

Correctional Research and the Institutional Review Board- Protection or Obstruction?

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Why Prisoner Research?

- Research is critical to developing evidence based methods for handling incarcerated persons.
- Ideal Environment for research, but few studies in correctional environments since 1959
- Emerging therapies denied to inmates because they cannot access clinical trials and expanded access

Why NOT Prisoner Research- 2

- The history of prisoner research
- Their protected status,
- Prisoner research is fraught with **pitfalls**
- Generally requires scrutiny by a fully empanelled Institutional Review Board specifically designed to handle research in this area.



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Prisoners- “Protected Class”

- Research on Prisoners- **PITFALLS**
- Administrative
- Legal
- Ethical
- Societal (Media)
- How to avoid them



Background- 1

- 1. A brief analysis of the development of the IRB process;
- 2. A Quick Review of 45CFR46 and its applicability;
- 3. Requirements of Institutional Review Boards which are engaged in approving prisoner research;

Background- 2

- 4. recent actions of OHRP;
- 5. Recent actions of IOM at request of Secretary of Health and Human Services; and
- 6. the Nuts and Bolts of how to do a Successful IRB Submission for prisoner research



Development of IRB Process

- Grew out of the Belmont Report (Named for the room they met in at the Smithsonian- not their Chairman or members)
- Belmont Report empanelled because of the times

Pre- Belmont Report

- Nuremberg Trials- International Military Tribunals for War Crimes
- Doctor's Trials- Part of IMT- 23 Doctors put on trial for experimentation on prisoners

The Doctors Trial

The Medical Case of the Subsequent Nuremberg Proceedings



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Doctor's Trial

- Defense- Similar things are happening in the United States
- Seven of 23 found NOT GUILTY
- Nine of 23 were sentenced to prison and all had their sentences reduced in time
- 7 of 23 were hanged in Landsberg Prison in Bavaria on June 2, 1948



Defense Arguments in this Trial

- 1. Several German doctors had argued in their own defense that their experiments differed little from previous American or German ones.
- 2. No international law or informal statement differentiated between legal and illegal human experimentation.
- Unfortunately, there was some **validity to their argument**

Nuremberg Code

- Drs. Andrew Ivy and Leo Alexander, American doctors who had worked with the prosecution during the trial were concerned about that possible validity
- Presented 6 Concepts of Permissible Medical Research to the Court- later became 10
- This became known as the Nuremberg Code

Nuremberg Code- 2

- 1. The voluntary consent of the human subject is absolutely essential.
- 2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature

Nuremberg Code-3

- 3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

Nuremberg Code-4

- 4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
- 5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

Nuremberg Code-5

- 6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
- 7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

Nuremberg Code-6

- 8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
- 9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

Nuremberg Code-7

- 10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

Nuremberg Code-8

- Neither Germany nor the United States adopted the tenets of the Nuremberg Code into any of its laws
- Therefore from 1947 until 1959 there were no “Illegal Experiments on Human Subjects.”

Parentetical- the Nuremberg Code

In 1953, Secretary Wilson of the U.S. Department of Defense included the Nuremberg Code, verbatim, as the official Department of Defense policy applicable to the Army, Navy and Air Force services in a memorandum with regard to "human volunteers in experimental research." Unfortunately, the memorandum was classified as "**top secret**" until 1975, so its distribution—and perhaps implementation—may have been severely limited.

Parenthetical- the Nuremberg Code

- In Re Cincinnati Radiation Litigation (874 F. Supp. 796, Southern District, Ohio), which involved radiation experiments and impoverished patients, Judge Beckwith stated that "the Nuremberg Code is the law of humanity," and that the Nuremberg Code "may be applied in both civil and criminal cases by the federal courts in the United States."

In Re: Cincinnati

- 1995- "Radiation Experiments Conducted by the University of Cincinnati Medical School with Department of Defense Funding," (Experiments conducted in 1972- Cancer patients radiated without knowledge or consent to determine dose extent of radiation (LD50))

Parenthetical- the Nuremberg Code

- In the 2001 case of Grimes v. Kennedy Krieger Institute (782 A.2d 807, Court of Appeals, Maryland), which involved lead experiments involving children in public housing, Judge Cathell stated that “the Nuremberg Code . . . should be the preferred standard for assessing the legality of scientific research on human subjects.”

