

#### ABOUT IDCR

IDCR, a forum for correctional problem solving, targets correctional physicians, nurses, administrators, outreach workers, and case managers. Published monthly and distributed by email and fax, IDCR provides up-to-the moment information on HIV/AIDS, hepatitis, and other infectious diseases, as well as efficient ways to administer treatment in the correctional environment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education. IDCR is distributed to all members of the Society of Correctional Physicians (SCP) within the SCP publication, *CorrDocs* ([www.corrdocs.org](http://www.corrdocs.org)).

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#### RESEARCH IN CORRECTIONS

By David Paar\*, MD, David Thomas\*\*, MD, Jacqueline Thomas\*\*, DO, Danielle Thomas\*\*, MS-IV, and Courtney Colton\*\*, IDCR

**DISCLOSURES:** \*Consultant: Gilead, Abbott, Boehringer Ingelheim, Speaker's Bureau: Gilead, Bristol Myers Squibb, GlaxoSmithKline, Abbott, Boehringer Ingelheim, \*\*Nothing to disclose

Whether or not the inclusion of incarcerated individuals in clinical research studies is justified has generated heated debate over the later part of the past century. Some have advocated that no research study can ethically include prisoners living in an inherently coercive environment, while others counter that incarceration does not strip an individual of his or her ability to make an informed decision regarding participation as a research subject.

Much of this debate is fueled by the competing concerns of protecting inmates as a vulnerable population while respecting their individual autonomy. This conflict is waged against the backdrop of a historical legacy of unethical treatment of incarcerated, institutionalized and other vulnerable groups during clinical research studies.

#### HISTORY OF RESEARCH IN PRISONS IN THE TWENTIETH CENTURY

Research involving prisoners has had a troubled past. During the early part of the twentieth century, there were well-documented instances of investigators in the United States, and elsewhere, using prison inmates to study the pathogenesis, prevention, and treatment of a variety of illnesses including cholera, beriberi, pellagra, and tuberculosis. Notorious experiments, such as the transplantation or injection of human or animal testicular material into senile men, were conducted, and, although rare, reflected the belief at the time that inmates were a population that could be subjected to experimentation that could not be performed on the general population. The unique vulnerabilities of inmates in these studies were often exploited. For example, many of the participants were death row inmates, some of whom died following injection of cholera toxins or similarly dangerous procedures. "Volunteers" were recruited by promising them clemency if they survived the experiment -

an incentive that today would be considered highly coercive - while other participants received special privileges or compensation such as cigars or cigarettes. Many inmates who participated in studies during this period did not give truly informed consent. Few understood the risks and benefits, if any, of the research protocols, and some may not have even been asked to participate.<sup>1,2,3</sup>

The Second World War had a significant impact on the inclusion of prisoners in research investigations. On the one hand, with the onset of the war, investigators appealed to inmates to make a patriotic contribution to the war effort by participating in medical research that would assist the military. The research included injections of blood from cattle to investigate alternate sources of blood products, studies of atropine as an antidote, as well as experiments in which subjects were infected with sleeping sickness, dengue fever, gonorrhoea, malaria, and agents of gas gangrene.<sup>1,2,3</sup>

However, at the conclusion of World War II, the discovery of human experimentation conducted by the Nazis on those they had imprisoned led to a wide scale re-evaluation of the ethics of research of human subjects and the study of the incarcerated in particular. The Nuremberg War Crime Tribunal was convened to investigate and punish war time crimes perpetrated by the Nazis, including hideous trials performed by the Germans in concentration camps. In 1947, the tribunal produced the Nuremberg Code, a set of 10 basic tenets, which was drafted as the standard by which to judge physicians and scientists during their trial at Nuremberg. It became an ethical standard for research for decades.

The first of these tenets, that "the voluntary consent of the human subject is absolutely essential . . . [and] should be so situated as to be

*Continued on page 2*

#### WHAT'S INSIDE

IDCR-o-gram .....	pg 5
State Laws 101 .....	pg 6
IDCR 101 .....	pg 7
In The News .....	pg 8
Self-Assessment Test .....	pg 9

