STATEMENTS ON INTRODUCED BILLS AND JOINT RESOLUTIONS (Senate - January 22, 1997)

HUMAN RESEARCH SUBJECT PROTECTION ACT

Mr. GLENN. Madam President, I rise today to introduce the Human Research Subject Protection Act of 1997. I send the bill to the desk.

The PRESIDING OFFICER. The bill will be received and appropriately referred.

Mr. GLENN. Madam President, if I approached any Senator here and I said, `You did not know it, but the last time they went to the doctor or went to the hospital, your wife or your husband or your daughter or your son became the subject of a medical experiment that they were not even told about. They were given medicine, they were given pills, they were given radiation, they were given something and were not even told about this, were not even informed about it, yet they are under some experimental research that might possibly do them harm--maybe some good will come out of it, but maybe it will do them harm also--but they do not know about it,' people would laugh at that and say that is ridiculous. That cannot possibly happen in this country. Yet, that very situation is what this piece of legislation is supposed to address.

I have been in public life and have served this country for many years. Frankly, I do not think too many things that I see surprise me anymore about our laws and about Government. Three years ago, though, I began to learn about a gap in our legal system that does truly concern me. In 1993 the Governmental Affairs Committee began to investigate the cold war radiation experiments. These experiments are one of the unfortunate legacies of the cold war, when our Government sponsored experiments involving radiation on our own citizens without their consent. They did not even know the experiments were being run on them. It was without their consent.

One of the most infamous of these experiments took place in my own State of Ohio, when scores of patients at the University of Cincinnati were subjected to large doses of radiation during experimental treatments, without their consent, without their informed consent. During the course of this investigation, I began to ask the question, what protections are in place to prevent such abuses from happening again? What law prohibits experimenting on people without their informed consent?

What I found, when I looked into it, is there is no law on the books requiring that informed consent be obtained. More important, I believe there is a need for such a law, as there continue to be cases where this basic right--I do view it as a basic right--is abused. As I started out, I would like to put this on a personal level for everyone of my colleagues. You just think about your own family, your own son, your own daughter, or grandchildren who might be, the next time they go to a doctor, the subject of some medical experiment that they are not even told about. I do not think there can be many things more un-American than that.

With the introduction of this bill today I hope to begin the process of correcting some serious gaps in our legal system. I want to make clear right now I am not seeking to bring medical research to a screeching halt. Please do not anybody at NIH, or anybody doing research throughout this country, think we are trying to stop that. We are not. That is not my intent and not the intent of this bill.

This country has the very finest health care system in the world, in part because of basic research. In fact, in large part because we have put more effort, more resources, more of our treasure into health research than any other nation in this world. In fact, I believe most people are not opposed to participating themselves in scientific research, if they are told about the pros and the cons. That is the goal of this legislation, to make sure that people have the appropriate information to make an informed choice about their medical treatment.

Everyone listening today probably has heard of the Nuremberg Code. That is the list of 10 ethical research principles which were produced as part of the judgment against Nazi physicians who engaged in truly heinous medical experiments during World War II.

The first principle of the Nuremberg Code states that the voluntary consent of the human subject of research is absolutely essential. Unfortunately, as we look back through our history since the late 1940's, it appears that researchers in America may not have taken all that Nuremberg lesson completely to heart.

I ask my colleagues what the following names might have in common: thalidomide, Tuskegee, and Willowbrook?

Well, the answer is that these are all sad examples of unethical research conducted in the United States, and in the United States well after the Nuremberg Code was issued, adopted and worldwide attention had been focused on some of the abuses of that time during World War II.

Given this history, I find it astounding that even after Nuremberg, the thalidomide babies, Willowbrook, Tuskegee and the cold war radiation experiments, and who knows how many other cases, we still don't have a law on our books requiring that informed consent--those two words, `informed consent'--be obtained prior to conducting research on human subjects.

I have had research conducted on me because of my past activities before I came to the Senate in the space program and so on, but I knew what was being looked at, what was being tried. I knew the objectives of it, and I was willing to do that. I was happy to do it. But it was informed consent that I had personally, and I knew what I was getting into and glad to do it.

