PAPERS

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Bioterrorism and bioethics: Challenges for industry, government and society

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Abstract

The emerging threat of bioterrorism raises important challenges for the biotechnology industry. Not only do new ethical issues arise for companies seeking to take advantage of opportunities for product development; so too must industry continue to grapple with longstanding issues that arise from advances in human genetics and medical research. No longer will it be sufficient to focus bioethical attention only on whether the 'ethics' of a clinical trial is as good as the 'science' (an important justification for pharmaceutical and biotechnology research). The threat of bioterrorism requires that economic, political and ethical considerations be given increased attention.

Keywords: *bioterrorism, bioethics, research, industry, health policy*

INTRODUCTION

In February 2002 many of the world's biotechnology companies, venture capitalists and scientists met in Zurich for a meeting called BioSquare. At the historic Meisen Palace, the American Ambassador to Switzerland opened a unique evening panel discussion that focused on the ethical, legal and scientific issues arising from the threat of bioterrorism. Coming just four months after several anthrax-laced letters were sent to members of the US Congress, the public and the news media, the issues discussed that evening could not have been more timely.[1]

One of the issues addressed by the panel (of which I was a member) was whether it is ethically defensible for biotechnology companies to shift their emphasis from traditional drug discovery and development for common diseases, to preparing tests, antibodies and vaccines in the global fight against bioterrorism. Several questions logically followed: Would it appear unseemly for companies to redirect some or all of their research portfolios from drug discovery and development to bioterrorism preparedness? How would companies engaged in similar areas of research respond when some choose to redirect their resources while others choose to stay on their current course? How will competition be affected? More generally, how might the increased attention on bioterrorism preparedness affect domestic priority setting? In this paper I respond to these questions and outline some of the key ethical issues facing both the public and private sectors as they jointly prepare to address them.

BIOTERRORISM: DEFINITIONS AND ACCELERANTS

At the time of this writing (September 2002) it is still not certain whether the anthrax letters – and more specifically the five deaths attributed to these letters – were acts of terrorism or not, let alone whether they were foreign or domestic in origin. Current scientific analysis suggests that the anthrax was of relatively recent origin and had probably been weaponised in one of a small number of US laboratories. Nor has the US Federal Bureau of Investigation determined whether or not the letters could be strictly defined as acts of 'terrorism'. This is not surprising given the ongoing debate about the difficulties inherent in clearly defining

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'terrorism'. For example, Adam Roberts has noted that while its original usage as described in the *Academie Française* in 1798 referred to a 'system or rule of terror' – including the use of terror by a government against its own citizens primarily associated with political assassination – terrorism now appears in several varieties:

The definition of 'terrorism' has evolved over time

> In the half century after the Second World War, terrorism broadened well beyond assassination of political leaders and heads of state. In South East Asia, the Middle East and Latin America there were killings of policemen and local officials, hostage taking, hijacking of aircraft and bombing of buildings. In many actions civilians became targets. The causes espoused by terrorists encompassed not just revolutionary socialism and nationalism, but also religious doctrines rejecting the whole notion of a pluralist world of states.[2]

But whether or not the anthrax letters meet a strict or flexible definition of terrorism misses the point. The threat alone, coupled with growing evidence of the scientific capacity to develop such weapons, has elicited increased attention from governments, the private sector and society. In the US a major spending bill, 'The Public Health Security and Bioterrorism Preparedness and Responses Act of 2002', was passed by the US House of Representatives by a vote of 425–1; the Office of Homeland Security was established (with discussions ongoing to elevate this cabinet level entity to the status of a Department); and personal security – including increased sales in gas masks and bomb shelters – has become a growth industry. A 9th July, 2002, *USA Today* survey found that 54 per cent of those polled believed that their community's public health system was not prepared to respond to a biological or chemical terror attack. These actions, when coupled with the science arising from the Human Genome Project, provide some explanation for why the present threat of bioterrorism could not have emerged at a better (or worse) time.[3]

Bioterrorism preparedness has elicited public and legislative respause

Consider that in 1995 Barry Bloom predicted that 'The power and cost effectiveness of modern genome sequencing technology mean that the complete genome sequences of 25 of the major bacterial and parasitic pathogens could be available within 5 years'.[4] A little more than five years later Fraser and Dando reported that this goal had been surpassed.[5] Indeed, just two years prior to the first anthrax-tainted letters, then-President Bill Clinton announced in a White House ceremony that the rough draft of the human genome had been sequenced – a 'big science' event that rivalled the *Apollo* moon landings or the development and detonation of the atomic bomb. Genome science certainly adds to the scope and power of bioterror; but it also may also turn out to have an unintended accelerant effect on the public conversation about bioterrorism, namely the tendency towards a type of genetic exceptionalism: the reduction of medical and health information to its constitutive genetic basis. As society ponders the effect of this new threat, it will be important to keep it in perspective.

