

Human Subjects Protection Review:
A Good Idea gone Wrong. How to Fix it
and Turn it into a Competitive Advantage

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The Government of Ireland wishes to develop an advanced research and technology based economy for the future prosperity of its citizens. This includes health care. Ireland also wishes to be a compassionate society. Universities and Academic Health Centers are in a world wide competition for the best faculty and more research funding.

Research related to human subjects requires prior approval by a local review board (sometimes referred to as an IRB or institutional review board). The Irish government has come to the realization that they could have a competitive advantage in attracting researchers and funding if they could have an excellent review process. The same strategy could be used by individual Universities and academic institutions. The reason for this possible competitive opportunity is that the required process of organizational review and approval for research on human subjects is a fine idea gone wrong.(1,2,3) It started plausibly enough. The National Institute of Health (USA) wished to be assured that patients who participate in research they fund are informed, understand the possible risks and benefits, voluntarily choose to participate and have assurance that the information they provide is kept confidential and anonymity is assured. To this end, Academic Institutions receiving such funds must create a review process (an Institutional Review Board or IRB) to be assured that the research does provide such protection to subjects.(4)

The process typically requires the researcher to fill out an IRB proposal which includes information on funding sources, investigators, study design, consent documents, and procedures for confidentiality. These proposals are reviewed by IRB staff and faculty volunteers. Revisions can be requested and the process can take weeks or even over a year. With time this review process has spread through out the world and is being applied to all research using human subjects in these institutions. An organization like a drug company that does not take externally funded research does not have to comply with these rules. Researchers at institutions taking external funding are required to receive education and maintain certification to demonstrate that they understand the issues involved.

What could be more sensible? How could such a worthy undertaking get out of hand?

“If we knew what we were doing, it would not be research”

“You can’t organize research.”

“Test everything,hold fast to that which is good.”(5)

These quotes define that part of research which is totally encompassing, unpredictable, creative, exploratory and perhaps paradigm breaking. This is a very different stage in the scientific process than the large, carefully planned trials, described in detail, which are at the heart of successful NIH grant proposals and doctoral dissertations.

The day dreaming, asking a few questions, the pre-pilot study, thinking about this patient, relooking at the data, asking a new question, conversations in the corridor are descriptors of this exploratory mode of research which is totally consuming. If each one of these queries required IRB review a social or clinical

science researcher would be filling out 30 IRB proposals a day. In truly high intensity research institutions, every activity, every moment of the researcher's day are observing, discussing, asking, and carrying out thought experiments along with the large scale trials such as those funded by NIH. If one envisions research in this way, the current IRB review process applied without thought could be destructive.

One author (DN) was in a taxi in New York City. Because he is not interested in baseball, he asked the driver what the price of a taxi medallion was. To operate a cab in some cities you have to have a medallion. Drivers often want to talk about this important part of their life. The question is of scholarly interest. The medallion price reflects the present value of the monopoly conferred on the owner. This driver said that a medallion cost \$140,000. In five years he will have paid off his bank loan, own his medallion, then he will sell it and retire as a rich man to his family home in rural Jamaica.

Is this research? One definition of research is if it is generalized knowledge and published. With the publication of this paragraph, this conversation has been turned into research. If so, should IRB approval have been obtained? Should informed consent be obtained from the driver? This conversation happened about 40 years ago and if the driver were still alive he might be about 100 years old.

Have I maintained confidentiality so this driver is anonymous? Any reader can write to the NIH and declare that I violated IRB policy. If NIH agreed that the above violation was egregious, they could halt all NIH funding to my university. This paragraph of civil disobedience, if it is that, could be costly indeed.

The zone of dishonesty.

If the benefit to the researcher for obtaining the funding for a research project is large enough and the cost of IRB approval is proportionally small then approval will be sought. What about research where the benefit is smaller than the effort required for review? Two things can happen. The research is not done. The small grant is turned away as now not being worth it. The second response is dishonesty. This project is defined as non research. We will not publish the results of our pre-pilot study and therefore it is not research. We will look at the data and, if our hypothesis looks to be supported, we will apply for IRB review. In hospitals this activity can be redefined as "quality improvement" or just "good patient care" This will probably suffice until some one decides to publish the results. That would define it as research. The harm or benefits to patients could be the same what ever label is used. This regulatory system is based on a logic that does not fit many circumstances and is not based on actual measured harm averted.

Quality Improvement in Health care.

Every health care institution is expected to be working to improve care with the goal of making care better. Plan, do, study, act (PDSA) cycles are employed to improve processes so that they are better now than before. Outcomes should be measured and benchmarked against other institutions. Multiple small incremental changes are tried and evaluated over time. (6) As such this does not necessarily come under the IRB review process. However if the team finds a nice result they might wish to tell others about it through a publication. This makes it research and for some requires IRB approval. This approval can only be given prospectively and not after the improvement project has started. Here is another domain where the IRB logic does not fit reality. (7,8,9)

“Sticks and stones will break my bones, but names will never hurt me.”

