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

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Standing agenda item: review of developments in the field of science and technology related to the Convention

Science and technology developments that have potential benefits for the Convention

Background information document submitted by the Implementation Support Unit*

Summary

The Seventh Review Conference decided that the 2012 to 2015 intersessional programme would include a Standing Agenda Item on review of developments in the field of science and technology related to the Convention. The Conference also decided that under this item, States Parties would consider new science and technology developments that have potential benefits for the Convention, including those of special relevance to disease surveillance, diagnosis and mitigation. During regional group consultations in early June, States Parties requested a background paper on this topic. This paper provides an overview of advances of possible relevance. It is based on the background information document on new scientific and technological developments relevant to the Convention prepared for the Seventh Review Conference (BWC/CONF.VII/INF.3). The annex, in English only, provides a more detailed account with references to the scientific literature.

I. Detection

1. Being able to detect that a disease event is occurring, to track causative agents, and start diagnostic practices prior to symptoms speeds up the timeframe in which a response can be organized. This can reduce the impact of a disease event and possibly reduce the

* Late submission, as document was requested by States Parties after due date.

desirability of instigating an outbreak in the first place. Recent advances in science and technology have provided a range of new capabilities in this arena, including: different approaches; research into in-building early warning and response systems;[1] use of satellite data;[2] the identification of pre-clinical disease indicators;[3] the use of engineered bacteria that glow when in the presence of a biological stressor;[4] visual sensors for tracking of pathogens and toxins;[5] as well as improvements in environmental detection of agents.[6]

II. Diagnostics

2. There have been a number of recent advances in the production of cheap and portable equipment for diagnosing diseases.[7] Some devices may enable the creation of rudimentary diagnostic capabilities in parts of the world currently lacking such capabilities. The also offer interesting opportunities to move some diagnostic tools and techniques to the point of care – or at least into a regional, rather than national, context.[8] There have also been advances in rapid diagnostic capabilities, which would also enable a faster, more efficient and tailored response, including through: new approaches to differentiate between bacterial and viral infections;[9] genotyping pathogens and identifying reassortment events;[10] the identification of single particles of pathogens or toxins;[11] the real-time diagnosis of fungal pathogens;[12] broader use of mass spectrometry; advances in microscope technology; as well as the use of sequencing capacity as a public health tool.[13] There have also been advances in developing faster assays for toxins.[14]

III. Prevention and prophylaxis

3. There has been progress in creating broad spectrum vaccines as well as new approaches for developing vaccines.[15] A range of novel mechanisms to pre-empt disease are also being developed. There has also been progress in finding ways to improve upon our natural immune systems.[16] Researchers also report improvements in delivery techniques for prophylactics.[17]

1 http://www.nti.org/gsn/article/researchers-designing-wmd-shield-for-buildings/
2 http://www.economist.com/node/13688152
3 http://www.biomedcentral.com/1471-2105/9/486
4 http://www.nti.org/gsn/article/researchers-develop-lab-on-a-chip-technology-to-test-water-safety/
5 http://www.spectroscopyonline.com/spectroscopy/article/articleDetail.jsp?id=376468
6 http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G10/639/27/PDF/G1063927.pdf?OpenElement
7 http://www.newscientist.com/article/dn14410-ipodsize-microscope-could-become-lifesaving-gadget.html
8 http://www.popsci.com/technology/article/2010-02/fingerprint-sized-paper-lab-chip-costs-just-penny
9 http://pubs.acs.org/doi/abs/10.1021/ac200596f
10 http://wwwnc.cdc.gov/eid/article/17/4/10-1726_article.htm
11 http://www.eurekalert.org/pub_releases/2006-11/uog-sbu111506.php
12 http://www.ncbi.nlm.nih.gov/pubmed/15893831
13 http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023400
14 http://aem.asm.org/content/74/14/4309.full
15 http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000921
16 http://www.nature.com/nature/journal/v476/n7361/full/nature10356.html
17 http://www.technologyreview.com/news/419880/a-flu-vaccine-without-the-needle/

IV. Therapeutics

4. Developing novel antibiotic capabilities remains a priority for the fight against disease. The last few years have seen: the creation of novel classes of antibiotics; progress in their characterization; success in improving their efficacy; identifying new targets; advances in understanding how bacteria overcome antibiotics; and better discovery tools. Progress in antiviral therapy, includes: the development of a pan-viral drug; the discovery of new drugs; improvement in understanding of how viruses work; the discovery of an anti-viral virus; virucidal proteins; proteins to disrupt viral adhesion to host cells; proteins that disrupt viral replication; as well as high-affinity binding reagents that demonstrate an antiviral activity. Bioprospecting has continued to identify potential therapeutic compounds. There have also been advances made in dealing with toxins including through genetic manipulation of host mechanisms, nanoparticles to trap toxins, as well as antibody approaches to allow them to be flushed from the body.

