

Chapter 2

Experiments of Concern

Human knowledge and understanding of the natural world is, presumably, both desirable in itself and a means to the provision of other human goods, such as health and longevity. Moreover, human freedom, including freedom of intellectual inquiry, is agreed on all hands to be an intrinsic human good. Accordingly, there is a presumption in favour of allowing research in the biological sciences, as there is in other areas of human knowledge. In short, research in the biological sciences is morally permissible, absent special considerations in relation to specific kinds of such research. What, if any, research in the biological sciences is morally impermissible?

Research in the biological sciences undertaken for the purpose of weaponising biological agents so that they can be used to kill or cause illness in human populations is presumably morally impermissible, whether the research in question is undertaken by state actors, (non-state) terrorist groups, criminal organisations or malevolent individuals. So much is proclaimed in the Biological Weapons Convention (BWC), notwithstanding the fact that arguments have been used from time to time to justify the use of biological weapons in the context of a just war. It has been argued, for example, that some biological weapons are more “humane” than some conventional weapons. It has also been argued that biological weapons development during peacetime may play an important role in deterrence [79]. It is not within the scope of this report to discuss the moral complexities arising from the use of various forms of weaponry, albeit this is an important and somewhat neglected topic. However, we note that, in so far as biological weapons are a species of weapons of mass destruction (WMD), there is a *general* moral objection to their development and use, namely, that inevitably they target civilian populations and not merely combatants. As such, they violate the so-called *jus in bello* condition of just war theory; the condition that, among other things, gives expression to the moral principle of civilian immunity in war.

An analogue of the moral principle of civilian immunity in conventional wars between nation-states is the moral principle not to deliberately target civilians that is adhered to by some—but obviously not all—*non-state* actors engaged in armed struggles. For example, for most if not all of its history the African National Congress (ANC) in its armed struggle against the apartheid government in South Africa adhered to this moral principle; military and police personnel were regarded by the ANC as legitimate targets but not ordinary civilians. On the other hand, terrorist

groups such as al Qaeda obviously violate this moral principle, as would any terrorist group using biological weapons as WMDs.¹ Naturally, terrorist groups might use “new generation” biological weapons that are able to target particular individuals, e.g., a biological weapon of assassination. However, use of such a biological weapon would not constitute use of a WMD.

In addition to the general concern that biological weapons may serve as WMDs is the concern that their effects are, generally-speaking, hard to predict and control. The fact that biological weapons are relatively inexpensive and easy to produce (in comparison with other WMDs) also means that the potential for an arms race in the context of biological weapons is especially worrisome. These features constituted central rationales behind the BWC.

At any rate, our assumption in this report is that research in the biological sciences undertaken for the ultimate purpose of stockpiling or using weaponised biological agents is in fact morally impermissible. The moral problem that now arises concerns research in the biological sciences that is not undertaken *by the original researchers* for the ultimate purpose of stockpiling or using weaponised biological agents, but might be used by secondary researchers (or other users) for these impermissible purposes, i.e., the moral problem presented by so-called dual-use dilemmas.

As already noted, a particularly morally problematic species of the dual-use dilemma arises in the case of research undertaken to enable the assessment of the potential threat posed by the biological weapons (BW) of other nation-states (including nation-states who might seek to use BW as instruments of terror against civilian populations) or the biological agent focused projects of non-state terrorist groups. Such ‘threat assessment’ research involves experimenting with the offensive applications of pathogens so as to determine appropriate counter-measures. In order to develop defences against a putative BW agent, it is necessary to understand:

- The underlying mechanisms for pathogenicity, including infectivity and virulence
- The way in which a micro-organism evades the human immune system or acquires resistance to antibiotics and
- The ways in which the agent may be dispersed, and its infectivity by each route

However, an understanding of these factors is also exactly what would be required for the development of BW [72]. An analogous point can be made in relation to non-state terrorist groups engaged in, for example, developing improvised equipment that could be used to grow a biological agent.