Anonymous Children’s Rhyme

What is harm? The nice feature of this rhyme is that it draws so bright a line between harm and no harm that every child can see the difference. IRB’s are not so fortunate. Actually it might be easier to reduce harm, but that is not what IRBs do. The goal is not to eliminate harm, but rather to be assured that subjects understand the possible harm and that the risk they undertake are proportional to the possible benefits.

Doctor Smith tells patient Jones: It may be that this blood test will tell us if this drug will work for your arthritis. I do not want to raise false hopes but this might work. If my thinking is right I will certainly tell my colleagues (consistent with my Hippocratic Oath to teach).

Is this good care or research or both? If the result is generalizable and if “telling my colleagues” is equivalent to publication, then IRB approval would be needed. If so, how is harm defined? Every child knows that being stuck with a needle is an “ouch”, but here this depends whether the experienced phlebotomist or the student draws the blood. What harm could “false hopes” engender? It does not have to be this way.

The many ways to promote good and reduce harm.

Society has evolved many ways to promote good behavior and prevent harm. See Table 1 which lists 13 theories or perspectives on the drivers of good, appropriate behavior. A number of these theories have the support of professional groups, academic departments and organizational structures promoting their ideas. These theories exist because they have face validity to many and are often supported by research evidence. First order thinking about the right way to achieve the goals of IRB calls for thought about what is the combination of these social forces to best achieve the goals of efficiency, productive research and patient protection. The wrong combination can lead to bizarre results and unintended consequences.

Table 1
Theories of the Drivers of good social behavior

Field, description	Mechanism	Comment
The law	The sanctions provided by civil and criminal law	Relevant for major failures malpractice
Political Science	Government laws and regulations Driven by public opinion, legislators And administrative regulations	IRB regulations as they now exist
Economics	The invisible hand of competition Rewarding good performance in the long run. Monopoly power is destructive	The power of choice Recommended here.
Social Sciences Sociology Cultural Anthropology	Culture and socially defined roles promote preferred behavior	Arguably the strongest driver, but it can not be legislated
Psychology	Personal attitudes, perception and motivation to excel	Deming built his theory of quality improvement on this assumption. The power of education
Social Psychology	The social pressure of personal Relationships	The desire to help.
Management	Leadership, hierarchy, organizational Policies and procedures	The organizational context of IRBs
Molecular biology and Evolution	Behavior patterns driven by DNA and survival	Parent child bonding as a template for social behavior like the doctor patient relationship
Accreditation	External review of standards	AAHRPP for IRBs
Public Performance Reporting	Creating social pressure to perform	Made possible through the spread of computers

Religion	True religious commitment drives good behavior	Over most of human history this has been the dominant theory
Professionalism	An ethical education, qualifications, licensure and membership oaths	The Hippocratic Oath The philosophy of medical education
The Public media	watch dog function exposing bad behavior	See references 5,6 A vivid story drives public opinion

This is not an exhaustive list

Consider bank robbery. It is a crime. It is clearly defined. The harm can be measured in dollars stolen. If you do it you go to jail. What if this approach were used for human subjects protection? Harm subjects and you are punished. What if the current human subjects review process were applied to bank robbery? You would have to pass a written exam before you could enter the bank and get permission each time you entered after appropriately completing of a long questionnaire. There are organizational methods to promote appropriate behavior. Harm people and you are punished. Create a corporate culture of humaneness. Such a strong culture is probably the most powerful way to achieve such day to day good behavior. Unfortunately this does not fit the regulatory tool kit and mind .Universities want to reduce racial prejudice and end sexual harassment. Think of applying the IRB review process to these harms. Think about these approaches to reducing t harm and how these methods would work if applied to human subjects review. Hospitals want to avoid mistakes such as wrong leg amputations. Compare how these processes for harm reduction and safety could be applied to human subjects review.

There are legal remedies; criminal and civil. Purposely hurting people is a crime. The victims can sue.

Harm insurance could be bought by the researcher to compensate for injury, not unlike malpractice insurance. The university could buy this for all its researchers. Researchers could be bonded. Researchers could have medallions like taxi owners which they will forfeit if they cause unaccepted harm. Accreditation is another option. There is an accreditation organization for IRBs; the Association for the Accreditation of human Research Protection Programs or AAHRPP. (www.aahrpp.org) Some IRBs use this accreditation to demonstrate their excellence to the world. The emphasis of this accreditation appears to be on having appropriate policies in place and adhering to them. This is where hospital accreditation was from the 1920s to the current century. Now The Joint Commission on Accreditation of Healthcare organizations is more focused on outcome measures publicly reported and compared.

There are market solutions. Patients come to teaching hospitals because on balance they prefer this care which mixes research, teaching and care. Too much harmful research and patients will go elsewhere.

Research institutions might be allowed and invited to create their own mix of these methods. The outcomes of these alternatives should be measured and compared. One key to improvement is to change this process from a rules based approach to an outcome based approach. This would require measuring the results of the review process. What is to be done while waiting for the results of such comparative trials between regulatory approaches? To the Optimist problems provide opportunities.