## RESEARCH IN CORRECTIONS... (continued from page 1)

able to exercise free power of choice without . . . the intervention of any element of force, fraud, deceit, duress . . . or coercion . . . ." has been widely interpreted as excluding prisoners from research since incarceration is a necessarily coercive condition. However, in the U.S., the prevalent opinion in the medical community, endorsed by the American Medical Association, was that the Nuremberg Code pertained to Nazi atrocities, but not to the increasingly prevalent medical experiments being conducted using inmates in state and federal jurisdictions. In fact, the post-war flourishing of medical experimentation within the U.S. penal system was being driven by increased federal funding to investigate medical illness, the formation of academic-pharmaceutical alliances, and the need to test various products in human subjects to meet U.S. Food and Drug Administration regulations.<sup>1,2,3,4</sup>

Prisoners were enlisted in a broad range of clinical studies and the inclusion of inmates in investigation became routine. In Holmesburg Prison, a county facility in Philadelphia, in the late 1960's inmates were recruited to participate in studies that explored everything from simple detergents and diet drinks to retinoic acid, dioxin, and chemical warfare agents. The list of sponsors of these investigations included not only pharmaceutical companies and other corporations such as Dow Chemical, but also the U.S. Army. However, in the early 1970's the public conscious shifted and began to look unfavorably upon research conducted in prisons. This change was influenced by well-publicized revelations of the serious side effects associated with medications, such as birth defects caused by the tranquilizer thalidomide and the Tuskegee syphilis experiments, which were not conducted using inmates, but did involve another vulnerable population: black men in the U.S. rural south. By the late 1970's, legislation had been passed preventing federal inmates from participating in clinical trials and very few state jurisdictions continued their clinical research programs using inmates.

### THE BELMONT REPORT AND 45 CFR 46

In response to the growing public concern regarding abuses during clinical research, the National Research Act was signed into law on July 12, 1974. This federal law created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, hereafter referred to as "The Commission". One of The Commission's charges was to identify the basic ethical principles that should underlie the conduct of biomedical

and behavioral research involving human subjects and to develop guidelines, which should be followed to assure that such research is conducted in accordance with those principles. The Belmont Report resulted from an intensive four-day period of discussions held at the Smithsonian Institution's Belmont Conference Center supplemented by monthly deliberations of The Commission held over a four-year period. It was published in The Code of Federal Regulations (CFR), commonly called the federal register or common rule, on April 18, 1979 as a statement of the Department of Health, Education, and Welfare's policy of ethical principles and guidelines for the protection of human subjects of research. Later this department evolved into the Department of Health and Human Services (DHHS) which remains responsible for the protection of human subjects involved in biomedical research through the Office of Human Research Protection (OHRP). The three basic principles that were detailed in this report were respect for persons, beneficence, and justice. Respect for persons has two important components: individuals should be treated as autonomous agents and those with diminished autonomy are entitled to protection. The report itself directly addresses the issue of prisoner participation in research:

"[R]espect for persons demands that subjects enter into the research voluntarily and with adequate information... In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities, for which they would not otherwise volunteer.... Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma."

These passages accurately state the equipoise that persists to this day regarding prisoners as research subjects. How to best balance between not "depriving" the inmate of an opportunity to participate and protecting the inmate from coercion remains the enduring challenge of this issue with vocal advocates of each position weighing in.

The federal legislation, published in the Code of Federal Regulations, that deals with the protection of human research subjects is called Title 45 CFR Part 46 and is commonly referred to as 45 CFR 46. It

became law in 1978, was revised in 2001 and provides some guidance regarding the inclusion of prisoners in research. 45 CFR 46 applies to all research involving human subjects that is conducted, supported by, or otherwise subject to regulation by any federal department or agency. It provides direction on how agencies and institutions can file letters of assurance that they will comply with these regulations, direction on the composition and duties of institutional review boards (IRBs) that oversee federally funded research, requirements for informed consent, and documentation of informed consent. Subpart B of this law lists additional protections for pregnant women, human fetuses, and neonates, and Subpart C lists additional DHHS protections pertaining to biomedical and behavioral research involving prisoners as subjects (6 45 CFR 46).

The additional protections of Subpart C provide for prisoners that participate in biomedical research including: 1. Inclusion of a prisoner or a prisoner representative on the IRB reviewing the research; 2. Assigning additional duties to the reviewing IRB to be sure that the research is permissible, free of undue influence, safe, accessible and fair to all inmates, presented in understandable language, and does not have any effect on parole. Permissible research involving prisoners includes: "(A) study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects; (B) study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects; (C) research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary [of the Department of Health and Human Services] has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; or (D) research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research,

*Continued on page 3*

## RESEARCH IN CORRECTIONS... (continued from page 2)

the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice in the Federal Register, of the intent to approve such research."<sup>6</sup>

