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on

Toxin and bioregulator weapons: preventing the misuse of the chemical and life sciences

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Introduction: The Chemical Weapons Convention (CWC) and the Biological and Toxin Weapons Convention (BTWC) were designed, with the inclusion of a General Purpose Criterion (GPC), to be comprehensive in the substances encompassed and responsive to technological change. Both are intended *inter alia* to cover and prevent weaponization of naturally occurring and synthetic toxins and bioregulators; the threat from which continues to grow with advances in, and convergence of, the chemical and life sciences and associated technologies. However, through longstanding textual ambiguities, exacerbated by inconsistencies and failures in State Party implementation, the envisioned BTWC and CWC overlapping protection in reality masks a dangerous regulatory gap, which risks both regimes failing to effectively prevent or address development of toxin or bioregulator weapons.

Recently there are welcome signs that the Organisation for the Prohibition of Chemical Weapons (OPCW) has begun to focus upon toxins, at least with regard to strengthening its capabilities to investigate their alleged use, notably through the work of the Scientific Advisory Board (SAB).[i] In our monograph -*Toxin and Bioregulator Weapons: preventing the misuse of the chemical and life sciences*[ii] - we identify areas of concern meriting collective consideration by the CWC States Parties at the forthcoming 5th Review Conference and beyond, as summarised below.

'Dual use' toxin and bioregulator research for CBW defence: Biological and chemical weapons (CBW) defence establishments undertake research and associated activities related *inter alia* to toxins, bioregulators, bioregulatory pathways and physiological systems, and measures to facilitate agent dissemination and uptake. The necessity of such 'dual use' research - having potentially benign and malign applications - is recognised and specifically permitted, when it is conducted for "protective purposes" under the CWC, or for "prophylactic, protection and other purposes" under the BTWC. To increase confidence and prevent misperceptions, States are required to report on such work through Annual CWC Article X Declarations and encouraged to submit similar details through the BTWC Confidence Building Measures. Unfortunately, public transparency in this area is currently limited and insufficient to address disquiet surrounding the intentions and applications of such research and associated activities conducted by many State CBW defence establishments. For example, we examined open-source information from a State in the Americas indicating a range of contemporary toxin and bioregulator research of potential 'dual-use' application had been carried out by military and military-related institutions and researchers. This included investigation of staphylococcal superantigen functioning; production of engineered non-toxic botulinum toxins through 'rational design'; employment of recombinant technology to develop a non-toxic SEB mutant; and work on aerosolised ricin and aerosolised botulinum toxin.[iii] Even though this State is far more open than many others; given the lack of full public reporting and transparency for certain facilities and programmes, it is not possible to determine the purposes for which all such research has been undertaken or to which it will be applied.

Novel toxins: Dual-use toxin research of potential concern extends far beyond previously investigated weapons agents. Military and non-military institutions and scientists have discovered and investigated a growing range of 'novel' toxins that could be weaponised, including those derived from indigenous poisonous plants, amphibians, reptiles, scorpions and marine animals. In some cases

the stated intent and associated activities were clearly medical or for other "protective purposes". In others the intention was unstated or unclear. And, in certain cases the purpose appears explicitly to be for toxin weaponization. We examined a series of papers published by scientists from an Asian State's defence research establishment and related bodies detailing their investigations of toxins derived from native stinging and poisonous plants. In 2018, these scientists argued that because the BTWC "banned the use or stockpiling of most of the pathogenic bio-threat agents" this would "necessitate… search [for] some novel natural bio-threat agents from stinging plants that may be used as future bio-weapon for self-defence purposes." They consequently undertook a study to "identify, characterize and screen the potential of […] stinging plants on the basis of their secondary metabolite contents that may be used for the formulation of novel future bio-threat agents for self-defence."[iv] They subsequently identified "several poisonous plants that can be used for the development of novel multi-system targeted warfare agents for defensive applications.". They identified "poisonous components" from ten candidate plants and investigated their "mode of action", which could "have harmful effect on various biological systems like nervous, cardiac, digestive, respiratory, dermal, etc simultaneously."[v] Some of the toxins investigated as potential agents – such as aconitine - are highly toxic and can be lethal; others though not as poisonous could still potentially be employed as "less lethal" toxin weapons.[vi]

