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## A Global Architecture for Medical Counter-Measure Preparedness Against Bioviolence

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## ARTICLE

**A GLOBAL ARCHITECTURE FOR MEDICAL  
COUNTER-MEASURE PREPAREDNESS  
AGAINST BIOVIOLENCE**

BARRY KELLMAN\*  
&  
ZACHARY CLOPTON\*\*

*It's time for a comprehensive effort to tackle bio-terror. We know that the successful deployment of a biological weapon—whether it is sprayed into our cities or spread through our food supply—could kill tens of thousands of Americans and deal a crushing blow to our economy.* Presidential Candidate Barack Obama (2008)<sup>α</sup>

*[I]t is more likely than not that a weapon of mass destruction will be used in a terrorist attack somewhere in the world by the end of 2013. . . . [T]errorists are more likely to be able to obtain and use a biological weapon than a nuclear weapon. . . . [T]he U.S. government needs to move more aggressively to limit the proliferation of biological weapons and reduce the prospect of a bioterror attack.* Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism<sup>β</sup>

*“[B]iological weapons are considered the least complicated and the easiest to manufacture of all weapons of mass destruction.” “The destructive power of these [biological] weapons is no less than that of nuclear weapons.”* Quotations attributed to Al Qaeda<sup>χ</sup>

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<sup>α</sup> ScienceDebate2008.com, Barack Obama's answers to the top 14 science questions facing America (Aug. 30, 2008), <http://www.sciencedebate2008.com/www/index.php?id=42>.

<sup>β</sup> COMMISSION ON THE PREVENTION OF WMD PROLIFERATION AND TERRORISM, WORLD AT RISK: THE REPORT OF THE COMMISSION ON THE PREVENTION OF WMD PROLIFERATION AND TERRORISM, at xv (2008), available at <http://www.preventwmd.gov/report>.

<sup>χ</sup> BARRY KELLMAN, BIOVIOLENCE—PREVENTING BIOLOGICAL TERROR AND CRIME 73 (2007) (citing *al-Ma'asada al Jihadiya*—The Jihadi Lion's Den Website).

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In a world of incalculable dangers, there are fortunately only a few ways that enemies could seriously subvert global security and stability. Of these, *bioviolence*<sup>2</sup> is arguably among the most salient.

These dangers are emerging from the confluence of bioscientific capacities unimaginable only a few decades ago. No one should cast aspersions on this science. From bioscience's labs emerge the promise of ridding humanity of scourges that have afflicted our species since our predecessors left Eden. Yet, biting the apple of knowledge has consequences, no matter how benign scientists' motives might be.

Their great achievements—understanding and manipulating life—inseparably carry the capacity to create weapons that could inflict catastrophe. A lethal bioweapon could cause deaths or economic losses that exceed anything other than, perhaps, a nuclear weapon, yet it is much easier to make than a nuclear weapon. The number of victims would depend on where an attack takes place, the type of pathogen, and the sophistication of the weapon-maker; there is widespread expert consensus that a high-end attack could produce in excess of ten thousand casualties, perhaps far more.s] The extraordinary speed and spread of scientific development means that more powerful and more diverse bioweapons are on the horizon.<sup>3</sup>

The stakes could not be more serious. Smallpox, humanity's preeminent killer, was eradicated from nature—one of humanity's greatest accomplishments. Remaining strains were secured in laboratories for research purposes. However, scientists will soon (if not now) be able to synthesize it by fusing genetic components. What if other orthopox viruses—monkeypox or camelpox—can be manipulated to have grievous implications for human-to-human transmission and rampant lethality? What if these innovative applications of bioscience can be made resistant to the vaccines and therapeutics that are stockpiled against smallpox? In the wrong hands, how many thousands, or potentially millions, of people would die? What would be the ramifications for social order?

Diseases once thought to be eradicated and for which scant natural immunity remains can be re-synthesized. The polio virus has been produced

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1. *Id.* at 1 (“*Bioviolence* is the infliction of harm by the intentional manipulation of living micro-organisms or their natural products for hostile purposes.”).

2. See Margaret A. Hamburg, M.D., Senior Scientist, Nuclear Threat Initiative, Testimony Before the Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism (Sept. 10, 2008), available at [http://www.preventwmd.gov/9\\_10\\_08\\_margaret\\_hamburg/](http://www.preventwmd.gov/9_10_08_margaret_hamburg/).

3. According to the U.S. Defense Science Board in 2001, “major impediments to the development of biological weapons—strain availability, weaponization technology, and delivery technology—have been largely eliminated in the last decade by the rapid global spread of biotechnology.” *Id.*

from genetic precursors. Soon, it may be re-synthesized to be contagious even among vaccinated populations. Consider genetic manipulation of measles—one of the great killers in human history—so that the immunizations received in early childhood offer no protection. On the horizon is the specter of creating altogether new pathogens.

Various bacterial agents such as plague or tularemia could be altered to increase their lethality or to evade antibiotic treatment. Scientists can generate antibiotic-resistant bacteria to determine how readily those bacteria might become resistant to new treatments. In Australia, scientists introduced a gene into mousepox (a cousin of smallpox) to reduce pest populations—it worked so well that it wiped out 100% of affected mice, even mice with immunity against the disease.<sup>4</sup> Insertion of a gene into a virus's DNA is not rocket science now; in a few years, it will be elementary.

Perhaps the greatest fear today is manipulation of the flu. The genomic sequence of the Spanish Flu virus that killed upwards of fifty million people nearly a century ago has been widely published and could be reconstructed. The Avian Flu is even more lethal albeit not readily contagious, via casual aerosol delivery. How difficult would it be for a malevolent bioscientist to manipulate any of these viruses to augment its contagiousness and transmit it throughout population centers? A decade ago, these dangers were fanciful; today, they are on the horizon; within a decade, they will be pedestrian.

According to the National Academies of Science, “[t]he threat spectrum is broad and evolving—in some ways predictably, in other ways unexpectedly. . . . In the future, genetic engineering and other technologies may lead to the development of pathogenic organisms with unique, unpredictable characteristics.”<sup>5</sup> Every passing day it will be slightly easier to commit a violent catastrophe than it was yesterday, and so on. As far as can be seen is the prospect of bioscience for life inseparably intertwined with bioscience for violence.

These bioviolence dangers are distinguishable from every major weapon including nuclear weapons. Other weapons have tracked an ancient paradigm: ever larger concentrations of industrial strength lead to ever more destructive weapons leading in turn to ever more powerful concentrations of political power. Even today, making nuclear weapons requires an industrial infrastructure that demands the apparatus of statehood. New dangers of bioviolence, however, invert that age-old paradigm. Weapons of mass annihilation can be made without anything like a nation-state's industrial infrastructure, perhaps by a single individual. Whatever their motives, a nano-fraction of humanity can now inflict a species-wide catastrophe that

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4. See Ronald L. Jackson et al., *Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox*, 75 J. VIROLOGY 1205, 1205–10 (2001).

5. NAT'L RESEARCH COUNCIL, GLOBALIZATION, BIOSECURITY, AND THE FUTURE OF THE LIFE SCIENCES 49 (2006).

breaches the progress of history. Thus, we stand on the threshold of an age when ever fewer people can cause ever greater suffering to ever larger populations. It is this new reality that holds the secret to emerging dangers and calls for a revolution in our conception of global order.

This is not a hypothetical concern. Terrorist organizations have expressed interest in acquiring bioweapons. The eleventh volume of Al Qaeda's *Encyclopedia of Jihad* is devoted to chemical and biological weapons. Al Qaeda has announced that "biological weapons are considered the least complicated and the easiest to manufacture of all weapons of mass destruction." Before 9/11, Al Qaeda operatives purchased anthrax and plague from arms dealers in Kazakhstan, and Al Qaeda has repeatedly urged followers to recruit microbiology and biotechnology experts. Following the Taliban's fall, five Al Qaeda biological weapons labs in Afghanistan tested positive for anthrax.<sup>6</sup>

Their reasoning might be reprehensible, but it is certainly not irrational. For anyone who views modernity as an abomination, the stark reality is that the 9/11 attacks, the bombing of the Madrid and London subways, mass murder in Mumbai, bombings in Jakarta, and numerous smaller attacks have all put civilization on edge—but to what effect? Western armies still traverse the world, and western economies still determine winners and losers. From our enemies' perspective, the stakes must be raised!

Bioviolence is the easiest and most effective way to ravage global security. Envision a series of attacks against States closely allied with the United States, timed to follow local officials' expressions of friendship to visiting U.S. dignitaries. The attacks would carry a well-publicized warning: "If you are a friend of the United States, receive its officials, or support its policies, thousands of your people will get sick." How many attacks in how many cities would it take before international diplomacy, to say nothing of international transit, is seriously undermined?

The truly unique characteristic of some bioweapons—distinguishing them from every other type of weapon—is contagion. No other type of weapon can replicate itself and spread. Any other type of attack, no matter how severe, occurs at a certain moment in time at an identifiable place. If you are not there, you are angry and grief-stricken but not physically injured. An attack with a contagious agent can uniquely spread through time and space, potentially imperiling everyone. A bio-offender could spread disease to unsuspecting victims who would themselves become extended bioweapons carrying the disease indiscriminately.

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6. See Harold Kennedy, *Military Officials Warn Al Qaeda to Attack with WMD*, NATIONAL DEFENSE, Feb. 2005, at 28, 28–30; see also CENTER FOR NONPROLIFERATION STUDIES, AL-QA'IDA'S WMD ACTIVITIES (May 13, 2005), [http://cns.mii.edu/other/sjm\\_cht.htm](http://cns.mii.edu/other/sjm_cht.htm); and Alan Cullison & Andrew Higgins, *Files Found: A Computer in Kabul Yields a Chilling Array of al Qaeda Memos*, WALL ST. J., Dec. 31, 2001, at A1. For a fuller discussion, see generally KELLMAN, *supra* note 1, at 72–80.

All this leads to the most important characteristic of bioviolence: it raises incomparable levels of panic. Bioviolence is about planes flying empty or perhaps not flying at all. It is about people refusing to interact with each other for fear of unseen affliction. It is about canceling public entertainment and tourism—even going to a movie would be too dangerous. Bioviolence is about hiding our children. Everyone will be potentially vulnerable to our dread of disease. No one would know when an attack is over, and no government can credibly tell an anxious population where and when safety can be assured.

Ultimately, if one's ambition is to rattle the pillars of modern civilization, and perhaps cause it to collapse, effective use of disease would set in motion political, economic, and health consequences so severe as to call into question the ability of existing governments to maintain their citizens security. To stop modern civilization in its tracks, bioviolence is the way to go.

The notion that no one will ever commit catastrophic bioviolence is untenable. Simply stated, there are capacities to do harm, and there are people who want to devote those capacities precisely to do harm. There should be no doubt that we are vulnerable to a rupture, and the day that disease is effectively used as an instrument of hate will profoundly change everything.

#### THE IMPERATIVE OF MCM PREPAREDNESS

This article considers international anti-bioviolence initiatives to promote medical counter-measure (MCM) preparedness. *Preparedness* refers to policies that should be implemented now—pre-attack—to optimize post-attack response effectiveness. Preparedness policies focus on: detecting commission of an attack, diagnosing the attack agent, administering medical treatment to victims, limiting the spread and severity of that attack, restoring and sustaining social order and the rule of law, and remediating the consequences of that attack.

By no means is preparedness the whole answer. Other *prevention* policies are essential to deny potential perpetrators access to weaponizable pathogens, to track and confine the trade in such pathogens or weaponization equipment, or to oversee bioresearch that has uniquely dangerous applications. Moreover, there are aspects of preparedness not directly committed to MCMs (e.g., improving diagnostic and biosurveillance capabilities) that are no less important; indeed, no MCM distribution system can operate effectively if other response activities are in disarray. All these prevention and other preparedness policies are omitted from discussion here only to focus attention on the details of what needs to be done to promote MCM preparedness.

Yet, even amid a healthy respect for the broad array of necessary anti-bioviolence measures, there are good reasons to focus on MCM prepared-

ness. First, if MCMs are available, the victims can be treated and the consequences of an attack can be contained. In a bio-attack's wake, there is no higher priority than minimizing suffering and death and stanching the spread of disease. Second, by reducing damage and containing losses, we can deter attacks. A culprit who seeks to inflict mass violence and panic will be less inclined to use disease in the face of organized and efficient measures to limit consequences.

Importantly, engaging the international community on MCM preparedness could have powerfully beneficial repercussions. This is a singular topic that is in everyone's interest to advance because an effective plan for MCM stockpiling and distribution could be dual-use—it could be a major system for addressing natural pandemics as well as bioviolence. Engagement of international organizations and the private sector, along with many States could thus transform this entire policy arena, designing an integrated global system where benefits are shared, responsibilities are common, and security is mutual.

While bioviolence MCM preparedness can be dual-use, such preparedness is distinguishable from natural disease preparedness in at least four noteworthy respects. First, law enforcement has a pivotal role because bioviolence is a crime of human intentionality. Second, bioviolence caused by intelligent perpetrators is distinguishable both spatially and temporally from the spread of natural disease which tends to disperse in predictable patterns. An intentional actor whose goal is to frustrate response efforts could commit attacks in multiple, non-contiguous countries, confounding even the best preparations to deliver MCMs. Third, a bioviolence attack might pose far more acute needs for response and care especially at the moment and site of attack. Fourth, the public attitude in response to an attack is likely to be different than to a natural disease outbreak. Again, the factor of human intentionality alters perceptions about public safety and security that are not merely measured by mortality counts, and bioviolence inevitably suggests recurrence which further undermines public confidence. All these implications present unique challenges for bioviolence preparedness.

