COMMENTARY

RETHINKING THE BIOLOGICAL AND TOXIN WEAPONS CONVENTION?

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THE CONVENTION ON THE PROHIBITION OF THE DEVELOPMENT, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction (BTWC) has been in force since 1975. The convention was the first arms control treaty to ban an entire class of weapons, and it has served as the absolute norm against the use of biological weapons.¹

The core of the BTWC has been and remains Article I, in which member state parties agreed “... never in any circumstances to develop, produce, stockpile or otherwise acquire or retain microbial or other biological agents, or toxins ... that have no justification for prophylactic, protective or other peaceful purposes.”²

The BTWC also contains provisions for review conferences to be held every 5 years to enable reflection on the continued viability of the treaty and allow member nations to consider BTWC issues and questions that accrue during the intervening years. To date, consensus has been that the BTWC rests on solid foundations and remains an effective instrument for the guidance and oversight of biological weapons. But we question the accuracy of this assessment, given that such affirmations may not fully reflect or appreciate the dual-use or direct-use (military) implications of emerging bioscience and associated technologies.

When the BTWC was first negotiated in 1972, the goal was to limit states’ use of biological or biologically derived agents as battlefield weapons. The second section of Article I prohibits “weapons, equipment or means of delivery de-

signed to use such agents or toxins for hostile purposes or in armed conflict” and formally codifies this proscription.² Over time, the BTWC has evolved so as to be relevant to the control of bioterrorism, largely through national implementation of requirements for states to control activities within their jurisdictions (as defined by Article IV). The BTWC has also evolved through practice (rather than formal changes to the convention language) to include recognition of the convention’s importance for public safety and health.

However, as biotechnology develops (and in some cases, rather rapidly), we question whether, in what ways, and to what extent new developments in bioscience and biotechnology may affect the convention. Assembled member states are tasked with examining whether the articles of the convention remain viable, given the exponential increases in biotechnological capabilities. Apropos of this responsibility, we argue that current and anticipated near-term advances in the biosciences necessitate more detailed and perhaps broader identification of what constitutes a “weaponizable agent” in the context of the BTWC. In short, we ask if the BTWC remains relevant for identifying and guiding the emerging categories of what constitutes a weaponizable biological agent. If so, how should the language of the BTWC be updated to more accurately describe relevant advances in the biosciences? If not, is a new framework required to better apprehend the implications of these advances in bioscience, and what would such a framework entail?

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A REVISED FRAMEWORK

We believe that biological agents can be parsed into 6 categories, rather than the 2 that are directly explicated by the current BTWC (Table 1).

The first category, traditional biological warfare pathogens, includes those agents such as anthrax, smallpox, and tularemia that can be considered as possessing utility only as weapons. No therapeutic or other uses have been identified for these pathogens. Thus, the pathogen is the weapon, which when processed and deployed would constitute a biological warfare attack.

The second category, traditional BW toxins, could be prepared and deployed as biological warfare agents and are also referenced in the BTWC. But many toxins also have applications in biological research and medicine. For example, tetrodotoxin is used to identify and manipulate sodium channels in in vitro preparations of neurobiological and cardiovascular studies. Clinically, *Clostridium botulinum* is used at low concentrations to control muscle spasms, manage chronic migraine, and treat overactive bladder and is somewhat widely used (as Botox) in cosmetic procedures. Similarly, conotoxins have been clinically used to treat convulsive disorders and stroke, to induce neuromuscular blockade, and for cardioprotection.^{3,4} Thus, these toxins (and the following 4 categories of agents) are considered as having dual use, which complicates their management in both commercial and military or proliferation applications, but also clearly limits their use under the provisions of the BTWC.⁵⁻⁷

The third category, derived biopathogens, has been distinctly considered in light of their somewhat unique properties. Of note is that certain bacteriophages are being used to treat bacterial infections and/or as probiotics, and phage therapies have been viewed as “magic bullets in the war on superbugs.”⁶ Phage use has interesting potential for highly targeted applications, incurring only mild side effects due to phage exposure throughout human evolution.⁷ But the same approaches could be employed toward bio-warfare. Developing synthetically derived chimeric pathogens employing the characteristics from multiple pathogens (eg, such as one with the virulence of influenza and the mortality of rabies) is illustrative of the nefarious potential that such agents could afford.⁸ Such use would be recognized as a violation of the BTWC.⁹

The fourth category is biomodulator agents, which can therapeutically be used to up-regulate weak or compromised immune systems. Neuromodulators have also been clinically used to treat certain neurologic and psychiatric disorders. In considering weaponizable applications, agents in this category (and those that follow) can be used to enhance or degrade aspects of cognitive and behavioral performance to either (1) positively affect capabilities of “friendly” personnel, or (2) negatively affect capacities of adversaries (including civilians). Biomodulators are not directly prohibited by the BTWC, although by inference, biological-derived biomodulators would be, while synthetic ones likely would not be prohibited.

The fifth category, artificial biotechnology, describes modifications at the cellular level. The therapeutic uses of

Table 1. What Is Covered Under the BWC? What Should Be Covered Under the BWC?