Grimes v. Kennedy Krieger Institute
(782 A.2d 807, Court of Appeals,
Maryland),

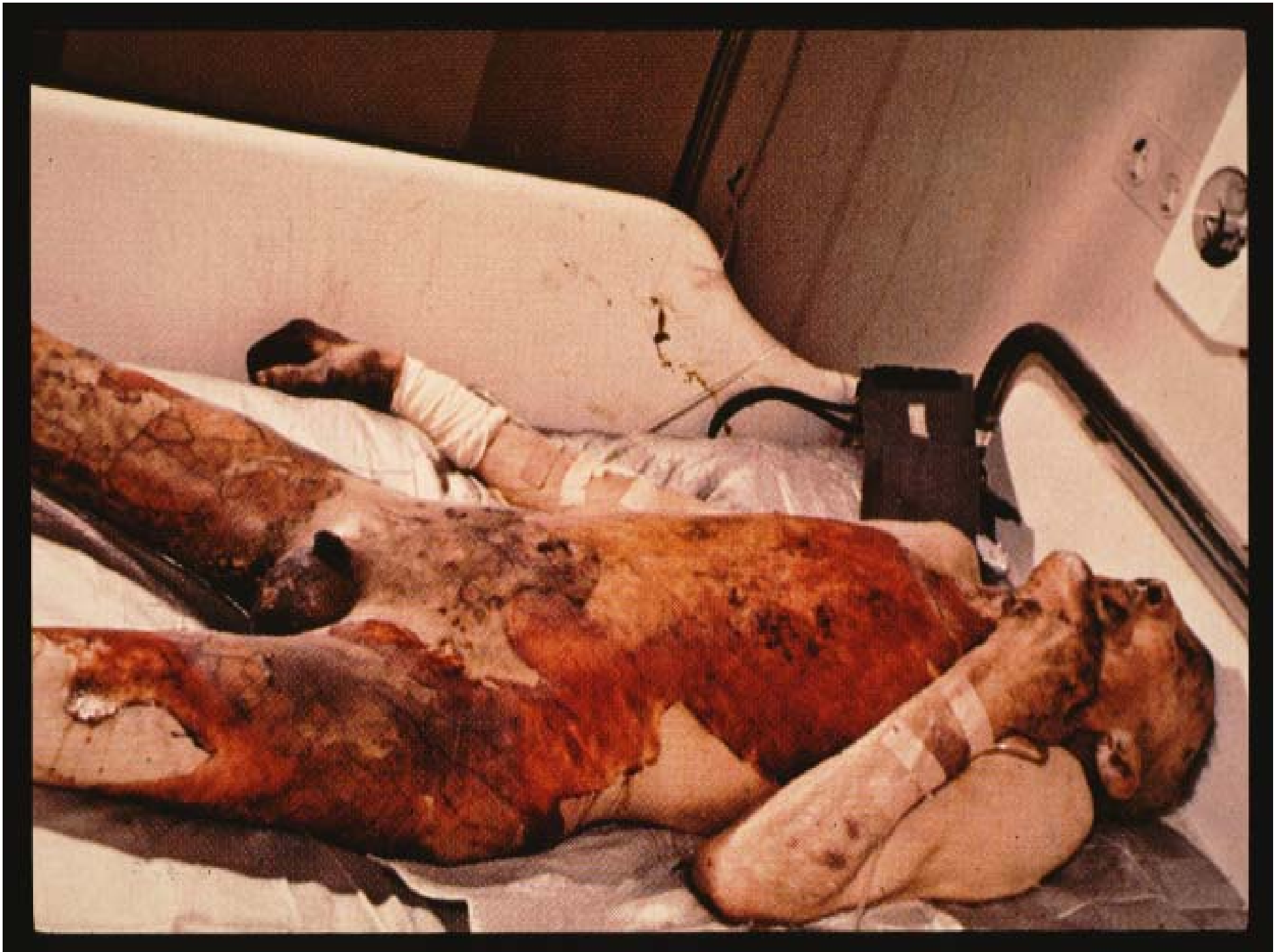
- Johns Hopkins Study- **1990-1994**
- Children in homes with intentionally only partial lead ablation to determine effects
- "Children.... accumulate lead in their blood from the dust, thus helping the researchers to determine the extent to which the various partial abatement methods worked "

Grimes v JHU (Krieger)

- The researchers and their Institutional Review Board apparently saw nothing wrong with the search protocols that anticipated the possible accumulation of lead in the blood of otherwise healthy children as a result of the experiment, or they believed that the consents of the parents of the children made the research appropriate.

With Nothing Illegal- What Can Occur?