#### A. *The U.S. Approach to MCM Preparedness*

In the United States, the Department of Health and Human Services (HHS) administers Project BioShield, a comprehensive plan to encourage development of CBRN countermeasures.<sup>7</sup> The Office of the Assistant Sec-

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7. Project BioShield Act of 2004, Pub. L. 108-276, 118 Stat. 835 (codified in scattered sections of 42 U.S.C.); see U.S. Department of Health & Human Services, Project BioShield, <http://www.hhs.gov/aspr/barda/bioshield/index.html> (last visited Oct. 21, 2009); and HHS Public Health Emergency Medical Countermeasures Enterprise Strategy for Chemical, Biological, Radiological and Nuclear Threats, 72 Fed. Reg. 13109, 13113 (Mar. 20, 2007); see also FRANK GOTTRON, PROJECT BIOSHIELD: PURPOSES AND AUTHORITIES 1 (2009).

retary for Preparedness and Response (ASPR) has lead responsibility for MCM procurement and funding.<sup>8</sup>

Within ASPR, the Biomedical Advanced Research and Development Authority (BARDA) has authority for managing MCM planning. BARDA's directive is to "coordinate an integrated, systematic approach to planning for and executing research, development and acquisition of medical countermeasures for public health emergencies."<sup>9</sup> BARDA is responsible for driving MCM analysis and prioritization; coordinating approaches to research, development, and drug acquisition; and executing advanced development and procurement of MCMs for CBRN threats and pandemic influenza. BARDA facilitates communications between the U.S. government, the biomedical industry, and other R&D participants through workshops, web portals, and dialogues, as well as providing a degree of transparency.<sup>10</sup>

BARDA leads the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE), a multi-agency collaboration including the Centers for Disease Control and Prevention (HHS/CDC), the Food and Drug Administration (HHS/FDA), and the National Institutes of Health (NIH). PHEMCE's mission areas include defining and prioritizing MCM requirements, focusing research, development, and procurement activities in order to obtain those identified requirements, and then establishing deployment and use strategies for those products.<sup>11</sup> To prepare an MCM development and procurement strategy, PHEMCE gathers information about existing threats and their medical/public health consequences and available MCMs in order to assess the development pipeline, current levels of preparedness, concepts of use, product specifications, and the estimated costs of their development and acquisition. PHEMCE thereupon determines the require-

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8. HHS Public Health Emergency Medical Countermeasures Enterprise Strategy for Chemical, Biological, Radiological and Nuclear Threats, 72 Fed. Reg. 13109, 13109 (Mar. 20, 2007); Homeland Security Presidential Directive (HSPD) 18 directs the U.S. MCM effort to concentrate efforts on countering the threats of weapons of mass destruction. *See* Homeland Security Presidential Directive 18: Medical Countermeasures Against Weapons of Mass Destruction, 43 WKLY. COMP. PRES. DOC. 128, 132 (Jan. 31, 2007).

9. PAHPA Stakeholders Meeting, Biomedical Advanced Research and Development Authority (Nov. 8, 2007), [http://www.hhs.gov/aspr/conferences/pahpa/2007/barda\\_pahpa\\_stakeholder\\_meeting\\_v4b\\_sgh\\_508.pdf](http://www.hhs.gov/aspr/conferences/pahpa/2007/barda_pahpa_stakeholder_meeting_v4b_sgh_508.pdf); NATIONAL BIODEFENSE SCIENCE BOARD, AMENDED CHARTER (2008), <http://www.hhs.gov/aspr/omsph/nbsb/nbsbamendedcharter.pdf>.

10. U.S. DEP'T OF HEALTH AND HUMAN SERV., PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURES ENTERPRISE, BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY, DRAFT BARDA STRATEGIC PLAN FOR MEDICAL COUNTERMEASURE RESEARCH, DEVELOPMENT, AND PROCUREMENT 1 (2007), *available at* <http://www.hhs.gov/aspr/barda/documents/draftbardaplan.pdf>.

11. *See* HHS PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURE ENTERPRISE, IMPLEMENTATION PLAN FOR CHEMICAL, BIOLOGICAL, RADIOLOGICAL, AND NUCLEAR THREATS 5-6 (2007), *available at* [http://www.hhs.gov/aspr/barda/documents/phemce\\_implplan\\_041607final.pdf](http://www.hhs.gov/aspr/barda/documents/phemce_implplan_041607final.pdf).



ments and priorities for each type of MCM and identifies and prioritizes near-, mid-, and long-term development and acquisition programs.

BARDA receives scientific and technical input from the National Biodefense Science Board (NBSB) which tracks bioscientific trends and provides recommendations for biodefense research and development activities. Research and development programs engage the National Institutes of Health (NIH), particularly the National Institute of Allergy and Infectious Diseases (NIAID), which has primary responsibility to see that promising drug candidates are awarded contracts through Project BioShield's funds. NIH/NIAID can expedite reviews of promising biodefense drugs by simplifying the application process.<sup>12</sup>

The Strategic National Stockpile (SNS), managed by HHS/CDC, is designed to provide medical supplies to protect Americans against a public health emergency that potentially exceeds local readiness and capacity.<sup>13</sup> The SNS formulary was initially designed to combat specific severe threats;<sup>14</sup> it now contains a broader set of antibiotics, medical supplies, antidotes, antitoxins, antiviral drugs, vaccines, and other pharmaceuticals valued at approximately \$3.5 billion.<sup>15</sup> The Director of CDC has the authority, in consultation with the Surgeon General and the Secretary of HHS, to order the deployment of the SNS upon approval by ASPR. Distribution of SNS assets has been the subject of elaborate state and national planning efforts, which include the formation of private sector partnerships to assist in the critical areas of asset storage and transportation.<sup>16</sup>

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12. For example, the NIAID has used \$35.6 million to award contracts and grants to promote basic research and development with the intent that the medical countermeasures will one day be acquired by the government. See *Project BioShield Reauthorization Issues: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 109th Cong. 5–12 (2006) (statement of Alex M. Azar, II, Deputy Secretary, Department of Health and Human Services) [hereinafter *Project BioShield Reauthorization Issues*].

13. To receive SNS assets, an affected state's governor's office can request the deployment of the SNS assets from CDC or HHS, which will evaluate the situation and determine a prompt course of action. Each state is required to develop plans to receive and distribute SNS medicines and medical supplies to local communities. See Centers for Disease Control and Prevention, *Strategic National Stockpile* (Mar. 31, 2009), <http://www.bt.cdc.gov/stockpile/>.

14. The SNS formulary was designed in response to the CDC's Category A threat: anthrax, botulism, plague, smallpox, tularemia and viral hemorrhagic fevers.

15. See TODD PIESTER, CENTERS FOR DISEASE CONTROL STRATEGIC NATIONAL STOCKPILE OVERVIEW 6–8, 22 (2008), available at [http://emergency.cdc.gov/coca/summaries/pdf/SNS\\_070108.pdf](http://emergency.cdc.gov/coca/summaries/pdf/SNS_070108.pdf). The SNS will continue to broaden its scope. According to the PHEMCE Implementation Plan, acquisitions of emergency medications through and beyond FY 2013 will include: broad spectrum antibiotics; broad spectrum antivirals for ebola, junin, marburg, and variola viruses; anthrax vaccine and antitoxin; point-of-care diagnostics for all biological threat agents; and filovirus medical countermeasures. HHS PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURE ENTERPRISE, *supra* note 11, at 15–19.

16. For examples of state and local efforts, see the work of the National Association of County and City Health Officials (NACCHO). National Association of County and City Health Officials, *Strategic National Stockpile*, <http://www.naccho.org/topics/emergency/SNS/index.cfm> (last visited Oct. 21, 2009).

Notably for this article's focus, the Pandemic and All-Hazards Preparedness Act (PAHPA) directs the HHS Secretary to "provide leadership in international programs, initiatives, and policies that deal with public health and medical emergency preparedness and response."<sup>17</sup> On behalf of the Secretary, ASPR leads HHS international preparedness efforts and response activities in close collaboration with the Office of Global Health Affairs (OGHA), the CDC, and FDA. Within ASPR, the Office of Medicine, Science and Public Health (OMSPH) provides expert advice on international issues, and officials within the Office of the Assistant Secretary interact directly with the international community.

*B. The Need for a Global Approach to MCM Preparedness*

No one can be certain about where a bioviolence attack might occur. What is certain is that a sufficiently severe attack will have global implications, wholly ignoring borders. The stuff of bioviolence—pathogens, laboratory equipment, and knowledge—is ubiquitous and growing more so. Once a bioweapon is prepared, perpetrators from anywhere can slide across national boundaries and release disease anonymously. Moreover, vulnerabilities are global. If a highly contagious agent is used, the interests of international security demand that its spread be stanching. If a noncontagious agent (e.g., anthrax) is used, the potential for massive loss of life (perhaps from repeated attacks) would horrifically damage the global economy and diplomacy.

Even if by some magic potion Americans could be immunized against every bioviolence agent, the prospect of witnessing attacks that devastate allies, transform developing societies into despair, cancel transport and trade, and sow worldwide panic would beget a profoundly catastrophic environment. In this context, globalization and interdependency are not mere clichés. To plug a vulnerability somewhere but leave huge gaps elsewhere is to build a dam from a sieve. If only for the potential magnitude of loss, perhaps counted in millions of lives and trillions of dollars, Americans would be gravely wounded by a foreign bioviolence attack.

Yet, global bioviolence MCM preparedness is appallingly inadequate. Consider smallpox, arguably among the gravest of potential bioviolence agents. When smallpox was formally declared eradicated nearly three decades ago, WHO had 200 million doses of vaccine. In the intervening years, that number has decreased to about 2.5 million doses, located in a single site near Geneva.<sup>18</sup> Some nations have developed their own stockpiles. Altogether, stockpiles of smallpox vaccine are less than 800 million doses –

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17. Pandemic and All-Hazards Preparedness Act (PAHPA), Pub. L. No. 109-417, 120 Stat. 2831 (codified in scattered sections of 42 U.S.C.).

18. See WORLD HEALTH ORGANIZATION, SMALLPOX GLOBAL VACCINE RESERVE: REPORT BY THE SECRETARIAT (2005), available at [http://apps.who.int/gb/ebwha/pdf\\_files/WHA58/A58\\_9-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA58/A58_9-en.pdf).

enough for at best 12 percent of the world's population assuming ideal distribution. Over 80 percent of these doses are stockpiled in six countries; slightly less than 50 percent belong to the United States.<sup>19</sup> Ten countries have appreciable stockpiles of vaccine (relative to their population size). Only four of these countries are outside NATO and the G-8: Israel, Singapore, South Africa, and Malaysia.<sup>20</sup> Nearly all other countries have little or no vaccine.<sup>21</sup> Even under optimal conditions to meet an emergency, approximately seven months would be needed for full surge production; even then, global smallpox vaccine manufacturing capacity would be about 40 million doses per month.<sup>22</sup>

These deficiencies were demonstrated in the 2005 Atlantic Storm exercise on smallpox response:

Although some countries had enough to vaccinate their entire population, others had only enough of the vaccine for one percent of their citizens, or even less. "When I saw the list [of vaccine stocks], that was a shock to me, how little prepared many countries are, even rich Western countries," said Klaas de Vries, who played the Dutch Prime Minister.<sup>23</sup>

The lack of an international architecture for MCM preparedness undermines the entire U.S. anti-bioviolence strategy by insinuating that American scientific genius is to be isolated exclusively to self-protection. Bluntly stated, it is illegitimate to assert that while threats of bioviolence are inherently international in scope and consequence, MCM preparedness against those threats should be pursued independently by each sovereign nation.

Finally, it can be argued that MCM preparedness is obligatory under the WHO's International Health Regulations (IHR) which require that States develop, strengthen, and maintain the capacity to respond promptly and effectively to public health emergencies of international concern and maintain a national public health emergency response plan.<sup>24</sup>

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19. See Bradley T. Smith et al, *Navigating the Storm: Report and Recommendations from the Atlantic Storm Exercise*, 3 *BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY PRAC. & SCI.* 256, 256–67 (2005).

20. G8 nations include: United States, France, Germany, Italy, Japan, United Kingdom, Canada, and Russia. A complete listing of NATO members is available at [http://www.nato.int/cps/en/natolive/nato\\_countries.htm](http://www.nato.int/cps/en/natolive/nato_countries.htm).

21. Smith et al., *supra* note 19.

22. See WORLD HEALTH ORGANIZATION, *supra* note 18.

23. Daniel S. Hamilton & Bradley T. Smith, *Atlantic Storm: A Simulated Bioterrorist Attack Demonstrated the Weakness of International Public Health and Security Systems when Dealing with a Sudden Outbreak of Highly Infectious Diseases*, *EMBO REP.*, Jan. 2006, at 4, 6.

24. See WORLD HEALTH ORGANIZATION, *INTERNATIONAL HEALTH REGULATIONS 40–42* (2005), available at [http://www.who.int/csr/ihr/IHR\\_2005\\_en.pdf](http://www.who.int/csr/ihr/IHR_2005_en.pdf). The IHRs recommend that national plans enable authorities:

- a) to determine rapidly the control measures required to prevent domestic and international spread;
- b) to provide support through specialized staff, laboratory analysis of samples . . . and logistical assistance . . . ;

### C. *The GHSAG Initiative*

The most important recent international effort to reduce bioviolence dangers is the agreement of the Global Health Security Action Group (GHSAG) to focus attention on a global infrastructure for distributing medicines worldwide. GHSAG includes ministerial level participation from the United States, Canada, France, Germany, Italy, Japan, Mexico, and the United Kingdom, as well as leadership of the European Commission and the World Health Organization. It has no *de jure* authority, but its high level participants can coordinate and commit to devoting substantial resources to advance common health objectives.<sup>25</sup>

In the 2008 Ministerial Statement, GHSAG members formally recognized that international coordination is necessary for delivery of MCMs to patients:

Regarding medical countermeasures, we considered the need to develop a sustainable global infrastructure that would allow us to work together to counteract the health consequences of natural or man-made threats. Our initial efforts will focus on sharing infor-

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- c) to provide on-site assistance as required to supplement local investigations;
  - d) to provide a direct operational link with senior health and other officials to approve rapidly and implement containment and control measures;
  - e) to provide direct liaison with other relevant government ministries;
  - f) to provide, by the most efficient means of communication available, links with hospitals, clinics, airports, ports, ground crossings, laboratories and other key operational areas for the dissemination of information and recommendations received from WHO regarding events in the State Party's own territory and in the territories of other States Parties; [and]
  - g) to establish, operate and maintain a national public health emergency response plan, including the creation of multidisciplinary/multisectoral teams to respond to events that may constitute a public health emergency of international concern . . . .

*Id.*

25. See Global Health Security Initiative, Ministerial Statements: Brussels, Belgium (Dec. 2008), <http://www.ghsi.ca/english/statementbrussels2008.asp>. The 2008 Ministerial Meeting produced the following commitments:

- On risk and crisis communications, we agreed to continue our collaboration to strengthen our collective knowledge and to apply the principles of risk and crisis communications in specific situations.
- We agreed to enhance our laboratory capabilities by improving the transportation of diagnostic specimens and reference materials; facilitating the exchange of scientific expertise among members; and strengthening diagnostic capacities, both within and beyond member laboratories. This will be extended to an international network of radiobioassay laboratories.
- We supported increased GHSI coordination to improve global early alerting and reporting, including risk assessment and integrated analysis of CBRN and pandemic influenza threats, and recognize that the GHSI can bring added value in stimulating the timely exchange of information toward the prevention of risks to health.
- We agreed to enhance our preparedness for CBRN threats and pandemic influenza by collaborating in moving towards a sustainable global infrastructure, including research and development, for medical countermeasures.
- We welcomed the proposal of Commissioner for Health Ms. Androulla Vassiliou to have a joint cross-national exercise organised between the GHSI partners and the European Union in 2010. The exercise will support the work of the GHSI in the area of risk and crisis communications.