I think most people feel the same way. If they know what they are getting into and they feel there is a good purpose to it, they are willing to do it. But to do research on people when they don't even know what the research or the medicines or the radiation is that is being tried on them, I think is unconscionable.

What it comes down to is there are no criminal fines or penalties for violating the spirit or the letter of that Nuremberg Code that should be the basis of all of our informed consent in this country.

In fact, our own Constitution says, `The right of the people to be secure in their persons . . . shall not be violated.'

So there is no explicit statutory prohibition against improper research. I must add that just because there is no law on the books does not mean there are no protections for people from unethical medical or scientific research.

These tragic incidents I have mentioned have resulted in changes in the way human research subjects are treated. I don't want to misrepresent this, because there is a very elaborate system of protections that have developed over the years. Unfortunately, though, this system does have some gaps and, if enacted, I believe this legislation will close those gaps.

Let me briefly describe the system that is currently in place.

Regulations governing the protection of human research subjects were issued by the Department of Health, Education, and Welfare in 1974 and may be found at part 46 of title 45 of the Code of Federal Regulations.

In 1991, 10 years after a recommendation of a congressionally chartered Presidential advisory board, 16 other agencies adopted a portion of this rule, a portion of the rule to apply to research that these agencies sponsored. And at that point, these regulations became known as the common rule.

The common rule requires research institutions receiving Federal support and Federal agencies conducting research to establish committees, and these are known as--the shorthand version is IRB's--Institutional Review Boards. Their job is to review research proposals for risk of harm to human subjects and to perform other duties to protect human research subjects.

The common rule also stipulates requirements related to informed consent, how researchers must inform potential subjects of the risks to which they, as study participants, agree to be exposed.

It should also be noted that HHS regulations contain additional protections not included in the common rule for research involving vulnerable populations; namely, pregnant women, fetuses, subjects of in vitro fertilization research, prisoners and children. No other Federal agency has adopted these additional protections.

Several mechanisms have been developed by HHS and research institutions over the years to extend the common-rule protections to more people. For example, many, but not all, research institutions which receive some Federal support voluntarily apply common-rule guidelines to all research conducted at their institutions.

Additionally, in order to receive approval for a drug or device from the Food and Drug Administration, a research institution or pharmaceutical company must comply with the requirements of the common rule as administered by the FDA.

In addition to the Federal regulations, most professional medical societies and associations have adopted ethical codes of conduct regarding research.

The first such ethical code, called the Helsinki Code, was adopted by the World Medical Association in 1964. So it has been on the books for a long time. Since that time, other prominent organizations, like the American Medical Association, the American Society for Clinical

Investigation, and the American Federation of Clinical Research have also adopted such ethical codes.

Most recently, in October 1995, the President exhibited, I believe, strong leadership and established the National Bioethics Advisory Commission, NBAC. This had been a long time coming. It had been suggested, but no one had ever gone ahead and done this, and the President exerted the leadership and established the NBAC.

Quite simply, the scientific and ethical issues which the NBAC are supposed to evaluate represent some of the most important, some of the most complex and controversial questions of our time. NBAC's input will be critical to informed policymaking for both the legislative and executive branches.

The two primary goals of NBAC are to, first, evaluate the current level of compliance of Federal agencies to the common rule, and, second, evaluate the common rule and advise both the executive and legislative branches on any changes that might be needed to it.

I very strongly support the work of the NBAC but recently have become extremely concerned to hear that more than 15 months after its establishment, the NBAC is still operating with a volunteer staff. It was my understanding that a number of Federal agencies supported the creation of the NBAC and agreed to back up their support with resources and staff. Some NBAC members have stated in public meetings that they are frustrated with the progress the Commission is making and attribute the slow pace to the lack of resources. Additionally, the resource problem may be limiting the number of meetings of the Commission.

Further, if this problem is not resolved in the near term, the Commission may have to stop meeting altogether. I sent a letter to the President's science adviser a few days ago, Dr. John Gibbons, to express my concerns about this. Dr. Gibbons was working to resolve this funding problem, which I view as an urgent priority.