BIOETHICS AND BIOTERRORISM

Bioethics, generally understood as the study of moral problems in medicine, research and policy, has a long history of emphasis on the moral obligations of individuals (primarily healthcare providers and scientists) and an emerging set of common values, principles and ideals. While there is a healthy and productive dialogue within the academic bioethics community about the sufficiency of various theories or approaches to resolving significant moral problems, there is considerable agreement that whatever the approach – whether based on a set of universal ethical principles, human virtues or other moral perspectives[6] – the *object* of morality is to engage in the moral life. While approaches may differ, many believe that

The 'common morality' is a set of shared beliefs

a 'common morality' does exist that binds all persons in all places, and that human rights are the favoured form of such a universal core of morality.[7] For example, irrespective of culture, ethnicity, political orientation or religion, few would disagree that non-maleficence (avoiding harm) is a widely – even universally – accepted value.[8]

Similarly, there are numerous statements, codes and guidelines intended to reflect wide agreement on particular bioethics issues. Some of these are specific to the conduct of research involving human subjects.[9] Other statements, such as the *Universal Declaration on the Human Genome and Human Rights*[10] are aspirational in tone but enjoy the support of the member states of the United Nations. Few would disagree with the letter or spirit of Article 1 of the Biological Toxic Weapons Convention of 1972:

> Each State Party to this convention undertakes never in any circumstances to develop, produce, stockpile or otherwise acquire or retain 1. Microbial or other biological agents, toxins or whatever their origin or method of production, of types or in quantities that have no justification for prophylactic, protective or other peaceful purposes.

Agreement about common principles, beliefs may not be shared

Agreement notwithstanding, however, most civilised societies recognise that the threat of bioterrorism challenges contemporary bioethical analysis precisely because those who would engage in it do not share in a common morality that abhors violence against humanity. The history of state-sponsored eugenics programmes, from Nazi Germany more than a half century ago to the more recent atrocities revealed in Rwanda and the former Yugoslavia are evidence that while a set of principles, theories or approaches can describe why these actions are wrong, they alone will not prevent abuse. It is somewhat worrisome, however, that examples abound of the use of deadly bacteria or viruses used as instruments of war. The number of countries that have studied or used deadly biologicals – Germany, France, Japan, the United States, the United Kingdom, South Africa, the former USSR and Iraq[11] – is as diverse as the list of diseases used – anthrax, smallpox, plague, botulism, tularaemia, and viral haemorrhagic fevers, such as Ebola; diseases determined by the Centers for Disease Control and Prevention to present the greatest risk to society. (They are considered Category A diseases because they cause high death rates or serious illness, are relatively easy to spread, could cause public panic or require special steps for public health preparedness.)

Any morally sensitive person can explain that terrorist acts that are intended to injure or kill innocent persons violate all reasoned positions that defend human rights. What is needed is a set of actions, policies and behaviours that decrease the perceived need to use this method of political action against individuals and states. This requires sensitivity to cultural, political, economic, religious and moral considerations – and to date the effort to achieve consensus on such policies has flummoxed philosophers, theologians and politicians alike. Yet, this is precisely the point at which institutions in civil society can play such a crucial role.

BIOTECH ETHICS

The global biopharmaceutical industry recognises that there are new opportunities to develop diagnostic tests, prophylaxis and treatments in response to biological and chemical warfare. Yet these very opportunities present certain ethical challenges, and walking the line between appropriate ethical behaviour and opportunism requires skill. Writing in the January 2002 issue of the entrepreneurial trade journal *Start-Up* Deborah Erickson summarised the risks and opportunities for companies considering moving into the marketplace in aftermath of the 11th September, 2001, attacks:

> Growing awareness of the likelihood of bioterrorism is revealing what some biotechnology executives consider 'inescapable opportunities' to protect the general public as well as military personnel. Given the variety of vulnerabilities becoming evident, it's no wonder that executives across the biotechnology industry are considering how they might leverage their know-how in new ways to support national defense . . . Yet many of the opportunities in biodefense seem limited by the fact that the government would be the only customer.[12]

