

"NCI Management of Radiation Studies"

Statement of

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Good morning, madame chairman, and members of the Subcommittee. I am Richard Klausner, Director of the National Cancer Institute (NCI). I am pleased to testify before you today about NCI's role in radiation research, specifically about studies of exposure to Iodine 131 and its relationship to thyroid cancer. In my testimony I will describe NCI's mission, the process for scientific discovery, the management of complex scientific studies, the NCI study of I-131 exposures, our role in studies associated with the aftermath of the Chernobyl accident, and actions I have taken to strengthen oversight, management, and communication of NCI's radiation studies.

Introduction

The National Cancer Institute has a long and distinguished history in radiation research including studies of how radiation is involved in the causes of cancer and how it is used most effectively in the treatment of cancer. Today, NCI is staffed with several of the world's leaders in the field of radiation epidemiology and radiation dosimetry. When Public Law 97-414 instructed the Department of Health and Human Services to estimate the thyroid doses of iodine-131 received by people exposed to fall-out from the Nevada nuclear tests, NCI was asked to take on this responsibility. In October 1997, I testified before the Senate Appropriations Subcommittee on Labor, Health and Human Services and Education and presented the results of that study. Following that hearing, and at the request of the Department of Health and Human Services (DHHS), the National Academy of Sciences (NAS) and Institute of Medicine (IOM) reviewed the data and prepared a report entitled "Exposure of the American People to Iodine-131 from Nevada Nuclear-Bomb Tests: Review of the National Cancer Institute Report and Public Health Implications." Their report focused on (1) assessing the soundness of the NCI analyses and estimates including those developed separately from the main report, (2) the risk of thyroid disease from iodine-131 fallout, (3) evaluating the benefits and harms of recommending a program of routine screening for thyroid cancer, and (4) identifying strategies for communicating with the public about risks and responses. We are in the process of carefully studying the report, findings, and recommendations and are working with the Department of Health and Human Services and the Centers for Disease Control

and Prevention and its Advisory Committee on Energy Related Epidemiologic Research (ACERER) to implement their advice most effectively.

In April of 1986, a nuclear reactor accident took place at Chornobyl in Ukraine. Following the accident, large numbers of people were exposed to iodine-131 and, for many of them, actual measurements were made of radioactivity in their thyroid glands. With the availability of such measurements, the Department of Energy (DOE) felt that if a study of the exposed children in Ukraine and Belarus could be designed and implemented, it might be extremely valuable for determining the risk of thyroid cancer as a function of the dose of iodine-131 received. Because of NCI's experience and expertise in this field, in 1990 the DOE asked the NCI to take responsibility for planning and working with scientists of the then Soviet Union to develop long-term studies of health effects, specifically in the thyroid, that might result from exposure to I-131 from the Chornobyl accident. DOE asked that Dr. Bruce Wachholz, the Chief of our Radiation Effects Branch, manage the scientific aspects of the program. We were pleased to be able to actively participate in this study, because of the unique opportunity this tragic accident afforded us to complete the risk assessment of I-131 and thyroid cancer that was called for in P.L. 97-414. I will discuss this study in greater detail later in my testimony. Shortly after this request, the dissolution of the Soviet Union took place, and we have subsequently been working with the new independent governments in Belarus and Ukraine. In close cooperation with scientific colleagues in Belarus and Ukraine, a U.S. working group has worked with comparable working groups in each country to develop research protocols for studies of thyroid cancer in large cohorts of children and adolescents in both countries. These studies are now in progress.

NCI's Mission

The ultimate goal of the National Cancer Institute is to prevent or cure cancer. The United States Congress in 1937 established the National Cancer Institute and in 1971 reaffirmed its commitment to cancer research with the passage of the National Cancer Act. Today, as we approach the 21st century, we can take pride in our accomplishments, but our pride is tempered by the knowledge that we still have much to do to achieve our goal.

