OPINION

Biologists napping while work militarized

As researchers discover more agents that alter mental states, the Chemical Weapons Convention needs modification to help ensure that the life sciences are not used for hostile purposes, says **Malcolm Dando**.

SUMMARY
- Number of possible biological warfare agents on the rise
- Future targets could be emotions, immune responses or fertility
- Lack of engagement with problem among life scientists
- Weapons conventions need to catch up

In October 2002, Chechen rebel fighters held more than 750 people hostage at a Nord-Ost production in a theatre in Moscow. The siege was broken only after special military forces used what the Russian Health Minister, Yuri Shevchenko, later described as a mixture of substances derived from fentanyl — an opiate developed in the 1950s as an anaesthetic. Widespread relief that many of the hostages were saved was tempered by 124 of them being killed by the gas.

Chemicals with effects like those of fentanyl are often known as 'incapacitating agents'. These substances affect biochemical processes and physiological systems to produce a disabling condition such as unconsciousness, and in higher concentrations can cause death. With effects that last from hours to days, they are distinct from standard riot-control agents such as CS gas, which cause sensory irritation that disappears shortly after termination of exposure.

That Russian special military forces resorted to using fentanyl in Moscow is a possible harbinger of the wider militarization of advances in the biological sciences.

Designer weapons

Attempts to exploit benignly intended research for hostile purposes are not new. After the Second World War, the international medical community began to discover compounds that alleviated symptoms of mental illnesses such as depression and mood swings. These findings weren't accompanied by a good understanding of how the drugs worked. Nevertheless, they prompted nations to ramp up their efforts to find chemicals suited to military use. In fact, in 1959, the chairman of the UK government's secret Chemistry Committee of the Advisory Council on Scientific Research and Technical Development told his colleagues that the committee was "looking for agents which would produce, not cure, psychoses"[1].

> "Some researchers are actively facilitating the development of new chemical weapons."

Between the early 1950s and 1970s, researchers working in laboratories that eventually became the US Army Medical Research Institute of Chemical Defense studied chemical agents that affect the central nervous system. Indeed in 1961, the US military weaponized BZ — a drug that had originally been studied as a possible therapy for gastrointestinal diseases. BZ is one of a group of chemicals that act on the brain and can cause delirium; people exposed to it may fall into a stupor, struggle to speak, show poor coordination and have difficulty processing thoughts.

Despite the long-standing interest the defence industry has shown in drugs that alter people's physiological and mental states, a lack of knowledge has hampered attempts to use them. For example, by 1966, the US military had stockpiled munitions capable of delivering BZ, but its mode and site of action were poorly understood, and its effects varied widely from person to person. This and other problems led to its abandonment. The United States destroyed its stocks by 1990, several years before the Chemical Weapons Convention (CWC) entered into force in 1997.

Current biochemical threats range from lethal chemical agents to traditional and genetically modified biological agents. In general, biological agents such as anthrax cause governments the most concern. Only a few pathogens are suitable for military use, however. For example, smallpox could prove useful as a weapon because it is highly contagious; anthrax because it has a life cycle that involves the production of long-lived spores. The limited range of possibilities means that there is a good chance of developing countermeasures such as vaccines or antibiotics against these agents. Even if efforts are made to modify them — for example by introducing genes that encode antibiotic resistance — the problem of designing countermeasures is potentially surmountable because the range of effective manipulations that can be made is also limited.

But recent scientific and technological advances could transform the biochemical-threat landscape. Indeed, in 2003, military analysts from the Counter-proliferation and Technology Office of the Defense Intelligence Agency in Washington DC predicted that emerging biotechnologies were likely to lead to a "paradigm shift" in the development of biological warfare agents[2]. They warned that it would soon become possible to engineer agents to target specific human biological systems at the molecular level.