I am very glad to announce--as a matter of fact, it was just today--that these groups in Government that are interested in this had a meeting under Dr. Gibbons' leadership, and the $1.6 million that was supposed to accrue from these different agencies to be used by the NBAC is now forthcoming. So the NBAC is now funded so they can do the job they were originally supposed to do.

We are very glad to say that has happened just today, and I am glad it happened today, just when I am introducing this bill, because it looks as though we now truly are moving to support the NBAC that did not receive the kind of monetary support, the kind of funding that we thought it was going to have when it was first formed a year and a half ago.

There are a number of existing mechanisms that do protect human research subjects today. In fact, in March of 1996, the GAO reported to me that the testing protection system has reduced the likelihood of serious abuses from occurring. However, the GAO also pointed out a number of weaknesses and gaps in the current system.

There are at least four areas, four major gaps.

First, not all agencies have adopted the common rule, including agencies that currently sponsor research involving human subjects. The Department of Labor and the Nuclear Regulatory Commission are examples of agencies that sponsor such research but those agencies have not adopted the common rule, which I think they should have.

Second, the common rule's research is voluntarily applied in many cases. Most institutions which receive Federal funds will voluntarily apply the common rule to all research conducted at their institution. However, not all research institutions adopt this policy. And in any case, if any improper research is discovered at these institutions, there are very few steps available to the Federal Government to do much about it.

Third, a private institution or a researcher who conducts nonfederally funded research or is not seeking approval of a drug or device with the FDA does not have to apply the principles of the common rule to its research. In other words, there is a huge area of all the private medical research out there that is not under the common rule unless they just choose themselves to just voluntarily do it.

Fourth, no Federal agency, other than HHS, has applied the additional protections described in 45 CFR 46 for vulnerable populations--pregnant women and their fetus, children, prisoners--to their own research. So the purpose of this legislation is to help close the gaps that exist within the current system for protecting research subjects.

Well, is there really a problem out there?

Is this just a paper loophole that I am trying to close?

Unfortunately, Mr. President, there are ongoing problems with inappropriate, ethically suspect research on human subjects. It is difficult to know the extent of such problems because information is not collected in any formal manner on human research.

The Cleveland Plain-Dealer in my home State of Ohio has recently reported in a whole series of articles, after much investigation of this issue. And I quote from them:

What the government lacks in hard data about humans, it more than makes up for with volumes of statistics about laboratory animals. Wonder how many guinea pigs were used in U.S. research? The Agriculture Department knows: 333,379. How many hamsters in Ohio? 2,782.

So we have all this data on animals and little on human beings. I would hasten to add that the guinea pigs the Plain-Dealer refers to are the four-legged kind too and not the guinea pigs that are humans being used for research.

The reason we know so much about the use of animals in research is that we have laws governing the handling and treatment of them.

For example, the Animal Welfare Act requires that certain minimum standards be maintained when using animals in research.

Let me give you some recent examples which indicate why, notwithstanding the common rule and the other protections that are in place, I think additional protections are needed in statute.

In 1994-95, in an effort to explore the rights and interests of people currently involved in radiation research conducted or sponsored by the Federal Government, the Presidential Advisory Committee on Human Radiation Experiments conducted an in-depth review of 125 research projects funded by HHS, DOE, DOD, VA, and NASA. According to the ACHRE report:

Our review suggests that there are significant deficiencies in some aspects of the current system for the protection of human subjects.

The ACHRE found that documents provided to IRB's often did not contain enough information about topics that are central to the ethics of research involving human subjects. In some cases the committee found it was difficult to assess the scientific merit of a protocol based on the documentation provided.

ACHRE's report states that some consent forms studied by the committee are--and I quote--

. . . flawed in morally significant respects, not merely because they are difficult to read but because they are uninformative or even misleading.

The report states further:

Our review also raises serious concerns about some research involving children and adults with questionable decision-making capacity.

And the ACHRE concludes:

All told, the documents of almost half the studies reviewed by the committee that involved greater than minimal risk [to the subject] raised serious or moderate concerns.