We have reached a turning point in our fight against cancer. Between 1991 and 1995, the cancer death rate and the incidence rate showed their first sustained drop since record keeping began in the 1930s. For several types of cancer - children's cancers, breast, colon and rectal, Hodgkin's and testicular - the decreasing death rates reflect cumulative research successes over the past several decades. Continued advances in our knowledge base have been a vital component in the recent decline in the cancer death rate - a decline that has translated into thousands of lives saved. However, while the decline in the cancer death rate is evidence of our successes and reflects the collective knowledge and technical advances achieved, we still face an enormous challenge to more fully grasp the underlying causes of cancer - an understanding that is the keystone of further progress. Our success will continue to be measured in terms of fewer deaths, fewer new cases, increased life expectancy, and improved quality of life for cancer survivors. Our goal of a

reduced cancer burden can only be achieved through continued expansion of our knowledge base that supports the successful translation of discoveries into treatments that benefit all people who are at risk for and who have cancer.

Clinical Studies in an International Setting

The NCI is an institution of science, and our operations are driven by the processes of science. The culture of science is one of continued questioning, testing of hypotheses against evidence, critique by peers, validation of research results, and modification and extension of results as new findings emerge from the community of researchers. In this culture the pursuit of new knowledge must be the primary goal.

Importantly, much scientific research is conducted in a collaborative manner. Complex projects require the collective wisdom of multidisciplinary teams of experts and are never performed by individuals working in isolation. Members of these research teams provide the diverse and broad expertise that is necessary to ask and answer major questions relating to human health. International collaborations are particularly challenging. Culture, local customs, and language differences must be surmounted; administrative, legal, and logistical barriers overcome; and effective communication and trust established before the collaboration can even address its scientific goals.

Complementing scientific excellence, we must also have scientific and administrative mechanisms that provide oversight and accountability to our research projects and programs. Oversight of NCI activities is provided by various groups, including the Presidentially-appointed National Cancer Advisory Board, the Board of Scientific Counselors (for intramural research, conducted by NCI staff), and the Board of Scientific Advisors (for extramural research). In addition, certain individual projects, such as major clinical studies, often require specific oversight, in the form of data monitoring committees or advisory groups. These committees, functioning independently of those directly involved in the project, protect the interests of the people participating in the research and provide advice to project leaders on the future conduct of the study. They are integral to safeguarding the scientific integrity and ethical foundations of major clinical studies. Thus, it is crucial that the administrative and procedural requirements associated with clinical research serve the needs of the particular project and, in essence, be tailored to them.

The Chernobyl experience shows much about the complexity of organizing and conducting a major clinical research study in an evolving and fluid international context. This study is a comprehensive clinical epidemiologic investigation requiring an effective integration of scientific, ethical, legal and regulatory requirements in a highly volatile political environment. The project directors are Ukrainian and Belarussian scientists, and they are studying the incidence of thyroid cancer in residents of these two countries who were exposed to radiation from the Chernobyl disaster. U.S. contributions include scientific expertise, guidance, training, advice, equipment and supplies, and partial funding.

Clinical studies conducted in the U.S. must adhere to the highest ethical standards and must guarantee that patients and subjects are fully informed of the potential risks and benefits of their participation in the study. In this country, we have policies and procedures, based in law and regulation, to ensure that all clinical studies satisfy these requirements. Approval and oversight for research protocols are vested in Institutional Review Boards (IRB) in each research center involved in such studies, whether in the U.S. or abroad, which are responsible for ensuring the ethical conduct of the study. In other countries, these processes often are not as well defined; sometimes they are actually non-existent and must be established before a clinical study can start. In newly democratic countries, the concept of voluntary participation in a government-sponsored study is not always clearly understood, either by the sponsors or by the participants. In the case of U.S. involvement in the Chernobyl studies being conducted by scientists in Ukraine and Belarus, as in other foreign countries where we are working, all of the regulations and procedures that apply to clinical research in the U.S. must be followed, and we therefore had to educate our foreign collaborators, as necessary, on these processes. Our ability to effectively accomplish this training had a direct impact on project implementation and execution, effective management of protocol benchmarks, and realistic achievement of proposed study outcomes.

Additionally, effective international cooperation requires significant lead time for establishing the critical interpersonal relationships needed to work together effectively and surmount the barriers already noted. NCI staff and their foreign partners have successfully established these relationships, which now constitute a firm basis for moving forward with the Chernobyl investigations.