In relation to the dual-use dilemma in the biological sciences, the approach of the US National Research Council (NRC) in its influential 2004 report, *Biotechnology Research in an Age of Terrorism*, is to map the range of these dual-use dilemmas by identifying and taxonomising a set of salient “experiments of concern”. We accept this approach in the context of our attempt to isolate the morally permissible from the morally impermissible in relation to dual-use research

¹ See Miller [86].

in the biological sciences. Our first task, then, is to map the terrain of such dual-use dilemmas; hence, our recourse to experiments of concern.

According to the NRC report “experiments of concern” are those that would:

1. Demonstrate how to render a vaccine ineffective
2. Confer resistance to therapeutically useful antibiotics or antiviral agents
3. Enhance the virulence of a pathogen or render a non-pathogen virulent
4. Increase the transmissibility of a pathogen
5. Alter the host range of a pathogen
6. Enable the evasion of diagnosis and/or detection by established methods or
7. Enable the weaponization of a biological agent or toxin [102].

Other possible categories are:

8. Genetic sequencing of pathogens
9. Synthesis of pathogenic micro-organisms
10. Any experiment with *variola* virus (smallpox)
11. Attempts to recover/revive past pathogens.

Experiments of Concern

Demonstrate How to Render a Vaccine Ineffective

The Dual-use Dilemma: It may be important to know, for public health reasons, whether and/or how a particular vaccine can become ineffective so that the vaccine can be improved or alternative protective measures can be investigated and adopted. The deployment of vaccine-resistant biological agents against a target population, however, would circumvent an important medical defence.

Examples: Vaccine-resistant mousepox. In 2001 the *Journal of Virology* published an article describing the accidental discovery of a group of Australian scientists who were attempting to produce an infectious contraceptive for mice, which periodically breed out of control in parts of Australia. The scientists spliced a single foreign gene into a mild mousepox virus in the hope of creating a genetically engineered sterility treatment. The gene—interleukin-4 (IL-4)—helps regulate immune system reactions. The effect, however, was to create a strain of mousepox so virulent that it killed both mice with natural resistance to mousepox and mice that had been vaccinated against mousepox [26]. A disturbing implication of this result is that adding an IL-4 gene might similarly increase the virulence of smallpox (or some other poxvirus that infects humans) and potentially allow the virus to overcome vaccination (which is our only defense against smallpox). The genetic engineering technique used in this study is relatively straightforward and described in standard microbiology textbooks. No extraordinary equipment or facilities are required. To employ the technique on smallpox, however, one would need access to the smallpox virus (which, officially anyway, only exists in two secure facilities worldwide).

Project Jefferson. In September 2001 the *New York Times* revealed the existence of a classified US biodefence project (Project Jefferson) which, in early 2001, involved the production of a vaccine-resistant strain of anthrax bacteria [152]. The purpose was to reproduce results of Russian research published by *Vaccine* in 1997. The researchers inserted genes from *B cereus* into *B anthracis* and showed that the engineered bacteria were highly lethal against hamsters, even when they had been inoculated with Russia's standard anthrax vaccine [44, 142]. The US officials involved in Project Jefferson were reportedly mindful of the BWC and the need for protective intent. Accordingly, the project aimed to produce only small quantities—1 g or less—of the modified anthrax [85, p. 309]. Though the Soviets allegedly had the capacity to produce 4,500 metric tons of anthrax yearly [85, p. 254], strictly speaking even one gram of anthrax is a large quantity, capable of infecting thousands of people if a suitable dried spore preparation is made.

When Project Jefferson produced a vaccine-resistant, genetically modified biological agent, it was only verifying something that had already turned up in the scientific literature. It is a different matter to produce modified pathogens that no one, potential adversary or otherwise, has ever created.

Cowpox. Some novel pathogens only exist as disease threats because scientists created them. In 2003, for example, a team of US scientists at St Louis University led by Mark Buller, supported by a National Institute of Allergy and Infectious Diseases (NIAID) biodefence grant, repeated a previously-published Australian experiment on mousepox (described above) [26] with the intention of developing a pharmaceutical countermeasure. In the experiment, mice infected with genetically-modified mousepox virus recovered when treated with a combination of antiviral drugs. As mousepox is closely related to the *variola major* (smallpox) virus, the result led Buller's team to hope that a treatment against genetically engineered smallpox could be developed [121]. Later, however, the scientists went further by applying the mousepox enhancement technique to the cowpox virus which, unlike mousepox, infects humans. The rationale was reportedly “[t]o better understand how easy or difficult it would be to apply the same kind of genetic engineering to the human smallpox virus and make it more lethal” [140]. Although such work has been justified as “necessary to explore what bioterrorists might do”, other scientists have questioned the utility and wisdom of enhancing viruses [116, 157].

