and

WHEREAS, thousands of Airmen stationed in Thailand, prepared aircraft and flew missions over Vietnam; and

WHEREAS, Marines and Soldiers fought in Laos and crossed into Cambodia; and

WHEREAS, distinguishing types of service in an theater of operations is a bad precedent, when "boots-on-the-ground" veterans are differentiated from all other Armed Forces participants, especially when this Nation is currently at war; and

WHEREAS, exposures to chemicals, toxins and heavy metals can be spread more widely by airborne drift or water-borne runoff than calculated patterns;

NOW THEREFORE BE IT RESOLVED, that the Reserve Officers Association of the United States, chartered by the Congress, urge the Congress, the Department of Defense and the Department of Veterans Affairs, to retain current definitions of service in any theater of operations ensuring that individuals are recognized for their service and remain eligible for health benefits regardless of manner of exposure whether on land, sea, or in the air.

Time Sensitive—submitted by ROA Headquarters Staff
Adopted by the ROA National Convention, June 28, 2008

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