Management

This committee has asked about how NCI manages its research programs, with particular focus on radiation studies. My understanding of the questions and concerns directed toward NCI is that they focus on oversight and management of the Chernobyl study, rather than the scientific questions being asked. With the Chernobyl project, the management approach must and does reflect the inherent characteristics of this type of a comprehensive, complex clinical study. It is designed to respond to changing parameters that require flexibility to address myriad issues that will inevitably arise purely because of the nature of the study itself. In our large, complex clinical trials, we often use a team approach to address specific problems as they arise, while at the same time providing for proper oversight that is removed from the day-to-day operations. Decisions are generally made by consensus, and we draw the necessary pool of talent, expertise, and experienced individuals in building these teams. Collective oversight may look sloppy or chaotic to those who are used to a simpler, more defined, hierarchical management structure, but past experience has proven that this process works. The aforementioned model has been applied to the Chernobyl studies in Belarus and Ukraine, although it is important to emphasize once again that we are not running these studies. We are cooperating with the scientists and physicians in those countries who are responsible for carrying them out. We provide guidance, financial assistance, training, and other assistance, but ultimately one must remember that we cannot and should not be making unilateral decisions. As I

mentioned previously, the complexity of doing a large clinical study is further complicated by the many cultural, economic, political, and fiscal challenges of working in these countries.

It may be helpful to try to explain why the involvement of real people in clinical studies poses such challenges. Our "management" plan for a clinical study is the clinical research protocol. Among other things, a clinical research protocol defines the patient accrual rate necessary to achieve numbers that will support the rigorous statistical analysis needed to substantiate a finding. We know from years of experience that a certain number of patients will drop out of a study, will be unable to complete the intervention, or that we will be unable to enter sufficient patients on the study because of an inability to obtain a sufficient supply of a drug, or due to a lack of interest among the cancer community for the particular study. One example of a clinical trial that has presented major obstacles is bone marrow transplantation, where the wide availability of this technology as routine patient care has greatly reduced our ability to attract patient volunteers into a research setting. Protocols have been in place for years that attempt to compare existing treatment approaches to state of the art therapy; but because the study design requires that patients be randomly assigned to one treatment arm or the other, we have not been able to enter sufficient numbers of patients onto the study. When treatments are offered outside a research setting, patients don't have to risk randomization - they can simply choose whether or not to receive bone marrow transplantation. Does that mean we should give up trying to get an answer? Absolutely not. But delayed patient accrual has forced us to drastically alter our projections as to how long it will take us to complete this incredibly important study. Therefore, it is critical to understand the impact that patient accrual and follow-up has on the conduct of even the most simple clinical study, and why the management of the study must be flexible enough to accommodate such events.

The I-131 Study: Estimating Exposure to Fallout

In late 1982, Congress enacted a requirement, as part of the Orphan Drug Act (P.L. 97-414), that the Secretary of the Department of Health and Human Services undertake three studies: 1) to conduct scientific research and prepare the analysis necessary to develop valid and credible assessments of the risks of thyroid cancer that are associated with thyroid doses of Iodine 131; 2) to develop valid and credible methods to estimate the thyroid doses of I-131 that are received by individuals from nuclear bomb fallout; and 3) to develop valid and credible estimates of the exposure to I-131 that the American people received from the Nevada atmospheric nuclear bomb tests. Parts 2 and 3 were addressed in a report released last year by NCI. The first part of the mandate is still the subject of ongoing research, and I will come back to this point a little later in my testimony. However, I would like to point out that this legislation was very specific in its charge to "...conduct scientific research and prepare analyses necessary to develop valid and credible assessments of the exposure to Iodine 131."

Almost one year ago, I appeared before the Senate Appropriations Subcommittee on Labor, Health and Human Services and Related Agencies to deliver to Congress the long-awaited NCI report, "Estimated Exposures and Thyroid Doses Received by the American

People from Iodine-131 in Fallout Following Nevada Atmospheric Nuclear Bomb Tests." Because this committee has also expressed interest in many of the same issues that were raised last year, I have appended to this statement last year's testimony and ask that it be entered into the hearing record. I said last year, and I will repeat before you today, that a more clear, more rapid, and more aggressive plan for dissemination of the results to the public was called for. That said, I also believe the dissemination we made was unprecedented for a study of this magnitude and complexity. Further, we were able to take advantage of a new technology, the Internet, to provide access to over 100,000 pages of data that would otherwise have been inaccessible to most individuals.