Industry has the capacity to respond to bioterrorism but must do so responsibly

No one doubts that industry has the capacity – working alone or in partnership with government – to develop the basic science and medicines needed to respond to the threat of biological and chemical warfare. But with opportunity comes ethical responsibility. Among the most challenging of these responsibilities is the obligation to use valuable resources wisely. Companies that choose to redirect their product pipeline to bioterrorism and away from other areas should be prepared to defend this decision, especially in light of the opportunity cost to other diseases whose funding sources and priority status will be negatively affected. This is a matter of fairness in the distribution of scarce resources. Representative of the concern that needed resources may be siphoned away from health research is the comment by Mohamed Ahkter of the American Public Health Association who stated: 'Prior to 9-11 we were focused on the HIV-AIDS problem, focused on teenage pregnancy, focused on immunizing kids . . . Those things are now on the back burner.'[13] History recalls a time in the USA when children and pregnant women were 'therapeutic orphans': excluded from clinical trials because of a reluctance to expose them to the risk of research.[14] While this situation may be remedied by new Food and Drug Administration (FDA) regulations that encourage research on children and women, the main ethical issue – namely that it is an injustice to deprive certain persons or groups of the potential benefits of research directed at their disease or condition – may emerge in discussions about research on bioterrorism.

Public health priorities may be affected

It is a curious debate: if resources are redirected to research on problems related to bioterrorism, will these resources be less available for research on (for example) current and known health problems – resulting in society as a whole becoming the next therapeutic orphan? To address this issue convincingly, two objections need to be overcome.

The first is that since there is a finite amount of research resources, such that any dollar directed *towards* one area is automatically diverted *away* from another, research on bioterrorism problems is somehow taking money away from more urgent and tangible ones. It is hard to say whether this is true, particularly given the significant amount of research funding appropriated to infectious disease research that focuses both on bioterrorism preparedness *and* basic science. Many agencies and department of the US government have increased funding for bioterrorism research. Illustrative of this was the proposed increase of US$1.2bn in bioterrorism funding at the National Institute of Allergy and Infectious Diseases, as part of the *The NIAID Counter-Bioterrorism Research Agenda,* described by the US Health and Human Services Secretary Tommy Thompson as 'an accelerated program to expand research on bioterrorism agents and to quickly develop new diagnostics, drugs and vaccines to protect the public.'[15] The Pharmaceutical Research and Manufacturers Association (PhRMA) announced on 3rd April, 2002, that: 'infectious diseases – both those that could result from a bioterrorist attack and those that occur naturally – are the target of 256 medicines and vaccines in development'.[16] Given that the increased emphasis on bioterrorism-related funding is found in both public and private sector priorities, it is hard to claim that

companies are somehow taking advantage of bioterrorism to develop products at the expense of others in their pipeline.

Progress in science comes with ethical responsibilities

The second objection is more pervasive, namely that the risk of bioterrorism provides an opportunity for progress in any area of science that previously was considered unimportant, dangerous or somehow contrary to the value society assigns to research in general. Much as I am sympathetic to the caution that the late philosopher Hans Jonas offered when he argued that 'progress is an optional goal, not an unconditional commitment, and . . . its tempo in particular, compulsive as it may become, has nothing sacred about it',[17] I find that I am equally sympathetic to the view that encourages development of the basic and applied science that increases the capacity of humanity to not only survive, but flourish. Holding both views means that the social activity of research – whether supported by public or private sources – carries with it an obligation to deploy resources wisely and not frivolously. Such a view explains why it is necessary to give good reasons why society's resources – including the human resources of volunteers and patients who might be enrolled in research – should be expended and for what cause. (I turn to this topic in more detail below.)

Industry has condemned the misuse of biotechnology

There is some evidence that the industry recognises that it has such responsibilities regarding the justification of research. For example, the Biotechnology Industry Organization (BIO) released a 'Statement on Ethical Use of Biotechnology to Promote Public Health and National Security and to Fight Against Bioterrorism'.[18] The BIO statement condemns the use of bioterrorism by reaffirming 'its long-standing policy opposing the use of biotechnology to develop weapons' and outlines its ongoing support for biotechnology research 'to promote and protect the public health and national security'. The PhRMA released its own statement summarising its official positions on compliance with the Biological Toxic Weapons Convention (BTWC) including recommendations for strengthening the BTWC.[19] Both statements have in common an attempt to strike a balance between safety and security on the one hand, and promotion of research and development on the other. These are important statements of commitment, and to the extent they are effective, are deserving of public support.