That is a horrible indictment.

As I mentioned earlier, from December 15 to 18, 1996, the Cleveland Plain-Dealer published a series of articles entitled `Drug Trials: Do People Know the Truth About Experiments.'

And I want to give credit to the people that worked on that. Keith Epstein, has covered Capitol Hill here and has written much and done much investigative reporting working on this, as did Mr. Sloat, S-l-o-a-t, Bill Sloat. Those two fellows worked on this and did a great job in pointing out some of the problems that still exist. And we have talked to them about some of these things.

The Plain-Dealer uncovered a number of disturbing cases, very disturbing cases as a matter of fact, where people were either unaware of the fact that they were involved in research or were not provided full information about potential side effects of research. The series raises very serious questions about the adequacy of our current system of protecting human research subjects.

The Plain-Dealer found, for example, of `4,154 FDA inspections of researchers testing new drugs on people [since 1977] . . . more than half the researchers were cited by FDA inspectors for failing to clearly disclose the experimental nature of their work.'

Another serious finding in this series is that researchers who receive the most severe penalty by the FDA, being designated `Disqualified Investigators,' have little fear of this fact being found out by their peers or patients. One of the articles discusses potentially serious problems in the way research

conducted outside of the United States is incorporated into applications for drug approvals in the United States.

The Plain-Dealer uncovered much evidence to suggest that the Federal Government continues to sponsor research where informed consent is not obtained. And this fact disturbed me greatly also.

On November 14, 1996, the Wall Street Journal published an article that examined the practice at one pharmaceutical firm, Eli Lilly and Co. in using homeless alcoholics in their clinical trials. The article raises some disturbing questions about the quality of the phase I trials conducted by this one company. Also serious ethical questions are raised concerning the appropriateness of paying homeless alcoholics significant sums to be human guinea pigs. It is not clear from the article whether these tests were reviewed by any IRB.

On December 27, 1996, the New York Times reported on a New York State appeals court ruling which found that the State's rules governing psychiatric experiments on children and the mentally ill were unconstitutional. The court found that the rules did not adequately protect people who, because of age or illness, cannot give informed consent to take part in drug tests or other experiments. The article mentions 10 to 15 of the 400 psychiatric experiments covered by the ruling as being `privately financed' and therefore outside the coverage of Federal rules.

How would you like it if your father, mother, son or daughter, husband, wife was in one of those institutions and was having experiments conducted on them without your knowing about it or without them knowing about it? That is what we are up against.

(Det er interessant, hvordan man i stigende grad bruger private aktører til at udføre det beskidte arbejde, for derved at omgå loven).

On August 15, 1994, the New York Times reported on ethical and legal questions regarding a company's efforts to promote a drug that can make some children grow taller than they otherwise would. The drug in question, Protropin, has been approved by FDA for use in children whose bodies do not make sufficient quantities of human growth hormone. However, once approved, doctors may prescribe it for other purposes at their discretion. In this case the company was apparently surveying schools for short children and then trying to funnel those children to doctors who would prescribe the drug whether or not the children lacked the human growth hormone. This unapproved research was occurring without the oversight of an IRB. And at least 15,000 children have taken this drug.

Another illustration of the precarious coverage of the common rule occurred in 1995 when it became known that researchers from the Center for Reproductive Health at the University of California Irvine, were fertilizing humans and implanting theses in different mothers without the consent of the donor. This research was not being funded by any Federal agency; however, NIH was funding more than $20 million worth of other research at the university. Even though several internal and external investigations by the university and the district attorney were being conducted on this experiment, a clarifying moment occurred when investigators from OPRR visited UC Irvine early last year. These investigators reminded university officials of the common rule; the fact that the university had agreed to apply it to all research conducted there--through OPRR's assurance

process; and that NIH was currently funding a good deal of research at the institution. Within a week of OPRR's visit, the university took public action to halt the research and formally investigate the researchers.