According to 45 CFR 46, permissible research includes not only social, behavioral, and psychological research, but also therapeutic trials using pharmaceutical agents for medical conditions that particularly affect inmates (though the use of placebos in this situation requires additional safeguards.) The example given in the law specifically mentions hepatitis, but the health condition that came to the forefront as a condition particularly affecting prisoners was HIV infection and AIDS. Under pressure from patients and patient advocacy groups, HIV clinical research moved from the strictly academic setting to a variety of other patient sites including non-university affiliated hospitals, private physician offices, and community consortiums. In the 1990s, when effective HIV treatment therapies were under investigation in multiple clinical trials, HIV clinical trials at some academic sites re-entered the prison setting. In this case, inclusion of prisoners was often justified as a means to provide access to cutting-edge therapies to persons living with HIV who were incarcerated. At several major medical centers, HIV research was extended into correctional facilities. For example, clinical trials being conducted at The University of Texas Medical Branch in Galveston and the University of Miami in Florida were offered to inmates in the Texas Department of Criminal Justice and the Florida Department of Corrections, respectively. Additionally, behavioral research regarding AIDS in the incarcerated population were being conducted by Yale and Brown Universities in their respective state jurisdictions. Not all of these studies fell under the purview of 45 CFR 46, as these regulations apply to federally funded studies and some of these investigations were funded by pharmaceutical industry support. Allowing prisoners to participate seemed

appropriate since life-saving treatment, not available outside of clinical trials, became available to incarcerated patients with AIDS.

In 1998, one of the pharmaceutical manufacturers of HIV medications implemented a non-comparative trial of a combination of three nucleosides for the treatment of HIV in prisoners only. Many prisoner advocates became concerned that prisoners were being exploited in the name of medical research since all of the pharmaceutical agents in this trial were available outside of clinical trials and there was already some question in 1998 if three nucleosides alone were adequate therapy for HIV infection.<sup>7</sup> Today we know that triple nucleoside therapy is inferior to either protease inhibitor-based or non-nucleoside reverse transcriptase inhibitor-based potent combination therapy and is not recommended as first line therapy for HIV infection. Subjecting prisoners to the choice of receiving what might be inferior treatment seemed to exceed the limit of minimal risk that 45 CFR 46 had set as a standard. The scientific research community was again faced with the difficult question of how best to protect prisoners.

As a result, a group of concerned correctional clinicians organized a conference, "Clinical Trials in Corrections." Over 100 like-minded individuals and representatives from the Office of Human Research Protections attended this meeting, and proceeds were published in 2001 in *AIDS Reader*.<sup>13</sup> What happened next had a chilling effect on pharmaceutical medical research using prisoners as subjects. The IRBs at the University of Texas Medical Branch, the University of Miami, Brown University, and Yale University were reviewed by the OHRP and received "letters of determination"<sup>8</sup> that the composition of the IRBs and their procedures to ensure the protection of prisoners were inadequate. Enrollment in clinic trials was suspended at the University of Texas Medical Branch at Galveston<sup>9</sup> and the University of Miami.<sup>10</sup> Although each of the Universities cited above eventually received permission

to resume research with prisoners, virtually no clinical trials using pharmaceutical agents are being conducted in the state prison systems today. Behavioral, social, and psychological research continues to be pursued by many institutions using prisoners as subjects.

## COMMENT

It has now been over 30 years since 45 CFR 46 Subpart C has been enacted. Whether an inmate can ever act autonomously and what the standard of minimal risk for an inmate remains unclear.<sup>11</sup> Three issues are at the crux of this question. First, are prisoners and the general population well served by not having federal funding for clinical research using pharmaceutical therapies in the incarcerated population; second, does the law serve its goal to protect a vulnerable population; and third, does the federal law impact upon non-federally funded research? Secretary Tommy Thompson of the DHHS has speculated that it is past time that Subpart C be evaluated again (personal communication). To this end, the DHHS has asked the Institute of Medicine of the National Academy of Sciences to investigate the impact of Subpart C, and to determine if there should be any change in the current law. The Committee of Ethical Considerations for Revisions to the DHHS' Regulations for Protection of Prisoners Involved in Research was impaneled and will examine whether the conclusions reached by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in the 1970's remain appropriate today.<sup>12</sup> The committee will hold five public meetings at which they will collect data from invited panelists who work or perform research in the correctional setting and will also hold two workshops to further inform the process. Three of the public meetings have been held: March 16, 2005, National Academies of Science, Washington, D.C., May 4, 2005, The National Academies of Science, Washington, D.C., and July 18, the Gladstone Institute, San Francisco, CA. The committee's final report is expected in March, 2006.