Brain research projects: Over the last two decades, the technologies available to neuroscientists have developed rapidly and made it increasingly possible to understand the neuronal circuits in the central nervous system (CNS) that underly our behaviour, and the roles played by bioregulators in such processes. The obvious advantages of this work, for example in helping people with brain dysfunctions and injuries has led States to initiate large-scale brain research projects over recent years. In certain countries scientists from military medical institutions and other defence related facilities are involved in much of the research. Research strands of the national brain project of one Asian State and associated work on neurological systems and associated bioregulators (including noradrenaline, 5-HT, serotonin and orexin) in a variety of simple animal models – such as fruit flies, zebrafish and mice - have potential dual-use applicability. In addition, in order to better understand more complex human behaviours and the mechanisms that produce them, large-scale work is also being carried out in this Asian state on the nervous system and responses of non-human primates (NHPs), like macaque monkeys. This has important 'dual-use' implications as previous biological weaponeers did not restrict their work to manipulation of basic functions of the brain, but also sought to influence human emotions, cognition and consequent behaviour. Work within this State's national brain project includes studies of higher functions of the brain using advanced biotechnology with NHP as test subjects. The research seeks to explore the neural basis of cognition including how molecules and cells establish synaptic contacts and generate neural circuit activities. While the purported purposes of such research are benign, there are risks of potential malign application including to inform or facilitate development of bioregulator weapons to attack, influence or subvert human cognition.[vii]

"Less lethal" weapons: Concerns about the malign application of toxins, bioregulators, and other substances of biological origin, as well as their synthetic analogues, have extended to their development and use as so-called, often misnamed, "less lethal" weapons.

A particular focus of disquiet among many CWC States Parties, as well as medical and scientific bodies, has been development and use of weapons employing central nervous system (CNS)-acting chemicals. These are a disparate group of toxic chemicals whose purported purpose as weapons is to cause prolonged but nonpermanent disability or incapacitation. They include centrally acting agents producing loss of consciousness, sedation, hallucination, incoherence, paralysis, and disorientation. Many putative agents have low safety margins, and inappropriate doses cause serious, sometimes permanent health effects, even death. Certain States have previously conducted research

into a range of CNS-acting chemicals, including pharmaceutical chemicals and/or bioregulators, and related bioregulatory pathways, potentially for law enforcement and military purposes.[viii]

Whilst the development and use of weaponized CNS-acting chemicals in armed conflict was clearly prohibited under the CWC, there has been continuing debate as to whether certain CNS-acting chemicals could be employed for law enforcement. In December 2021, the 26th Conference of States Parties adopted a Decision, in the form of an "Understanding", clarifying that the CWC *did* prohibit aerosolized use of CNS-acting chemical agents for law enforcement purposes.[ix] Although a landmark advance, the threat of CNS agent weaponization remains. Whilst 85 States supported the "Understanding", the vote was opposed by 10 States,[x] and there is concern that certain of these may not feel constrained by its prohibitions. Notable among the opponents was a State that previously conducted research and development of CNS-acting weapons and whose security forces in 2002 used aerosolized fentanyl derivatives to end a terrorist siege, causing the deaths of more than 120 hostages from poisoning and asphyxiation.[xi] Subsequent dual-use research into CNS-acting chemicals has been reported by this State's scientists as well as by scientists from two other States that also opposed the CSP-26 Decision.[xii] The task now falls on all CWC States to implement the CSP-26 Decision fully and consistently.

Riot control agents (RCAs) are defined under the CWC as chemicals not listed in one of the treaty Schedules that rapidly produce sensory irritation or disabling physical effects that disappear within a short time following termination of exposure. In addition to chemically synthesized chemicals, these agents include a number of substances of biological origin, notably capsaicinoids. The CWC permits the use RCAs for "law enforcement including domestic riot control purposes," [xiii] but only provided they are used in "types and quantities" consistent with such purposes.[xiv] However, they have been frequently misused for serious human rights violations, most commonly in non-custodial settings to restrict, intimidate, or punish those participating in public protest the world over; and also in the prisons, detention centres or police stations of certain countries to ill-treat individuals. [xv] A recurring medical concern has been their use in excessive quantities in the open air or in confined spaces where the targeted individuals cannot disperse. In such situations, serious injury or death can result including from the toxic properties of the chemical agents or from asphyxiation.[xvi] A particularly shocking case has been the inappropriate use of excessive amounts of tear gas by the police of an Asian State to quell disturbances at a football match on 1 October 2022. The use of tear gas, the resulting crowd panic and stampede, compounded by overcrowding and locked exits, led to the deaths of over 130 people with hundreds more injured.[xvii]