On October 10, 1994, the New York Times reported on a New York doctor who adopted two types of drugs approved by FDA for cancer treatment and stomach ulcers for an unapproved use to perform nonsurgical abortions. The article quotes the doctor saying that in 121 of 126 cases his approach was successful. The remaining five cases required surgery to complete the procedure. Because the drugs were FDA approved and the doctor was not funded or connected to federally sponsored research, no IRB or approved informed consent procedures were required. Apparently, each patient signed a three-page consent form, but this was not approved by an IRB. According to the Times, once FDA approves a drug, physicians are generally allowed to use it for off label purposes.

Now Mr. President, some of the issues discussed in these articles are problems with how the common rule itself is being applied. Some of these examples illustrate the gaps in the common rule coverage. My legislation will address both the coverage and the application of the common rule.

Now how precisely would the legislation work?

It would require all research facilities to register with HHS. Registration shall include: First, statement of principles governing the research facility in its conduct of human subject research; second, designation of the official responsible for all human subject; third, designation of membership roster of IRB(s); and fourth, attestation that the research facility is complying with the protection requirements of the common rule.

The legislation includes a grandfather provision for all research entities which currently have negotiated project assurances with HHS. The vast majority of research facilities have such assurances.

The legislation contains a 3-year reregistration requirement.

The legislation includes criminal penalties for failure to comply with the act. Therefore, if enacted it would be a felony offense to experiment on someone without their informed consent.

The intent therefore of this legislation is twofold: First, to fill in the gaps of coverage of the common rule by requiring all research involving human subjects to abide by the rule; and second, to elevate the importance of conducting research ethically, the bill provides criminal fines and penalties for failure to comply with the requirements of this law, and by extension 45 CFR 46.

Finally Mr. President, my legislation would codify a recommendation which the Advisory Committee on Human Radiation Experiments made regarding the conduct of classified research involving human subjects.

Specifically, the advisory committee recommended that informed consent of all human subjects of classified research be required, and that such requirement not be subject to waiver or exemption. Under current rule and executive order, it is possible to waive informed consent and IRB review for

classified research. Title II of this legislation would prohibit the waiver of either informed consent or IRB review for classified research.

The advisory committee also recommended that human subjects of classified research be provided with certain information regarding that research. My legislation would require that such subjects be information concerning: First, the identify of the sponsoring Federal agency; second, a statement that the research involves classified information; and third, an unclassified description of the purpose of the research.

Mr. President I have tried today to briefly lay out the case for the need for the legislation I am introducing. I know that my colleague from Ohio, Senator DeWine, is also concerned about the issues I have raised today, and about those that appeared last month in the Plain Dealer. I believe that he has requested that the chairman of the Labor and Human Resources Committee hold hearings on this subject. I think that is entirely appropriate. And I hope that this legislation could be considered in that process. I look forward to working with the Labor Committee in this regard.

I do not claim to have the magic bullet solution with this bill. However, I believe there are some key principles which should guide the Senate's consideration of this legislation. These principles are:

First, informed consent and independent review of experiments involving human subjects must be required.

Second, anyone who violates the right of research subject to have informed consent, should be held criminally responsible for that violation.

I want to put this in personal terms once again. You can imagine your spouse, husband, wife, father, mother, children, being experimented on without your knowledge or their knowledge. That is unconscionable, and we should not permit that. This legislation will close many of the loopholes that permit that to happen now.

As the legislative process moves ahead, it is certain that the bill will undergo scrutiny and amendments. But I think the outcome, if this legislation is enacted into law, will be improved protections for all Americans.

Madam President, obviously, I welcome any cosponsors on this legislation. I will be sending out a `dear colleague' letter to all the offices, and I hope we get a good response to that. I think there are very few Senators who will not back this when they hear what can happen then to them, their families, and their constituents back home, if we do not pass something like this.

I think this is many years overdue. I don't want to scare people to death with this, because I think most of the research in this country is conducted in a way that is good and is with informed consent--in most cases. But just the few examples that I have mentioned here today, as well as the articles in the Cleveland Plain Dealer and New York Times I quoted from, indicate there is still a very major problem in this area and one that we want to close the gaps on so that no American is subjected to experiments like this, unless they know exactly what is going on and have given informed consent.

Thank you. I yield the floor.