Confer Resistance to Therapeutically Useful Antibiotics or Antiviral Agents

The Dual-use Dilemma: The production of a pathogen which is resistant to existing treatments can be for genuinely peaceful purposes. A scientist might, for example, set out deliberately to generate antibiotic-resistant bacteria to determine whether or not, or how, a bacterial strain *can* become resistant. Such information would be relevant to recommendations about how best to administer the antibiotic; and resistant bacteria could be used to test alternative and/or new antibiotics.

Researchers may additionally study, and thus select for, resistant microbes in order to demonstrate the activity of an antimicrobial, to confirm the mechanism of an antimicrobial, and to discover the functions of microbial proteins. For these and other reasons, scientists routinely conduct experiments to assess the ability of pathogenic micro-organisms to acquire resistance (and produce resistant pathogens in the process): “[i]n vitro and in vivo selection for drug resistance has become part of the standard of all drug characterization and development” [51]. Drug resistant microbes able to defeat the defences that are erected by the human immune system and supplemented by existing medical technology, however, could make attractive biological weapons.

Examples: Drug-resistant mousepox. Given the perceived need, especially in light of the bioterrorist threat, for treatment against poxviruses such as smallpox, camelpox, and monkeypox, Australian scientists tested the efficacy of the antiviral cidofovir (which had previously proven effective against poxviruses in animal models) in the protection of varieties of mice against varieties of the mousepox virus [52]. While the drug was generally effective in protecting mice against mousepox, it was found that the more virulent strain of mousepox created by genetic engineering insertion of the IL-4 gene into the mousepox (*ectromelia*) virus (as described above) was resistant to the anti-viral effects of the drug. This might indicate that other drugs should be investigated and/or developed for protection against genetically engineered poxviruses. But it also reveals (to would-be bioterrorists) that insertion of the IL-4 gene into poxviruses may produce super-strains of disease that are drug-resistant (as well as possibly vaccine-resistant, as described above).

Drug-resistant plague and anthrax. The Soviet biological weapons program allegedly led to development of a strain of anthrax resistant to five antibiotics and a strain of plague resistant to all antibiotics. Insofar as this was part of an offensive biological weapons program—and because the purpose of the original researchers was malign—these are clear examples of impermissible research. A hypothetical example of dual-use research, however, would be the attempt to reproduce such pathogens for bio-protective purposes. If it is confirmed that creation of such pathogens is possible, and if the characteristics of such pathogens are determined, then we will know more about the kinds of threats (both natural and unnatural) we may need to prepare to protect ourselves against. The results of such research, however, could potentially be used by bioterrorists or others with harmful intentions.

Enhance the Virulence of a Pathogen or Render a Non-pathogen Virulent

The Dual-use Dilemma: For public health reasons, it may be important to know whether and/or how the virulence of a pathogen that exists in nature can increase. An ‘enhanced’ pathogen deployed in a biological attack, on the other hand, would inflict more human damage than normal.

Examples: In 2002 the *Proceedings of the National Academy of Sciences (PNAS)* published the results of an experiment involving the engineering, from published DNA sequences, of a protein—known as SPICE—produced by the smallpox virus. The study revealed the ways in which, and the extent to which, this protein defeats the human immune system. This could be important knowledge in the event that smallpox re-emerges because “[d]isabling SPICE may be therapeutically useful” [53]. But the results potentially provide information on how to increase the virulence of the closely related *vaccinia* virus (which is used in the smallpox vaccine).

In 2003 *PNAS* published the findings of scientists who had accidentally created a more virulent form of tuberculosis (TB) when trying to alter the genetic structure of *Mycobacterium tuberculosis* bacteria [60].

