

To: The Editor  
Nature Magazine  
London, England

and

The Editor  
Science Magazine  
Washington, D.C.

Gentlemen:

We have written this short statement in the hope that it will initiate some discussion, in print and privately.

Are there any good experiments using human cells and viruses that should not be done?

Even if one chose to, one could not experiment on human beings. We accept, therefore, that a boundary exists past which we must indulge our curiosity. Work with somatic human cells in culture has proceeded without any apparent hesitation, defining the inner or "do-able" side of this boundary. For example, at the boarder today we find work on human-nonhybrid cell lines and heterokaryons, human tumor cells and putative human tumor viruses, extension of the host-range of avian and murine TV to the human host cell, while well within it are experiments on detection of inborn errors of metabolism in cells in culture and on transplantation of human organs.

Now a class of experiments with human germ cells (e.g., in vitro fertilization, cloning, introduction of "absent" genes, or gene therapy) is becoming possible. Should those experiments be on the same side as experiments on skin-biopsy cells, or should they be cloned with experiments on people?

A second related class of experiments involves the reverse Process: putting human genes or the nucleic acid of human viruses into cells of other species, or into prokaryotic cells. The dangers (e.g., of creating a tumor virus that can grow inside a bacteria like E.Coli which normally sits in the human gut) are

immense.

Before work continues on either of these two classes of experiments, we suggest a portion of any scientist's right to follow his nose without regard to consequences should be surrendered. We ought to ask ourselves whether the experimental results are worth the calculable and unknown dangers to ourselves and to the general population. We propose that in this field if no other, we are obliged to ask ourselves whether the experiment needs to be done, rather than if it ought to be done, or if it can be done. If it is dangerous, or wrong, or both, and if it doesn't need to be done, we just ought not to do it.

Precedents for regulation exist:

1. Federal grantees sign a paper promising that research on human subjects will follow detailed guidelines which safeguards the rights and health of volunteers and any other persons involved in the work.
2. Peer site visits precede most research grants.
3. Drug companies and medical investigators in this country must report their data to the FDA whether or not their technique or drug is eventually licensed for medical use.
4. Hospitals are licensed by state medical boards.

We suggest the following extensions of these precedents:

- (1) All laboratories that work on animal virus genetics, on human cells, on human viruses, or on any tumor viruses, must be licensed by the NIH-NCI, just as hospitals are licensed by medical boards. This procedure must extend beyond grantees to include: drug companies, foundations, universities, hospital research wings, and state and local health department laboratories.

CIA  
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In response to a general but vague concern about the dangers of the work we do, we have drawn up this set of comments and suggestions. We would welcome your response.

Bob Pollack  
Joe Sambrook

28/6/71

9/11

## General Laboratory Practice

1. Autoclave all garbage leaving the lab.
2. Use disposables wherever possible. After they are used, autoclave them and dispose into the regular garbage.
3. Never mouth pipette anything that has the slightest chance of being infectious. Use only bulb pipettes in sterile areas.
4. Do not allow any dirty stuff to accumulate. Store it in closed pots filled with an autoclavable disinfectant (7X is best).
5. Use laboratory coats whenever possible. The disposable paper type is best. If you use the regular sort, autoclave them before they go to the laundry.
6. Clean up all spills immediately and swab the area with disinfectant (Osyl is best, but Clorox 1% is cheaper and works).
7. Wash or shower in and out of the lab.
8. Ban all visitors from the working areas.
9. No eating, drinking or smoking in the lab.
10. If any of the laboratory staff is sick or pregnant or is taking immunosuppressive drugs (even for hay fever) he should not work.
11. All laboratory staff should have regular medical check-ups, and samples of their sera should be taken at six-monthly intervals.

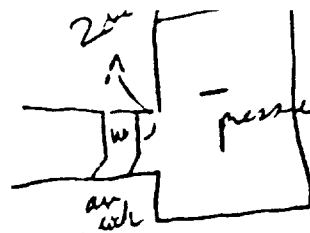
*distillate  
system  
checked -  
for use*

Biological Material within the Lab

1. Although all cells and cell extracts should be treated as if they were infectious, particular care is required in handling large quantities or highly concentrated virus stocks. Use gloves and put disposable diapers down on the working surfaces.
2. Utmost care is required in handling nucleic acids isolated from viruses or cells, since host range limitations are overridden, and the immune system is bypassed.
3. Biohazard tape, like radioactivity tape, should be used seriously or not at all.
4. Interspecific fusion of cells may possibly lead to the induction of latent viruses, or the creation of new strains of viruses. Any mixtures of cells or viruses must therefore be treated with great care.
5. Among the cell types commonly used in the laboratory, probably the most dangerous are cultures of primary cells. Try to use established cell lines wherever possible. Among these cell lines, probably the most dangerous are those that are known to carry RNA-tumor-like viruses (L cells, HeLa cells).
6. There may be a case for encouraging people to work on non-primate cells when their question does not require primate material.