- PRIVATE RESEARCH
- UNIVERSITY RESEARCH
- GOVERNMENT RESEARCH



PRIVATE (PHARMACEUTICAL COMPANY) RESEARCH

- Prior to 1959 no drug came to the American market without first being tested on prisoners.
- Personally witnessed the “Pfizer” Building on the grounds of a Michigan prison
- Holmesburg Prison outside of Philadelphia

PRIVATE (PHARMACEUTICAL COMPANY) RESEARCH-2

- From 1962 to 1966, a total of 33 pharmaceutical companies tested 153 experimental drugs at Holmesburg prison alone. (Alan Hornblum, *Acres of Skin*, Routledge, NY, 1998)

University Based Research

- Dr. Albert Kligman, Professor of Dermatology at the University of Pennsylvania- entered the aging prison, he was awed by the bare torsos of hundreds of inmates walking aimlessly before him and by the potential they held for his research- "All I saw before me were acres of skin. It was like a farmer seeing a fertile field for the first time."

University Based Research- 2

- Grimes v. Johns Hopkins University (Krieger Institute)- Lead studies in children
- “the IRB involved here, the Johns Hopkins University Joint Committee on Clinical Investigation...abdicated [its] responsibility, instead suggesting to the researchers a way to miscast the characteristics of the study in order to avoid the responsibility inherent in nontherapeutic research involving children.”

GOVERNMENT BASED RESEARCH

- USPHS Syphilis Study in Alabama
- Oregon and Washington state prisons (a total of more than 130 prisoners were irradiated),
- Live cancer cell injection at the Ohio state prison
- Mind Control Experiments in Pennsylvania State Prison

Where are we?

- Holmesburg prison closed in 1977. Prison research ended when **states** began to limit, if not forbid, research involving prisoners.
- On November 16, 1978, the Department of Health and Human Services (DHHS) provided guidelines for "Protection Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects." - Revised in 1991

The Declaration of Helsinki

- Declaration of Helsinki came into being in 1964 after considerable deliberation and review by the World Medical Association (WMA), which is an international organization comprised of medical professional organizations from 27 different countries
- Not really important in US because of Belmont Report

The Declaration of Helsinki

- Three Sections
- FIRST SECTION- 9 general Rules
- SECOND SECTION- 18 basic Principles
- THIRD SECTION- 5 additional Principles
- US Membership in WHO through the AMA
- US Government did not adopt Declaration of Helsinki (FDA Alludes to it occasionally)

The BELMONT REPORT

- 1974- Congress passed the National Research Act- Established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (“National Commission”)
- Their work product became known as the Belmont Report

CHARGE TO COMMISSION

- 1. identifying the basic ethical principles pertaining to biomedical and behavioral research involving human subjects;
- 2. developing guidelines to help ensure that biomedical and behavioral research would be conducted in accord with these basic ethical principles; and
- 3. recommending policy action to the Secretary of the *then*-Department of Health, Education and Welfare (now DHHS)

Belmont Report

In 1978- The Belmont Report is the culmination of the National Commission's work with regard to the first two responsibilities

Suggested to Congress that the report be adopted in total

Congress declined to do that and passed 45CFR46

Belmont Report- 2

- To this day, the Belmont Report is regarded as the preeminent statement in the U.S. of ethical principles pertaining to human subject research, and is considered by many to be the foundation upon which federal human subject research policy rests.

Belmont Report- 3 Sections

1. Briefly addresses the special concern about distinguishing research from practice, and when therapy is combined with research.
2. Discussion of the three basic ethical principles in human subject research
3. Commentaries about applying the three basic ethical principles

Ethical Principles

- 1. RESPECT FOR PERSONS
- 2. BENEFICENCE
- 3. JUSTICE

- The Belmont Report has never been modified or amended since its creation in 1978

RESPECT FOR PERSONS

- AUTONOMY
 - Individuals are autonomous
 - Persons with diminished capacity deserve protection
- Therefore acknowledge autonomy and protect those with diminished capacity
- Autonomy- Self Determination – Voluntary and Informed consent to make a decision

Beneficence

- Secure a person's well being beyond an obligation
- 1. DO NO HARM
- 2. MAXIMIZE POSSIBLE BENEFITS AND MINIMIZE POSSIBLE HARMS

JUSTICE

- Who receives the benefits of research and who bears its burdens
- "Fairness of Distribution"
- Gets to the question of prisoners- is it unfair to exclude them based solely upon their incarcerated status?