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## LETTER FROM THE EDITOR

Dear Colleagues,

This issue is dedicated to clinical trials in corrections. Prior to 2000, several correctional practitioners and facilities were involved in clinical trials in order to permit the incarcerated population to gain the benefits of investigational drugs and other therapies that could only be obtained through trials. In 2000, the Office of Protection from Research Risks (currently named Office for Human Research Protections) investigated every clinical trial from every major university, correctional system, and quality Institutional Review Board involved in prisoner research. That investigation caused most of the aforementioned programs to stop enrolling new patients and taper their existing efforts.

Many of us involved in correctional healthcare felt that both society and our patients were inadequately served by this act. Although mostly minor violations were documented, the tone created by the investigation lead to irreparable damage to clinical trials in corrections. Universities decided it was not worth the effort and correctional administrators wanted no part of any potential controversy.

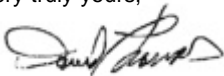
The advantages of clinical trials in correctional populations, both for the inmates and society, and the advocacy for them, are phenomenal. There was a pervasive feeling that affording this benefit to our patients was going to be impossible, even though many of us continually brought the issue of clinical trials in corrections to the highest levels of authority.

In the last year of his position as Agency Head of the Department of Health and Human Services (DHHS), Secretary Tommy Thompson personally determined that there might be real value to inmates and society if the question of clinical trials within clinical settings were evaluated again. To that end, the DHHS asked the Institute of Medicine of the National Academy of Sciences to reevaluate the pertinent parts of Federal law pertaining to prisoner inclusion in research.

It should be our job to advocate for our patients in this area and to remind the committee of two specific items: first - the effect of Federal law is far more reaching than the words of the statute themselves and, second - the current situation discriminates against legitimate scientific inquiry and encourages unregulated research which may be performed solely for remuneration.

After reading this issue, readers should be familiar with the history of research involving prisoners, 45 CFR 46, the Belmont Report and the requirements for conducting research involving prisoners. Readers should also be able to identify when research requires approval by an Institutional Review Board.

Very truly yours,



David Thomas\*, MD

*\*Nothing to Disclose*

### Faculty Disclosure

In accordance with the Accreditation Council for Continuing Medical Education Standards for Commercial Support, the faculty for this activity have been asked to complete Conflict of Interest Disclosure forms. Disclosures are listed at the end of articles. All of the individual medications discussed in this newsletter are approved for treatment of HIV and hepatitis unless otherwise indicated. For the treatment of HIV and hepatitis infection, many physicians opt to use combination antiretroviral therapy which is not addressed by the FDA.