This situation could dramatically worsen as development, marketing, and deployment of systems capable of delivering significant amounts of riot control agents over wide areas or extended distances intensifies. In addition to potential misuse for collective mistreatment or punishment of crowds, such wide-area riot control agent delivery mechanisms could be employed as force multipliers in conjunction with firearms, making lethal force more deadly on a large scale. Although nominally developed for law enforcement, they also may be incorporated into military arsenals in the future and used in armed conflict in contravention of the CWC and, in the case of capsaicinoids, the BTWC. The OPCW SAB in its February 2023 report for the forthcoming Review Conference has voiced concerns over the "continued development, testing, production, and promotion of diverse" wide-area riot control agent delivery mechanisms. It warned that "the capabilities being developed increasingly resemble military equipment. These systems could be repurposed and filled with other chemicals," including chemical warfare agents, central nervous system-acting chemicals, and bioregulators.[xviii] Civil society researchers – notably from Bradford University and the Omega Research Foundation - have documented development and promotion of wide-area riot control agent delivery mechanisms, including indoor dispersion devices, water cannons, external area denial devices, multi-barrel projectile launchers, large-caliber projectiles, and delivery mechanisms mounted on remote weapons systems, unmanned ground vehicles, and drones.[xix] In recent years proliferation, use and misuse of wide area RCA delivery mechanisms has begun. In 2018 the security

forces of a Middle East State used tear gas drones in response to mass protests, in some cases against peaceful protestors, bystanders, journalists and field medical facilities. [xx] In 2022 this State authorised further employment of such RCA drones for law enforcement purposes.[xxi] In 2019[xxii] and 2021[xxiii] respectively, the security forces of a second Middle East State and a State in the Americas inappropriately employed multi-barrel launchers to fire salvoes of tear gas projectiles into protesting crowds.

Recommendations

It is important that the OPCW collectively review these diverse scientific and technological developments; and assess and respond to associated potential threats. Consequently, CWC States Parties at the 5th Review Conference, should:

- Reaffirm the importance of the GPC as a vital safeguard ensuring the Convention's comprehensive scope and future-proofed prohibition *inter alia* of all naturally occurring and synthetic toxin and bioregulator weapons.
- Establish a consultative process to develop guidelines on how the "types and quantities" principle of the GPC should be applied in practice. The consultative process should explore specific challenges to the GPC arising from contested interpretation as to the range of toxic chemicals (including toxins and bioregulators) and associated delivery mechanisms that could be legitimately employed for law enforcement, and the nature of what constitutes legitimate use. It should specifically address:
    - *Riot control agents:* Clarifying nature and scope of activities consistent with "law enforcement including domestic riot control". Building upon previous work of the Scientific Advisory Board identifying chemicals (including those of biological origin) that fulfil the definition of RCA,[xxiv] guidance should be developed as to quantities of identified RCAs that can legitimately be employed in law enforcement. Such guidance should acknowledge relevant obligations under international human rights law, to ensure such RCA employment is proportionate, necessary, and does not endanger life or health.
    - *Delivery mechanisms:* Determining which delivery and dispersal mechanisms purportedly intended for RCAs (including those of biological origin and their synthetic analogues) and potentially applicable to other toxic chemicals, are inappropriate for law enforcement purposes and would consequently breach Article II.1 of the Convention. Such prohibited means of delivery should at a minimum include artillery shells, aerial bombs, mortar shells, cluster munitions, and other mechanisms that are indiscriminate or deliver quantities of RCAs likely to cause death or serious injury to those targeted. Guidance should be provided as to which RCA means of delivery can be legitimately employed in law enforcement and if so under what circumstances and with what constraints.
    - *CNS-acting chemical agent weapons:* Following adoption of the "understanding" by the 26th Conference of CWC States Parties, aerosolised use of CNS-acting chemical agents for law enforcement purposes is effectively prohibited. Further guidance is, however, needed to define "CNS-acting chemicals" and the range of chemicals that would be covered by the "understanding". Consequently, States should support the SAB recommendation that the Director General establish a TWG to study current developments concerning CNS-acting chemicals.[xxv] Additional guidance is also required in order to ensure that any existing or future law enforcement weapons that use toxic chemicals (including toxins and bioregulators) that act on other *core* human physiological processes beyond the CNS are also prohibited. Guidance should further clarify that not only aerosolised but all weaponised use of such toxic chemicals for