*Id.*

mation on research and development; improving diagnostics capacity; developing strategies for shelf life extension of stockpiled medical countermeasures; and collaborating on the development of specific therapeutics, vaccines, and/or diagnostic tools for specific threats.<sup>26</sup>

GHSAG's interest in MCMs includes addressing regulatory issues related to MCM licensing and distribution. GHSAG members are planning to share best practices and discuss potential avenues for cooperation.

Yet, global MCM preparedness is not simple. Advancing MCM preparedness on a global level is fundamentally more problematic than advancing comparable initiatives domestically. The expense and logistical challenges multiply greatly when the target is all of humanity, not just a single country. Even more troubling, there is a daunting governance deficit; no explicit structure is authorized to process such initiatives. Every proposed initiative requires identification of an implementation mechanism, and any State can frustrate collective action. A truly global approach is easier said than done.

In this context, GHSAG's narrow membership deserves attention. There is an inherent tension between inclusion and the need for consensus; the more that a truly global body must respect the voices of nearly two hundred sovereigns, the less that it will generate consensus on what to do.<sup>27</sup> Indeed, GHSAG's efficacy can be attributed to the fact that it includes only eight nations plus a regional organization (the European Commission) and one international organization (the WHO). These nations are hardly representative of the world: six are involved in both NATO and the United Nations Western European and Others Group (the United States is a partial member). China and India, which together represent one-third of the world's population and are among the fastest growing economies, are not included. GHSAG includes no Islamic, African, South American, or former Soviet Union nations, and only one Asian nation (Japan).

While GHSAG's limited membership no doubt contributes to its ability to advance initiatives, a useful middle ground between its very narrow membership and something truly global (perhaps engagement at the level of the G-20) might offer benefits in terms of engagement and resources that would be worth the difficulties of reaching consensus among a larger group.

Worth mentioning is a group with fifteen member states that has unquestionable *de jure* authority to address threats to international peace and security (certainly including bioviolence): the United Nations Security Council. Among experts, there is little confidence that the UNSC will soon take up the challenge of bioviolence MCM preparedness; untangling the

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26. *Id.*

27. Moises Naim, *Minilateralism: The Magic Number to Get Real International Action*, FOREIGN POLICY July–Aug. 2009, at 136.

many political reasons why this body might be an ineffective planning venue are far beyond this article's scope. Yet, as will be discussed, to get from where we are today to a preparedness system that is truly global means adjusting national laws, adapting programs of international and regional organizations, and perhaps creating new institutional frameworks (hopefully minimal). Much of these modifications might proceed more expeditiously with direction from the one international body that is legitimately constituted to sustain security.

*D. Article Focus: Legal Challenges of a Global MCM Preparedness Strategy*

Progressive action to stockpile and distribute MCMs requires an altogether unique degree of international cooperation and thus can strengthen the development of international law. Attention needs to be devoted to legal constraints on governments' authority to take necessary action as well as to the potential for substantial intrusion into personal liberties and proprietary rights. Addressing these legal issues now, before a bioviolence attack, will not only facilitate expeditious response, it will refine modalities of global planning and build confidence.

The following sections of this article focus on legal challenges organized under four broad categories: (1) risk assessment and management; (2) incentivizing research and development of new MCMs; (3) facilitating MCM licensing and emergency authorization; and (4) planning for MCM stockpiling, delivery, and dispensation. These challenges are integrated, and initiatives to meet these challenges are continuous and mutually reinforcing.

It is crucial to emphasize that this article is an outline of a strategy. Many potential issues and initiatives are discussed with reference to mechanisms currently advanced by relevant international organizations. Each initiative could be the subject of its own lengthy article. Presenting these initiatives in rapid succession might convey an impression that they are undemanding, without political objection or intractable problems that might impede their implementation. Nothing could be further from the truth. These initiatives must be implemented in an astoundingly dysfunctional world order that hurls obstructions at every step.

The objective here is to portray a map for advancing global MCM preparedness not because the journey is simple but because only with a map can policy makers gain perspective about the magnitude of the undertaking they confront. A map necessarily omits many details. Its purpose is to depict the key components and to draw their interconnections. To get to the destination of improved security from bioviolence will be an arduous undertaking. It may be easier, hopefully, with an understanding of where we need to go.

## I. RISK ASSESSMENT AND MANAGEMENT

The first task of MCM planning processes is risk management: the process of constructing, evaluating, implementing, monitoring, and revising strategies for reducing losses from future hazards and dealing with the recovery process should a hazard occur. This includes an assessment process to prioritize risks, identify existing and near-term available MCMs for high priority risks, and allocate scarce resources for developing those MCMs.<sup>28</sup> These prioritization decisions critically set the boundaries for the system's future response capability and help to ensure a comprehensive and risk-prioritized biopreparedness strategy.

Related to risk management is the need to resolve disparities of terminology with regard to biorisks and MCMs. Harmonization of research lexicons and stage nomenclature for MCM R&D can reduce the costs of collaboration and encourage engagement of private and academic sectors. Simply, everyone should use the same research and regulatory language.<sup>29</sup> Research can be shared more readily and technology advances can be measured more reliably and fairly against one another for both scientific and contracting purposes.

Today, assessing and managing risks is done exclusively on the national level. Even in Europe where the European Commission might be expected to assess and manage risks regionally, most relevant decisions are left to national authorities. Worldwide, the upshot is that pivotal decisions

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28. In 2006, the Department of Homeland Security (DHS) completed a Bioterrorism Risk Assessment; it continues to review and improve its processes. Current U.S. bioterrorism risk assessment principles are the following:

- *Risk analysis needs to address bioterrorism uncertainties:* Probabilistic risk assessment is a proven technique that can be used for managing the risks from bioterrorism.
- *Bioterrorism risk analysis requires access to multidisciplinary expertise:* Key disciplines include biology, epidemiology, psychology, public communications, decision analysis and risk analysis, operations research, probability, and statistics.
- *Risk analysis must be responsive to dynamic terrorism threats:* Risk analysis must take into account changing threat conditions and their resource implications over time. Intelligent adversaries will adjust their strategies and tactics to counter the U.S. ability to detect, prepare for, and respond to their attacks. Therefore, the nature of risk is a continuing evolution and will always be difficult to estimate.
- *The purpose of risk assessment is to support risk management:* Policy makers should develop risk mitigation measures that are informed by risk analysis, including assessment of social, psychological, direct, and indirect economic impacts, and should apply such measures in a manner that consciously seeks to avoid unintended consequences.

COMM. ON METHODOLOGICAL IMPROVEMENTS TO THE DEP'T ON HOMELAND SECURITY'S BIOLOGICAL AGENT RISK ANALYSIS, NAT'L RESEARCH COUNCIL, DEPARTMENT OF HOMELAND SECURITY BIOTERRORISM RISK ASSESSMENT—A CALL FOR CHANGE 9 (2008) (summarizing and discussing the Department of Homeland Security's 2006 Bioterrorism Risk Assessment report).

29. The U.S. government has established a Technology Readiness Levels (TRLs) scheme that standardizes the designation of the stage of development for evolving technologies and provides a common understanding of technological status. See DEP'T OF DEFENSE, TECHNOLOGY READINESS ASSESSMENT (TRA) DESKBOOK, at H-1 to H-28 (2005), available at [http://www.dod.mil/ddre/doc/May2005\\_TRA\\_2005\\_DoD.pdf](http://www.dod.mil/ddre/doc/May2005_TRA_2005_DoD.pdf).

are not so much made inconsistently; they are typically ignored altogether whether due to lack of awareness of biothreats, political disputes about these threats' strategic relevance, or funding disputes about relative priorities. Viewed from afar, there is a woeful lack of decision-making capacity that is the necessary foundation of preparedness. In this anarchic environment, private sector participants who might produce MCMs or develop distribution capabilities are dissuaded from becoming engaged.

In the absence of an authoritative body that makes critical choices about assessing risks and developing capacities to manage those risks, it is difficult to understand how global MCM preparedness can proceed effectively. Briefly, these choices include:

1. How and by whom should a global list of biothreat agents be selected? How should criteria for selection be harmonized in view of disparate perspectives on the threats, pre-existing vaccination levels, and overall health conditions?
2. How should each agent's potential consequences—its lethality, virulence, contagiousness, etc.—be weighed against an MCM's benefits and costs including its side effects; its per unit cost of production; and the capacity to produce it before or immediately after an outbreak? And, how quickly it can be delivered to an infected area and dispensed?
3. Should resources focus on pre-attack immunization or on treatment? Widespread immunization is expensive with no guarantee that a selected disease will occur. Reliance on post-attack treatment, however, can leave populations vulnerable to large losses. (The United States civilian population treatment strategy relies primarily on post-event prophylaxis or post-exposure treatment, although it has stockpiled MCMs against threats of potential catastrophic consequence—e.g., smallpox—to dispense to potentially every American as needed.)
4. How should MCM R&D cope with various agents? Currently, most MCMs are “one-bug, one-drug.” Increasingly, MCM research will focus on broad spectrum treatments and platform technologies that facilitate prompt production of MCMs. (The U.S. National Strategy for Medical Countermeasures against Weapons of Mass Destruction targets the use of existing approaches for developing medical countermeasures to address challenges posed by traditional CBRN agents while calling for a flexible capability to develop new MCMs.<sup>30</sup>)

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30. See Homeland Security Presidential Directive 18, *supra* note 8. HSPD-18 lays out three principles to guide this effort:

- Integrate fundamental discovery and medical development to realize novel medical countermeasure capabilities.
- Establish a favorable environment for evaluating new approaches.
- Integrate the products of new and traditional approaches.



5. How will each MCM be dispensed? With regard to a specific disease agent, is comprehensive vaccination or ring vaccination preferable?<sup>31</sup> Similarly, some MCMs must be dispensed by public actors (e.g., vaccines), while others can be distributed directly to and self-administered by individuals (e.g., oral antibiotics).

International law cannot and should not answer these questions. International law should, *inter alia*, identify the authoritative body for making these decisions, the substantive and procedural standards that such decisions should satisfy, and the degree of transparency and reviewability of such decisions.

Altogether, there is value in having an official international body that defines priorities for MCM development and incentivizes how potential developers pursue those priorities. While a fully authoritative global body with powers comparable to BARDA-PHEMCE-NBSB is unrealistic, a more limited initiative is to establish an international biopreparedness panel or task force that defines harmonized criteria for risk management, enabling governments to better assess probabilities of specific bioviolence attacks and their predictable consequences. This task force could also usefully build an information exchange platform among scientific researchers, funders, and private sector biodefense entities for the purpose of communicating research and development opportunities and challenges to decision makers, thereby optimizing global competition for producing and developing promising anti-bioviolence MCMs.

This task force should be international in scope so that it can harmonize MCM preparedness planning worldwide. While the WHO and related organizations should be engaged in these activities, and while this task force should be international in scope, bioviolence risk management is not centrally a public health function and entails determinations about threats and security that exceed WHO's mandate.

At minimum, this task force should establish a platform for gathering scientific input and forging scientific consequence on risk management questions. Moreover, it should track ongoing trends and opportunities that can be exploited to promote and streamline future biodefense research and development activities. At maximum, it could form an international MCM

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*Id.* at 131–32. Recently, the University of Pittsburgh Medical Center and GE Healthcare announced a collaboration aimed at the construction of an advanced development and production facility for the manufacture of vaccines and therapeutics to counter a range of biological threats. Press Release, University of Pittsburgh Medical Center, UPMC and GE Healthcare Collaborate to Protect United States from Bioterrorism, Infectious Diseases (Oct. 12, 2009), available at <http://www.upmc.com/MediaRelations/NewsReleases/2009/Pages/UPMC-GEC-Bioterrorism-Infectious-Diseases-Protection.aspx>.

31. Cheun-Yen Lau, *Ring Vaccination vs. Mass Vaccination in the Event of a Smallpox Attack on the United States*, AMERICAN COLLEGE OF EMERGENCY PHYSICIANS, Sept. 2004, available at <http://www.acep.org/ACEPmembership.aspx?id=39246>.

development strategy, plan for its implementation, and serve as an organizational structure to handle the attendant procedural and administrative tasks. An intermediate role, in addition to gathering scientific input and forging consensus, would be to promote harmonization of the entrepreneurial aspects of bioviolence risk management by promoting innovative procurement modalities that incentivize MCM development and production.<sup>32</sup>

## II. INCENTIVIZING MCM RESEARCH AND DEVELOPMENT

Discovering and producing effective bioviolence MCMs is a risky business. It is difficult to predict which specific pathogen perpetrators of bioviolence will use. Developing MCMs against each of these pathogens is costly and time consuming. On average, developing a new drug takes nearly ten years, and costs between \$800 million and \$1.7 billion.<sup>33</sup> These substantial resources would be devoted to drugs that, in the end, may not be approved for distribution.<sup>34</sup>

Even if approved, profits from sales might not cover the costs of development. Bioviolence does not occur frequently, and the odds of exposure to a disease that might be used in an attack are low. “[T]he global market for just one cholesterol-lowering agent exceeds the global market for all vaccines together, not just those that comprise a security countermeasure.”<sup>35</sup> With such small and uncertain markets for MCMs, most private medicine developers choose to forego expensive MCM research, development, and production.

Governments and other MCM purchasers can impel private sector participation by providing R&D assistance, identifying R&D priorities, facili-

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32. For example, milestone contracts that provide for installment deliveries can lower contracting risks, assuring steady revenue and encouraging rapid delivery. Payment terms might also allow purchasers to pay a discounted price for MCMs that have yet to be approved with a remainder to be paid later upon full approval; MCM producers could thereby avoid the risks of conventional all-or-nothing contracting even as governments retain periodic opportunities to evaluate the products. In the non-price context, useful terms might include requiring producers to absorb the cost of storing products and maintaining their surety or allowing for the designation of vendors as exclusive suppliers. Terms might also include designating vendors as the exclusive suppliers to ensure a continued relationship or protect intellectual property concerns. Contracts could require producers to create and maintain unused excess production capacity to be tapped or “surged” during an emergency. The United States has considered these terms in legislation governing use of its special reserve fund to purchase stockpile assets. *See* 42 U.S.C. § 247d-6b(c)(7)(C)(ii) (2006); *see also* Jonathan B. Tucker, *Developing Medical Countermeasures: From BioShield to BARDA*, 70 *DRUG DEV. RES.* 224, 226, 231 (2009) (discussing specific requirements for MCM contracting).