As I also stated last year, this delay in publication did not have an adverse impact on public health, a position reaffirmed recently by the Institute of Medicine (IOM) in the report issued on this topic September 1. As I mentioned in my testimony last year, DHHS had requested that the IOM undertake a review of the findings in NCI's I-131 report and that it make recommendations on appropriate public health measures. To carry out this evaluation, the IOM assembled two groups of expert scientists, clinicians, public health representatives and members of the public, and after several months of open meetings, committee deliberations, and consultation with other experts in many scientific and medical disciplines, released their findings and recommendations. I was impressed with the thoroughness and completeness of their process, the clarity of the recommendations, and the recognition of and sensitivity toward the need for better ways to communicate information about radiation risk to the public. This latter point is probably the most daunting challenge we face as a federal entity: how to provide complex information to the public in a clear, relevant, and understandable way. We at NCI face this challenge repeatedly. For example, many women, even those without any risk factors, fear that they will develop and die from breast cancer. However, most women don't know that more women die from lung cancer than breast cancer, and even more women die from heart disease than either of these two cancers. Environmental exposures, such as pesticides, radon, and others that are involuntary, are often viewed as being more hazardous than voluntary exposures that we often don't even think about as being hazardous. One of the IOM recommendations was that the Department of Health and Human Services undertake the research necessary to determine how to most effectively present information about risk so that it will be better understood by the public. I agree that this is a most worthwhile endeavor, and what is learned will almost certainly be of assistance to NCI in communicating to the public about cancer risk in general.

Chornobyl

I would like to return to the first portion of the Congressional mandate regarding research related to the risk of developing thyroid cancer as a result of exposure to I-131. The best way to determine the link between exposure to I-131 and the development of thyroid cancer is to actually find people who have been exposed and monitor their health. In the scientific literature, it has long been questioned whether exposure to I-131 leads to thyroid cancer. It was not until the early 1990s, in the aftermath of the Chornobyl accident, that notable increases in cancers began to be reported. Even after these reports began to appear, however, we still did not know the relationship between the dose of I-

131 received and the risk of developing thyroid cancer. All of our previous "estimates" of that risk are based on extrapolating what we know about external radiation, which is based on many assumptions and is a very crude method for making such an estimate. NCI attempted to obtain more precise and valid data about exposure to I-131 and thyroid cancer from the population in Utah that was downwind from the Nevada Test Site, but these studies were inconclusive. However, children exposed to radiation from the Chernobyl accident may have received hundreds of times the dose received by children in the U.S. As I noted earlier in my statement, the exposures resulting from the Chernobyl accident, unfortunate as they were, now provide us with the opportunity to attempt to correlate exposures to and thyroid doses from I-131 with the onset of thyroid cancer and other health outcomes. We want to understand the dose relationship so that we can extrapolate back to a range of doses, specifically those in the U.S.

I have been asked many times to explain the difference between the risk estimate that was prepared last year when we released the I-131 report and the risk assessment we are trying to obtain from the Chernobyl study. Essentially, the difference is that the estimate prepared last year was not based on actual exposure of individuals to Iodine 131; it was rather an approximation of the number of cancers one might expect based on *what is known and published* about the relationship between exposure to radiation and the effect or outcome (thyroid cancer). This type of risk estimate can be prepared at any time using data available and already published in the scientific literature from many sources. The most important thing to remember about a risk estimate is to pay attention to all of the qualifiers, or limitations, that accompany it. The less that is known about an exposure, the broader the estimate will be, and the more uncertain the ability to validate its accuracy.