But much work still needs to be done to translate these somewhat aspirational policies into action. Industry action on bioterrorism will have to occur against the background of public perception that some companies have not always taken seriously their commitment to ethical behaviour. For example, concerns have been expressed about the ethical standards for conducting research both domestically and internationally. Internationally, criticism has been directed at the pharmaceutical industry regarding the '10/90 disequilibrium' problem: of the roughly US$50–60bn spent on health research internationally, only 10 per cent is spent on health problems affecting 90 per cent of the world's population.[20] The public perception may extend to the sources of support for some research. For example, while relatively unknown to the general public, many companies have had long-standing military contracts with the US Government's Department of Defense: the Defense Advanced Research Projects Agency (DARPA) spent nearly US$170m on biological defence in 2001.[20]

These examples illustrate only that industry action in ethically charged areas always runs ethical risks. Industry will need to make clear its case for adopting a business plan that responds to this changing environment. How can this be done? First, industry can be clear about how it sets priorities. Given the 'inescapable opportunities' that exist, industry will need to explain how the research and development it funds meet both current and long-term threats without appearing to merely capitalise on those economic opportunities. Second, it

Industry must exercise humility in advising on foreign policy

need not adopt the apparent strategy of the federal government that seems to link many policy decisions (domestic and foreign) with bioterrorism. Third, the biotech industry must exercise restraint in becoming an instrument of foreign policy construction. In his keynote address to BIO's annual meeting in Toronto, Carl Feldbaum made a case for industry formulating 'its first foreign policy, one which is cognizant of the miserable judgments and mistakes of other industries – and avoids them'.[21] Given the difficulty governments face in developing foreign policy in this area, industry must exercise a certain humility with respect to the expertise it can lend; limiting it to areas of health, economics and science. For example, industry runs the risk of appearing opportunistic and disingenuous by offering views about what is or is not in the national interest.

RESEARCH INVOLVING HUMAN SUBJECTS

Human subjects research on preventive strategies present certain challenges

Many have recognised the need to reform the federal system for protecting human subjects in research.[22–25] For example, the National Bioethics Advisory Commission (NBAC) recommended that the US federal system for the protection of human subjects needs to be replaced with a single, comprehensive set of rules that covers both publicly and privately sponsored research, and overseen by a national office.[25] Research on preventive strategies and possible cures for bioterrorist attacks presents some unique problems: how can vaccine studies be ethically conducted when the risks to subjects are so high (the possibility of serious disease or death from the agents being tested)? How can the informed consent of volunteers be obtained? How, in light of the federal research ethics rules that discourage institutional review boards (IRBs) from assessing the risks to persons other than the subjects involved in the study itself, can the risks to society be fully assessed? Given the lessons learned from the investigation and reports on experiments conducted with conscripted subjects uncovered by the Advisory Committee on Human Radiation Experiments (ACHRE),[22] it will be difficult to design Phase I and II studies involving human exposure to toxic or lethal pathogens. This problem was alleviated to some extent with the recent adoption of proposed FDA rules that had been languishing since 1999 that amend certain human subject protections. The new rules permit testing the efficacy of new drugs or biologicals

> . . . used to reduce or prevent the toxicity of chemical, biological, radiological, or nuclear substances when adequate and well-controlled efficacy studies in humans cannot be ethically conducted because they would involve administering a potentially lethal or permanently disabling toxic substance or organism to healthy human volunteers without a proven treatment in field trials (assessment of use of the substance or product after accidental or hostile exposure to the substance) are not feasible.[26]

One of the consequences of these new rules is that the majority of bioterrorism research will be carried out on animals, or be conducted with cellular-based and computer-aided modalities. But this situation is not without its own set of important ethical issues, particularly in studies involving the use of human biological materials.[27] Guidance is still lacking regarding the issues associated with informed consent for the collection, storage and prospective future use of these samples. Hundreds of millions of samples exist in the nation's pathology laboratories and repositories – many collected without research-explicit informed consent – all of which may be valuable resources for bioterrorism research; and yet if these samples are identifiable it is incumbent upon federally funded researchers to obtain informed consent from the sources for research use. This may prove a daunting task on feasibility grounds, let alone whether people would

Risk/benefit assessment

Informed consent for research on tissue samples

consent to the use of their samples for military research.

The problems for prospective collection of samples for future use raise just as profound a question: if an individual gives a sample that is collected with the intention of using it for future medical research (whether research in general or research on a specific disease or condition), how will researchers disclose the possibility that this sample may be used for bioterrorism studies?