law enforcement purposes, no matter how they could be delivered, should be prohibited.

- Update and strengthen routine OPCW industry monitoring and verification measures applicable to toxins and bioregulators, as well as analytical methods and databases available for challenge inspections and investigations of alleged use. In prioritising activities, the States Parties should note the SAB Temporary Working Group on Biotoxin's "strong recommendation" that OPCW capabilities (at least for investigation of alleged toxin use) should focus on nine "most relevant" toxins. In addition to ricin and saxitoxin which are listed in Schedule 1, the seven other "most relevant" toxins of concern were determined to be abrin, aflatoxins, botulinum toxins, epsilon toxin, Staphylococcus aureus enterotoxins, T-2 toxin; and tetrodotoxin.[xxvi] The SAB TWG also recommended that the OPCW continue to monitor developments in relevant S&T fields and further modify the list of "most relevant" toxins as required.[xxvii] Furthermore, the SAB TWG recommended that the "OPCW should continue to monitor developments on compounds of biological origin, in the field of bioregulators in particular, for indications of increased risk of misuse as weapons".[xxviii]

  Consideration should also be given to updating the CWC Schedules by adding further toxins that have been or may be utilised in weapons programmes. Once again consideration should be given to inclusion of the seven "most relevant" toxins listed by the SAB TWG on Biotoxins. The OPCW should also consider updating the Schedules to include indicators of new types of potential chemical agents (and their precursors) of concern, including those of biological origin, notably bioregulators such as Substance P. An additional approach to consider is modification of existing verification provisions relating to "Other Chemical Production Facilities" (OCPFs) so as to capture OCPFs that could support State-level bioregulator weapons production[xxix].
- Explore how the CWC and BTWC States Parties and organisations can work together more effectively to prevent hostile application of naturally occurring toxins, bioregulators, and their synthetic analogues. At the institutional level, the OPCW Technical Secretariat and the BTWC Implementation Support Unit should strengthen existing information exchange, cooperation, and collaboration to respond to the implications of the growing convergence of the chemical and life sciences.

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[i] OPCW, Analysis of Biotoxins Report of the Scientific Advisory Board's Temporary Working Group, Technical Secretariat, SAB/REP/1/23, 20 April 2023

[ii] Crowley, M. and Dando, M. Toxin and bioregulator weapons: preventing the misuse of the chemical and life science research, Palgrave Macmillan, November 2022. https://link.springer.com/book/10.1007/978-3-031-10164-9

[iii] For further details of relevant activities and publicly available scientific research papers see: Crowley and Dando (2022) op.cit. pp.176-194.

[iv] Gupta, S. M. et al. Phytochemical Analysis of Indian Stinging Plants: An Initiative Towards Development of Future Novel Biothreat Agents for Self-defence. Proceedings of the National Academy of Sciences, India Section B: Biological Sciences, 2018, 88(2), pp.819–825.

[v] Gupta, S. M. et al. Himalayan Toxic Plants of Defense Importance. ACTA Scientific Medical Sciences, 2018, 2(3), pp.44–48.

[vi] For further details of relevant activities and publicly available scientific research papers see: Crowley and Dando (2022) op.cit. pp.79-86.

[vii] For further details of relevant activities and publicly available scientific research papers see: Crowley and Dando (2022) op.cit. pp.57-60.

[viii] For further details of relevant activities and publicly available scientific research papers see: Crowley and Dando (2022) op.cit. pp. 60-63, 78, 101-103, 109-113, 124-128, 150-161.