We knew people were concerned about their risk of developing thyroid cancer as a result of the fallout from the Nevada Test Site. I asked NCI staff to review and evaluate all available data on thyroid cancer, including incidence and mortality data, to see if there was any way to identify a change that might be related to I-131 exposure. These analyses did not find any such relationships that were statistically significant. NCI scientists were able, however, to obtain risk estimates for I-131 indirectly, based on the known relationships between thyroid cancer risk and exposure to radiation from external sources. To do this, they had to make reasonable assumptions about the relative effectiveness of radiation from these two types of radiation. This method resulted in a very broad estimate that ranged from 11,300 to 212,000 excess cases of thyroid cancer that might have been caused by exposure to I-131, but without a risk coefficient, the cause and effect relationship was based on assumptions. In their report, the IOM stated that, based on their own epidemiologic analyses, the excess of cancer cases is probably in the lower part of the range estimated by NCI. If the Chernobyl studies are successful, a much better estimate, with less uncertainty, will be possible because we will have direct evidence about thyroid cancer risk in persons exposed to I-131 that we can combine with the estimated doses from the Nevada Test Site.

How did NCI get involved in the Chernobyl study? As I mentioned in the beginning of my testimony, the Department of Energy (DOE) requested that one of our scientists, Dr. Bruce Wachholz, manage the scientific aspects of a large clinical radiation epidemiology

study to be conducted in the former Soviet Union. This study grew out of an international agreement between Soviet President Gorbachev and President Reagan that called for bi-national cooperation in undertaking research to better understand the health consequences of radiation exposure resulting from the Chernobyl release. Dr. Wachholz's background in radiation biology, his experience with radiation dosimetry, and his familiarity with similar multi-disciplinary studies made him an obvious choice to lead this project on the U.S. side. Drawing from a pool of consultants who had previously served as advisors on other radiation studies, Dr. Wachholz assembled a prestigious working group to assist in the development and management of this activity. As a result of collaboration between U.S. and Belarus and Ukraine scientists and discussions with international organizations, the study was framed, the protocol was designed, and an assessment of available resources in the host countries (Ukraine and Belarus) was pursued. It is important to remember that this is a study of exposed individuals in Belarus and Ukraine, being carried out by scientists and physicians in those countries, with advice and assistance from U.S. collaborators.

These studies are large, complex, and long term. We estimate that they may continue for 10-15 years. A timetable with target completion dates was developed as part of the protocols, and in addition a management plan was developed to assist us in guiding the overall project. The primary objective of the study is to carry out valid and credible assessments of the early and late morphologic and functional changes in the thyroid glands of persons exposed to radiation from radioactive materials released as a consequence of the Chernobyl Nuclear Power Plant accident. The emphasis is on obtaining data that allow us to develop a risk coefficient for thyroid cancer as it relates to dose, sex, and age in 1986 and on comparing the relative effectiveness of I-131 with that of x-ray and gamma irradiation in inducing thyroid cancer and other thyroid conditions.

From early 1991 through early 1994 (Belarus) and early 1995 (Ukraine), a U.S. working group, several members of which had previous experience with these types of studies, collaborated with working groups in Belarus and Ukraine, respectively, to develop the research protocols. Specific tasks were clearly spelled out, and approximate time lines were included. At the same time, government officials in Belarus and Ukraine were informed about the role of and need for an IRB and, following a period of training and education, established IRBs in their respective countries. During this period, another challenge facing the working groups was the need to interpret and translate all documents between Russian or Ukrainian and English. The protocols were negotiated and approved by the international working groups and subsequently approved by IRBs in each country and by the NIH Office of Protection of Research Risks (OPRR). The Belarus protocol was signed and implemented in May 1994; the Ukraine protocol followed a year later, and was signed in May 1995. The delays in Ukraine arose due to a number of problems, including initial difficulties at the Ministerial level, including a hesitation to identify specific officials or agencies that would be responsible for the study. Once these difficulties were resolved, the degree of cooperation began to improve. However, we found that at times limited progress was made between NCI's visits, although these visits were pivotal in stimulating further activity. In 1997, the first study participants were screened at clinics set up for this purpose in Minsk and Kiev, and in mobile facilities.

