

**Vulnerability
in
Human Subjects Research**

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Overview

- What is vulnerability in the research context?
- An overview of vulnerable groups (and the research that's been done on them)
- What should we do to address the concerns?

What is Vulnerability?

Some research populations are vulnerable and need special protection. The particular needs of the **economically and medically disadvantaged** must be recognized. Special attention is also required for

- **those who cannot give or refuse consent** for themselves, for
- **those who may be subject to giving consent under duress**, for
- **those who will not benefit personally** from the research and for
- **those for whom the research is combined with care.**

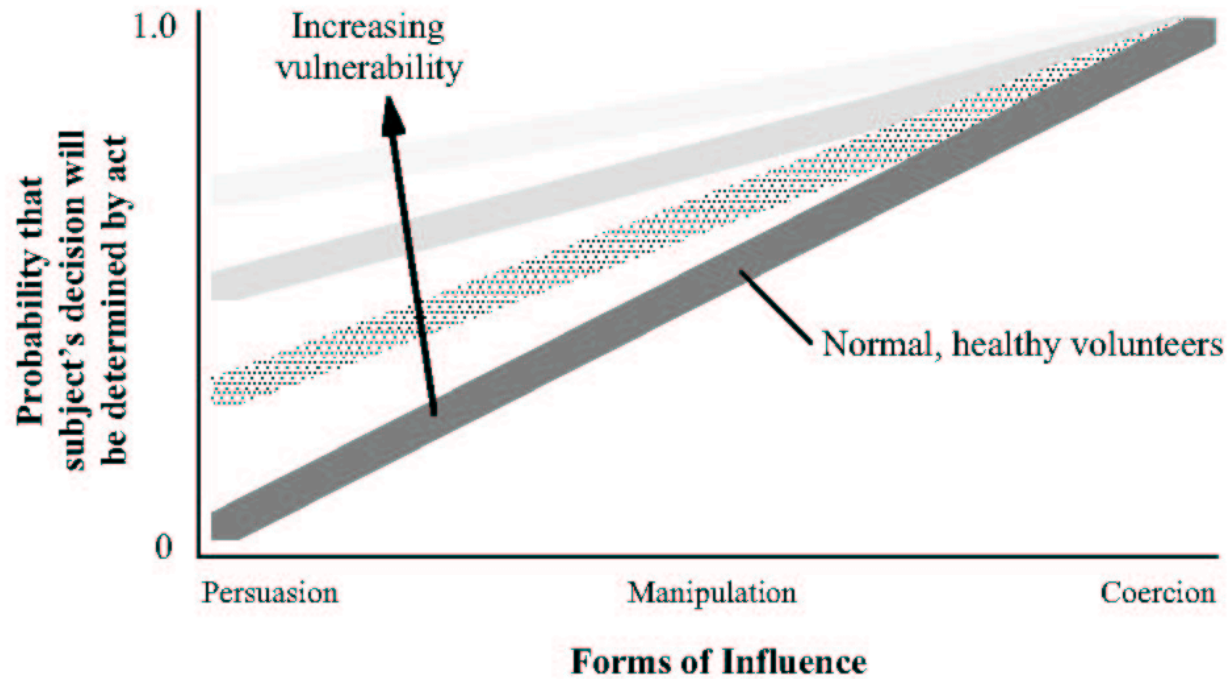
(Declaration of Helsinki, ¶8 (2000))

What is Vulnerability (continued)?

- Vulnerable persons are those who are **relatively (or absolutely) incapable of protecting their own interests**. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.
Council for International Organizations of Medical Sciences (CIOMS), International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 13 (2002).
- Because of this, these persons (and members of groups) are **susceptible to harm** (physical, psychosocial and dignitary) **and exploitation** by researchers, sponsors, and others

Other factors...

- background conditions in the community or country where the research is conducted. Examples are **inadequate experience or capacity for conducting ethical and scientific review of proposed research; poor local infrastructure; untrained personnel; limited technical capacity for conducting the proposed research; and limited availability, accessibility, and sustainability of health care and treatment options outside the research setting.** Joint United Nations Programme on HIV/AIDS (UNAIDS). *Ethical Considerations in HIV Preventive Vaccine Research* (2000).
- “the **absence of an effective mechanism for oversight of research.** If a country lacks mechanisms for identifying and sanctioning researchers who violate laws, regulations, or fundamental ethical standards in carrying out the research, then all research subjects are potentially vulnerable” Macklin R. Bioethics, vulnerability, and protection. *Bioethics* 2003; 17:472-486.



Vulnerable individuals are particularly susceptible to acts having the purpose or effect of having potential subjects behave in a desired way.

Nelson & Merz, *Med Care* 2002; 40 (9 Suppl.): V69-80

So, WHO is vulnerable?

- **women** (and their fetuses) (!) (see subpart B of 45 CFR 46)



STEPHANIE KLEIN-DAVIS | The Roanoke Times

Mellisa Williamson, 35, a Bullitt Avenue resident, worries about the effect on her unborn child from the sound of jackhammers.



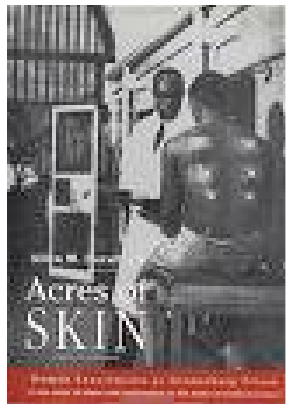
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- **prisoners** (see subpart C of 45 CFR 46)

Holmesburg Prison



Albert Kligman



So, WHO is vulnerable?

- women (and their fetuses) (!) (see subpart B of 45 CFR 46);
- prisoners (see subpart C of 45 CFR 46);
- **children** (see subpart D of 45 CFR 46) (*Dr. Schreiner will discuss*)



“This is gonna hurt like hell.”

So, WHO is vulnerable?