33. *Project BioShield Reauthorization Issues*, *supra* note 12, at 7.

34. “It is estimated that of every 5,000 ‘candidate’ drugs that look promising on the lab bench, only 5 enter clinical trials, and only 1 of those achieves FDA licensure.” Bradley T. Smith et al., *Developing Medical Countermeasures for Biodefense*, 7 *BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY PRAC. & SCI.* 42, 42 (2009), available at [http://www.upmc-biosecurity.org/website/resources/publications/2009/biomemo/2009-03-27-devel\\_med\\_cntrmeasures.html](http://www.upmc-biosecurity.org/website/resources/publications/2009/biomemo/2009-03-27-devel_med_cntrmeasures.html).

35. *Project BioShield Reauthorization Issues*, *supra* note 12, at 7.

tating regulatory approval, and guaranteeing future procurement contracts. Initiatives that reduce barriers and risks associated with potential MCMs can encourage producers to brave the dangerous beginning R&D stages. For example, MCMs for smallpox<sup>36</sup> and anthrax<sup>37</sup> that the United States widely stockpiles are the result of policies that have substantially altered typical market dynamics associated with pharmaceuticals.

This section considers two legal aspects of incentivization: (1) protecting MCM producers from potential liabilities; and (2) clarifying producers' patent rights.

#### A. *Liability Protection of MCM Producers*

MCMs could cause injury or even death among healthy recipients who might seek damages from producers. This risk of liability weighs heavily against expending vast sums to produce vaccines, deterring substantial investments on new MCMs with potentially unknown effects.<sup>38</sup> The variability of liability regimes across countries adds legal uncertainty.

Providing liability protection could ease pharmaceutical companies' concerns, especially during an emergency. Yet, there are substantial fairness issues that should militate against broad immunity that substantially infringes on victims' remedies. Efforts should be made, therefore, to harmonize liability standards worldwide for MCM development so as to both incentivize MCM development and respect victims.

Accomplishing harmonization of liability standards means addressing two questions: first, how should risks of loss be assigned between the producer and the public? And second, how should activities be distinguished for purposes of deciding how to assess liability?

##### 1. *Assigning Risk of Loss*

Administration of MCMs raises important questions of individual versus community welfare. At least three models for assigning risk of loss are available. First, a government could administer the MCM, substitute itself for the producer in any dispute, or indemnify a producer who might be held liable. The normal liability standards would apply: the victim would have to show that the MCM caused the harm; the difference from normal standards is that the government, not the producer, pays damages. Although protec-

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36. Strategic National Stockpile, *supra* note 13.

37. *Id.*

38. In the United States in the 1980s, adverse reactions to vaccines created liability concerns for producers which caused them to stop producing vaccines that, in turn, led to a decline in child vaccination rates. Remaining manufacturers increased their prices to cover liability costs which led to significant vaccine shortages. See AM. MED ASSOC., REPORTS OF BOARD OF TRUSTEES, LIABILITY PROTECTIONS FOR ADULT VACCINES 47–48 (June 2005), available at <http://www.ama-assn.org/ama1/pub/upload/mm/38/a-05bot.pdf>.

tive of producers, this approach compels government acceptance of burdensome litigation of individual claims.

A second approach is to establish a no-fault compensation scheme whereby the government compensates victims without concern as to whether the producer was at fault—recovery is allowed so long as the victim suffers any stipulated injury presumed to be caused by the medicine. This is the approach of the United States National Vaccine Injury Compensation Program,<sup>39</sup> as well as of the Smallpox Emergency Personnel Protection Act of 2003.<sup>40</sup> Its virtue is to minimize any risk to the producer and simplify victims' recovery, but it disregards whether the producer might have engaged in misconduct.

The third model, used by the U.S. Public Readiness and Emergency Preparedness (PREP) Act,<sup>41</sup> is to immunize producers and to permit victim recovery from a specially established fund for claims of loss due to use of MCMs in a public health emergency. However, immunity does not apply in cases of willful misconduct. A victim must choose whether to collect from the "Covered Countermeasures Process Fund"<sup>42</sup> or prove that the producer's misconduct caused the losses. This approach's virtue is to enable the victim to recover from the fund while also disallowing immunity if the producer is at fault.

Each nation can adopt (or adapt) any of these models so long as each nation insulates producers from alleged losses due to the risks of using their MCMs (but not losses due to producer malfeasance). Indeed, the WHO uses this approach when administering vaccine donation programs.<sup>43</sup>

## 2. *Criteria of Liability*

For any of the approaches that turn on fault, it is important to clarify what activities might justify extending liability to a producer. Liability should be imposed on a producer that:

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39. 42 U.S.C. § 300aa-10 (2006).

40. Smallpox Emergency Personnel Protection Act of 2003, Pub. L. 180-20, 117 Stat. 638 (codified in scattered sections of 42 U.S.C.).

41. 42 U.S.C. § 247d-6d to -6e (2006).

42. See Dep't of Health and Human Serv., Health Resources and Services Administration, Countermeasures Injury Compensation Program, <http://www.hrsa.gov/countermeasurescomp/default.htm> (last visited Oct. 21, 2009).

43. In regards to H5N1, "Bird Flu," the WHO plan states, "[w]ith regard to liability associated with a WHO H5N1 influenza vaccine stockpile, manufacturers and/or suppliers are responsible for developing vaccines in accordance with WHO standards. Countries requesting vaccine from the stockpile would assume responsibility for their use. It was recommended that the terms of a disclaimer to reflect responsibility for liability should be developed in advance to circumvent delays in a pandemic situation." WORLD HEALTH ORGANIZATION, GLOBAL PANDEMIC INFLUENZA ACTION PLAN TO INCREASE VACCINE SUPPLY: PROGRESS REPORT 2008, at 15 (2008), available at [http://www.who.int/vaccine\\_research/Global\\_Pandemic\\_Influenza.pdf](http://www.who.int/vaccine_research/Global_Pandemic_Influenza.pdf). The WHO will follow these same mandatory disclaimer procedures for its H1N1 donation program set to begin in November 2009. Lisa Schlein, *Developing Countries to Get Swine Flu Vaccine*, VOICE OF AMERICA NEWS ONLINE, Sept. 25, 2009, <http://www.voanews.com/english/2009-09-25-voa43.cfm>.

- fails to provide full and accurate disclosure about the risks of its products to regulatory authorities during the approval process;
- delivers substandard product due to production errors, poor handling procedures, or other forms of negligence (or worse); or
- fails to provide sufficient use instructions or fails to warn users of potential risks.

There are other situations that are harder to resolve. For example, if the producer's estimate of the harmful consequences of using the MCM is too low or its estimate of the MCM's benefits is too low, should there be liability? If the mistake was not willful, it still might be the case that the producer undertook insufficient study (especially in the case of a drug authorized for emergency use); imposing liability could deter seeking authorization without time-consuming testing. A more perplexing grounds for liability is where the MCM works as anticipated, but the producer fails to deliver as much as promised, or as quickly as promised, perhaps due to the challenges of meeting unanticipated "surge production" demands. Again, even if the producer acted in good faith, there is reason to impose liability in that the producer's promise of supply was the basis of the government's decision; knowledge that such a promise might become the basis of liability will induce producers to offer such promises more carefully.

Altogether, international law should guide and harmonize the criteria of liability protections for MCM producers. There will be benefits from uniform and predictable rules that can foster increased investment in MCM research and development. Failure to protect the system against such liabilities should be regarded as a breach of State responsibility.<sup>44</sup> State responsibility applies for undermining the international harmonization of liability that is essential to the effectively administering a global MCM infrastructure.

### B. Patent Protection

The intellectual property rights associated with MCMs are a vexing issue demanding international resolution. In the context of bioviolence, the key question is how States can gain access to MCMs if the patent holder is unwilling or unable to deliver in sufficient quantities.

MCM producers argue that the high risks of making safe and effective vaccines would make no economic sense if, having configured a critical

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44. The U.N. International Law Commission, in its 2001 Draft Articles on Responsibility of States for Internationally Wrongful Acts, posits, "There is an internationally wrongful act of a State when conduct consisting of an action or omission . . . constitutes a breach of an international obligation of the State." U.N. International Law Commission, *Report of the International Law Commission on the Work of Its Fifty-third Session* ¶ 76, U.N. Doc A/56/10 (Apr. 23–June 1, 2001 and July 2–Aug. 10, 2001), available at <http://www.un.org/law/ilc/>.

drug, someone could readily copy and sell it for a price that need not reflect the sizeable research investment. From developing nations' perspective, paying a price that reflects research costs plus profit is virtually impossible. They could produce the drug at a fraction of the cost, and their populations desperately need these medications; they argue that the pharmaceutical sector's pursuit of exorbitant profits should not be a death sentence for millions of innocent people.

Under the World Trade Organization's (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) Article 31, States may grant *compulsory patent licenses* that allow domestic producers to manufacture a patented item without the patent holder's consent, provided such licenses must be limited to meeting domestic needs, not for export, and the original patent holder is to be paid adequate compensation.<sup>45</sup> As of 2008, forty-four WTO member-States had ratified Article 31bis.<sup>46</sup> Significantly, paragraph (b) requires:

[S]uch use may only be permitted if, prior to such use, the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time. This requirement may be waived by a Member in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use.

The policy that compulsory licenses be granted for domestic needs has been criticized for failing to provide relief to least developed countries that lack a domestic pharmaceutical manufacturing capacity. So, in 2003, the WTO Council announced that a country may produce generics of patented drugs for export if another country is in need. The importing country must inform the Council what products it seeks and how much—perhaps a time-consuming obstacle during an unforeseen public health emergency when MCMs are immediately needed. National patent regimes may include specialized provisions allowing States to circumvent patents for national security reasons or in times of emergency (in which bioviolence certainly would fall).<sup>47</sup>

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45. Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1C art. 31, Apr. 15, 1994, 33 I.L.M. 81, available at [http://www.wto.org/english/docs\\_e/legal\\_e/27-trips.pdf](http://www.wto.org/english/docs_e/legal_e/27-trips.pdf).

46. Erin M. Andersen, *Unnecessary Deaths and Unnecessary Costs: Getting Patented Drugs to Patients Most in Need*, 29 B.C. THIRD WORLD L.J. 85, 101 (2009).

47. Rahul Rajkumar, *The Central American Free Trade Agreement: An End Run Around the Doha Declaration on Trips and Public Health*, 15 ALB. L.J. SCI. & TECH. 433, 442 (2005). For example, in 2003, El Salvador published a Trade Policy Review describing the country's Law on the Promotion and Protection of Intellectual Property (LFPPI). The LFPPI provides for the grant of a compulsory license in emergencies or national security contexts, if it is non-assignable, non-exclusive, and provides adequate remuneration to the rights holder. The Council for TRIPS reviewed the Salvadoran LFPPI and found it to be in compliance with international agreements. *Id.* at 457.

Some States have already issued compulsory licenses for domestic use (e.g., Thailand, discussed below), and in at least two cases, pairs of countries have invoked Article 31bis's procedure (Canada-Rwanda in 2007 and India-Nepal in 2008).<sup>48</sup> Notably, the issue of whether a State may grant a compulsory license for a bioviolence MCM arose in connection with the 2001 anthrax attacks. Canada overrode the patent on Cipro, a strong antibiotic. The Bush administration's threat to circumvent Cipro's patent protection evoked a promise from Bayer, the patent holder, to supply the drug at a deeply discounted price.

Many unanswered questions belie Article 31(b)'s utility in the context of a bioterror event.<sup>49</sup> Who should assess the grounds for compulsory licensing? Under what conditions? In what timeframe? Further, the language of Article 31(b) uses undefined terms—"reasonable commercial terms and conditions" and "reasonable period of time"—which could slow any negotiating process. Perhaps the most complex problem is whether a nation should be able to claim an emergency exception to issue a compulsory license if an attack has *not yet occurred*? Most bioviolence agents act too quickly to allow a post-attack licensing and production process. Does a nation *need* a compulsory license simply because the product costs more than a State would like to pay? Consider the case of Thailand which issued compulsory licenses for HIV/AIDS drugs but also a heart disease medicine called Plavix—not surprisingly, international criticism was much stronger for the latter than the former.<sup>50</sup> While the threat of HIV/AIDS is a clear

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48. See Andersen, *supra* note 46, at 105, 112. According to Andersen:

On July 19, 2007, Rwanda took the first step in the Article 31bis process and informed the WTO of its intention to import compulsory-licensed pharmaceuticals for public health reasons. In September 2007, Canada became the first country to issue a compulsory export license and granted Apotex, a Canadian generic drug manufacturer, permission to supply TriAvis, a combination AIDS drug, to Rwanda.

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In early 2008, Nepal became the second country to apply for an import-license under Article 31bis. Indian drug-manufacturer Natco Pharma responded, and sought out a compulsory license to produce generic versions of two anti-cancer drugs. Natco has proposed to manufacture 45,000 doses of the drugs, and, subject to Article 31(h), remunerate the patent-holders a five percent royalty.

*Id.* at 103–04. See also George Tsai, *Canada's Access to Medicines Regime: Lessons for Compulsory Licensing Schemes Under the WTO Doha Declaration*, 49 VA. J. INT'L L. 1063, 1075–79 (2009).

49. See Taiwo A Oriola, *Against the Plague: Exemption of Pharmaceutical Patent Rights as a Biosecurity Strategy*, 7 U. ILL. J.L. TECH. & POL'Y 287, 329–30 (2007).

50. Cynthia M. Ho, *Patent Breaking or Balancing? Separating Strands of Fact from Fiction Under TRIPS*, 34 N.C. J. INT'L L. & COM. REG. 371, 421–22 (2009) (“Thailand’s license on Plavix drew particular attention from patent owners as the first step on a slippery slope towards licensing any and all patents if heart disease were considered an emergency. . . . ‘Combating HIV has always been seen by activists, if not others, as a health emergency, and under WTO rules, patents can be broken in emergencies. However, it’s hard for anyone to argue that heart disease meets such stringent tests.’”); and Andersen, *supra* note 46, at 107 (“When Thailand issued a compulsory license in 2007, both the United States and the European Union condemned its actions, censuring the country and putting it on a ‘priority watch list.’”).

reality in many states invoking compulsory licenses, can the same be said for anthrax?