Increase the Transmissibility of a Pathogen

The Dual-use Dilemma: For treatment and public health planning purposes, it may be important to know whether a naturally-occurring infectious disease threat could be worsened by the evolution of a pathogen into a more transmissible form. Attempts to enhance transmissibility might thus yield valuable knowledge. A pathogen might be more useful as a biological weapon, however, if it is more easily transmitted through a population.

Examples: H5N1 influenza. The World Health Organization (WHO) has sponsored research to find out whether H5N1 avian influenza could trigger a human pandemic. The hope is that, by “reassorting” (mixing) H5N1 with human influenza viruses in the laboratory, scientists may determine how dangerous the hybrid virus would be and the likelihood of it causing a pandemic. Such experiments could help determine whether there is some natural barrier to the reassortment of H5N1 or whether the world has simply been lucky [19].

Switching the virus between different hosts is also believed to lead to increased transmissibility, especially if one of those hosts is the pig. A number of influenza laboratories are considering mixing birds with pigs to determine if the virus will mutate to increase its transmissibility, and potentially be of greater threat to humans.

Smallpox-Ebola chimera. A project of the Soviet bioweapons project allegedly aimed to produce a hybrid “chimera” of smallpox and Ebola. The purpose was to create a pathogen highly contagious like the former and highly virulent like the latter. It can thus be characterised as a project which aimed to increase the transmissibility of Ebola. (Such research would also fall under the third category of concern insofar as its purpose was to increase the virulence of smallpox.) The Soviet project should not be considered dual-use; insofar as this was conducted as part of an offensive biological weapons program this is clearly impermissible research. A hypothetical example of dual-use research, however, would be the attempt to

construct such a chimera with the protective aim of discovering whether or not the Soviets or others may have succeeded in such a project. If it is discovered that creation of such a chimera is possible, and if the characteristics of such a pathogen are determined, then we will know more about the kinds of things we need to prepare to protect ourselves against. The knowledge about how to create such a virus, on the other hand, could be used to cause extreme devastation by those with malevolent intentions.

Alter the Host Range of a Pathogen

The Dual-use Dilemma: In an era of renewed concern about emerging infectious diseases, it may be important for human health to know whether a non-zoonotic disease can become, or is close to becoming, a zoonotic agent. Medically important research might thus result in an animal disease that could sicken humans. The use of such an agent in a biological attack could be devastating because, as was the case with the severe acute respiratory syndrome (SARS) coronavirus, people have no immunity and have not been selected for resistance to the disease.

Examples: An important area of research into infectious diseases examines why some pathogens infect multiple hosts whereas others are highly host-specific. By what processes, for example, did HIV become able to infect humans as well as chimpanzees? Understanding what determines host-specificity or host-limitation is important for research into emerging diseases of humans, animals and plants. An example of high risk research might be experiments to determine whether a species-specific virus such as camelpox could be adapted to readily transmit in humans by insertion of *variola* genes.

Myxoma virus was used for the biological control of rabbits and does not replicate in humans. However, genes are now being identified which when engineered into the *myxoma* virus could overcome host specificity and allow the virus to infect humans [27].

Enable the Evasion of Diagnosis and/or Detection by Established Methods

The Dual-use Dilemma: In relation to ongoing infectious disease threats to human health, it may be important to know whether a pathogen has the potential to mutate naturally into an undetectable form so that new diagnostic/detection techniques may be devised. Pathogens engineered to evade diagnosis and/or detection, however, would be well-suited for a covert biological attack; and the delay in diagnosis and subsequent treatment would increase the resulting human damage.

Examples: Microencapsulation of pathogen particles would be one way of avoiding antibody-based detection, although this technique has no analogue in nature. As such, microencapsulation would only be carried out for an offensive BW purpose (such as delivery of a pathogen to the lower intestine) or to investigate the requirements for protection against such a threat.

Altering gene sequences may be a way of testing the robustness of molecular detection systems. It may be useful to understand the circumstances under which natural mutations would be likely to render a diagnostic system ineffective.

Enable the Weaponization of a Biological Agent or Toxin

Experiments of this kind test the bounds of permissibility most severely. Weaponized agents do not exist in nature, and so (absent the threat of biological weapons attack) there is no ongoing public health imperative for protective mechanisms as there is against a naturally occurring infectious disease threat.