[ix] Organisation for the Prohibition of Chemical Weapons, Decision: Understanding regarding the aersolised use of central nervous system-acting-chemicals for law enforcement purposes, CWC Conference of States Parties, 26th Session, 2021.
[x] CWC coalition, 26th Session of the Conference of the States Parties (CSP-26), 2021, www.cwccoalition.org/ csp26-summary/.
[xi] Riches, J, Read, R., Black, R., Cooper, N. &Timperley, C. Journal of Analytical Toxicology 36, 647, 2012.
[xii] Crowley, M. & Dando, M. Down the slippery slope? A study of contemporary dual-use chemical and life science research potentially applicable to incapacitating chemical agent weapons, Bath University, 2014; Crowley, M. & Dando, M. (2022) op.cit., pp.125, 101-102.
[xiii] OPCW, Chemical Weapons Convention, 1993, Article II.9
[xiv] OPCW, Chemical Weapons Convention, 1993, Article II.1.a.
[xv] For illustrative cases see, Amnesty International, Tear: an investigation, https://teargas.amnesty.org/#top; Crowley, M. Chemical Control, Palgrave Macmillan, London, UK, 2016, pp.50-80.
[xvi] See for example, Crowley, M. (2016) op.cit., pp. 48-49 and pp. 72-75.
[xvii] There has been widespread media reporting of this case. See for example Lamb, K. and Tereisa, A. Tear gas, locked gates led to Indonesian soccer stampede, spectators say, Reuters, 4 October 2022
[xviii] OPCW, Report of the Scientific Advisory Board on Developments in Science and Technology to the Fifth CWC Review Conference, RC-5/DG.1, 22 February 2023, paragraph 80.
[xix] Crowley, M. (2016) op.cit. pp.92-106; Crowley, M. Tear Gassing by Remote Control, Remote Control Project/Bradford University/Omega Research Foundation, December 2015.
[xx] UN Human Rights Council, Report of the Detailed Findings of the Independent International Commission of Inquiry on the Protests in the Occupied Palestinian Territory, A/HRC/40/CRP.2, 18 March 2019; Greenwood, F. and Zaqqout, O. Drones Don't Wear Uniforms. They Should, Foreign Policy, 22 May 2018; Al Jazeera, Israeli Drone Targets Journalists, 12 November 2018.
[xxi] Breiner, J. Israel Using Drones to Tear Gas Palestinian Demonstrators in West Bank, Haaretz, 28 April 2021,
[xxii] Amnesty International, Suppressing Protests: French Less-Lethal Weapons Used In Lebanon, January 2021; Amnesty International, Lebanon: New evidence reveals French law enforcement equipment unlawfully used to crush protests, 28 January 2021.
[xxiii] Human Rights Watch, Colombia: Egregious Police Abuses Against Protesters, 9 June 2021; Amnesty International, Cali: In the epicentre of repression: human rights violations during the 2021 national strike in Cali, Colombia, AMR 23/4405/2021, 30 July 2021.
[xxiv] OPCW, Technical Secretariat, Office of Strategy and Policy, Note by the Technical Secretariat, Declaration of riot control agents: advice from the Scientific Advisory Board, S/1177/2014, 2014; See also OPCW, Scientific Advisory Board, Response to the Director-General's Request to the Scientific Advisory Board to consider which riot control agents are subject to declaration under the Chemical Weapons Convention. SAB-25/WP.1., 27 March 2017.
[xxv] OPCW, SAB 5th Review Conference Report (February 2023) op.cit., paragraph 31.
[xxvi] OPCW, SAB TWG on Biotoxins (April 2023) op.cit., Strong Recommendation 3.
[xxvii] OPCW, SAB TWG on Biotoxins (April 2023) op.cit., Recommendation 5.
[xxviii] OPCW, SAB TWG on Biotoxins (April 2023) op.cit., Recommendation 6.
[xxix] This was originally proposed by the late Dr Jonathan Tucker. See: Tucker J. The body's own bioweapons, Bulletin of Atomic Scientists, Volume 64, number 1, March/April 2008, pp. 16–22 & 56–57.