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 HIV/AIDS, Human Rights, Drug Policy and  
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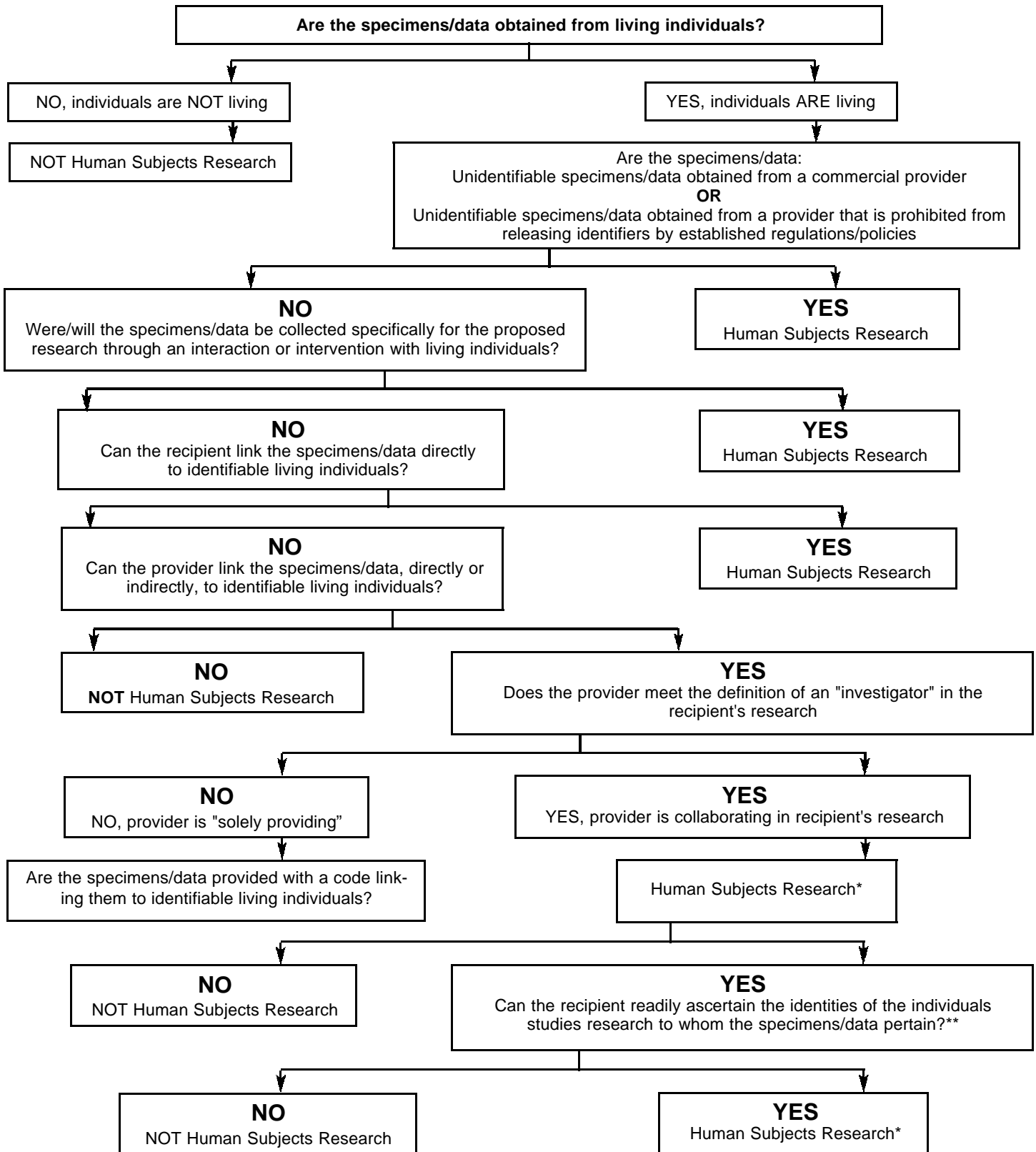
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# IDCR-O-GRAM: Is the Research I want to Conduct Subject to IRB Approval?



## STATE LAWS 101\*

State	Legislation
California*	Specific legislation including criminal penalties for failure to comply; requirement that all clinical investigators - no matter the source of funding - present to all human subjects a document known as the "Experimental Subjects Bill of Rights," and comply with other parts of its extensive statute
Florida**	Florida has its own Review Council for Humans Subjects, but this only applies to research performed in Department of Health or Department of Children and Family facilities (or by contract with those agencies). The correctional systems have no similar protective agency.
Georgia***	Georgia has specific restrictions on cancer and THC research and surgical procedures under investigation.
Kentucky^	Kentucky has a Cabinet for Health Services, which has specific requirements for research funded through the state.
Maryland^^, North Carolina^^	Maryland and North Carolina have adopted the Federal statute for all state participants in research.
Wisconsin, Pennsylvania, Texas, Ohio, Virginia	Wisconsin, Pennsylvania, Texas, Ohio, and Virginia have all adopted the basic precepts of the Federal statute, but have made modifications by their legislatures. For instance, Ohio requires fully informed consent even for proposals that have minimal risk.
New York <sup>o</sup>	New York has the most complex of the statutes, adopting both the Federal 45 CFR 46 and overlaying certain state requirements. Prisoner research requires the specific approval of the Commissioner of the Department of Health. The New York statute directly attempts to limit single practitioners or small groups from conducting clinical research by specifically requiring "All individuals seeking to conduct research must affiliate themselves with an agency or institution that has...a human research review committee."

Of the state laws, only New York has specific requirements for prisoner research. States lacking specific requirements for prisoner research must adhere to state provisions on research. Almost all states permit a researcher to opt out of the state statute if the researcher is performing their research under a Federal-wide assurance and agrees to follow 45 CFR 46.

\*CA Health & Saf. Code # 24171-24179.5 (2003) et. seq.

\*\*FI Stat. 381.85(2003) & 743.07 (2003).

\*\*\*GA O.C.G.A. 33-24-59.1 (2002); & 39-1-1 (2003) & 360-121-01-05 (2003).

^KY 900 KAR 1:060 stat. 4(1)(a) (2003) & 920 KAR 1:060 ("Protection of Human Subjects") (2003).