- women (and their fetuses) (!) (see subpart B of 45 CFR 46);
- prisoners (see subpart C of 45 CFR 46);
- children (see subpart D of 45 CFR 46);
- **members of hierarchical groups**, such as the military, employees or ...

SECRET

SECRET

No. S.1/5801/HW

Legal 1 (Mr. Griffith-Jones)
Ministry of Supply
The Adelphi

Death of L. A. C. Maddison

We discussed on 14th May, 1953, this case where the above-named airman died at the C.D.E.E. Porton, while undergoing tests with G.B. gas.

You explained to me the system whereby volunteers for these and similar tests had been obtained for many years (at least as far back as 1929) and you informed me that there had never been any fatal accident previously during such tests at Porton, although about a week before Maddison's death one of the subjects of the tests on the G.B. gas had shown alarming symptoms which, however, had soon passed off.

It may be that in law the Minister would be under no liability for the death of L.A.C. Maddison if it could be shown that there had been no negligence on the part of M.O.S. personnel, but I do not think that you would be wise to try to take this point, partly because in dealing with a dangerous but largely unknown substance like G.B., it would be difficult to show that there had been no negligence (a very high degree of care being required in relation to dangerous substances), and partly because the terms of the information to be brought to the notice of personnel to encourage them to volunteer (Appendix "A" to W.O. Memo. 112/Misc/5850 A.G.1(A) of 6th November, 1950) - terms indicating that there was not the slightest element of danger, have proved to be somewhat misleading. In my opinion compensation will in practice have to be paid in this case, though in determining its amount you will need to have regard to any pension which may be payable by the Minister of Pensions.

As for the future of experiments of this nature, I would advise as follows:-

- (1) If fatal accidents of this kind occur in the future I think that the Minister should pay appropriate compensation and that he ought not to seek to adopt some system of indemnities or "blood chits" designed to throw the responsibility upon the persons volunteering for the tests. Apart from any question of the deterrent effect of such a system, it would probably be ineffective in law at any rate where the subjects of the tests are under 21.
- (2) The Minister should not resume tests with G.B. gas in the conditions operating when L.A.C. Maddison met his death until all reasonable steps have been taken to discover why the gas proved fatal to him and not to the other subjects. It may be that Maddison had some personal idiosyncrasy which made him specially sensitive to the gas. This needs to be investigated. It would not be right for the Minister to put further groups of men through this particular test, when these further groups may well contain personnel with similar idiosyncrasies. The occurrence of the alarming symptoms to the other subject during the previous week shows that there is a definite element of unknown danger present. Whether it would be right to continue with modified tests, where smaller

quantities of G.B. were used, will depend on the circumstances. I am, however, sure that all reasonable steps should be taken to prevent further fatalities. The occurrences at present under

Porton Down

the system whereby volunteers for these and similar tests had been obtained for many years (at least as far back as 1929)



Ronald Maddison, RIP

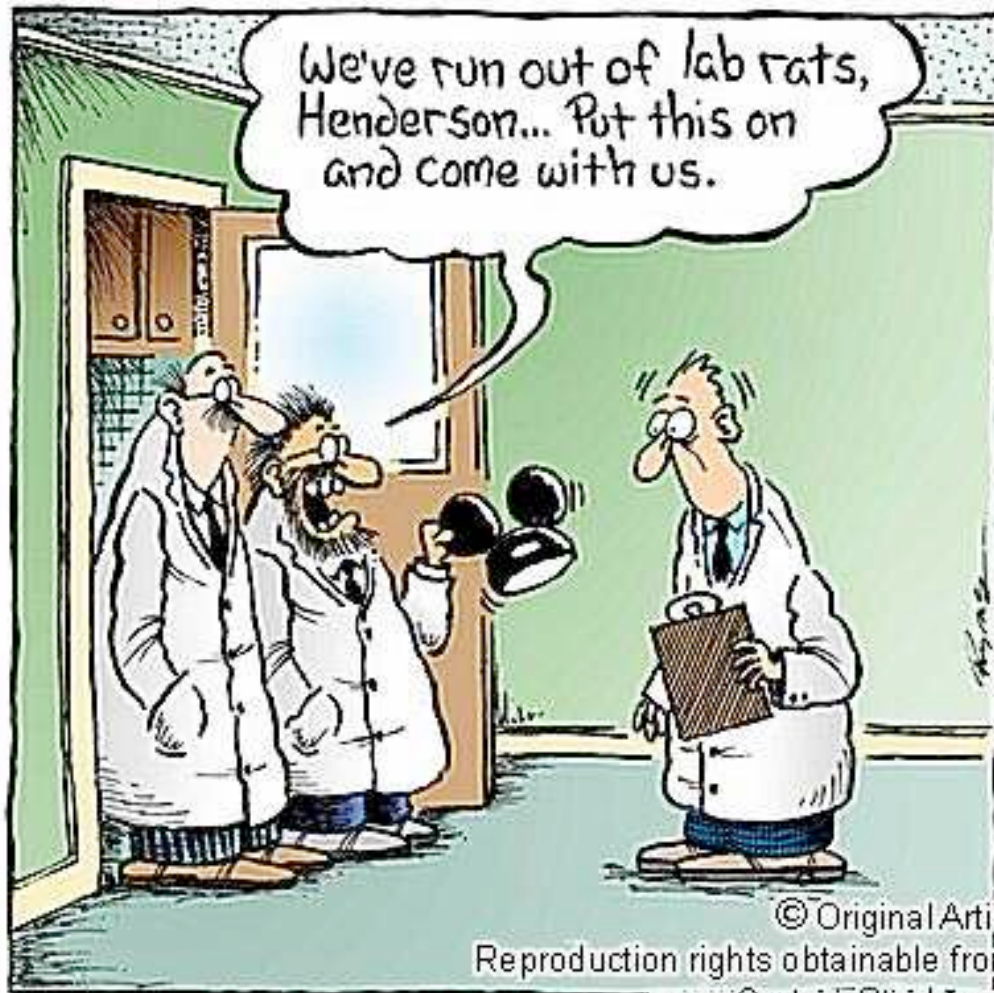
To test the effectiveness of nerve agents such as Sarin, servicemen were offered about £2 and a pass for three days' precious leave if they volunteered to take part in tests.