Every research institution should have on its web site a section that says “We have the best human subjects review process, because...” This will happen for the following reason. Administration will not do this proactively, but rather to respond to pressure. Every researcher considering a job at this institution should ask this question. Every private granting agency should ask this question. The parents of every prospective student should ask this question. When notable research institutions see excellent junior faculty leave because they can not get their research done, when Drug companies take their research funds to another country, and graduate students go to the competing universities, eventually administration will respond.

A recent study of the American Board of Internal Medicine sought IRB review from 46 academic health centers for the identical evaluation of an educational program. They reported that 4 withdrew, 8 received expedited review, 4 found the study exempt, and 30 were reviewed. This review process took from less than a week to 56 weeks with a mean of 18 weeks.(11, 12, 13)

The rapid turn around centers are at a competitive advantage for research funds. This points out the lack of agreed upon policies for approval. Clinical laboratories use standardized specimens to check their test results and calibrate them with other labs and against national standards. One could imagine a similar approach for IRBs

A good test question for prospective students and parents to ask is the this:

Suppose the following were to happen here.

In an undergraduate seminar on “Introduction to business administration” The instructor asks several students to interview a graduate about his successful business career. How did he do it? The graduate is flattered and pleased. The students write up a report, which is passed on to the college’s alumni magazine and published. “Recent grad makes good: I owe it all to my mother and my education” the article says. An anonymous person writes to the university IRB to say that this is research on a human subject without IRB approval. This triggers an IRB investigation.

What would happen here? Back up your answer with data.

What if the reply was as follows: We would require IRB approval (That our medical school's NIH funding is more important than good undergraduate education goes unspoken) This seminar lasts for six weeks and our review process takes three months. The faculty member was disciplined and not rehired and the students had critical reports entered into their academic records greatly reducing their chances to get into graduate school. The incident was reported to the Federal Government. It does not matter that no one was harmed and everybody benefited, we follow the rules.

The university with the best answer to this question and others like it should attract this good student.

Measuring and managing the process.

For this process to work well several goals are desired.

The value of research in the organization should go up.

The costs of the review process should go down This includes the costs of delay (An 18 month delay in an African based HIV/AIDs trial can be measured in deaths caused by delay of otherwise unavailable treatment) The cost to the IRB staff, volunteers and office. And the opportunity cost to the researcher for time involved. In some cases IRBs price discriminate, charging drug companies thousands of dollars for the review and less or nothing for others.

The amount of uninformed risk and harm for subjects should go down. May we suggest the following metrics as a place to start.

The number of accepted scientific posters by researchers per week compared to the expected number tracked over time. It is creative research that could suffer from this process and posters are closer to measuring this than is the amount of funded research. The number of new subjects recruited into current studies week by week compared to the expected numbers and report this information in real time.

Survey researchers about the process. How many hours did this application take to complete?

What projects did you not do because the review costs were greater than the benefits?

Measure the IRB office costs per review and the length of time from submission to acceptance.

How many punishments and warnings have been handed out for what causes?

The hardest to measure is the process outcomes of unaccepted harm. Patients are regularly surveyed about their satisfaction with care. Add an additional question to this survey. On a five point scale, how willing would you be to participate in clinical research which might improve care for patients like you?

Clinical laboratories check their equipment and methods by comparing their measurements to many other laboratories using identical samples with a known true answer. If the lab's result differs it is time to make corrections in the process. Do the same for a standardized IRB application to see how local results differ. There are some examples of project directors seeking approval from 30 different organizations for the same study and getting very different responses in terms of time to approval.(11, 12) Unlike the clinical laboratory test samples there

are no gold standard answers. Researchers considering doing research should ask to see the results of such bench mark comparisons. They should know that what other universities approve in a month had a year long delay here.

Put all this information on the university or national web site. Have a designated person in the university hierarchy who has the explicit assignment of increasing creativity, lowering review costs and reducing unaccepted harm. Have an ongoing quality improvement team working on improving the measured outcomes by improving the process. A good IRB should be doing its own quality improvement research on its process and outcomes.

A competitive Advantage

Universities all over the world are competing to be the best. Good universities are seen as the power behind an advanced technological economy. The market for junior researchers and students has become global. Some Universities are fortunate enough to be able to compete with new wealth: for example in Dubai, Singapore, Shanghai, and Alberta. Other countries can not rely on such wealth. One of these is Ireland which aspires to have a high technology research driven economy for the benefit of all its citizens. Ireland also wants to be a compassionate country where patients are willing to help improve the care of fellow citizens. The government has come to see that an excellent human subject review process could be their competitive advantage. Now some research is funded for four years rather than three to allow time for the IRB process to be carried out. That implies that there could be a 25% saving in the costs of research. By raising this to the national agenda, convening a national task force to examine these issues and beginning to collect data, they may be on the way toward being a country which attracts international students, faculty and funding. In Norway a single review is good for the entire country.(1) Their IRB process can be done on line. If researchers leave the USA to go to Norway and Ireland perhaps NIH will take notice.(14) NIH might fund some pilot projects from research universities which would like to develop alternative approaches. Spending money to solve this problem is nice, but it pleases us to know that aspiring graduate students and junior faculty could lead this transformation toward a more sensible process by asking tough questions, demanding data based answers and making choices.

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