The Dual-use Dilemma: Understanding weaponization processes may facilitate the development of protections against a potential BW perpetrator (including a nation-state contemplating a terrorist attack on civilians). Our focus here will be on the weaponisation of biological agents by nation-states, as opposed to the processes for delivery of biological agents that might be used by non-state actors contemplating a terrorist attack. (We do not thereby mean to imply that the threat assessment in relation to the latter is not important; clearly it is of enormous importance.) Weaponization for “threat assessment” purposes is likely to be interpreted by outsiders as simply the production of BW, thus endangering the norm against their production, driving a biological arms race, and making biological attacks more likely.

Examples: Project Clear Vision. In September 2001, the *New York Times* revealed the existence of a classified US biodefence project (Project Clear Vision) which, from 1997 to 2000, involved building and testing a Soviet-model bomblet for dispersing bacteria [152]. This involved tests of bacteria bomblets, built according to a Soviet design, and conducted by Battelle, a military contractor in Columbus, Ohio. The bomblets were reportedly filled with simulant pathogens and tested for their dissemination characteristics and performance under different atmospheric conditions. Experiments in a wind tunnel revealed how the bomblets, after being released from a warhead, would fall on targets [85, p. 295]. Before the testing took place, some US government legal experts had argued the experiments were not a breach of the BWC provided they were not intended for offensive purposes. Other officials argued that a weapon was, by definition, meant to inflict harm and therefore crossed the boundary into offensive work: “A bomb was a bomb was a bomb” [85, p. 288].

Biological agent grenade. In February 2003 a patent was issued to the US Army for a “rifle-launched non-lethal cargo dispenser” that can be filled with “smoke,

crowd control agents, *biological agents*, chemical agents, obscurants, marking agents, dyes and inks, chaffs and flakes” [emphasis added] [10]. In December 2005, after concerns were raised that the development and production of such a weapon would breach the BWC, the US Patent and Trade Office approved a change to the patent which removed the term ‘chemical/biological agent’ [122].

Aerosolization. Small-scale aerosolization technology may be useful for administering individual doses of inhaled vaccine or antiviral therapy (such as ribavirin) to humans, and larger-scale aerosolization could be used for mass-vaccination of animals—for example, in the poultry industry. It is hard to imagine large-scale aerosolization being therapeutically useful for humans, although such technology would certainly have enormous value for the purpose of delivering BW agents. Such technology might also be developed and tested for protective purposes. One of the principal aims of the NIAID Biodefense Research Agenda, for example, is to “ensure adequate numbers of BSL-3 [Biosafety Level Three] facilities with aerosol challenge capacity” [161, p. 8].

NBACC. The National Biodefense Analysis and Countermeasures Center (NBACC), due to be completed in 2008, is intended to provide the United States with high-containment laboratory space for biological threat characterization and bioforensic research. According to the US Department of Homeland Security, NBACC will form part of the National Interagency Biodefense Campus at Fort Detrick, Maryland. Its programs will investigate the infectious properties of biological agents, the effectiveness of countermeasures, decontamination procedures, and forensic analysis. Part of NBACC is the Biological Threat Characterization Center, which will conduct laboratory experiments aimed at investigating current and future biological threats. The Center will also assess vulnerabilities, conduct risk assessments, and determine potential impacts in order to guide the development of countermeasures such as detectors, vaccines, drugs, and decontamination technologies [135].

Many of the activities to be undertaken by NBACC could readily be interpreted by outsiders as the development of BW under the guise of threat assessment. In particular, weaponization projects and the construction of novel (not previously existing) pathogens arguably constitute impermissible research. In a February 2004 presentation, George Korch, Deputy Director of NBACC, revealed that one of its research units intended to pursue a range of topics including “aerosol dynamics”, “novel packaging”, “novel delivery of threat”, “genetic engineering”, and “red teaming”. At one point in his presentation, Korch summarized the threat assessment task areas as: “Acquire, Grow, Modify, Store, Stabilize, Package, Disperse” [38, 115, 117]. Such language is identical to that which would describe the functions of an offensive BW program.