(<http://news.bbc.co.uk/1/hi/uk/426154.stm>)



Insert video of British troops in LSD experiment

<http://www.youtube.com/watch?v=SX7m4fqTLKU>



We've run out of lab rats,
Henderson... Put this on
and come with us.

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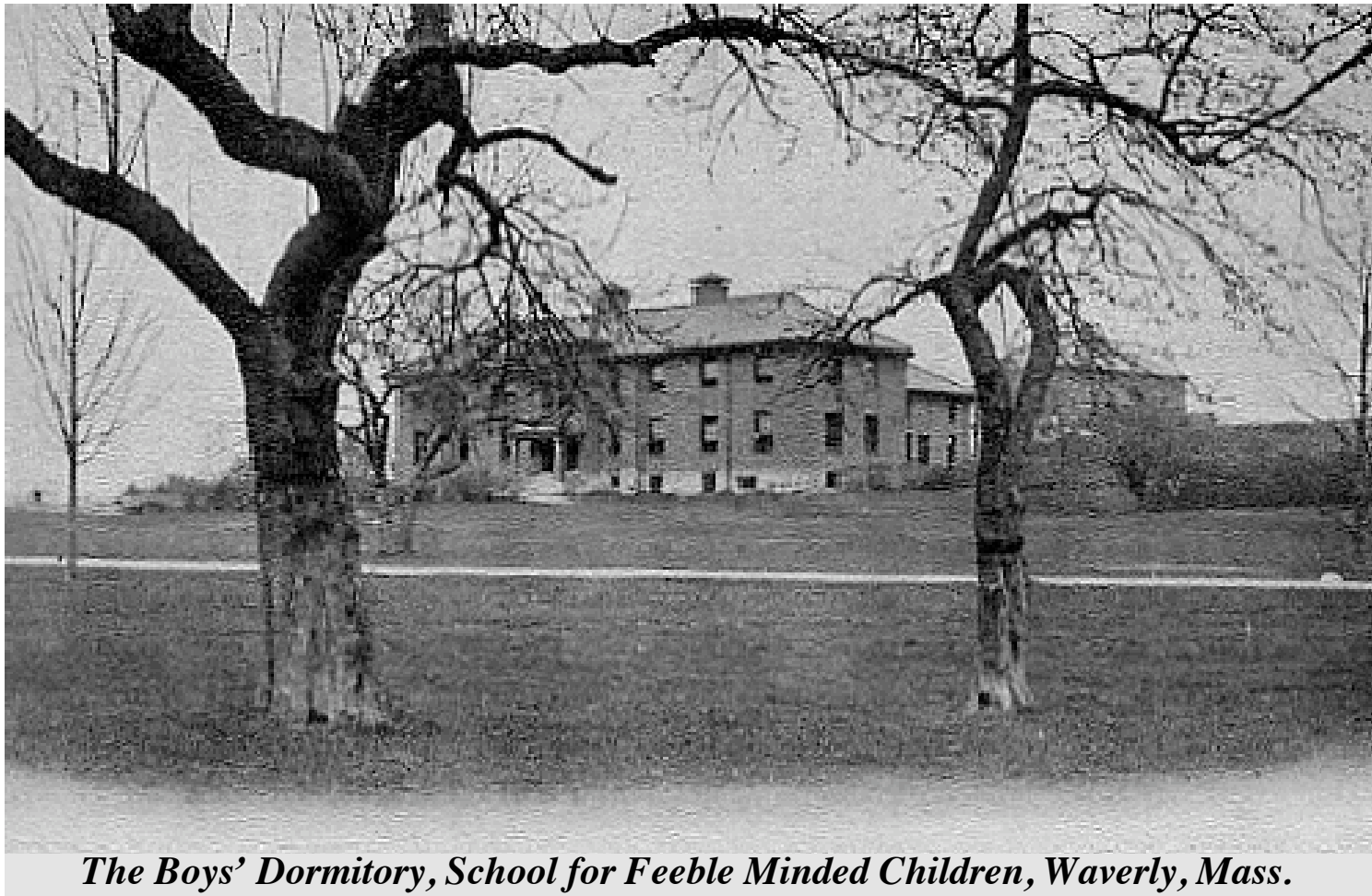


“The title of my science project is ‘My Little Brother: Nature or Nurture.’”

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- members of hierarchical groups, such as the military, employees or . . .
- **students** (especially the mentally infirm, and medical students)

The Walter E. Fernald State School

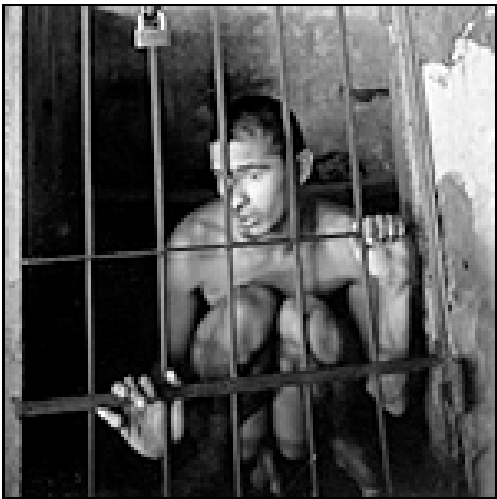


The Boys' Dormitory, School for Feeble Minded Children, Waverly, Mass.

Willowbrook State School



Saul Krugman



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- **persons with dementias**, mental disorders and residents of nursing homes



“Discouraging data on the antidepressant.”