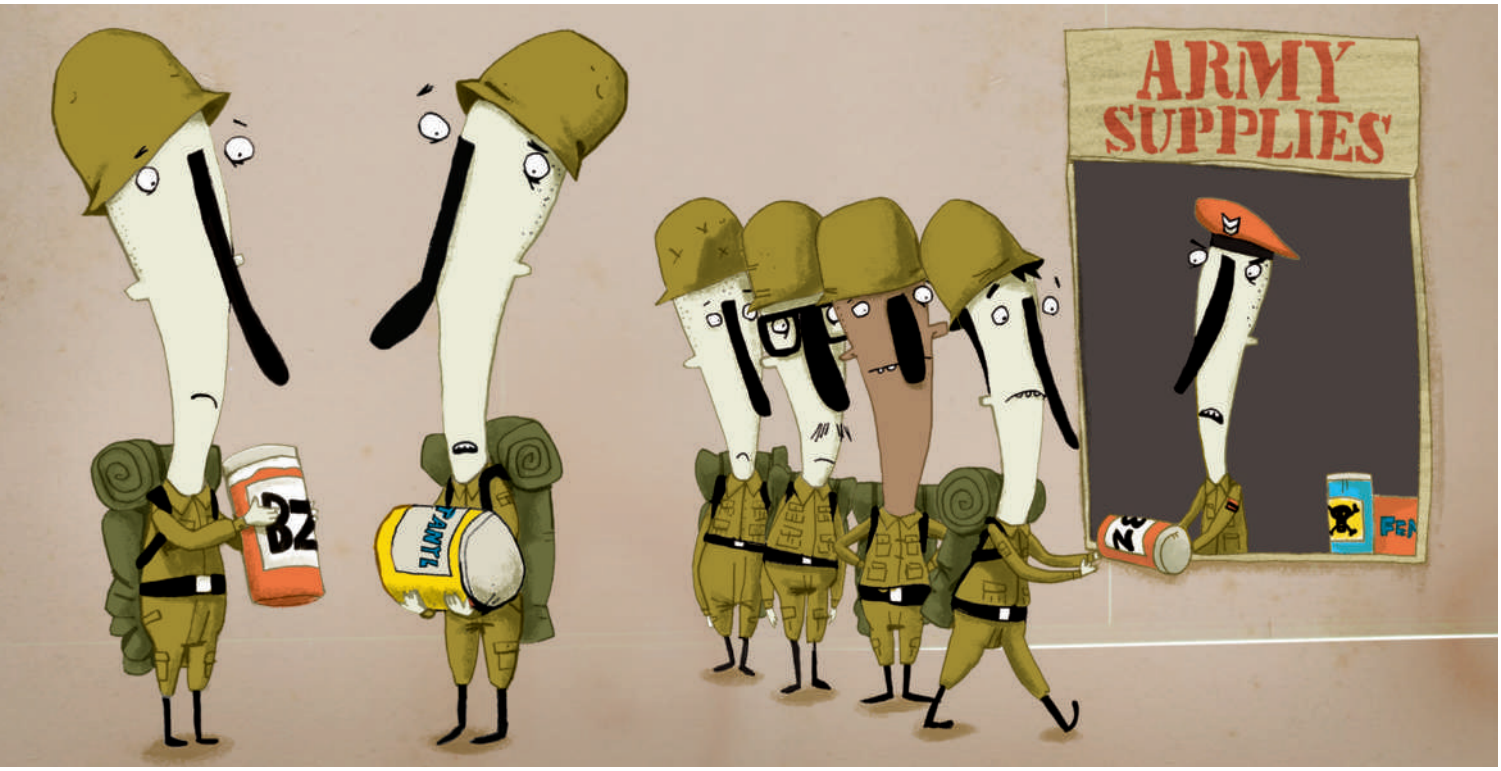
This idea of identifying crucial biochemical pathways, and then designing compounds to disrupt them is a leap from the traditional model of biological-agent development. It expands the options: there are likely to be thousands of potential molecular targets and numerous ways of disrupting each one.