Oversight is difficult under conditions of secrecy

In addition, the nature of this research means that many of the studies will be carried out in secret. In the absence of clear policy regarding classified research in the USA it is difficult to see how federal oversight of protocols involving the testing of bioweapons can be managed within the existing public IRB oversight system. Given the growing use of these committees, it goes without saying that the common problems some of them face – overwork, under-funding, inadequate training – will make local review of studies involving bioterrorism-related matters more difficult.

CONCLUDING THOUGHTS AND NEXT STEPS

Science has a long tradition of ethical responsibility, and industry is making important strides to develop comprehensive approaches to addressing some of the most vexing bioethical problems. But the threat of bioterrorism is not a singular problem that can be solved solely by comprehensive research guidelines and increased research funding, necessary as these activities would be. Bioterrorism simultaneously bridges domestic and foreign policy, national security and public health, science and medicine, business and technology; it engages business ethics, bioethics and environmental ethics. One expects that the leadership exhibited by industry in the search for the causes of, preventive measures and cures for disease in this environment will be undertaken with a renewed commitment to ethical integrity.

Bioterrorism bridges many areas of public policy

But there are a number of concrete steps that can be taken. The issues discussed above highlight the dilemma faced by all classified research in an open society: how can public accountability for federal research dollars be balanced against the state's interest in preventing the unintended consequences of the misuse of this same research? This would be an appropriate time for industry to exercise its leadership position to harmonise research regulations and guidelines to ensure that all science operates under a transparent and understandable system for the protection of human subjects. A laudable first effort would be to implement the relevant recommendations of ACHRE and NBAC relating to the oversight of research involving human subjects in the USA. For reasons arguably similar to (but no less controversial than) those for convening military rather than public tribunals to try suspected terrorists, one can imagine that such protocols may be undertaken under secret conditions to protect the 'national interest', or if not in secret then at least carried out by a single national panel similar to the Recombinant DNA Advisory Committee convened by the US National Institutes of Health.

A second step would be to devote resources (public and private) to study the ethical, legal and policy dimensions of bioterrorism preparedness, analogous to the Ethical, Legal and Social Implications (ELSI) research programme carried out under the auspices of the Human Genome Project.[28] A similar effort is needed to support an infrastructure of researchers to anticipate and address the ethical, legal and social consequences of research, development and policy in this area. If the threat of bioterrorism is important enough to devote significant societal resources to preventing its use, it would be unfortunate if resources were not equally devoted to understanding the social, political and ethical consequences as well. In this regard, the obligation falls on many shoulders, public and private alike.

A third step is to re-think the structures for examining the impact of technologies

on society. One innovative proposal was made by the Commission on National Security/21st Century, a bi-partisan commission chaired by former Senators Gary Hart and Warren Rudman. In January 2001, nine months before the anthrax letters, the commission released its final draft report in which they argued that:

Proposal to create a National Advisory Commission on Bioscience

> We need an institution that provides a forum for the articulation of all interests in the implications of the new biotechnology and other new technologies. Without such a forum, it is doubtful whether public confidence in the progression of bioscience can be sustained amid all the controversies it will surely provoke over the next 25 years. We need a place where government officials, scholars, theologians, and corporate executives can meet regularly to discuss issues of concern. We need an institution that can deal effectively with the other governmental agencies regularly involved in these issues; otherwise its findings will remain peripheral to the actual processes of decision. *We therefore recommend that Congress transform the current National Bioethics Advisory Commission into a much strengthened National Advisory Commission on Bioscience (NACB).*
>
> The NACB should focus on the intersection between bioscience, information science and nanotechnology for, as we have said, it is this intersection that will form the pivot of major transformation. Such a change will affect a wide range of public policy issues, including health, social security, privacy and education. Nor should the commission's mandate be limited to ethical questions. It should concern itself, as well, with the social and public safety implications of bioscience.[29]

The NBAC has already been transformed into another bioethics commission, the President's Council on Bioethics (PCB), but nothing in the Executive Order creating the PCB[30] leads one to conclude that they will be able to engage this topic with both the deliberateness and the speed necessary to assist policy makers. Reading the Hart–Rudman report again 18 months later, there is a profound prescience to their concerns. They imagined what many have been reminded of all too starkly in the past year: that bioterrorism blurs the lines between public health, medical research, technology development and foreign policy; that bioethics, biotechnology and the welfare of the biosphere are intimately connected.

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