Jewish Chronic Disease Hospital





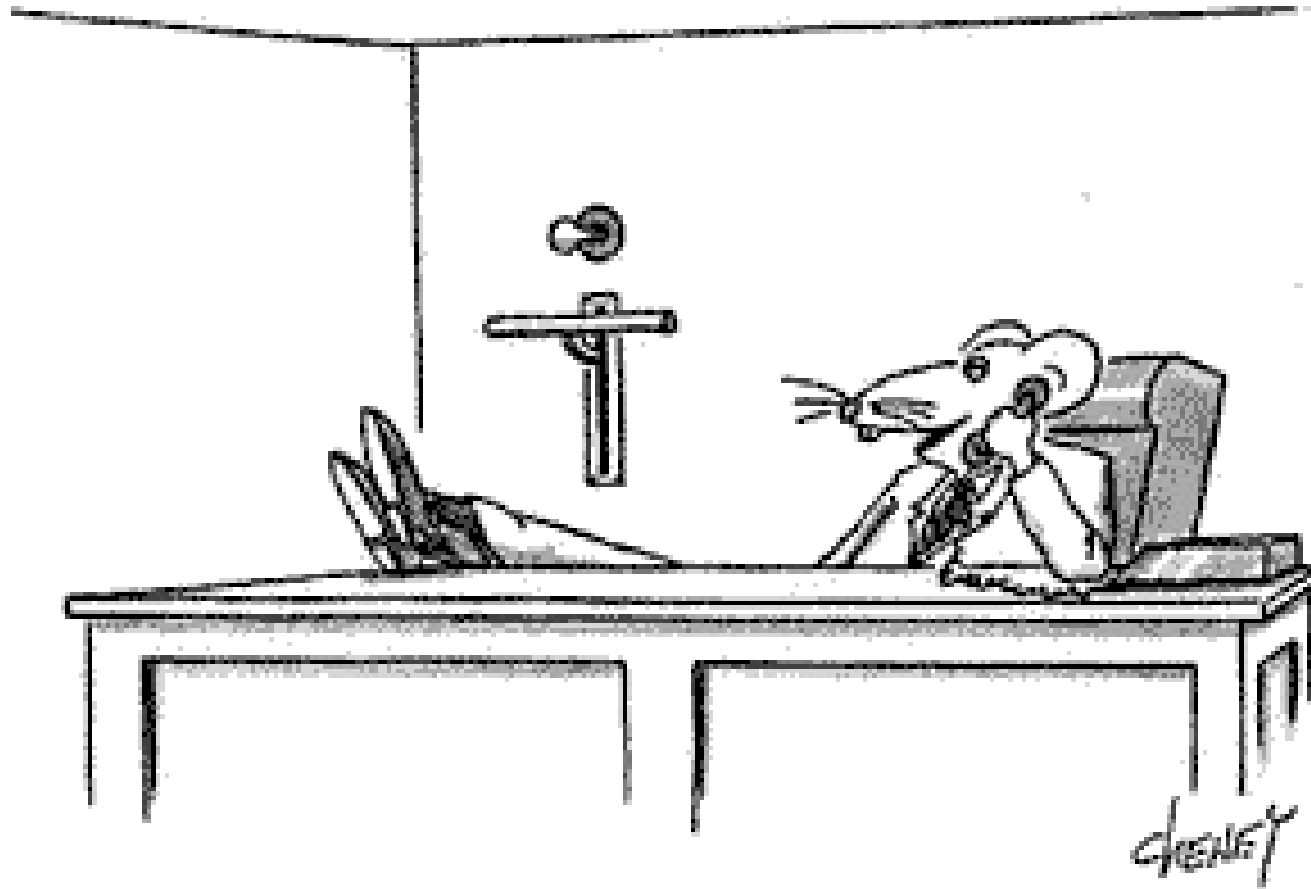
“Scientists have extended the life of the fruit fly.”



Stephen Crowley/The New York Times

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- students (especially the mentally infirm, and medical students);
- persons with dementias, mental disorders and residents of nursing homes;
- people receiving welfare or social assistance, **poor people**, and the unemployed



*“Oh, not bad. The light comes on. I press the bar. They write me a check.
How about you?”*

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- **patients in emergency rooms**

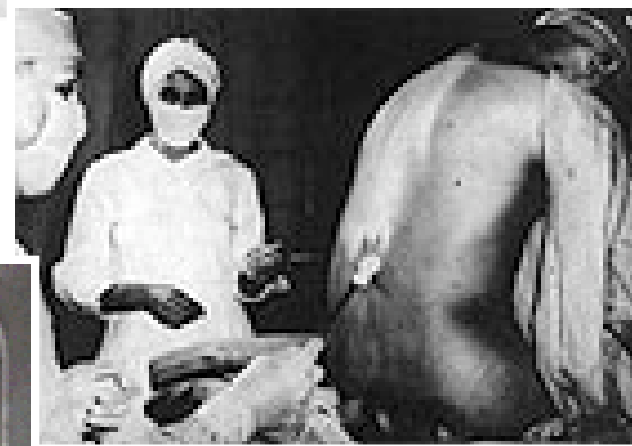


<http://sitemaker.umich.edu/temple/rampart>

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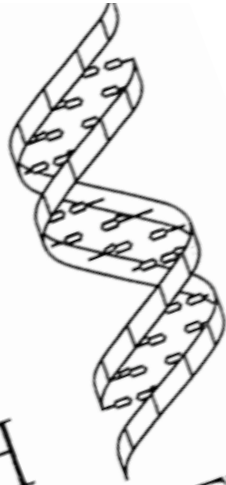
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- patients in emergency rooms;
- some **ethnic and racial minority groups**

Tuskegee Syphilis Study



Jewish
Men and
Women
Volunteers
Needed for
National
Institutes
of Health
Study

FAMILIAL CANCER IN THE JEWISH COMMUNITY



Familial Cancer and
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Jewish Community of
Greater Washington

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Sun.	TESTING	- ADAS ISRAEL
Tues.	Apr. 14	11:00 a.m. - 2:00 p.m.
	Apr. 23	5:00 p.m. - 9:00 p.m.
		(Israeli Independence Day Celebration)
Thurs.	Apr. 28	10:00 a.m. - 1:00 p.m.