^^MD Health Code Ann. Stat. 13-2001 and 2002 (2003).

^^^NC Gen. Stat. 58-3-255 (2004).

<sup>o</sup>NY Public Health Law 2444(3) (2004).

### IDCR-o-gram... (continued from page 5)

#### Footnotes

\*All human subjects research must obtain institutional review board (IRB) approval. Exceptions include when there is no effort to contribute to the general body of knowledge and the information will be used only for risk management or internal modifications of ones' own system or facility.

All DHHS-supported human subjects research involving prisoners as subjects must comply with all regulations set forth in 45 CFR 46 Subpart C. When prisoners are involved as subjects in research, composition of the IRB must satisfy the following requirements:

- A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB.

- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.

Research involving prisoners (or other vulnerable populations) cannot receive expedited IRB approval.

\*\* Examples of situations in which the recipient cannot link the specimens/data to living individuals include:

- The key to decipher the code is destroyed before the research begins
- The investigators and the holder of the key to the code enter into an agreement preventing the release of the key to investigators under any circumstances
- There are IRB-approved written policies in place preventing release of the key under any circumstances
- There are other legal requirements prohibiting the release of the key under any circumstances

#### Endnotes

Adapted from Office of Extramural Research. Research involving private information or biological specimens. (n.d.). Accessed August 17, 2005 from

<http://grants.nih.gov/grants/policy/hs/index.htm> and

NIH. Office of Human Research Protections. Guidance on the involvement of prisoners as research. (n.d.). Accessed August 17, 2005 from <http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.htm>

## Research 101: Types of Clinical Trials

Type of Trial	Purpose
Treatment Trials	Test experimental treatments, new combinations of drugs, or new approaches to surgery or radiation therapy
Prevention Trials	Look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vitamins, vaccines, minerals, or lifestyle changes.
Diagnostic Trials	Conducted to find better tests or procedures for diagnosing a particular disease or condition.
Screening Trials	Test the best way to detect certain diseases or health conditions.
Quality of Life Trials	Explore ways to improve comfort and the quality of life for individuals with a chronic illness.

## Clinical Trial Phases\*

	Phase I	Phase II	Phase III	Phase IV
<b>Description</b>	Initial studies	Controlled clinical studies	Expanded controlled and uncontrolled trials after preliminary evidence of the drug has been obtained	Post-marketing studies
<b>Purpose</b>	Assess the safety, tolerability, metabolism, and pharmacologic actions of the therapy in humans and the side effects associated with increasing doses	Evaluate clinical efficacy of the therapy for a particular indication or indications in patients with the disease/condition under study; determine the common short-term side effects and risks	Gather additional information to evaluate the overall benefit-risk relationship of the drug and provide adequate basis for physician labeling; definitively assesses efficacy of the new therapy, especially in comparison with currently available alternatives	Detect any rare or long-term adverse effects over a much larger patient population and timescale than was possible during the initial clinical trials; delineate additional information, including drugs' risks, benefits, and optimal use
<b>Number of People Given Drug</b>	20-80	100-300	1,000-3,000	Varies
<b>Additional Information</b>	Conducted in inpatient clinic, where subject can be observed by full-time medical staff; not blinded; often no placebo control	The development process for a new therapy often fails at this phase due to the discovery of poor efficacy or toxic effects	Double-blind randomized controlled trials; most expensive, time-consuming phase to design and run; once a therapy has proven satisfactory over Phase III trials, the trial results are usually combined into a large document containing a comprehensive description of the methods and results of human and animal studies, manufacturing procedures, formulation details, and shelf life. This collection of information is then submitted to the FDA for approval of the therapy.	Phase IV studies may be mandated by regulatory authorities or may be undertaken by the sponsoring company for competitive or other reasons; adverse effects detected by Phase IV trials may result in the withdrawal or restriction of a therapy

\*All clinical trials are conducted in phases.