From 1994 through 1996, and following the signing of the protocols, work was carried out on the development of the operational infrastructure as spelled out in the protocols. This included such efforts as the development of operating manuals; exploring and developing methods to identify and locate the cohorts in each country; establishing data coordinating centers, data management, and creating data flow sheets; obtaining tax exemptions on equipment and supplies; and developing appropriate financial transfer arrangements; and putting in place a program of quality assurance;. Completion of these tasks was further complicated by the need to integrate various organizational entities and operating units into a cohesive project in order to undertake a study of this complexity with its need for rigor and absence of bias. Again, there was a need to translate additional critical documents between Russian or Ukrainian and English and, very importantly, also adjust to several changes in Ministers in both countries. It is also fair to mention that, especially in the earlier years of the project, efforts were expended to overcome both the legacies of the Cold War as well as the significant scientific and cultural disparities.

My first meeting with DOE arose because of concerns they had about the progress and management of the study. I met with Dr. Paul Seligman, Deputy Assistant Secretary for Environment, Safety and Health, DOE in July 1996, and we agreed on a plan of action, including the establishment of a research support contract to develop and provide scientific and technical assistance in the project. In September 1997, NCI awarded such a contract to Columbia University following a full and open competition. The NCI official who serves as the Project Officer for this contract is Dr. Ihor Masnyk, who in recent years also has been the U.S. Associate Project Director.

Due to the considerable and complex pre-study activities that had to take place, it may appear that the Chernobyl studies have been slow to get underway. However, there were innumerable scientific, political, economic, and practical considerations and obstacles that were faced. These included changes in key government personnel (Ministers of Health) in Belarus and Ukraine, senior staff changes in Belarus, new laws and restrictions (such as import duties on technical equipment and financial transaction obstacles), changes in the physical location of key components, complex and changing organizational and interpersonal dynamics, delays in delivery of equipment and supplies due to the establishment of new foreign government oversight agencies, and many others.

Despite these delays, the study is moving forward. The cohorts have been established, study participants have been selected, methods for location of individuals are being evaluated, and feedback from individuals who have been invited to be screened is being gathered for evaluation. As of August 1998, in Belarus 2,869 patients have been screened, which is very close to the first year target of 3,000 screenings. In Ukraine, where screenings began three months ago, 529 study participants have been screened. Much of the credit for this progress is due to the ongoing activities of the working groups of consultants, whose members have provided regular and continuing guidance on these studies and have assisted in surmounting significant operational obstacles facing project execution. This U.S. assistance was provided by NCI staff and consultants (members of the working groups) through frequent trips to the study sites and regular monitoring of progress.

One of the specific milestones that is included in the protocols, and one that we have been asked to address, is the appointment of Bi-National Advisory or Oversight Committees. Such committees are required in each of the protocols, and based on the assumption that the studies would progress much more quickly, members were scheduled to be appointed during the first six months following the final approval (signing) of the protocols. Members are appointed by each national participant (five each from the U.S. and either Ukraine or Belarus), representing specific areas of expertise (endocrinology, radiation biology, radiation dosimetry, radiation epidemiology, and clinical sciences/pathology). The responsibilities of these oversight groups include those normally found in such studies done in the U.S., including recommending modifications of the protocols to the national authorities; approval of protocol modifications that have been agreed upon; review and approval of budgets prior to presentation to the national authorities; scientific and administrative oversight, including on-site visits and written scientific critiques; and developing a publication policy. All of these functions relate to the main activity of the studies, i.e. screening of participants. In addition, the Bi-National Advisory/Oversight Committees were given the responsibility to ratify the appointment of the Project Director in the study country. The process of identifying and appointing members for these committees has been quite slow, but all of the members of these committees have now been identified and we hope to schedule the first meetings in the near future. Has the absence of these committees had a negative impact on the conduct of the studies? We believe the answer, up to this point, is no; however with the accrual of study subjects, we have reached a point where the advice of the committees becomes important. Again, I must point out that these studies are cooperative, with NCI providing assistance but with the ultimate responsibility and authority resting with the Project Directors in the study countries. We believe that the study teams in Belarus and Ukraine match our own commitment to see the studies through to completion.