A potential test case for this question (and Article 31bis) could be Canada's Access to Medicines Regime (CAMR),<sup>51</sup> manifesting TRIPS Article 31bis and authorizing Canada's Commissioner of Patents to grant compulsory licenses permitting the manufacture and export of low-cost versions of patented pharmaceuticals.<sup>52</sup> Interestingly, one of the pharmaceuticals eligible for CAMR is 500mg oral Ciprofloxacin (Cipro)<sup>53</sup>—the subject of the 2001 dispute and exactly the drug and dose listed by the CDC as treatment for Anthrax.<sup>54</sup>

The straightforward point here is that bioviolence exposes a flaw in the TRIPS agreement's compulsory licensing provisions: a compulsory license may be issued only after a need for a particular product has been demonstrated. The system might work well enough regarding a disease like HIV/AIDS that is a present and ongoing medical threat. However, in a way that is unique from the role served by other medicines, bioviolence MCMs have limited utility until a crisis when the need for them will be overwhelming. Waiting until an attack to justify a compulsory license is too late, and will inevitably result in suboptimal, unpredictable outcomes. The United States' behavior following the anthrax attacks shows that, amid a bioviolence crisis, the patent protection system breaks down. This challenge of bioviolence preparedness is an area that international law can usefully address now before an attack, thereby encouraging producers to invest in new MCMs while ensuring that bioviolence victims get what they need during an emergency. Still, prospects for progress in this context are less than promising.<sup>55</sup>

### III. FACILITATING MCM LICENSING AND EMERGENCY APPROVAL

It is in every nation's interest to ensure that effective MCMs can be expeditiously put to use wherever needed. Typically, however, medicines may be dispensed only if licensed after thorough testing has demonstrated

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51. Canada's Access to Medicines Regime, Introduction, [http://www.camr-rcam.gc.ca/intro/index\\_e.html](http://www.camr-rcam.gc.ca/intro/index_e.html) (last visited Oct. 24, 2009).

52. Norway, the Netherlands, India, Korea, China, and the EU have passed similarly directed laws. CANADA'S ACCESS TO MEDICINES REGIME—CONSULTATION PAPER 2 n.5 (2006), available at [http://camr-rcam.gc.ca/review-reviser/camr\\_rcam\\_consult\\_e.pdf](http://camr-rcam.gc.ca/review-reviser/camr_rcam_consult_e.pdf); see also Tsai, *supra* note 48, at 1076 n.65.

53. Patent Act, R.S.C., ch. P-4, Schedule 1 (1985).

54. Centers for Disease Control and Prevention, Patient Information: Ciprofloxacin 500-mg Oral Tablet, <http://www.bt.cdc.gov/agent/anthrax/treatment/cipropatient.asp> (last visited Oct. 24, 2009).

55. The World Intellectual Property Organization (WIPO) has conducted negotiations toward substantive harmonization of international intellectual property laws under the auspices of the United Nations. However, these negotiations have not been generally successful, calling into question prospects for improving standards for compulsory licensing. Subhasis Saha, *Patent Law and TRIPS: Compulsory Licensing of Patents and Pharmaceuticals*, 91 J. PAT. & TRADEMARK OFF. SOC'Y 364, 364–65 (2009).



their safety and efficacy. Yet, many novel bioviolence MCMs have not been elaborately tested. Moreover, many MCMs are licensed only in a few developed nations. If an attack happens in a nation where an MCM is not licensed, an official might insist on seeking clarification of the unlicensed foreign MCM's certification, delaying or prohibiting dispensation altogether. Notably, such officials are not limited to a nation's licensing authority but may include officials (public or corporate) with authority to approve an MCM's transport and delivery as well as persons with local command and control responsibility. Regardless of such persons' position or motivation, the consequence of delay could be widespread illness and death.

While regulatory approval processes are expensive and time consuming for all pharmaceutical products,<sup>56</sup> these challenges multiply in the context of biopreparedness. The international scope of such an initiative means that producers must successfully navigate the procedures of many separate regulatory regimes. Moreover, in the unique context of catastrophic disease treatment, it may be necessary to allow for the emergency use of unapproved products or their unapproved uses. In a crisis situation, the best defense against an agent might be an MCM that has not yet been fully approved.

This section's simple assertion is that, at the moment of a bioviolence crisis, the last thing anyone should do is argue about the legal status of MCMs that can save lives or limit contagion's spread. Nor should the beneficial use of one nation's MCMs be restricted for use in a foreign nation due to inconsistent regulatory approval. Such legal controversies should and can be addressed now, in the pre-attack period of calm. Indeed, nothing discussed in this section poses an intractable problem; every issue raised here can be resolved in advance through rational planning processes.

Nations could agree to recognize each others' licensed MCMs if the licensing nation has approved them using internationally recognized standards. Alternatively, amid an emergency, the receiving nation could grant *emergency use authorization* (EUA). These two tactics basically differ by timing: if the attack has not yet happened, a process of mutual recognition of licensed MCMs is appropriate; if the attack has happened, then an EUA process is appropriate. Despite the functional resemblance of these two tactics, it should be noted that international mechanisms to harmonize standards for licensing medicines already exist as will be discussed; they need to be adjusted to specifically address bioviolence MCMs. By contrast, international harmonization mechanisms do not exist for EUAs; such mechanisms will need to be created.

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56. "For a long time, pharmaceuticals have been among the most extensively regulated consumer products; in most countries, governments regulate testing, development, production, marketing and liability and often even control distribution and prices." Kai P. Purnhagen, *The Challenge of Globalization in Pharmaceutical Law—Is an International Drug Approval System Modeled After the European System Worth Considering?*, 63 *Food DRUG L.J.* 623, 624 (2008).

### A. *Multi-National Harmonization of MCM Licensing Standards*

Each sovereign nation must license MCMs for use in its jurisdiction. Each State has developed its own procedures and requirements for such licenses; the exact information required, risk accepted, and procedures followed may differ among them. The fact that different regulatory processes invoke inconsistent standards for obtaining a license can be a disincentive to MCM preparation.

International efforts to harmonize regulatory approval processes can promote high standards and incentivize MCM development within a more predictable, uniform regulatory environment. Moreover, the process of internationalizing approval standards evidences the priorities of participating regulatory authorities. Finally, the more that pharmaceutical licensing processes can be centralized, coordinated, and harmonized, the faster informed decisions can be made in the event of an emergency, when time is of the essence and information may be fragmented. Notably, GHSAG's recent interest in MCMs includes addressing regulatory issues related to MCM licensing and distribution.<sup>57</sup>

Harmonization of standards for MCM regulatory approval is imperative. Standards should focus on quality control, staff, working areas, equipment and instruments, operating procedures, methods, reference materials, reagents, control samples, documentation, biosafety, and audits. Pharmaceutical manufacturing plants are enormously expensive investments and there are efficiencies to be gained by allowing such facilities to conform to a single set of requirements in each of these areas. Disparate national regimes may force manufacturers to alter their production methods for individual markets, or worse, they may simply decide that select minority markets are not worth pursuing.

Broadly viewed, there are two methods to address the need for consistent licensing standards and procedures. The first is through a system of centralized licensing—consistency is promoted by virtue of there being one authority with one set of rules. The second is for international/regional organizations to harmonize standards and procedures for national licensing, thereby encouraging nations to recognize each other's licensed MCMs.

#### 1. *Centralized Licensing*

*Centralized licensing* means empowering an authoritative body to apply agreed-upon standards and issue internationally valid pharmaceutical licenses. The WHO Prequalification Programme<sup>58</sup> is a centralized approval mechanism, originally designed to guide UN procurement agencies, that facilitates access to medicines that meet standards of quality, safety, and effi-

57. See Global Health Security Initiative, *supra* note 25.

58. World Health Organization, Prequalification of Medicines Programme, <http://apps.who.int/prequal/> (last visited Oct. 24, 2009).

cacy for HIV/AIDS, malaria, and tuberculosis. The list of approved products has evolved as a useful tool for purchasers of bulk medicines, including States and other organizations. For instance, the Global Fund to Fight AIDS, Tuberculosis and Malaria disburses money for medicines that the WHO process has prequalified.

In Europe, the European Agency for the Evaluation of Medicinal Products (EMA) has a centralized approval process that allows the EMA to issue an approval decision on new applications that become binding across the European Union. It is noteworthy that this mechanism has not been favored by pharmaceutical manufacturers seeking licenses for European distribution who seem to prefer to use EMA's alternative decentralized model discussed below due to individual Member States' larger, and therefore more predictable, bodies of law.<sup>59</sup>

Both the WHO and the EMA systems have considerable merit. Yet, the licensing of pharmaceutical products is widely understood as central to State sovereignty, although States have ceded some sovereignty in the international public health context—the WHO, for example, is authorized to use the territory of each Member as necessary to fulfill its objective and to exercise its functions.<sup>60</sup> A centralized licensing system for bioviolence MCMs, therefore, should not be portrayed as wholly unrealistic. Yet, more limited efforts at harmonization might be more realistic for now.

## 2. *Mutual Recognition Based on Internationally Harmonized Standards*

A second method involves regulatory authorities recognizing approval in a foreign jurisdiction and thereby granting certain exemptions in their own jurisdictions. However, States are reluctant to turn over approval processes to other States' regulatory bodies due to concerns about the efficacy of certain States' approval processes and different priorities relating to side effects, testing procedures, and outcomes.

These concerns may be addressed through harmonization of standards. Harmonization minimizes the differences among regulatory regimes, increasing the efficiency of applications and reviews based on consensus principles. As States apply more consistent standards, they should be more willing to accept results and decisions from other States. Among the reasons to promote harmonization are: (1) lowering new drug development costs for pharmaceutical companies; (2) reducing the time to bring new drugs to market; (3) increasing international cooperation in pharmaceutical industry regulation, thus improving regulatory efficiency and expertise; and (4) eliminating unnecessary duplication of clinical trials on human popula-

59. Purnhagen, *supra* note 56, at 635–36.

60. CONST. OF THE WORLD HEALTH ORGANIZATION, art. 67, available at [http://www.searo.who.int/LinkFiles/About\\_SEARO\\_const.pdf](http://www.searo.who.int/LinkFiles/About_SEARO_const.pdf).

tions, thus minimizing risks to research subjects and assuaging ethical concerns.<sup>61</sup>

An example of harmonization is Europe's "decentralized procedure" which establishes a licensing regime for mutual recognition.<sup>62</sup> Companies that obtain a license in an EU Member State may apply to another State for mutual recognition of that authorization. The second State *may* refuse reciprocal authorization, but that triggers negotiation and, if not resolved, mandatory and binding arbitration at the EMEA's Committee on Proprietary Medicinal Products (CPMP).<sup>63</sup> "Practically speaking, the result of the decentralized procedure has been the near eradication of disputes regarding mutual recognition as measured by referrals for CPMP arbitration."<sup>64</sup> The decentralized procedure has essentially created a system of mutuality.

Developing bilateral and multilateral agreements among regulatory authorities can enable them to coordinate their efforts and offer recognition to certain aspects of foreign approval processes. In the United States, the FDA works for mutual recognition and international harmonization of regulatory requirements and guidelines.<sup>65</sup> Accordingly, the United States (FDA) and Europe (EMA) have taken some small steps to promote cooperation for pharmaceutical licensing,<sup>66</sup> including agreeing to mutual recognition of Good Manufacturing Principles (GMP) inspections for pharmaceutical manufacturers.<sup>67</sup> The FDA and EMA have also agreed to procedures for the sharing of information, including post-authorization pharmacovigilance

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61. J. John Lee, Comment, *What Is Past Is Prologue: The International Conference on Harmonization and Lessons Learned from European Drug Regulations Harmonization*, 26 U. PA. J. INT'L ECON. L. 151, 155 (2005); see Purnhagen, *supra* note 56 at 632-34.

62. Lee, *supra* note 61, at 175-77.

63. 2004 O.J. (L 136) 1; see generally European Medicines Agency, Committee for Medicinal Products for Human Use, <http://www.emea.europa.eu/htms/general/contacts/CHMP/CHMP.html> (last visited Oct. 24, 2009).

64. Lee, *supra* note 61, at 176.

65. The FDA's policy on developing international harmonization of regulatory requirements and guidelines is intended to address how it participates with standards bodies outside of FDA, domestic or international. The policy also covers the conditions under which FDA intends to use the resultant standards, or other available domestic or international standards, in fulfilling its statutory mandates for safeguarding the public health. See Food and Drug Administration, International Programs: Harmonization and Multilateral Relations, <http://www.fda.gov/InternationalPrograms/HarmonizationInitiatives/default.htm> (last visited Oct. 24, 2009). The FDA has also established the Global Harmonization Task Force. See Food and Drug Administration, International Programs: Global Harmonization Task Force (GHTF) <http://www.fda.gov/InternationalPrograms/HarmonizationInitiatives/ucm114616.htm> (last visited Oct. 24, 2009).

66. Claudio A. Mereu and Philippe Delsaut, *EMA and the Marketing of Pharmaceuticals Across the European Union*, PHARMALICENSING.COM, [http://pharmalicensing.com/public/articles/view/994346010\\_3b44841a653f7](http://pharmalicensing.com/public/articles/view/994346010_3b44841a653f7) (last visited Oct. 24, 2009) (suggesting that the EMA is considering additional steps toward mutual recognition with the United States and others).

67. PHARMACEUTICAL GOOD MANUFACTURING PRACTICE, AGREEMENT ON MUTUAL RECOGNITION BETWEEN THE UNITED STATES OF AMERICA AND THE EUROPEAN COMMUNITY, <http://www.mac.doc.gov/mra/mra.htm> (last visited Nov. 23, 2009).

data, provided that the information is protected.<sup>68</sup> Finally, the FDA and EMEA (along with Japan) have taken significant strides toward harmonization through the ICH mechanism described below.

Coordination that is more broadly international could be promoted, for example, through the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The ICH harmonizes national regulatory processes in Europe, Japan, and the United States by producing a single set of technical requirements for registering new drug products.<sup>69</sup> Its objective is to ensure timelier introduction of new pharmaceuticals by reducing duplicative testing of new medicines without compromising safety, quality, and efficacy.<sup>70</sup> The ICH has encouraged more countries to integrate their regulatory policies and is extending harmonization efforts to advances in new medicines where increased regulatory cooperation can enhance the protection of international public health.