Indeed, a 1998 report from the Office of the US Under Secretary of Defense for Acquisition and Technology stated: “Stabilization and dispersion are proliferation concerns because these technologies increase the efficacy of biological agents” [163]. And in light of the planned NBACC activities as described by Korch, a 2005 US State Department report which assessed that “China maintains some elements of an offensive BW capability in violation

of its BWC obligations” appeared to reflect an American double standard on BW when it warned that:

From 1993 to the present, [Chinese] military scientists have published in open literature the results of studies of aerosol stability of bacteria, models of infectious virus aerosols, and detection of aerosolized viruses using polymerase chain reaction technology. Such advanced biotechnology techniques could be applicable to the development of offensive BW agents and weapons [136].

Genetic Sequencing of Pathogenic Micro-Organisms

The Dual-use Dilemma: Sequencing the genetic codes of entire pathogens or specific genes of pathogens could assist in understanding the nature of the pathogens and in the development of new vaccines or treatments for the diseases they cause. Sequencing also facilitates genetic diagnosis and detection. Gene sequence data could, on the other hand, be used to construct a pathogen for deployment against a target population with no natural immunity. Of particular concern are the facts that the smallpox genome has been published and that the published polio genome enabled artificial synthesis of a “live” polio virus as described below.

Examples: Anthrax. In a letter to *Nature*, Read et al. describe the sequencing of the Ames strain of *Bacillus anthracis* (anthrax). Reported benefits of the sequencing include identification of (1) virulence genes on plasmids, (2) “chromosomally encoded proteins that may contribute to pathogenicity”, and (3) “numerous surface proteins that might be important targets for vaccines and drugs” [49]. They conclude that “the complete sequence of *B. anthracis* is a step towards a better understanding of anthrax pathogenesis.” Though presumably true, the improved understanding of anthrax enabled by genetic sequencing could potentially be used by those who aim to increase the danger of anthrax—or to transfer its harmful characteristics to other microbes (including near genetic neighbours identified by the study) via genetic engineering—as well as those who aim to improve medical defenses against it.

Influenza. Research results published in 2005—on the complete genetic sequencing of the 1918 influenza A (H1N1) virus [63] and the “resurrection” of H1N1 using reverse genetic techniques [65]—revealed (and reproduced, in animals at least) the traits that made the virus so virulent. However, the decision to publish this information aroused concerns that would-be BW perpetrators could use it to reconstruct H1N1 for malign purposes. The danger of the virus is revealed by the fact that it killed between 20 and 100 million people in 1918–1919—more than have been killed by any single disease in such a short time period in human history. The newly created US National Science Advisory Board for Biosecurity (NSABB) was asked to consider the latter paper before publication and concluded that the scientific benefit of the future

use of this information on the 1918 virus far outweighed the potential risk of misuse. Similar issues relate to publication of the H5N1 influenza—i.e., bird flu—genome.

Synthesis of Pathogenic Micro-Organisms

The Dual-use Dilemma: Synthesis of the genomes of viruses theoretically allows the introduction (and precise positioning) of mutations or novel sequences that can be used to study the function of particular genes or regulatory sequences. It would be more usual (though perhaps less precise) to do this using conventional molecular biology—e.g., “infectious clones”—rather than genome synthesis [47]. Synthesis technology would obviate the need for would-be BW perpetrators to source pathogens from natural reservoirs in other parts of the world or from other laboratories. It can facilitate reconstruction of extinct pathogens (as mentioned above and below, with regard to the “resurrection” of the 1918 flu) and it could theoretically enable construction of novel pathogens.