Interagency Coordination

There is a wealth of expertise and experience among Executive Branch agencies from which we can learn. Among the steps I have taken since becoming NCI Director have been efforts to improve communications with other federal agencies, especially with our collaborators. As I mentioned earlier, in July 1996 I and several other NCI staff met with our colleagues from the Department of Energy to reach an agreement on the future management of the Chernobyl studies. This was an important meeting as it addressed many of the issues under consideration today, and it was intended to provide a template for future open, honest discussions about our progress on these very important studies. Last September, I met with my counterpart at the National Center for Environmental Health at CDC, Richard Jackson. We discussed the many areas in radiation research where we could learn from each other, and we signed a joint memorandum committing our agencies to work more closely together, to identify new opportunities to collaborate on research initiatives, and to provide a forum for our staff to regularly exchange information on our progress. I am extremely pleased with the success of our renewed commitment, and I am confident that this will quickly translate into better, faster dissemination of important health information to the public.

Summary

An organization must be flexible to respond to changing needs and correct problems as they are encountered or identified. Last year, following the release of the I-131 report, I put in place several mechanisms to correct weaknesses I had identified in the process of trying to understand why this report took so long to complete. First, I assigned to the Deputy Director, NCI, the responsibility for monitoring and oversight of all radiation research conducted or supported by NCI. This placed the central coordination and monitoring function directly in my office where I could be immediately informed of any delays in or impediments to this area of research. Second, I directed that a comprehensive tracking system be developed to ensure that Congressional mandates such as this one would be monitored regularly and status updates provided periodically for better oversight and monitoring. This system has been developed and will be fully operational this fall. Third, over the past two years I have had ongoing conversations with key DOE staff, and with the Minister of Health in Ukraine, and have received only positive feedback about the conduct and progress of these studies. There is ample evidence to show considerable activity on these studies, including frequent trips overseas, frequent communications with project directors in Belarus and Ukraine, meetings with the contractor, and increased ability to successfully deliver needed equipment and supplies overseas to the appropriate recipients. My staff meet regularly with DOE staff to discuss progress on this study and have been informed that progress is satisfactory. We presented an update of the Chernobyl study to the National Cancer Advisory Board last week, and we are planning a presentation to the ACERER in November.

With all of these mechanisms in place, was there more we could have done or should have done in monitoring the Chernobyl study? A more detailed reporting of protocol benchmarks versus actual progress may have brought greater visibility to the delays associated with this study. However, because of the nature of the delays, it remains unclear to me whether this reporting in itself would have expedited progress. It is the complexity of conducting an international study in an unstable climate that has impacted progress. Time lines, milestones, and targets are all in place and significant progress has been made. I will readily admit that the study milestones may have been overly optimistic, especially knowing today what we do about the political, economic, and regulatory difficulties we have encountered. For those who focus on meeting milestones, this perhaps is viewed as a fundamental flaw. However, I believe that the optimism was based on our experiences here in the U.S. and the understanding that in clinical studies there are many contingencies that cannot be anticipated. Finally, I have asked the question myself: would functioning Bi-National Advisory Committees have made a difference in progress on these studies? After discussing this question with many of my own advisors, I have concluded that the guidance and advice provided by the working groups were sufficient to identify problems, issues and solutions as quickly as possible. This advice came from multiple sources, including our consultants on the project and more recently the staff on the Columbia contract. Many of these consultants have been affiliated with the project in varying capacities over the years and bring very different perspectives and valuable advice. The formal Bi-National Advisory Committees were not intended to function in such an operational mode, and their most valuable role relates to

issues that are beginning to confront us now: issues of cohort identification; statistical strength; and our ability to complete the study as was originally conceived. I look forward to having these committees in place in the very near future so that they can begin their work.

I remain committed to ensuring that as long as NCI has responsibilities for these studies, they will be done well, in as timely a fashion as possible, and the results will be disseminated widely to the public and the scientific community. NCI clearly has the expertise needed to carry this out, and the responsibility to ensure that it is done well rests both with the scientific staff who manage the day to day issues and also with NCI management, where proper oversight must be maintained. I hope this testimony has clarified some of the issues of concern to the Subcommittee, and I will be pleased to answer any questions you may have.