There is also value in developing multilateral agreements among regulatory authorities to coordinate their efforts and offer recognition to foreign approval processes. Such coordination could occur through networks for regulatory authorities such as the WHO's International Conference for Drug Regulatory Authorities (ICDRA), a WHO-sponsored network that brings together national regulatory authorities to, among other activities, harmonize regulatory processes.<sup>71</sup> The WHO has also established the Developing Countries' Vaccine Regulators Network (DCVRN) to promote and support the strengthening of national regulatory capacity for evaluation of clinical

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68. Letter from Paul Weissenberg, Director, DG Enterprise European Commission and Thomas Lonngren, Executive Director, European Agency for the Evaluation of Medicinal Products, to Mark B. McClellan, Commissioner, Food and Drug Administration (Sept. 12, 2003), <http://www.fda.gov/InternationalPrograms/Agreements/ConfidentialityCommitments/ucm093991.htm>; Letter from Mark B. McClellan, Commissioner, Food and Drug Administration, to Paul Weissenberg, Director, DG Enterprise European Commission and Thomas Lonngren, Executive Director, European Agency for the Evaluation of Medicinal Products (Sept. 12, 2003), <http://www.fda.gov/InternationalPrograms/Agreements/ConfidentialityCommitments/ucm093989.htm>.

69. International Conference on Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH), Frequently Asked Questions, <http://www.ich.org/cache/html/2834-272-1.html> (last visited Oct. 24, 2009).

70. The ICH harmonization follows a five-step process. First, the ICH builds consensus around a proposed harmonization contained in a Concept Paper. Second, the Steering Committee signs off that there is sufficient scientific consensus on the technical issues for the draft guideline or recommendation. Third, the guidelines become the subject of normal regulatory consultation in three regions: the EU, Japan, and the United States. The parties share information gleaned from these regional/national processes. Fourth, the ICH working group assesses these comments, and if both regulatory and industry parties can be satisfied with a consensus guidelines, it is submitted to the Steering Committee for adoption. The fifth step is regulatory implementation. National/regional regulatory processes in the EU, Japan, and the United States are engaged to adopt the harmonized guidelines. *See id.*

71. *See* World Health Organization, International Conference of Drug Regulatory Authorities, [http://www.who.int/medicines/areas/quality\\_safety/regulation\\_legislation/icdra/en/](http://www.who.int/medicines/areas/quality_safety/regulation_legislation/icdra/en/) (last visited Oct. 24, 2009).

trial proposals and clinical trial data through expertise and exchange of relevant information.<sup>72</sup> The Global Harmonization Task Force (GHTF) also serves as an information exchange forum for countries with developing medical device regulatory systems.<sup>73</sup>

These international standards form the foundation for efforts to harmonize MCM production and acquisition processes, but to date, these standards do not specifically address the unique circumstances and disincentives of producing bioviolence MCMs. These efforts should specifically support harmonization related to bioviolence MCM development.

### B. *Emergency Use Authorizations*

To save lives following a bioviolence attack, unapproved MCMs that are the best (and perhaps, only) preventive, diagnostic, or therapeutic treatments for a given pathogen could be dispensed even though those MCMs are not authorized for use in less critical times. A few countries have taken steps to allow foreign MCMs to deal with emergency situations where no authorized products are available. For example, Germany issued an ordinance in 2003 that allows the importation, storage, and use of non-licensed drugs and vaccines.<sup>74</sup>

The absence of an internationally harmonized system to authorize emergency use of unapproved MCMs or their unapproved (“off-label”) uses, however, threatens to render them legally unusable in States that lack an EUA mechanism.<sup>75</sup> In a State having such a mechanism, it is unclear if it is comparable to another State’s mechanism. Such confusion disincentivizes MCM producers who need to know if their products will be used in an emergency. Moreover, such confusion leaves responsible officials ruminating about the implications of authorizing unapproved MCMs just when fast and appropriate decisions are most imperative.

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72. See World Health Organization, Developing Countries’ Vaccine Regulators Network Establishment, [http://www.who.int/immunization\\_standards/vaccine\\_regulation/dcvrn/en/](http://www.who.int/immunization_standards/vaccine_regulation/dcvrn/en/) (last visited Oct. 24, 2009).

73. “The Global Harmonization Task Force (GHTF) is a voluntary group of representatives from national medical device regulatory authorities and . . . industry. . . . [GHTF’s] purpose is to encourage convergence in regulatory practices related to ensuring the safety, effectiveness/performance and quality of medical devices, promoting technological innovation and facilitating international trade, and the primary way in which this is accomplished is via the publication and dissemination of harmonized guidance documents on basic regulatory practices.” Global Harmonization Task Force, General Information, <http://www.ghf.org/information/information.htm> (last visited Oct. 24, 2009).

74. See Meeting of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, Germany: Enhancing International Capabilities for Responding to and Mitigating the Effects of Outbreaks of Diseases—How to Overcome Legal Problems, July 15, 2004, available at [http://www.opbw.org/new\\_process/mx2004/bwc\\_msp.2004\\_mx\\_wp07\\_E.pdf](http://www.opbw.org/new_process/mx2004/bwc_msp.2004_mx_wp07_E.pdf).

75. See Stuart L. Nightingale et al., *Emergency Use Authorization (EUA) to Enable Use of Needed Products in Civilian and Military Emergencies, United States*, 13 EMERGING INFECTION DISEASES J. 1046, 1047–48, available at <http://www.cdc.gov/EID/content/13/7/pdfs/1046.pdf>.

Using the U.S.<sup>76</sup> and European<sup>77</sup> legal structures as models, the international community should work to harmonize EUAs worldwide. EUA harmonization provides predictability for industry and helps States align priorities and cost-benefit analyses. International harmonization should address three issues: What is the process for EUA decision-making? What are substantive decision-making standards? And, how should an authorization be operationally implemented, including remediation and post-event withdrawal of an authorization?

### I. *EUA Process*

Declaration of an emergency is requisite for considering EUAs.<sup>78</sup> Accordingly, each State's process for such declarations should be clear, and harmonization of such processes would enable multi-national integration of

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76. The Project BioShield Act of 2004 includes the Authorization for Medical Products for Use in Emergencies that addresses the off-label use of approved products and the use of unapproved products for prevention, treatment, or diagnosis under emergency circumstances. *Id.* at 1048; *see also* Project BioShield Act § 4, 118 Stat. at 853–59 (codified at 21 U.S.C. § 360bbb-3 (2006)). The FDA may approve the emergency use of drugs, devices, and medical products (including diagnostics) that were not previously approved, cleared, or licensed by FDA or the off-label use of approved products in certain well-defined emergency situations. Project BioShield Act § 4, 118 Stat. at 853–59. In addition to these statutory requirements, HHS, through ASPR, has established the Secretary's Emergency Use Authorization Working Group (EUA WG) which provides recommendations to the secretary and the FDA commissioner on use of EUAs, as well as facilitates education and communication about EUAs with healthcare professionals and the public. Nightingale et al., *supra* note 75, at 1048.

77. The legal foundation for emergency use of medicinal products in the European Community is addressed by two legal documents. First, EC Directive 2004/27 directs the Member States to pass domestic legislation allowing for the temporary use of unauthorized medical products in emergencies. 2004 O.J. (L 136) 34. It also specifies that such legislation must contain liability immunity for manufacturers and healthcare providers. *Id.* EC directives are not binding at the Community level but are expected to be transposed by each individual Member State. Second, EC Regulation 507/2006 (binding on all citizens and Member States) allows the EU Committee for Medicinal Products for Human Use (CHMP) to give certain products a conditional marketing authorization during emergency situations. 2006 O.J. (L 92) 6. The legal basis for such a conditional marketing authorization stems from Article 14(7) of Regulation (EC) No. 726/2004. *Id.*

78. In the United States, following the HHS secretary's Declaration of a Public Health Emergency justifying issuance of the EUA, the FDA commissioner, under delegated authority from the secretary of HHS, may issue an EUA after consultation, to the extent feasible and appropriate given the circumstances of the emergency, with the directors of the National Institutes of Health (NIH) and HHS/CDC, if she concludes that:

- 1) the secretary of Homeland Security determines there is a "domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiologic, or nuclear agent or agents";
- 2) the secretary of defense determines that there is a similar emergency or potential emergency threatening military forces; or
- 3) the secretary of HHS determines that there is a "public health emergency under section 319 of the Public Health Service Act that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents."

Nightingale et al., *supra* note 75, at 1048. For further description and specific examples of recent use, see Susan E. Sherman et al., *Emergency Use Authority and 2009 H1N1 Influenza*, 7 BI-SECURITY & BIOTERRORISM: BIODEFENSE STRATEGY PRAC. & SCI. 245 (2009).

response. Such preplanning is essential if regions are relying on a shared MCM stockpile strategy. Harmonized processes should specify types of information that could be relevant in the EUA context.<sup>79</sup>

The critical decision to approve a non-licensed MCM raises various subsidiary questions. First, what will be the evidentiary burden of proof for these decisions? Must a decision be beyond epidemiological or mathematical doubt, or simply based on a preponderance of available information? In this context, what are an MCM producer's obligations to furnish pertinent documentation (under especially frenzied conditions), and what might be the ramifications (liability) for producers who are later found to have withheld information? A parallel set of questions focus on the decision-maker: under what standards will a decider be held accountable? If an application is denied, is there a process for review or appeal? If so, how should procedural protections be modified to fit the urgency of an emergency authorization setting?

Perhaps the most important question in the international context concerns the evidentiary weight to be given to foreign States' decisions to approve an EUA. Much bureaucratic effort and MCM producer uncertainty could be alleviated by an internationally centralized mutual recognition system that allows a few (or just one) States' approval to suffice for all. While States do not routinely recognize extra-jurisdictional MCM approvals, emergency situations might make States more amenable to recognition. Part of emergency planning might include "emergency use recognition" provisions. Harmonization of procedures at the national level could facilitate eventual consensus for a centralized approval mechanism, like the WHO Prequalification Program (see above).

Mutual communication efforts should complement harmonization of States' EUA procedures. Regulatory authorities could develop information sharing agreements regarding potential MCMs, standardizing lexicons, and allowing for freer movement of information if an emergency is declared. This should include analyses of the emergency use MCM's efficacy and side effects. Moreover, harmonized procedures can introduce transparency with regard to the decision-making record, thereby reducing concerns of perceived bias and help ensure the integrity of the decision-making process. The FDA-EMEA Confidentiality Agreement suggests that States have already considered many of the legal and procedural issues related to information sharing and pharmaceutical licensing; similar agreements should be developed specifically for the emergency use context.<sup>80</sup>

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79. See Approval of New Drugs when Human Efficacy Studies Are Not Ethical or Feasible, 21 C.F.R. §§ 314.600–650, 601.90–95; see also Christopher-Paul Milne, *Racing the Globalization of Infectious Diseases: Lessons from the Tortoise and the Hare*, 11 NEW ENG. J. INT'L & COMP. L. 1 (2004).

80. See Letter from Paul Weissenberg, *supra* note 68; see also Letter from Mark B. McClellan, *supra* note 68.



## 2. *Substantive Standards*

Substantive standards for EUAs also require harmonization. In the United States, an EUA is a determination (based on review of available scientific studies) that an MCM's benefits outweigh its potential risks (both known and unknown), in addition to a demonstration that no alternative product is available.<sup>81</sup> In contrast, most nations' regulatory authorities must analyze many complicated issues by undertaking a *de novo* assessment of the potential determinants and by defining, again *de novo*, the metrics for deciding whether a specific determinant is satisfied. It would be useful, therefore, to have international guidance for specific determinants and the metrics for assessing those determinants in particular cases. The following list could be helpful in that context:

1. What is the magnitude of the threat in terms of the pathogen's lethality, contagiousness, and proximity to the relevant population? If the unapproved MCM is not used, what will be the likely magnitude of harm?
2. What is the timeframe for that threat—is it a clear and present danger? Within the relevant timeframe, is there more information that could be obtained that would likely produce a more informed judgment about the threat or about the proposed MCM?
3. What are the potential consequences associated with using the unauthorized MCM? How do these consequences compare to the consequences of not using it? Are there any alternatives to the use of the unapproved MCM? Should the same standards apply to unlicensed MCMs and off-label use of licensed MCMs?
4. Can the consequences of using the unapproved MCM be lessened by a refined dissemination strategy (e.g., not dispensing to persons who are immune-compromised or to young children)? What are the implications of dispensing the MCM to specific groups (e.g., first responders or the military) instead of the general population?

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81. In the United States, following the HHS secretary's Declaration of Emergency justifying issuance of the EUA, the FDA commissioner, under delegated authority from the secretary of HHS, may issue an EUA after consultation, to the extent feasible and appropriate given the circumstances of the emergency, with the directors of the National Institutes of Health (NIH) and CDC, if she concludes that:

- 1) the agent listed in the emergency declaration can cause a serious or life-threatening disease or condition; 2) on the basis of the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the medical product may be effective in diagnosing, treating or preventing this disease or condition or a serious or life-threatening disease or condition caused by another EUA-authorized product or an otherwise approved or licensed product; 3) the known and potential benefits of the medical product, when used to diagnose, prevent, or treat the disease or condition, outweigh the risks, both known and potential; and 4) no adequate, approved, alternative medical product is available.

Nightingale et al., *supra* note 75, at 1048.

5. Is the proposed MCM available in sufficient quantities? What will be the expense and logistical challenges associated with getting it to needed populations? Can this be done within an acceptable timeframe?

### 3. *Operational Implementation*

Operational matters subsequent to approval should be precisely planned and standardized. At least three phases of implementation deserve attention here: proper MCM use; recordkeeping; and remediation.

First, any emergency use law must require clear communication of the prescribed methods of use to response personnel or health care workers who will dispense the MCMs. They may need information on how to handle, store, and administer an unfamiliar product. They should also receive sufficient information to inform recipients of both their right of refusal (if any) and the product information necessary to make that decision. If there are restrictions on authorized use, that information must also be communicated to both dispensers and recipients.<sup>82</sup>

Second, States must maintain detailed records about the MCM's administration. Data about recipients of an MCM must be meticulously logged to track its side effects and its treatment efficacy. Similarly, recordkeeping allows administrators to communicate with recipients in order to adjust dosages, monitor recipients' pre-existing conditions, or advise them regarding subsequent changes in their health. Data should enter a feedback loop informing decision makers faced with new decisions or reviewing past ones, allowing them to revoke their designation if the products prove more dangerous or less effective than originally thought.<sup>83</sup>

Third, emergency authorization mechanisms should also consider remediation measures such as identifying and distributing a product that can treat an MCM's negative side effects. MCM EUAs should also include capacity for withdrawing approval either because the threat has dissipated or because the MCM is less effective or creates more harmful side effects than originally thought. Withdrawing emergency authorization may simply require the reverse process of authorization to issue a corresponding revocation. Initial authorizations may facilitate this by including "sunset" provisions that automatically revoke an authorization after a set period of time unless formally renewed.