Tables adapted from: National Institutes of Health. *Clinical Trials information*. (n.d.). Accessed August 3, 2005 from <http://www.clinicaltrials.gov/ct/info/whatis>

## SAVE THE DATES

### United States Conference on AIDS

September 28-October 2, 2005  
Houston, Texas  
Visit: [www.nmac.org](http://www.nmac.org)

### IDSA Conference

October 6-9, 2005  
San Francisco, CA  
Visit: [www.idsociety.org](http://www.idsociety.org)

### National Conference on Correctional Health Care (NCCHC)

October 8-12, 2005  
Denver, Colorado  
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### IDCR Pre-Conference Seminar at NCCHC

"Infectious Diseases in Corrections: An Integrated Approach"  
October 8, 2005  
Denver, Colorado  
Visit: [www.ncchc.org](http://www.ncchc.org)

### Society of Correctional Physicians Annual Meeting

October 9, 2005  
Denver, Colorado  
Visit: [www.corrdocs.org](http://www.corrdocs.org)

### "Drug-drug Interactions and Metabolic Complications of HIV"

Satellite Broadcast  
October 26, 2005  
12:30-2:30pm EST  
Visit:  
[www.amc.edu/patient/hiv/hivconf/index.htm](http://www.amc.edu/patient/hiv/hivconf/index.htm)

### APHA Meeting and Exposition

November 5-9, 2005  
New Orleans, LA  
Visit: [www.apha.org](http://www.apha.org)

### American Association for the Study of Liver Diseases Meeting

November 11-15, 2005  
San Francisco, CA  
Visit: [www.aasld.org](http://www.aasld.org)

### National Viral Hepatitis Prevention Conference

December 5-9  
Washington, DC  
Visit: [www.cdc.gov/ncidod/diseases/hepatitis.conference.htm](http://www.cdc.gov/ncidod/diseases/hepatitis.conference.htm)

### XVI International AIDS Conference

August 13-18, 2006  
Toronto, Canada  
Visit: [www.aids2006.org](http://www.aids2006.org)

## NEWS AND LITERATURE REVIEWS

### 24 vs 48 Weeks Pegasys/RBV for Co-infection: Which is Better?

In a randomized, controlled trial, 128 patients co-infected with HIV and HCV genotype 2 or 3 received 180 mcg Pegasys sq once weekly in combination with 10.6-13.0 mg/kg/day ribavirin (RBV.) All patients with undetectable HCV RNA at 24 weeks after initiation of therapy were randomized at 28 weeks to either stop treatment or continue treatment for 20 weeks, for a total of 48 weeks of treatment. A significantly lower relapse rate was found in the patient group receiving 48 weeks of treatment compared to those receiving 24 weeks of treatment (11% vs 40%.) Study authors concluded that the optimal duration of treatment in HCV genotype 2- and 3-infected patients co-infected with HIV is at least 48 weeks. *Zanini, Puoti, et al. Poster abstract MoPpLB0103. International AIDS Conference. Rio de Janeiro. July 25, 2005.*

### Texas Mandates HIV Testing for All Inmates

Texas Governor Rick Perry signed legislation on June 21 implementing mandatory HIV testing for inmates pending release from Texas' prisons. The policy will be adopted in the Texas Department of Criminal Justice by September 1, with the hope of preventing the spread of the virus both within and outside of the Texas prison system and to inform inmates of their HIV status. The University of Texas Medical Branch at Galveston, which administers healthcare to the majority of Texas' correctional facilities, recently reported that HIV prevalence within the Texas prison system is 2.1%.

*West M. Daily Texan. Accessed June 21, 2005 from [www.dailytexanonline.com/media/paper410/news/2005/06/21/University/Inmates.To.Take.Hiv.Test.Before.Release-958334.shtml](http://www.dailytexanonline.com/media/paper410/news/2005/06/21/University/Inmates.To.Take.Hiv.Test.Before.Release-958334.shtml).*

### Updates to the Guidelines for Use of ARVs in HIV-1-Infected Adults/Adolescents

The Panel on Clinical Practices for the Treatment of HIV Infection has issued the following supplemental recommendations, effective immediately, for the use of antiretroviral agents (ARVs) in HIV-1-infected adults and adolescents: (1) a regimen containing "tenofovir + didanosine + NNRTI"

should not be used as an initial regimen in ARV treatment-naïve patients and (2) lopinavir/ritonavir can be dosed as one single daily dose (6 capsules or 10mL - equivalent to 800mg lopinavir/200mg ritonavir) in treatment-naïve patients. Once-daily dosing is not recommended in treatment-experienced patients or in patients receiving concomitant efavirenz, nevirapine, amprenavir, fosamprenavir or nelfinavir.