PARTICIPATE

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are needed to
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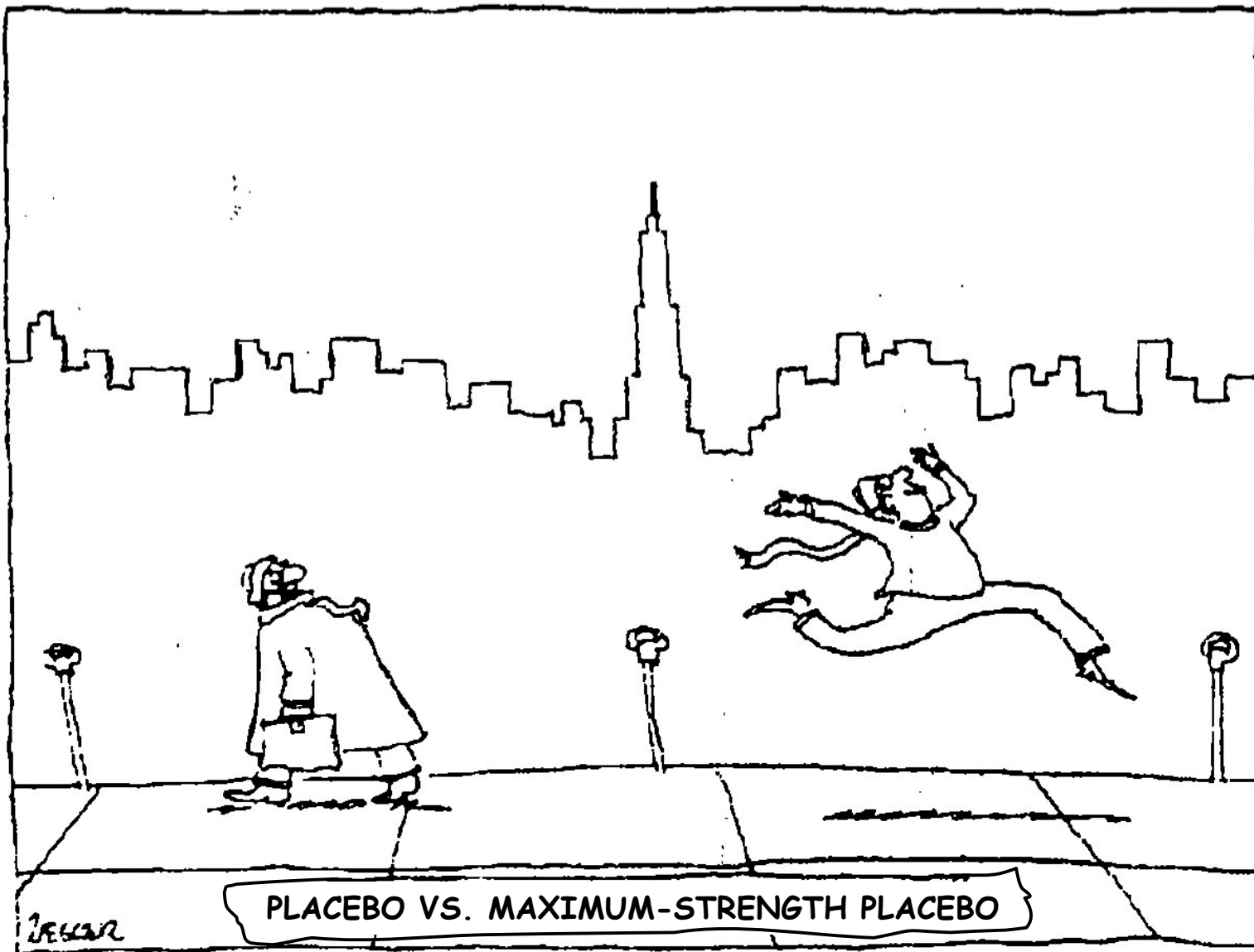
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- patients in emergency rooms;
- some ethnic and racial minority groups;
- **homeless persons**, nomads, refugees or displaced persons



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- some ethnic and racial minority groups;
- homeless persons, nomads, refugees or displaced persons;
- **patients** (including those with incurable disease)





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- patients in emergency rooms;
- some ethnic and racial minority groups;
- homeless persons, nomads, refugees or displaced persons;
- patients (including those with incurable disease);
- **individuals who are politically powerless**

The Director of Central Intelligence
Washington, D.C. 20505

MK-ULTRA

The Honorable Daniel K. Inouye, Chairman
Select Committee on Intelligence
United States Senate
Washington, D.C. 20510

Dear Mr. Chairman:

During the course of 1975 when the Senate Committee, chaired by Senator Church, was investigating intelligence activities, the CIA was asked to produce documentation on a program of experimentation with the effect of drugs. Under this project conducted from 1953 to 1964 and known as "MK-ULTRA," tests were conducted on American citizens in some cases without their knowledge. The CIA, after searching for such documentation, reported that most of the documents on this matter have been destroyed. I find it my duty to report to you now that our continuing search for drug related, as well as other documents, has uncovered certain papers which bear on this matter. Let me hasten to add that I am persuaded that there was no previous attempt to conceal this material in the original 1975 exploration. The material recently discovered was in the retired archives filed under financial accounts and only uncovered by using extraordinary and extensive search efforts. In this connection, incidentally, I have personally commended the employee whose diligence produced this find.

Because the new material now on hand is primarily of a financial nature, it does not present a complete picture of the field of drug experimentation activity but it does provide more detail than was previously available to us. For example, the following types of activities were undertaken:

- a. Possible additional cases of drugs being tested on American citizens, without their knowledge.
- b. Research was undertaken on surreptitious methods of administering drugs.
- c. Some of the persons chosen for experimentation were drug addicts or alcoholics.
- d. Research into the development of a knockout or "K" drug was performed in conjunction with being done to develop pain killers for advanced cancer patients, and tests on such patients were carried out.