Respect for Persons- Autonomy Beneficence- Justice

- Informed Consent
- Voluntariness
- Comprehension
- Information (Disclosure)
- Risk/Benefit
- Subject Selection

Belmont Report and the Prison

- Limited autonomy
- Lack of self-determination in most aspects of their life
- Coercive environment
- Some people feel inmates can NEVER give free informed non-coercive consent.
- Personal Experience

US Congress

- Did NOT accept the recommendation of the Belmont Report to accept their findings in total and create laws around it instead
- §289 of Chapter 6A in Title 42 of the United States Code lead to 45CFR46 (revised 1991)
- However the Department of HHS- Office for Human Research Protections recognizes the Belmont Report as an acceptable statement of ethical principles for assuring human subject protection.

Federal Regulations

- A mixture of protections that are difficult to navigate
- APPLY TO FEDERALLY FUNDED STUDIES ONLY
- HOWEVER- most Universities adopt the Federal guidelines for all studies- PRIVATE groups and non-University researchers MAY NOT HAVE TO ABIDE

PRISON STUDIES Particularly Vulnerable

- Universities and others who voluntarily adhere to Federal guidelines have much difficulty doing these studies and are caught in a regulatory spider web
- Private researchers or groups can ignore most if not all of the issues
- Therefore some states have specific enactments- (e.g. NY adopted Fed)

EXEMPT FROM REGULATION

- Some research may not be subject at all to the Common Rule or to any part of 45 CFR 46
- Research that is **not supported, conducted or otherwise regulated by a federal agency, or research that is funded by a federal agency that has not adopted the Common Rule.** (Most private & pharmaceutical research NOT University based)

Exempt from Regulation- 2

- The lack of a uniform, nationwide policy is often pointed out as a Prisoners as major weakness in our "system" of human subject protection.
- Therefore some entities, such as **state governments, professional organizations, and research institutions**, have adopted the Common Rule or even the entire set of regulations at 45 CFR 46 as their own policy for human subject protection

Exempt From Regulation

- May or May Not be TOTAL Exemption
- It DOES mean that Enforcement in these circumstances is NOT from the Federal agencies (They lack the formal jurisdictional authority)
- States- force of Law (Statutory and Common) Civil and Criminal
- Universities and Associations- may fire you or expel you

Many Federal Laws Regarding Research

- 45CFR46 established a "COMMON RULE" that all Federal Agencies could adhere to in their support of human research. Unfortunately some agencies involved in a lot of human research declined to agree to the "Common Rule" and created their own regulations (FDA)

45CFR45 Subpart A

- Establishes (HHS) the basic parts of human subjects protection
- Known as the “Common Rule”
- Adopted by 14 Federal Agencies, BUT NOT FDA; DOJ; FBOP and others
- NOTE- Subpart A is the ONLY part adopted as the “Common Rule”

45CFR46- Exceptions

- Subpart B- Pregnant Women, Fetuses and Neonate
- Subpart C- Prisoners
- Subpart D- Children
- ARE NOT PART OF THE "COMMON RULE"
- Therefore- if you are doing research for a common rule signatory on children- they MAY have different rules than this

Therefore at a MINIMUM

- Most of us have to deal with 45CFR46
- And its SUBPART C on Prisoners
- We also have to check for other
 - Federal agency regulations;
 - State Laws;
 - University Policies and
 - Professional Association requirements
 - And possibly some court cases

PRISONERS- FIRST NOTE Subpart

A

- Exemption- Note that 45 CFR 46.101(b), at footnote (1) does NOT permit any **exempt** research on prisoners- It MUST always come to a full IRB review (although some IRB's do contemplate exempt prisoner research).
- Therefore in my opinion a typical exempt study like educational observation which would be exempt anywhere MUST go through FULL review for the Incarcerated

For ALL Research

45 CFR 46.111 lists seven (7) requirements that must be satisfied as a condition for IRB approval of research

1. Minimal risks
2. Acceptable Risks
3. Equitable Selection of Subjects
4. Informed Consent
5. Documentation of Informed Consent
6. Safety Monitoring
7. Privacy & Confidentiality

For ALL Research

- Number 3 of 45CFR46.111- Equitable Selection of Subjects could present a problem and specifically mentions prisoners, pregnant women, mentally disturbed, children and disadvantaged
- THEREFORE IRB must have a heightened scrutiny of the NEED for prisoners in a study at the outset (before even getting to Subpart C)

45CFR46 Subpart C

- November 16, 1978 then revised 1991
- NO FEDERAL PRE-EMPTION OVER LOCAL LAW
- Therefore simply complying with Subpart 3 does not relieve you of state or local laws (e.g. FCC Congress pre-empts all local laws concerning radio sending and receiving devices (VA. Ban on Radar Detectors probably unconstitutional)