## IV. PLANNING FOR MCM STOCKPILING AND DELIVERY

MCMs are valuable only if they get to bioviolence victims when needed. The essence of *preparedness*, therefore, is stockpiling of sufficient

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82. Note that the CFR provides for exceptions and alternatives to the standard FDA labeling requirements for MCMs in the Strategic National Stockpile. See 21 C.F.R. § 201.26 (2007).

83. Nightingale et al., *supra* note 75, at 1049.

MCMs and rapid delivery, most likely across national boundaries as few nations have in-country vaccine manufacturers, and most likely during a period of mass panic.

These challenges must be confronted in a time frame that is measured in minutes. Envision, for example, dissemination of weaponized anthrax in a sports arena, infecting perhaps thousands of victims. The white powder must be collected and transported to a diagnostic facility for analysis; once confirmed as anthrax, producers of vaccine and antibiotics must accelerate production; those MCMs must then be transported to a cargo plane that will transport them perhaps thousands of miles to the target site where they must be dispensed to victims. All this must happen within less than 72 hours. Outside perhaps two dozen countries in the world, meeting this deadline is pure fantasy.

It should be noted that stockpiling of medicines, particularly vaccines against chronic diseases, is not unprecedented. For example, the WHO's International Coordination Group (ICG) stockpiles vaccines for yellow fever, meningitis, polio, and avian flu (H5N1)<sup>84</sup> and expert consultations are underway for stockpiling vaccines against the new H1N1 influenza.<sup>85</sup> Moreover, the GAVI Alliance (formerly the Global Alliance for Vaccines and Immunisation) stockpiles medicines against pneumococcal disease, rotavirus, and yellow fever.<sup>86</sup> While for a host of reasons these medicine stockpiling systems are not ideal analogues for a system of bioviolence MCM preparedness, they do offer some useful insights.

This section addresses MCM stockpile planning before turning to delivery planning.

#### A. MCM Stockpile Planning

*Stockpiling* is the epitome of planning. With unlimited resources, every nation should stockpile enough MCMs for its population, but *domestic* stockpiling of MCMs is inefficient and unrealistic for most nations. Instead, MCM stockpiling should be regional, where depots can be connected to transport systems that can move resources rapidly to where they are needed.<sup>87</sup> Key to regional stockpiling is detailed allocation arrangements

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84. See World Health Organization, Informal Consultation on Technical Specifications for a (WHO) International H5N1 Vaccine Stockpile, Oct 17, 2007, [http://www.who.int/vaccine\\_research/diseases/influenza/181007\\_agenda\\_octobre.pdf](http://www.who.int/vaccine_research/diseases/influenza/181007_agenda_octobre.pdf).

85. See WORLD HEALTH ORGANIZATION, RESPONDING TO THE AVIAN INFLUENZA PANDEMIC THREAT (2005), available at [http://www.who.int/csr/resources/publications/influenza/WHO\\_CDS\\_CSR\\_GIP\\_05\\_8-EN.pdf](http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_05_8-EN.pdf).

86. GAVI Alliance, New and Underused Vaccines, [http://www.gavialliance.org/vision/policies/new\\_vaccines/index.php](http://www.gavialliance.org/vision/policies/new_vaccines/index.php) (last visited Oct. 24, 2009).

87. In the United States, the Vaccine Management Business Improvement Project (VMBIP) represents the efforts of the CDC, state and local immunization program managers, and partner agencies to improve current vaccine management processes at the federal, state, and local levels. VMBIP has determined that centralized distribution of vaccine from two or three locations is

specifying priorities that minimize disputes or confusion during an emergency. With regard to stockpiling responsibilities (including States' obligations to contribute to stockpile contents), and equitable distribution and reservation of stockpiled MCMs depending on an attack's location and severity, the following critical choices deserve consideration:

1. Whether to rely on physical stockpiling versus surge capacity when an attack has been identified. In order to allow for rapid production of large volumes of product, surge capacity requires pharmaceutical manufacturers to sustain expert personnel and excess manufacturing capacity, as well as flexible drug "scaffolds" that provide a pharmaceutical base for assembling multiple pathogen-specific responses. In the United States, HHS awarded contracts to expand manufacturing surge capacity for pandemic influenza vaccines and certain other MCMs.<sup>88</sup> However, most States lack a domestic MCM industry, let alone one with excess capacity for producing MCMs.<sup>89</sup> To the extent that surge production is preferred, the international community should encourage investments in scaffolding technologies.
2. Whether to develop *Push Packages* or rely on *Vendor-Managed Inventories*. Push Packages are government-owned caches of supplies and medications, located in secure locations. Vendor-Managed Inventories (VMIs) are maintained in reserve by private vendors; governments may purchase them as needed. Typically, VMIs contain frequently used products that vendors can rotate to maintain shelf life.
3. How to locate stockpiles with optimal access to major cities and targets and proximity to transnational transportation networks. These determinations require the application of general planning principles to threat and capacity assessments individualized for each State or region.

In addition to these determinants, stockpile planning should focus on maintaining stockpile surety and security. *Surety* refers to the proper storage and maintenance of stockpile assets. Because MCMs spoil with time, stor-

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preferred to multiple state and local depots; centralization reduces storage risks and distribution costs and allows more visibility into vaccine supply. See Centers for Disease Control and Prevention, Vaccine Management Business Improvement Project, <http://www.cdc.gov/vaccines/programs/vmbip/default.htm> (last visited Oct. 24, 2009).

88. See HHS Press Office, HHS Awards Contracts Totaling More Than \$1 Billion To Develop Cell-Based Influenza Vaccine, May 4, 2006, <http://www.hhs.gov/news/press/2006pres/20060504.html>; see also BARDA MCM Progress: HHS PHEMCE Stakeholders Workshop, Arlington, VA, Sept. 24, 2008, available at <https://www.medicalcountermeasures.gov/BARDA/documents/080924barda-mcmprogress.pdf>.

89. A lack of domestic pharmaceutical manufacturing affects less developed nations' ability to produce even basic lifesaving medicines. Nations with such dire infrastructure problems will hardly be expected to make MCM production a priority. See Roger Bate, *Local Pharmaceutical Production in Developing Countries*, Jan. 2008, available at [http://www.fightingdiseases.org/pdf/local\\_drug\\_production.pdf](http://www.fightingdiseases.org/pdf/local_drug_production.pdf).

age of MCMs must satisfy unique environmental requirements such as temperature, moisture, and light. They must also be kept up to date to avoid the distribution of expired products. International surety standards should be incorporated into the international stockpiling guidelines and international stockpile agreements.<sup>90</sup> Relevant here are the WHO's *Guidelines on the International Packaging and Shipping of Vaccines*, including the *Model Quality Assurance System for Assessment of Procurement Agencies* that provides guidance for pharmaceutical storage and distribution.<sup>91</sup> The WHO's model system focuses on training, adequate storage, and sanitation including temperature and volume standards, stock rotation, safe transportation, compliance with labeling and insulated packaging standards, and maintenance of accurate and complete records.<sup>92</sup>

Security concerns are also important. Attack perpetrators might try to destroy MCM stockpiles, or panicked victims of an attack might assault the stockpile. Determinations about the best security options are likely to be nation-specific and depend on a given force's training, availability, and reliability.<sup>93</sup> Here again, planning is critical, including the following elements:

- providing law enforcement and fire control
- safeguarding and controlling access to restricted areas
- maintaining vehicle traffic control
- facilitating orderly entrance to and exit from the point of distribution (POD)
- providing crowd control within and outside of the POD
- maintaining command-and-control capability for security staff
- coordinating intra-POD security operations as well as security operations between PODs and local law enforcement

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90. See, e.g., WORLD ORGANIZATION FOR ANIMAL HEALTH, GUIDELINES FOR INTERNATIONAL STANDARDS FOR VACCINE BANKS (2008), available at [http://www.oie.int/Eng/Normes/Mmanual/2008/pdf/1.1.10\\_VACCINE\\_BANKS.pdf](http://www.oie.int/Eng/Normes/Mmanual/2008/pdf/1.1.10_VACCINE_BANKS.pdf).

91. See generally WORLD HEALTH ORGANIZATION, DEPARTMENT OF VACCINES AND BIOLOGICALS, GUIDELINES ON THE INTERNATIONAL PACKAGING AND SHIPPING OF VACCINES (2001), available at <http://www.who.int/vaccines-documents/DocsPDF99/www9942.pdf>; and WORLD HEALTH ORGANIZATION, MODEL QUALITY ASSURANCE SYSTEM FOR ASSESSMENT OF PROCUREMENT AGENCIES (2007), available at <http://www.who.int/medicines/publications/ModelQualityAssurance.pdf>.

92. See GUIDELINES ON THE INTERNATIONAL PACKAGING AND SHIPPING OF VACCINES, *supra* note 91.

93. In the United States, a combatant command within the U.S. military has been tasked with estimating necessary troop and resource requirements for distribution site security, yet the capability is not yet operational. If the SNS is deployed, each state is responsible for providing security for the SNS assets and distribution sites once they assume custody of the counter-measures. Under the 2004 version of Emergency Support Function (ESF) #13, federal law enforcement (through DHS and DOJ) may provide "protection of personnel and temporary storage facilities during the distribution of supplies from the SNS." DEPARTMENT OF HOMELAND SECURITY, NATIONAL RESPONSE PLAN (2004), available at [http://permanent.access.gpo.gov/lps56895/NRP\\_FullText.pdf](http://permanent.access.gpo.gov/lps56895/NRP_FullText.pdf). However, the most recent version of ESF #13, dated January 2008, does not discuss SNS security. Federal Emergency Management Agency, Emergency Support Function #13—Public Safety and Security Annex (2008), available at <http://www.fema.gov/pdf/emergency/nrf/nrf-esf-13.pdf>.

- coordinating facility parking and ensuring adequate water, sanitation services, and heating or air conditioning, as required.

Altogether, States should be encouraged to develop cooperative stockpiling arrangements with neighbors. International organizations should promulgate guidelines that serve as bases for multi-national stockpile agreements and help build capacity for achieving relevant benchmarks. Development of an international certification or a peer-review process for stockpile surety and security would be useful for specifying metrics that can be used for evaluating national plans. An example here is the WHO's International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control, which makes national distribution planning a requirement of participation.<sup>94</sup> Plans for MCM stockpiling should be re-assessed regularly, considering changing threat parameters, manufacturing capabilities, and new science regarding potential agents and countermeasures.

In this context, the planning for an international H5N1 vaccine stockpile is informative. Recognizing that having an international stockpile available at the start of a pandemic helps ensure that people initially in greatest need would benefit from treatment with antiviral drugs, the WHO plans to establish an international stockpile of antiviral drugs for rapid response at the start of a pandemic,<sup>95</sup> and it has urged countries to have a stockpile of drugs for aggressively fighting the disease and preventing a pandemic outbreak.<sup>96</sup> Critical determinants that have been identified include logistics associated with deployment and administration, licensing for use in individual countries, epidemiological triggers for deploying the stockpile, mass delivery mechanisms, and time frames for emergency delivery and administration.<sup>97</sup>

### B. MCM Delivery Planning

Distribution planning requires assigning responsibilities for triggering the delivery of stockpiled MCMs. A model international distribution plan should identify the types of authorities that are necessary and suggest levels of decision makers who should be involved in such decisions.<sup>98</sup> Also, au-

94. World Health Organization, International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control, <http://www.who.int/csr/disease/meningococcal/icg/en> (last visited Oct. 24, 2009).

95. World Health Organization, Informal Consultation, *supra* note 84.

96. Aditi Diya Nag, *The Bird Flu and the Invoking of TRIPS Article 31 "National Emergency" Exception*, 34 SYRACUSE J. INT'L. L. & COM. 689, 703 (2007).

97. WHO is working closely with groups engaged in mathematical modeling to develop early containment strategies. WORLD HEALTH ORGANIZATION, *supra* note 85, at 11.

98. See CENTERS FOR DISEASE CONTROL AND PREVENTION, ANNEX 5—SUGGESTED PREVENT PLANNING ACTIVITIES FOR STATE AND LOCAL PUBLIC HEALTH AUTHORITIES (2003), available at <http://www.bt.cdc.gov/agent/smallpox/response-plan/files/annex-5.pdf>; Centers for Disease Control and Prevention, Smallpox Response Plan and Guidelines, <http://www.bt.cdc.gov/agent/smallpox/response-plan/> (last visited Oct. 24, 2009).

thority needs to be assigned for selecting transportation methods to get stockpiled assets to the dispensation sites. International logistical organizations have powerful capabilities that could be useful in response to an act of bioviolence.<sup>99</sup>

Planners must also develop contingent plans for estimating what public and private assets and personnel will participate. Dedicated vehicles and equipment should carry MCMs, whether public civilian assets, military assets, or private assets. Use of military assets and personnel brings its own set of legal obstacles (e.g., *posse comitatus*) and similarly requires planning and training for this uncommon mission. Mobilizing public assets requires legal provision to re-assign vehicles, equipment and personnel. Commandeering or otherwise employing private assets also requires legal authorization. Even if the logistical plans identify public and/or private assets, personnel must be trained to protect and maintain the MCMs in the challenging circumstances of a bioviolence emergency.

Notably, the WHO Good Distribution Practices for Pharmaceutical Products addresses pharmaceutical distribution, recognizing that States employ different distribution models. Guidance addresses: organization and management; personnel; quality management; warehousing and storage; vehicles and equipment; containers and container labeling; dispatch; transportation and products in transit; documentation; repackaging and relabeling; complaints; recalls; rejected and returned products; counterfeit pharmaceutical products; importation; contract activities; and self-inspection.<sup>100</sup> In order to identify vulnerabilities in States' plans and promote confidence that States appreciate their responsibilities, this and other international mechanisms should be developed to evaluate national distribution plans, provide technical and financial assistance to national delivery authorities, and build linkages with the private sector.

This section focuses on the following key issues: (1) command and control responsibilities for MCM delivery; (2) stockpile dispensation; and (3) mandatory dispensation of MCMs.