*The argument that  
one cannot protect  
all risks does  
not ⇒ no  
pre should  
be taken*

## Laboratory Design



1. The laboratory should be as air-tight as possible (seal windows, have double-doored exits, etc.)
2. The input air should be filtered so as to be as nearly sterile as possible. (At least an air-conditioner, < uv-irradiator < electrostatic precipitator < coarse filter < Millipore Hepa filter.)
3. The outflow air should be sterile. Burning is best in combination with uv-irradiation and filtration. Aerosols are stable.
4. Critical handling areas for hazardous material (cells, viruses, nucleic acids) should not open directly to the outside, should be under negative air pressure compared with the rest of the laboratory, and should be equipped with uv lights.
5. There should be adequate wash-in/wash-out facilities. Minimally, these are sinks well stocked with disinfectants (PhisoHex, etc.); optimally, showers and changing rooms.
6. There should be a double-doored autoclave connecting the working area to the kitchen, so that all dirty material is sterile before the wash-up people see it.
7. Do not use horizontal flow hoods.
8. Have warning notices put on the entrances to the labs: no visitors, especially not children and pregnant women.
9. Biochemical work with biologically dangerous material is also dangerous. Desk centrifuges must have covers. The output from vacuum pumps of Spincos must pass through a trap (e.g., charcoal, N<sub>2</sub>O<sub>4</sub>.) Sonicators must be enclosed.

*Sonication of  
AV40 in 50ml  
1.1 ml*

Are there any good experiments using human cells and viruses that should not be done?

Even if you chose to, you could not experiment on human beings. You all accept, therefore, that a boundary exists past which you must not let your curiosity carry you. Work with somatic human cells in culture has proceeded without any apparent hesitation, so such work defines the inner or "do-able" side of this boundary. Now a class of experiments with human germ cells (e.g., in vitro fertilization, cloning, introduction of "absent" genes, or gene therapy) is becoming possible. Will you place those experiments on the same side as experiments on skin-biopsy cells, or will you group them with experiments on people? You have mobilization to consider this question before you begin the work.

A second related class of experiments involves the reverse process: putting human genes or the nucleic acid of human viruses with cells of other species, or into prokaryotic cells. The ethical problem here is minor, but the dangers (e.g., of creating a human tumor virus that can grow inside a bacteria like E. coli which normally sits in the human gut) are immense.

If you are going to work with either of these two classes of experiments, we suggest you surrender a portion of the scientist's right to follow his nose without regard to consequences. You ought to ask yourself if the experimental results are worth the calculable dangers. You ought to ask if the experimental techniques are over the boundary and amount to experimentation on people.

Finally, you ought to ask yourself if the experiment needs to be done, rather than if it ought to be done, or if it can be done. If it is dangerous, or wrong, or both, and if it doesn't need to be done, just don't do it. This is not censorship. You must accept a physician's responsibility if, by free choice, you work within these classes of experiments.

Precedents exist:

- (1) Drug companies and medical investigators in this country must report their data to the FDA whether or not their technique or drug is eventually licensed for medical use.
- (2) Hospitals are licensed by state medical boards.
- (3) Federal grantees sign a paper forswearing research on human subjects.
- (4) Site visits precede all research grants.

We suggest the following extensions of these precedents:

- (1) All laboratories that work on animal virus genetics, on human cells, on human viruses, or on any tumor viruses, must be licensed by the NIH-NCI, just as hospitals are licensed by medical boards. This must extend beyond grantees to include: drug companies, foundations, universities, hospital research wings, and state and local health department laboratories.
- (2) Peer group review of the physical state of a lab and of the overall competence of the investigators is now acceptable practice (e.g., site visits). A broad-based committee must be established whose purpose should be to hear the scientist who wishes to do these two classes of work justify his line of experimentation to the public at large. Scientific competence

is not at question. Rather it should be the burden of the investigator in these fields to demonstrate why he must do admittedly dangerous work.

- (3) Research in these two classes of work must be more public than similar work on other mammalian cells or viruses. A progress report should be filed with the NIH a few times a year, and it should be made public. No one should be permitted the freedom to do the first, most messy experiments in secret and present us all with a reprehensible and/or a dangerous fait accompli at a press conference.