Category	As a Weapon	As a Therapeutic
Traditional BW Pathogens (weaponization only)	<ul style="list-style-type: none"> • Anthrax • Smallpox • Tularemia • Could include modifications such as antibiotic resistance 	<ul style="list-style-type: none"> • None
Traditional BW Toxins (dual use)	<ul style="list-style-type: none"> • <i>Clostridium botulinum</i> toxin • Staphylococcal enterotoxin-B (SEB) 	<ul style="list-style-type: none"> • Conotoxin (neuropathy) • <i>Clostridium botulinum</i> (BTOX)
Derived Biotoxins (dual use)	<ul style="list-style-type: none"> • Chimera pathogen employing characteristics from multiple pathogens (eg, rabies, influenza) 	<ul style="list-style-type: none"> • Bacteriophages to treat bacterial infections
Biomodulators (dual use)	<ul style="list-style-type: none"> • Immunomodulators to cause immune systems to be over-stimulated • Neuromodulators for degrading performance 	<ul style="list-style-type: none"> • Immunomodulators to up-regulate immune system for fighting disease • Neuromodulators for treating mental illness
Artificial Biotechnology (dual use)	<ul style="list-style-type: none"> • Modification at cellular level • Use of nonbiological material to over-stimulate metabolic process to render adversary ineffective 	<ul style="list-style-type: none"> • Modification at cellular level • Use of nonbiological material to regulate metabolic process to cure disease
Biological Enhancements (dual use)	<ul style="list-style-type: none"> • Tunability, treatment, protection, optimization • Modification, enhancement 	<ul style="list-style-type: none"> • Use to prevent or cure disease • Regrow organs

such techniques include engagement of nonbiologic materials to regulate metabolic processes to mitigate or prevent disease. Examples include forms of cell protection, cell labeling, targeted precise delivery of cell-based therapeutic effects, and in situ regulation of physiologic processes.¹⁰ However, as with agents in the fourth category, the potential exists to employ such technologies to alter metabolic processes to either augment or degrade physiological capabilities and performance. For example, such agents could change metabolic processes so that warfighters would require less nutrition and/or rest to maintain peak performance. Conversely, by reversing intent, a state or nonstate actor could employ artificial biotechnology to attack an adversary: Such approaches could be used to impair metabolic processes, thereby rendering individuals or groups incapable of certain functions and thus imparting degrading effects on warfighter and/or civilian activities. Given their nonbiological derivation, they do not appear to fall within the purview of BTWC prohibitions.

The sixth and final category specifically defines biological enhancements and encompasses a wide range of interventions that could be used to improve aspects of performance (either temporarily or permanently). These techniques and technologies have therapeutic potential in their capacity to alter physiologic functions, facilitate salutary processes (and/or lessen pathologic mechanisms), and, in more *avant* applications, to regenerate tissues and possibly regrow organs. These same tools can be used to “tune” and/or augment physiological processes so as to afford protection and optimization (of key aspects of the performance) of operational military personnel. To date, the BTWC member nations have not specifically considered such enhancements as falling within their purview, and it remains unclear whether the BTWC or standards and instruments of international law would be best suited or applicable to such deliberation and engagement.

Of course, many of techniques and technologies remain experimental and not yet ready or viable for any form of operational deployment. However, the pace and extent of the field is such that several of these agents are currently being explicitly considered for their potential value to military or warfare applications, and indeed many are now poised for or iteratively entering testing and evaluative trials toward such use.^{11,12} In considering the current BTWC standing on these issues, some movement has been observed. Discussions of BTWC Article I at recent review conferences and meetings of state parties have largely considered questions and issues related to “microbial or other biological agents or toxins” that fall into the first 2 aforementioned categories. Discourse has also focused on the third category, derived biotoxins. However, substantive address of biomodulators, artificial biology, and (as noted above) the use biological enhancements as weapons is still vague or lacking altogether. A notable exception has been explicit mention of weaponizable neurotechnologies— inclusive of those devices and approaches that could be used

for warfighter performance optimization—by the Australia Group at the most recent review conference in late 2016.

A MORE RELEVANT BTWC?

The BTWC was established primarily to address those substances intended to or capable of exerting deleterious effects on adversaries. Therefore, we assert that recent trends and trajectories in global research and development, and the continued democratization of biotechnology, which is seeing nonstate actors with state-like capabilities, prompt more holistic consideration of the convention to address and discern broader classification(s) of biological agents and the international security issues they incur. We believe that absent a more fulsome and explicit discussion of the real and growing threat(s) posed by ongoing development and potential use of nontraditional biological agents as viable weapons, the BTWC is likely to become increasingly inadequate, if not irrelevant.

We recognize and acknowledge that the language of the BTWC was deliberately designed to be vague to avoid specifics that could foster constricted classifications, which could then be easily skirted.¹³ More granular language might not have enabled the BTWC to survive the relatively effective 40-year duration it has to date. But bioscience and technology are rapidly changing, and we are not calling for excessive or constrictive specificity. Rather, we argue for greater accuracy and precision in identifying those domains of agents (including devices) that could be weaponized. For example, an area clearly not suggested in the text of the convention is the use of bioscience to enhance human performance. This is conspicuous in light of ongoing and increasing interest in establishing programs to study and implement biological optimization of cognitive and behavioral performance of military personnel.^{14,15}

To be sure, issues related to enhancing or degrading aspects of human performance using biomodulators, artificial biology, and biotechnologies have been and are dealt with in forums other than the BTWC. However, these discussions tend to be academic and focus on the scientific advances and ethical, legal, and social issues. If and when questions and concerns about military use of emerging biotechnologies arise, these forums are characteristically limited in perspective.

In our view, the fact that such discourses are occurring, largely in the absence of important security implications or effect(s), fortifies the need for the BTWC to address these biotechnologies. We believe that failure to do so would render the BTWC somewhat myopic and diminish its relevance. Thus, while a fundamental reexamination of the BTWC would be challenging and perhaps arduous, we believe that, at minimum, querying the broader applicability of the BTWC to weaponizable capabilities conferred by biomodulators, artificial biology, and biological enhancements would be prudent, necessary, meaningful, and ultimately worthwhile.

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