Frontiers of concern

Concerns about this kind of expansion of biochemical threats have since been reiterated by scientific and medical communities. For example, in 2006, the US National Academies produced a report called *Globalization, Biosecurity, and the Future of the Life Sciences*. The authors argued that recent advances in our understanding of how bioregulatory compounds work, of signalling processes and of the regulation of human gene expression — combined with developments in chemistry, synthetic biology and in technologies such as nanotechnology — have "opened up new and exceedingly challenging frontiers of concern".

More recently, a 2008 US National Academies report entitled *Emerging Cognitive Neuroscience and Related Technologies*, similarly argued that in cases in which 'agonists' of a particular system have been found to enhance some cognitive trait, an 'antagonist' might be developed that could reduce it and vice versa. If dopamine agonists enhance attention, say, so dopamine antagonists might disrupt it. They also warned, among other things, that nanotechnologies could overcome the blood–brain barrier and "exploit existing transport mechanisms to transmit substances into the brain in analogy with the Trojan horse".

Some researchers are actively facilitating the development of new chemical weapons. For example, a research group from Pennsylvania State University in University Park has identified several drug classes as potential non-lethal agents or 'calmatives'[3], including benzodiazepines and α2-adrenoreceptor agonists, as well as individual drugs such



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as diazepam and dexmedetomidine.

Similarly, at the 4th European Symposium on Non-Lethal Weapons in 2007, researchers from the Institute of Experimental Medicine and Charles University in Prague described the effects on macaque monkeys of combinations of drugs that produce a rapid loss of aggressive behaviour[4]. They argued that the drugs could be "used to pacify aggressive people during … terrorist attacks". The same researchers have also investigated methods of aerosol delivery to human volunteers.

Those who support the development of incapacitating agents often argue that using them in conflict situations stops people being killed. Historical evidence suggests otherwise. At the Nord-Ost siege, for instance, terrorists exposed to the fentanyl mixture were shot dead rather than arrested. Likewise, in Vietnam, the US military used vast quantities of CS gas — a 'non-lethal' riot-control agent — to increase the effectiveness of conventional weapons by flushing the Viet Cong out of their hiding places.

Blind to misuse

The lack of engagement with this issue among life scientists in general is alarming. Some companies are already marketing oxytocin on the back of studies showing that a nasal squirt of the hormone increases trust in humans. Even though the effectiveness of commercial sprays is doubtful, such research opens up the possibility of a drug that could be used to manipulate people's emotions in a military context. Discussions with more than 2,000 practising life scientists in 13 countries over the past few years have taught me that few have considered such possible uses of their work.

There are problems with both the international conventions that protect us from the potential misuse of biological and chemicals research — the CWC and the Biological and Toxin Weapons Convention. The Biological and Toxin Weapons Convention, for instance, lacks an effective verification mechanism to ensure that nations are fulfilling their obligations.

Some have called for the CWC agreement to be amended to allow the use of novel incapacitating agents[5]. In the past 20 years, modern warfare has changed from predominantly large-scale clashes of armies to messy civil strife: think of Bosnia, Iraq and Afghanistan. The chemical agents described here are particularly suited to this style of warfare; it's not hard to find people in the military world who think they would be useful[5].

The CWC urgently needs modifying if it is to continue to help ensure that the modern life sciences are not used for hostile purposes. Most pressingly, the compatibility of the Convention with the development of non-lethal chemical agents for law enforcement needs careful scrutiny. Article II.9(d) states that "Law enforcement including domestic riot control" is exempt from the prohibition of the use of chemical agents. 'Law enforcement' could be taken by some to cover more than domestic riot control — which, in certain circumstances, would make it legal for the military to use agents such as fentanyl.

In my opinion, all use of novel non-lethal agents such as fentanyl for law enforcement should be prohibited, or at least heavily restricted. If, instead, we sit on our hands we must accept that new incapacitating agents are just the beginning. We will be, as the British Medical Association concluded in its 2007 study, *The Use of Drugs as Weapons*, "knowingly moving towards the top of a 'slippery slope' at the bottom of which is the spectre of 'militarization' of biology" including "intentional manipulation of peoples' emotions, memories, immune responses or even fertility". ■

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