I regret having to bring this issue to your attention, but I know that it is essential to your oversight procedures that you be kept fully informed in a timely manner.

Yours sincerely,

STANSFIELD TURNER

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- people receiving welfare or social assistance, poor people, and the unemployed;
- patients in emergency rooms;
- some ethnic and racial minority groups;
- homeless persons, nomads, refugees or displaced persons;
- patients (including those with incurable disease);
- individuals who are politically powerless; and
- **members of communities unfamiliar with modern medical concepts**

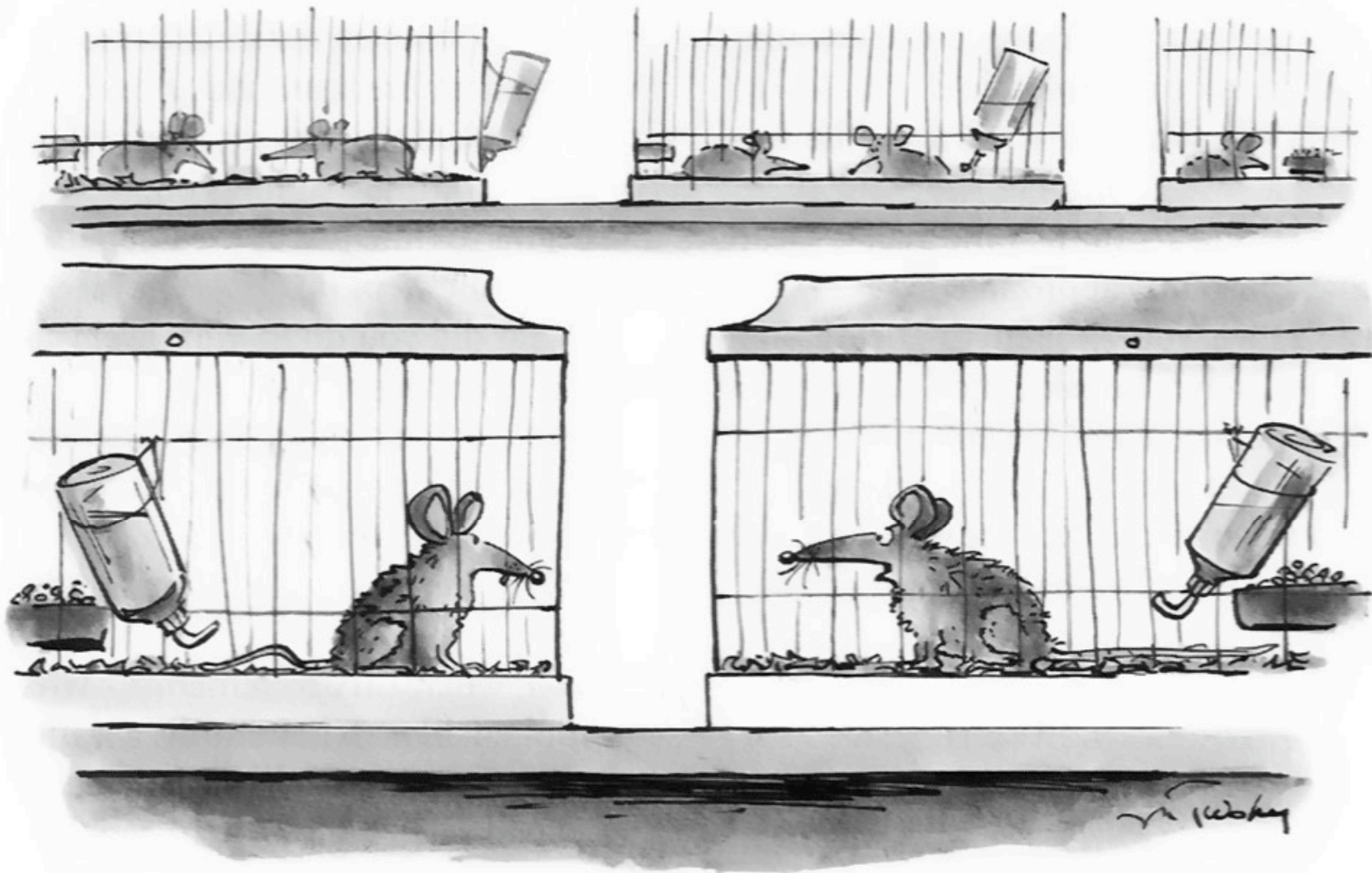
Sources: CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects, Guideline 13 (2002)