### *1. Command and Control Planning*

Command and control is critical to responding to a bioviolence attack. Accordingly, national response plans should address: hierarchies amongst would-be decision-makers; the powers delegated to each; command, control, and information systems that conform to that distribution of responsibilities; and training for all participants to perform their roles under

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99. For example, the World Food Program (WFP) specializes in providing air, water, and land transportation capabilities including rapid response, and deploys Augmented Logistics Intervention Team for Emergencies (ALITES) to carry out these responsibilities. See United Nations World Food Programme, Logistics, <http://www.wfp.org/logistics> (last visited Oct. 24, 2009).

100. See WORLD HEALTH ORGANIZATION, GOOD DISTRIBUTION PRACTICES FOR PHARMACEUTICAL PRODUCTS 3 (2005), [http://www.health.gov.il/download/forms/a3040\\_GDP.pdf](http://www.health.gov.il/download/forms/a3040_GDP.pdf).

pressure.<sup>101</sup> Command and control may also benefit from using operations centers that sustain situational awareness and a common operating picture, and facilitate information sharing between public health and law enforcement.

The variability of possible bio-events requires combining macro-level situational awareness and resources with micro-level execution. As central authorities typically have the most comprehensive situational awareness and can draw on the highest level of planning expertise, they can most efficiently allocate resources for distribution activities. Yet local authorities know the local geography, transportation routes, and available personnel; their control of distribution activities allows for nimble and precise responses that are tailored to their own circumstances. Thus, the coordination benefits of centralization must be balanced with the flexibility and local knowledge of decentralized approaches. Operational command and control should, therefore, connect local authorities with national and international officials and ensure that all decision-makers have effective legal authority.

## 2. *Specifying Conditions for Stockpile Dispensation*

States should be legally obliged and capable of making fine-grained decisions: how many of each MCM/asset should be deployed? How should shortages be handled? What happens if plans fall short of expectations? States also must ensure that officials and private persons execute their relevant responsibilities properly.

Lessons can be learned from the WHO's ICG Process for Stockpiling and Delivery of Vaccines. An emergency stockpile of vaccines, bundled with its injection materials and antibiotics, are held at the manufacturer's storage facilities.<sup>102</sup> The stocks can be requested by any country facing an epidemic; decisions are based on the epidemiological situation, pre-existing stocks in the country, intervention strategy, local coordination and operational aspects of the epidemic response, and how much of the particular vaccine is available.<sup>103</sup> Each nation must provide necessary information;

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101. In the United States, HSPD-8 calls for the creation of comprehensive training programs for first responders and directs HHS and other federal departments and agencies to establish a single point of access to federal preparedness assistance information; the actual assistance is typically deployed through state governments. Homeland Security Presidential Directive 8: National Preparedness, 39 WKLY. COMP. PRES. DOC. 1822 (Dec. 17, 2003). The DHS Office of Grants and Training (G&T) provides specialized training to enhance the capacity of first responders to deal specifically with terrorism involving weapons of mass destruction. A major program within the Office of G&T is the National Domestic Preparedness Consortium (NDPC) that identifies, develops, tests, and delivers training to state and local emergency responders. It includes the Center for Domestic Preparedness, as well as several state institutions. *See* National Domestic Preparedness Consortium, <http://www.ndpc.us/> (last visited Oct. 27, 2009).

102. INTERNATIONAL COORDINATING GROUP ON VACCINE PROVISION FOR EPIDEMIC MENINGITIS CONTROL (ICG), GUIDELINES FOR APPLYING TO THE EMERGENCY STOCKPILE 2 (2008), *available* at [http://www.who.int/csr/disease/meningococcal/ICG\\_guidelines\\_2008\\_02\\_09.pdf](http://www.who.int/csr/disease/meningococcal/ICG_guidelines_2008_02_09.pdf).

103. *Id.* at 2–3.



prepare an action plan for the mass vaccination campaign and reimburse the cost of goods shipped, including transport freight and insurance.<sup>104</sup> Vaccines that are used should be restocked before the end of the calendar year so that the total amount of annual stockpile is available for use in preventive campaigns in countries identified by WHO and UNICEF as being at high risk for the epidemic.<sup>105</sup>

With regard to bioviolence MCM dispensation, there are two leading tactics corresponding to the requisite method of delivery. Countermeasures that require injection or other specialized administration would likely be administered at a central point of distribution (POD). Other MCMs, such as oral antibiotics to combat anthrax, are capable of self-administration and could be delivered by postal workers or other decentralized means. The scale or severity of an outbreak is relevant to this decision.

POD sites should be stocked based on the estimated number of people to be treated. A 2008 RAND study laid out considerations for POD number and location, based on the per-POD throughput, characteristics of the community such as travel distance and population density, and trade-offs between minimizing and equalizing travel distances and deploying equal-sized PODs.<sup>106</sup> In addition, there should be medical supplies for dispensing MCMs and other assets needed for crowd control, communication, and emergency response.<sup>107</sup> Delivery plans should provide guidance for each potential pathogen/MCM combination.

MCMs that can be self-administered could be delivered by postal workers or other decentralized means. Indeed, according to a 2008 National Academies of Science (NAS) report, an emergency medical POD structure will have to contend with an abnormally large rate of throughput.<sup>108</sup> The NAS highlighted the potential of “push” mechanisms that would deliver

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104. *Id.* at 3.

105. See GAVI ALLIANCE INTERIM ANNUAL PROGRESS REPORT: GAVI YELLOW FEVER VACCINE STOCKPILE 1 (2004), available at [http://www.gavialliance.org/resources/13th\\_brd\\_Yellow\\_fever\\_stockpile\\_2.pdf](http://www.gavialliance.org/resources/13th_brd_Yellow_fever_stockpile_2.pdf).

106. The study recommends that all PODs meet the minimum requirements in the CDC's *Receiving, Distributing, and Dispensing Strategic National Stockpile Assets: A Guide for Preparedness*. See RAND HEALTH, RECOMMENDED INFRASTRUCTURE STANDARDS FOR MASS ANTI-BIOTIC DISPENSING 1 (2008), available at [http://www.rand.org/pubs/technical\\_reports/2008/RAND\\_TR553.pdf](http://www.rand.org/pubs/technical_reports/2008/RAND_TR553.pdf). Jurisdictions should consider a “rapid-dispensing protocol” to minimize the need for medically-licensed personnel at the POD site. *Id.* at xviii. Such a protocol would cover the following functions: “(i) directing clients through the POD; (ii) deciding which medication to dispense; (iii) disseminating information about the medication; and (iv) dispensing the medication.” *Id.* Plans should address preferred administration mechanisms and contingency plans in the event of complications. *Id.*

107. Such supplies might include surgical gloves, gowns, masks, respirators, needles and syringes, and public address systems. See Stephen Adams, Deputy Director, Strategic National Stockpile, Influenza A (H1N1) Update Meeting, *U.S. Strategic National Stockpile: Strategies for Influenza Mitigation* (July 2, 2009), available at [http://www.intramed.net/UserFiles/archivos/H1N1/steven\\_adams.pdf](http://www.intramed.net/UserFiles/archivos/H1N1/steven_adams.pdf).

108. INST. OF MEDICINE OF THE NAT'L ACADEMIES, DISPENSING MEDICAL COUNTERMEASURES FOR PUBLIC HEALTH EMERGENCIES: WORKSHOP SUMMARY 12 (2008).

countermeasures to individuals as part of a layered strategy to reach large numbers of people quickly and allow residents to shelter in place if there are environmental risks.<sup>109</sup> The report recommends types of public-private partnerships in this arena.<sup>110</sup>

National plans for rapidly dispensing stockpile contents in an emergency should engage the private sector in providing surge capacity, vendor managed inventories, and transportation assets.<sup>111</sup> Planning should include information technology necessary for maintaining and accessing medical records of persons who have received treatment. This is helpful—especially in emergencies—for tracking treatment success, location, and side effects, for avoiding hoarding, and for tracking the phases of a multi-phase treatment.

### 3. *Mandatory Dispensation of MCMs?*

A bioviolence attack will likely entail an extremely dangerous disease for which highly specific equipment and professionally trained first responders are needed. For purposes of dispensing MCMs, teams of first responders should be specifically prepared to address the unique problems of intentional outbreaks. Consideration should be given to pre-attack vaccination for first responders who will not have time to get vaccinated, much less to wait for the vaccine to take effect once an event occurs. Vaccination would assure responders that they are not jeopardizing their own health by

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109. *Id.* at 11.

110. The recommended types of partnerships include:

- Coordinating logistics, warehousing, and distribution of countermeasures.
- Setting up open points of dispensing (PODs) for dispensing countermeasures.
- Setting up closed PODs, usually by large employers for their employees and their families, thereby decreasing the volume of people at open PODs.
- Providing temporary labor to staff PODs and perform many other functions.
- Training and screening of volunteers.
- Preregistering individuals to screen for adverse health effects.
- Tracking and registering people who receive countermeasures.
- Providing education and communication for recipients of countermeasures.
- Providing security for open or closed PODs.
- Conducting research and development for new medical countermeasures.
- Providing technical assistance to private organizations to help them establish PODs.

*Id.* at 21.

111. In the United States, localities must submit distribution plans to the CDC, covering the public health department's coordination with traditional and nontraditional community partners; receiving, staging, and distributing medical materiel; laws to aid in the rapid dispensing of medications; and types and frequency of training, exercising, and evaluation of response plans. CDC reviews the plans annually. CDC works closely with localities to help identify and fix planning vulnerabilities and to test their capabilities through exercises. In doing so, CDC relies on a study prepared for the HHS Assistant Secretary of Preparedness and Response (ASPR), which recommends a point-of-dispensation plan with the following five stages: (1) orientation and paperwork; (2) registration; (3) medical assessment; (4) vaccination; and (5) form collection and exit. The U.S. government can usefully adapt this system to promote international dispensation capacities. See RAND HEALTH, *supra* note 106. These plans are in addition to the states' response plans, reviewed and tested by FEMA under Presidential Decision Directive 39. PRESIDENTIAL DECISION DIRECTIVE 39, U.S. POLICY ON COUNTERTERRORISM (June 21, 1995).

assisting. However, there are many potential agents to be vaccinated against, and vaccines can have potentially serious side effects. Therefore, a program of pre-attack vaccination for first responders must be accompanied by clear guidelines of the risks involved including data on which populations may have heightened risk.

Plans should also provide guidance on preparation of medical personnel for mass countermeasure administration, specifying the appropriate number of staff at each dispensation site. A 2008 RAND study recommends that jurisdictions be required to identify “core staff” in advance, leaving auxiliary personnel to be recruited ad hoc or borrowed from other government agencies or community organizations.<sup>112</sup> As discussed previously, legal provisions should be in place to address potential liability arising from the treatments.

A different problem pertains to dispensation of MCMs to the general population: what should be done about an individual who refuses to take them? That refusal may intolerably endanger others around him, raising a tension between public safety and individual liberties. During an outbreak, authorities will have little time to discuss the issue, much less engage in a protracted legal process to authorize mandatory administration of MCMs. The fact that various nations resolve these questions differently can impede a multinational response.

In planning for persons refusing treatment, States might consider offering a choice: accept medical intervention or be quarantined. In other words, temporarily forfeit control over one’s body or liberty. Due process concerns may arise if officials are authorized to determine that someone who refuses inspection or treatment ought to be quarantined. States and international organizations should be encouraged to develop national plans for such compulsory interventions.

#### CONCLUSION

The obstacles to a functioning global infrastructure for bioviolence MCM preparedness in the near future are legion. Naysayers could readily rattle off dozens of reasons why this or that initiative will not work, and they are right. As already mentioned, the world is remarkably dysfunctional, and implementation of progressive reform in this context faces near-infinite obstructions and frustrations. Moreover, there is scant evidence that global leaders consider such an infrastructure to be among their highest priorities.

The purpose of this article, however, has not been to assess the political odds that such an infrastructure will be built soon; it has been to draw a map of that infrastructure. For the moment, therefore, it is useful to shelve snide political realism and try to envision what a legally constituted global

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112. RAND HEALTH, *supra* note 106, at 45.

infrastructure for bioviolence MCM preparedness would look like. Significantly, necessary reforms require neither substantial expense nor drastic legal restructuring.

First, there would be an international panel or task force comprised of experts and serving a role broadly analogous to that of the Intergovernmental Panel on Climate Change, that: develops consensus criteria of risk; identifies existing MCMs for reducing those risks; resolves externalities associated with those MCMs; and promotes research and development of new risk reduction MCMs. This panel or task force would strive to harmonize research lexicons as it engages the best scientific and technical expertise worldwide. Because at least part of its focus will be on international threats, this panel or task force will need to have some connection to global law enforcement (Interpol, perhaps), in addition to science and public health communities. Its determinations, while not binding, will be the bases of all decisions throughout the MCM preparedness system, even as those decisions evolve over time.

Second, there would be widespread efforts to harmonize relevant national legislation concerning: liabilities of private pharmaceutical developers for the adverse consequences of their MCMs; mutual recognition of licensed MCMs and harmonized criteria for emergency use authorizations; transportation and distribution of MCMs in the wake of a bio-attack; and harmonized procedures for incorporating MCMs into effective response planning. While nations need not implement identical laws, each nation should have laws that address relevant issues, and outright inconsistencies and gaps within a State's own laws should be corrected. The oversight role of the United Nations Security Council in this regard could be pivotal.<sup>113</sup>

Third, some international organizations would adapt and accelerate key programs and initiatives. The WHO is pivotal in this context; fortunately, much of what the WHO would be expected to accomplish is already more or less in place. Notably, to address patent protections, the World Intellectual Property Organization (WIPO) should be engaged, and to address harmonization of licensing standards, the ICH should be engaged. There is no apparent need for a new international bureaucracy as much as there is a need to encourage a handful of existing international organizations to cooperate more effectively, specifically focusing on the challenges of bioviolence preparedness.

To conclude on a pessimistic note, it may be easier to envision political support for a global bioviolence MCM preparedness infrastructure to address the *second* catastrophic bio-attack. After one truly cataclysmic use of disease for hostile purposes, States' commitment and energy will un-

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113. Although far beyond this article's scope, there is the useful precedent of UNSCR 1540 which obligates every nation to implement laws for preventing the spread of weapons of mass destruction to non-State actors. Barry Kellman, *Criminalization and Control of WMD Proliferation: The Security Council Acts*, 11 THE NONPROLIFERATION REV. 142, 142-43 (2004).

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doubtedly rise to implement the appropriate legal modalities upon which a preparedness infrastructure can promote security against a repeat assault. Yet, in light of the potential magnitude of harm that bioviolence could cause, it may be suggested that the world not wait to prepare for the second attack. We should prepare now.