Prisoner- Subpart C

- Broad Definition- Person INVOLUNTARILY confined or detained for criminal or **civil** statute or in alternative sentencing arrangements
- Therefore a prisoner might be the person coming to your clinic who (unknown to you) has just been given probation instead of prison time for a crime-HOWEVER HHS has given letter rulings indicating that it DOES NOT mean parole or probation (Never been challenged)

Minimal Risk- Subpart C

- Amount of Harm of normal activities or routine medical, dental or psychiatric examination of a reasonable healthy person
- Therefore is an EGD minimal risk?

PRISONERS & IRB

At least one member of the Board shall be a **prisoner, or a prisoner representative** with appropriate background and experience to serve in that capacity

- Most of the IRB can have nothing to do with the Prison or prisoners (Cannot have an IRB made up of employees of a Department of Corrections)

Prisoner Representative

- NOT CLEAR IN STATUTE

“in the absence of choosing someone who is a prisoner or has been a prisoner, the IRB should choose a prisoner representative who has a “close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner.” (HHS)

- PERSONAL NOTE- I was then was not

Prisoner Research Itself

§ 46.306 (a)(2)

- (a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:
 - (1) the institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under § 46.305 of this subpart; and

Prisoner Research- Permissible

(2) in the judgment of the Secretary the proposed research involves solely the following:

- (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;

-

Permissible Medical Research

- (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** 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;

Permissible Medical Research

(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.**

BUT...control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted...experts... and published notice, in the **Federal Register**, of the intent to approve such research (There is no record of this ever happening)

Therefore NO Other Medical Studies and these Medical Studies may have **more** than minimal Risk (therefore you can do the EGD)

- Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS **shall not involve prisoners as subjects.**

What NOW

- You select your study predicated on the previous:
 - 1. Condition over represented in incarcerated persons
 - 2. Improves health or well being of the subject
- Then What Happens
- The IRB - SPECIFIC RESPONSIBILITIES

IRB Responsibilities- 1

- 1. Research must fall within one of the four categories of research permitted under Subpart C at 46.306(a)(2).
- 2. No Undue Influence on the Subject
- 3. Risks that prospective prisoners might accept by taking part in the research are similar to the risks that non-prisoners would accept (Another Undue Influence check)

IRB Responsibilities- 2

4. Prisoner subjects selected fairly and without the unnecessary involvement of prisoner officials or other prisoners
5. Information about research that is provided to prisoners is done in language that *prisoners* can understand
6. Research will have no effect on their parole or incarceration status

IRB Responsibilities- 3

7. Plans to provide such follow-up examination or care whether or not subject is still incarcerated

In Prisoner Research the IRB must Satisfy
All 7 Criteria BY LAW

Recent Developments

- June 20, 2003- Secretary HHS- Waiver- for epidemiologic studies- probably not necessary because they already fell under permissible studies.
- Secretary Tommy Thompson requested the IOM to look at the regulations on prisoner research and report to him about possibly permitting more research

IOM Report

- Personally- had the pleasure to present to them
- Very mixed feelings represented
- Recommended Some Expanded Research
- **BUT ALL PRISONER RESEARCH FALL UNDER FEDERAL REGULATIONS AND JURISDICTION**

Ethical Considerations for Research Involving Prisoners

- the IOM committee adds further protections both by expanding the population of prisoners covered by rigorous ethical rules and by recommending additional safeguards. The committee also acknowledges
- that access to research may be critical to improve the health of prisoners and the conditions in which they live, according to researchers and prisoners, as well as the prisoner liaison panel. However, research with prisoners should be conducted only if it offers a distinctly favorable benefit-to-risk ratio, not because prisoners are a convenient source of subjects

TODAY

- Neither Congress nor HHS has taken any steps to expand prisoner research or make all prisoner research come under Federal protective jurisdiction
- Therefore your IRB may disapprove your study which is safer than the one Pfizer is privately conducting with the same inmate subjects

TODAY

- We could still be in the situation following the Nazi War Crimes Doctors Trial
- Or the Holmesberg Prison Acres of Skin of 1979
- Or following the radiation experiments from the University of Cincinnati of 1995
- Or following the 1994 Lead Study on Children by Johns Hopkins
- These incidents are **not** ancient history



PERSISTENCE

IT'S OVER, MAN. LET HER GO.

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