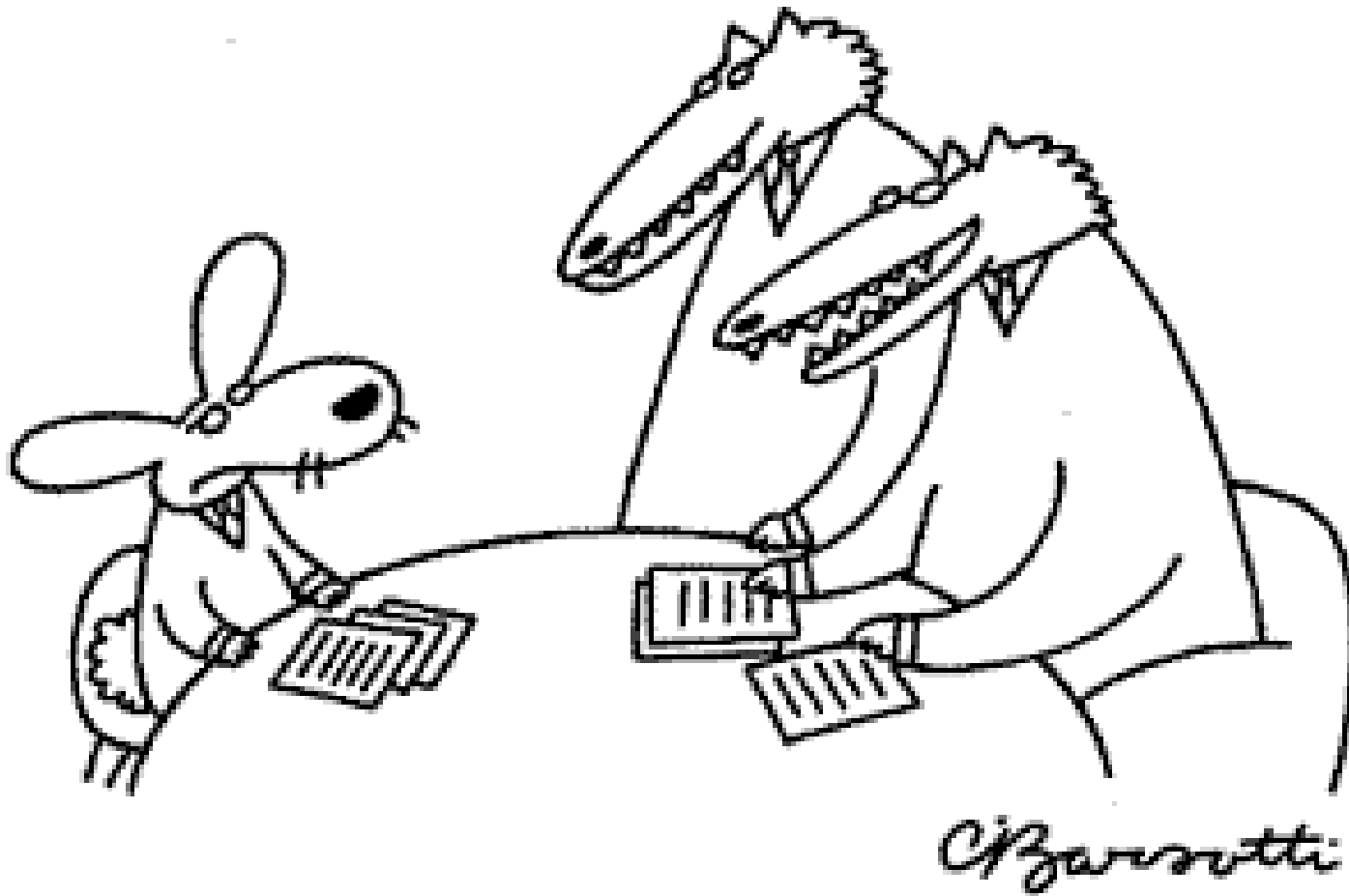
Insert “Dying for Drugs” clip about
Pfizer’s Trovan study in Kano, Nigeria



“They’re harmless when they’re alone, but get a bunch of them together with a research grant and watch out.”