Example: Polio. In an experiment carried out partly with the intention to draw attention to BW threats, American scientists sponsored by the US Department of Defence spent three years synthesising a *poliomyelitis* (polio) virus “from scratch”. Following the map of the polio virus RNA genome published on the internet, they bought and strung together corresponding DNA sequences, commercially available over the internet. This was used in a cell-free extract to create “live” virus that paralysed and killed mice [9]. One of the polio project scientists, Eckard Wimmer, said the experiment proved that eradicating a virus in the wild might not mean it is gone forever—conceivably, scientists may soon be able to apply the same technique to synthesise more complex viruses such as Ebola using blueprints available in scientific archives and from biological supplies purchased through the mail [36, 125, 137]. He said they “made the virus to send a warning that terrorists might be able to make biological weapons without obtaining a natural virus” [156]. Of particular concern is the possibility that the technique would enable artificial synthesis of smallpox. One reason the technical feasibility of the latter is doubtful, however, is the fact that the smallpox genome is so much larger—i.e., 200,000 base pairs in comparison with 7,500 for polio. Adding to such prospects, however, in December 2004 *Nature* described an unexpectedly sudden advance in synthesising longer strands of DNA: a research team synthesised a molecule 14,500 chemical units in length [46, 64]. While it took a number of years to initially synthesise polio, furthermore, Craig Venter has succeeded in synthesizing bacteriophages of comparable size (i.e., 6,000 base pairs) in a matter of weeks. This technology is advancing so rapidly that it is difficult to predict what will be possible in the future. Many now believe that synthesis of smallpox is possible.

Any Experiment with the Smallpox Virus

The smallpox virus (*variola major*) is a special case because it no longer exists in nature. As such, there is no public health imperative to defend against naturally occurring smallpox outbreaks. On 8 May 1980 the World Health Assembly (WHA) declared the successful eradication of smallpox worldwide, and by 1984 the World Health Organization (WHO) had authorized only the United States and the Soviet Union to each possess a single repository of the world's last samples of the virus.² In May 1990, US Health and Human Services Secretary Louis Sullivan proposed that the two countries should start working towards eliminating their collections of *variola* in order to ease fears that smallpox might be used as a biological weapon [92]. This sparked a debate over destruction versus retention of the virus that has continued to this day.

The Dual-use Dilemma: Understanding *variola* is important for developing medical defences in the event that a smallpox outbreak occurs as a result of a BW attack or the accidental leak of the virus from a laboratory. Because biosafety and biosecurity measures in laboratories are less than perfect, however, an increase in the number of personnel and facilities working with *variola* increases the likelihood of the virus escaping or being stolen and used in a biological attack.

Example: The WHA in 1999 established the Variola Advisory Committee (VAC). At its meeting in November 2005 the VAC noted, *inter alia*, further work on the primate model of human smallpox, which had been undertaken to facilitate the development of antiviral drugs and to meet associated licensing requirements. Recent experiments in primates, using different doses of virus, had induced disease with features similar to that of lesional smallpox and haemorrhagic smallpox in humans. These studies were considered useful in assessing the efficacy of antiviral drugs because they enabled greater understanding of specific organ and tissue sites of viral replication [164]. The relevance of this model is seriously questioned because very high levels of smallpox virus challenge were utilised, 10^9 for aerosol and 10^8 for intravenous challenges.

Attempts to Recover/Revive Past Pathogens

The Dual-use Dilemma: A number of attempts have been made to recover past pathogens from preserved frozen bodies. While the recovery of such pathogens may reveal important historical, evolutionary, and medical information, such patho-

²The samples are presently stored in secure freezers at the Centers for Disease Control and Prevention (CDC) in Atlanta and at the Centre for Research on Virology and Biotechnology in Koltsovo, Russia.

gens may be extremely dangerous to human populations if they are accidentally or intentionally released into the environment.

Examples: Journalist Gina Kolata describes numerous examples of successful and failed attempts by scientists to recover the 1918 flu from the lungs of frozen bodies in permafrost in Alaska and Norway [83]. Some of this research involved remarkably little oversight and precaution. One risk of this research is the possibility that the researchers themselves would be infected when exposed to the bodies in question—and the possibility that this could have sparked a global epidemic. More relevant to the dual-use dilemma is the fact that some of these researchers aimed to revive the frozen virus. While revival attempts have failed, recovery of and research on the 1918 flu virus from frozen bodies enabled the genetic sequencing and “resurrection” via reverse engineering discussed above. Both the revived virus, if attempts had been successful, and the information gained from the recovered frozen 1918 (H1N1) flu virus could be used for both beneficial and harmful purposes. Kolata also cites reports that Russian scientists have attempted to recover smallpox from frozen bodies. Attempts to recover/revive (particular strains of) other preserved pathogens are easily imaginable.