*NIH. Antiretroviral treatment guidelines. (n.d.). Accessed August 15, 2005 from [http://aidsinfo.nih.gov/guidelines/default\\_db2.asp?id=50](http://aidsinfo.nih.gov/guidelines/default_db2.asp?id=50)*

### Pancreatitis in HIV-Infected Adults

In a cross-protocol analysis of 20 Adult AIDS Clinical Trials Group (AACTG) study sites, rates of clinical and clinical/laboratory pancreatitis were relatively low. Seventeen of the 20 studies considered two definitions of pancreatitis: clinical pancreatitis and a combined definition of clinical and/or laboratory pancreatitis, defined as grade 3 or 4 amylase and/or lipase elevation. The remaining three studies defined pancreatitis as elevated serum amylase and a compatible clinical syndrome of nausea, vomiting and/or abdominal pain. Pancreatitis incident rates were calculated based on a Poisson distribution. Analysis of 17 studies reflecting 4 arms yielded a relatively low overall clinical pancreatitis rate of 0.61 per 100 person-years (PYs) and a higher clinical/laboratory pancreatitis rate of 2.23 per 100 PYs. Thus, the clinical/laboratory pancreatitis definition yielded a rate nearly four-fold higher than the clinical pancreatitis definition. Rates of pancreatitis in didanosine (ddl) arms seemed to be dose dependent. Pancreatitis rates for ddl/stavudine (d4T) trials were high at 4.16 per 100 PYs clinical and 6.25 per 100 PYs clinical/laboratory. The highest rates were seen with the combination indinavir/ddl/d4T. Study authors concluded that the combination of nucleoside reverse transcriptase inhibitors (NRTIs) and definition of pancreatitis has an impact on the incidence of pancreatitis. Further evaluation is needed to determine how much of this pancreatitis is directly caused by antiretroviral drugs and how much is attributable to preexisting comorbidities.

*Reisler R, et al. JAIDS. 2005; 39(2):159-66.*

## RESOURCES

### NIH Clinical Trials Website

<http://www.clinicaltrials.gov/ct/info/whatis>

### NIH Office of Extramural Research Human Subjects Website

<http://grants.nih.gov/grants/policy/hs/index.htm>

### DHHS Office for Human Research Protections (OHRP)

<http://www.hhs.gov/ohrp/>

### DHHS OHRP Guidance on the Involvement of Prisoners in Research

<http://www.hhs.gov/ohrp/humansubjects/guidance/prisoner.htm>

### The Belmont Report. Full report available at:

<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

### OHRP Human Subject Assurance Online Training

<http://ohrp-ed.od.nih.gov/CBTs/Assurance/login.asp>



## SELF-ASSESSMENT TEST FOR CONTINUING MEDICAL EDUCATION CREDIT

Brown Medical School designates this educational activity for one hour in category one credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through February 28, 2006. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. The following research examples are subject to IRB approval:
  - A. DHHS-supported research involving prisoners.
  - B. Research involving prisoners in which the information is used solely for internal modifications of one's own system/facility.
  - C. Research that involves prisoners, in which data may indirectly be linked to identifiable participants of the study.
  - D. A and B
  - E. A and C
  
2. The following statement(s) regarding clinical trial phases is/are false:
  - A. Phase II clinical trials are conducted to determine the short- and long-term side effects and risks of a new therapy/drug.
  - B. Phase III clinical trials typically involve 300-3,000 participants.
  - C. Phase I clinical trials assess the metabolism and safety of a therapy/drug and are blinded, controlled studies.
  - D. None of the above statements are false.
  - E. All of the above statements are false.
  
3. A prisoner or prisoner representative should be included on the IRB reviewing research involving prisoners, but is not necessary if a therapy/drug is not being given to prisoners during the study. True or false?
  - A. True
  - B. False
  
4. According to 45 CFR 46, permissible research involving prisoners includes the following:
  - A. The study of prisons as institutional entities, providing that the research does not present a high risk to the subjects.
  - B. The study or prisoners as incarcerated persons, providing that the research does not present a high risk to the subjects.
  - C. Research which has the intent of improving the health of the subject.
  - D. None of the above research is permissible under 45 CFR 46.
  - E. All of the above research is permissible under 45 CFR 46.

5. Research involving prisoners cannot received expedited IRB approval. True or false?
  - A. True
  - B. False

### IDCR EVALUATION

*5 Excellent 4 Very Good 3 Fair 2 Poor 1 Very Poor*

1. Please evaluate the following sections with respect to:

	educational value	clarity
Main Article	5 4 3 2 1	5 4 3 2 1
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2. Do you feel that IDCR helps you in your work?

Why or why not?

3. What future topics should IDCR address?

4. How can IDCR be made more useful to you?

5. Do you have specific comments on this issue?

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