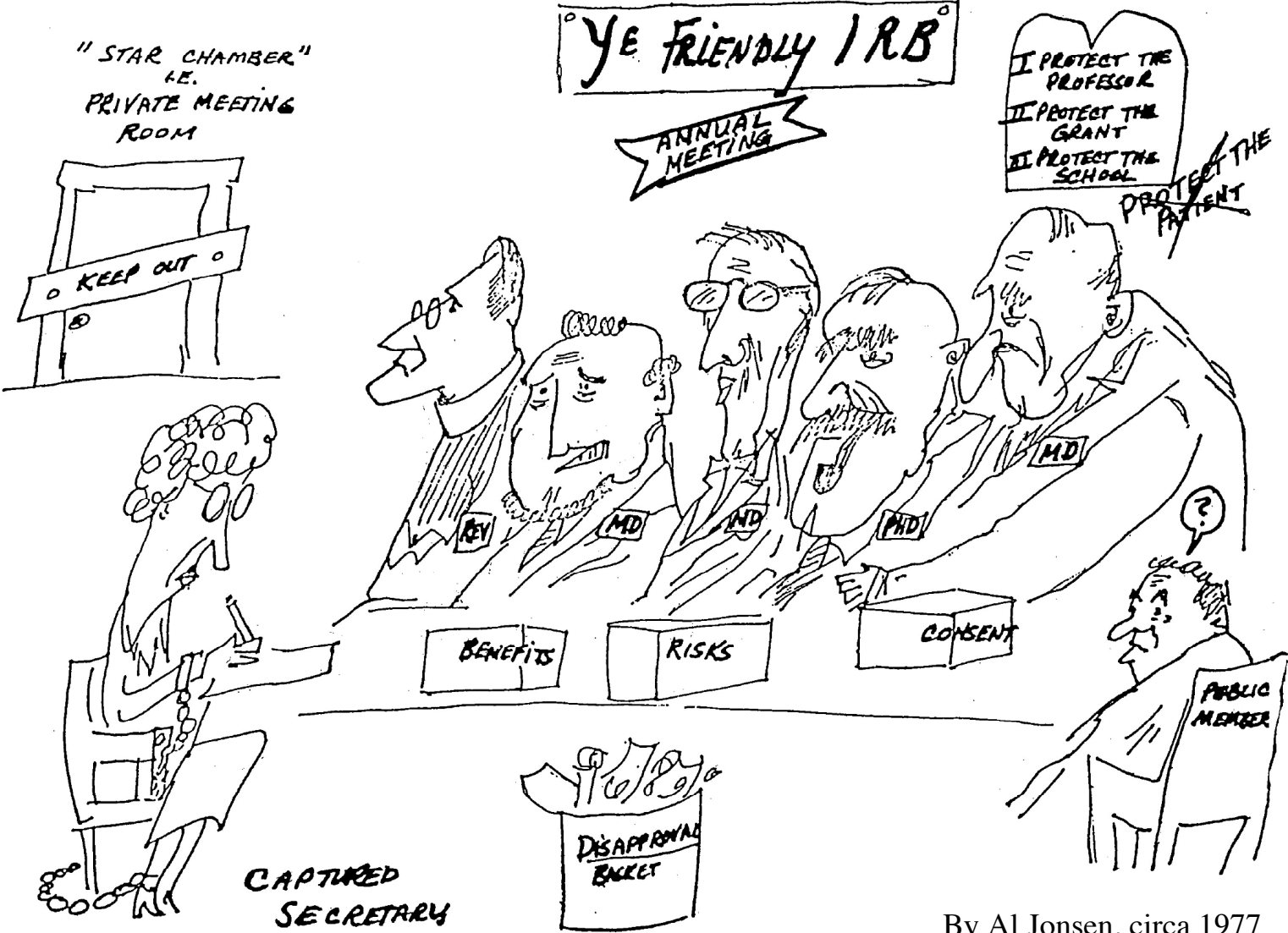


“What if these guys in white coats who bring us food are, like, studying us and we’re part of some kind of big experiment?”



“There. Now it’s all on paper. Feel better?”

What is the IRB's Role?



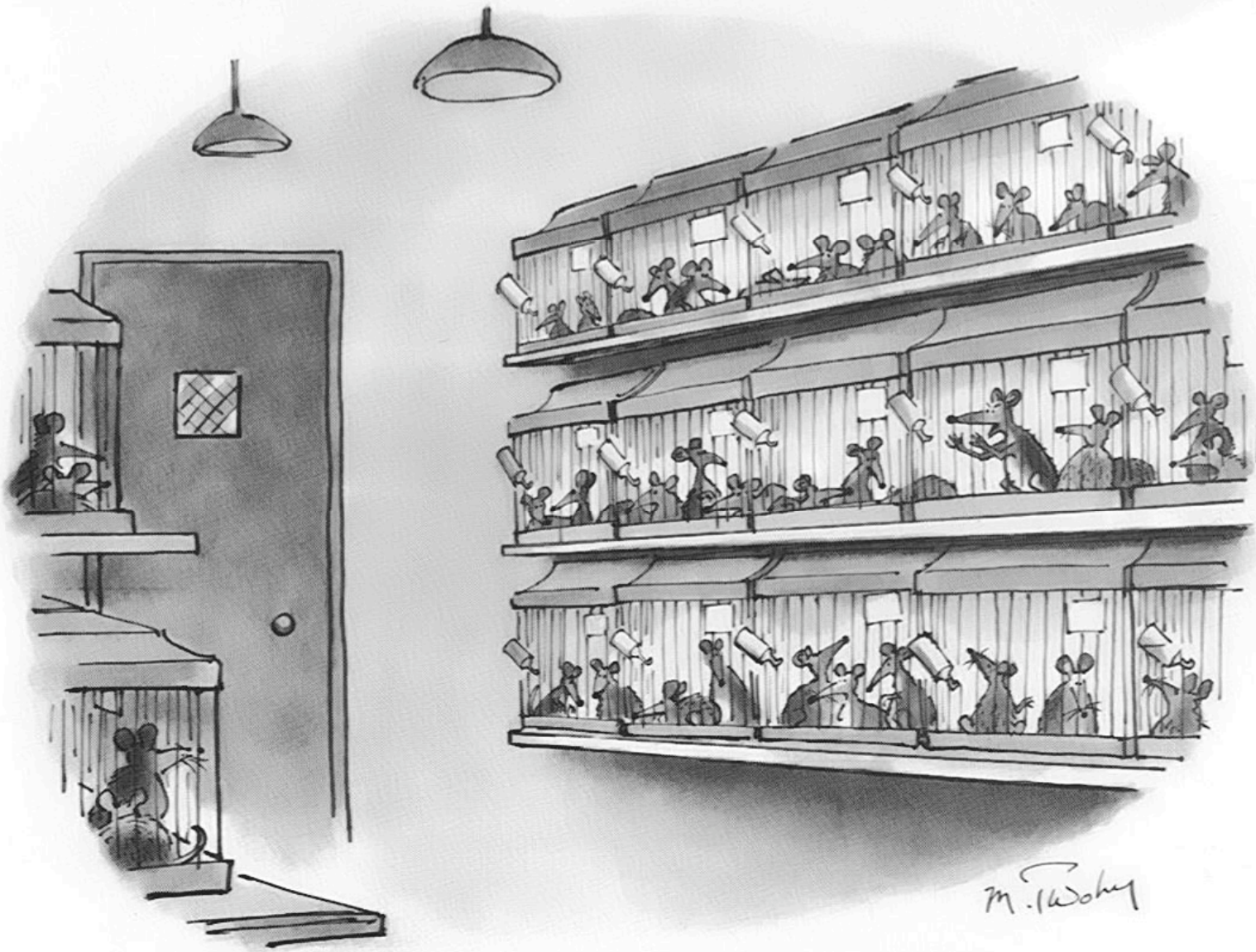
By Al Jonsen, circa 1977

Some questions to ask . . .

- Are potential subjects (PS's) legally competent?
- Are PS's capable of making reasoned decisions, free of coercion or undue influence? (Is the population at risk of incapacity?)
 - Does the researcher have plans and methods for assessment of capacity?
- Why are these PS's being included? Will the subjects or this population possibly benefit directly or indirectly from the research?
 - If not, FLAG!

What extra protections might be taken?

- Consent monitoring/testing
 - What standard is applied?
- Proxy/surrogate consent
 - Who is a capable and legal surrogate?
 - Best interest vs. Substituted judgment
- Advance consent (for those anticipating loss of capacity)
- Appointment of subject advocates
 - **When is it in a person's interest to be in research?**
- Empowerment
 - Negotiation with 'groups'; who can represent?
 - Local reviews; community advisory boards
- Exclusion



“When Dr. Henderson comes in, everybody play dead.”