V. Response capacity

5. There have been advances in determining whether a disease event involves cultured rather than natural pathogens,[18] as well as statistical approaches for separating out mixed data sets,[19] as well as the development of microbial forensic capabilities – all of which would assist in identifying if an attack has taken place and who might be responsible.[20] Research has also demonstrated the importance of effective quarantine measures in limiting impact. [21] Developments in decontamination technology, such as antibacterial foams and the use of nanoparticles, could facilitate a post-attack clean up.[22]

[18] http://news.rice.edu/2010/08/16/telltale-signs-of-bioterror/
[19] http://www.sciencemag.org/content/322/5898/44.1.full.pdf
[20] http://www.pnas.org/content/early/2011/03/01/1016657108.abstract
[21] http://wwwnc.cdc.gov/eid/article/16/8/09-1787_article.htm
[22] http://www.koat.com/print/29135497/detail.html

Annex

[ENGLISH ONLY]

Developments with possible beneficial consequences: a more detailed review

I. Detection

1. Being able to detect that a disease event is happening, to track causative agents, and start diagnostic practices prior to symptoms speeds up the timeframe in which a response can be organized. This can reduce the impact of a disease event and possibly reduce the desirability of instigating an outbreak in the first place. Recent advances in science and technology have provided a range of new capabilities in this arena, including: different approaches, such as through native air sampling techniques;[23] research into in-building early warning and response systems;[24] partial prediction systems for normal disease events based on satellite data;[25] the identification of pre-clinical disease indicators, such as the expression of switch-like genes;[26] the use of engineered bacteria that glow when in the presence of a biological stressor, such as a pathogen;[27]the use of membrane immunofiltration analysis with visual sensors for tracking of pathogens and toxins;[28] as well as improvements in environmental detection of agents by nanowire sensors or by immunographic methods.[29]

II. Diagnostics

2. There have been a number of recent advances in the production of cheap and portable equipment for diagnosing diseases.[30] Some of these devices may enable the creation of rudimentary diagnostic capabilities in parts of the world currently lacking such capabilities. The also offer interesting opportunities to move some of the diagnostic tools and techniques currently in use to the point of care - or at least into a regional, rather than national, context.[31] Relevant developments include: the creation of image sensing chips that could lead to the development of highly portable microscopes, similar technology has since been integrated into lens-less microscope prototypes that works with mobile phone technology; a cheap (US$10), pocket size polymerase chain reaction (PCR) machine that runs off two AA batteries which can be used to identify a number of pathogens; as well as the development of paper-based diagnostic ‘chips’ through advances in microfluidics and the use of silica nanoparticles.[32]

[23] http://online.liebertpub.com/bsp
[24] http://www.nti.org/gsn/article/researchers-designing-wmd-shield-for-buildings/
[25] http://www.economist.com/node/13688152
[26] http://www.biomedcentral.com/1471-2105/9/486
[27] http://www.nti.org/gsn/article/researchers-develop-lab-on-a-chip-technology-to-test-water-safety/
[28] http://www.spectroscopyonline.com/spectroscopy/article/articleDetail.jsp?id=376468
[29] http://daccess-dds-ny.un.org/doc/UNDOC/GEN/G10/639/27/PDF/G1063927.pdf?OpenElement
[30] http://www.newscientist.com/article/dn14410-ipodsize-microscope-could-become-lifesaving-
[31] http://www.popsci.com/technology/article/2010-02/fingerprint-sized-paper-lab-chip-costs-just-penny
[32] http://www.popsci.com/technology/article/2010-02/fingerprint-sized-paper-lab-chip-costs-just-penny

3. There have also been advances in rapid diagnostic capabilities, which would also enable a faster, more efficient and tailored response, including through: new approaches to differentiate between bacterial and viral infections;[33]the use of real-time reverse transcription PCR to genotype pathogens and identify reassortment events;[34] the use of Surface Enhanced Ramen Spectroscopy (SERS) to measure the change in frequency of a near-infrared laser as it scatters off viral DNA or RNA allowing the identification of single particles of pathogens or toxins;[35] the real-time diagnosis of fungal pathogens through Selected Ion Flow Tube-Mass Spectrometry (SIFT-MS);[36] as well as the use of sequencing capacity as a public health tool to identify causative agents as well as viral subtypes and reassortment events.[37] There have also been advances in developing faster assays for toxins, such as for the Clostridium botulinum Neurotoxin Type A.[38]

III. Prevention and prophylaxis

4. Certain recent advances have led to the identification of new vaccines. Progress has been made in the creation of broad-spectrum vaccines, such as a pan-influenza vaccine.[39] Genome wide analysis has also shown promising signs for the development of broad spectrum vaccines for bacteria, such as a single vaccine for common E. coli infections. [40] New approaches for vaccination have also been developed. One group reported having identified a standardised approach for genetically manipulating pathogens to make them harmless, whilst still inducing immunity in a mouse model. Another group discovered that they could prevent the replication of a variety of bacterial pathogens, such as those which cause tularaemia, plague, melioidosis, and brucellosis, by exposing a host to cationic liposomes non-coding DNA complexes (CLDC) mixed with pathogen membrane factors.[41]

5. A range of novel approaches to pre-empt disease are also being developed, including making use of advances in the understanding of infections to enable non-pathogenic bacteria to protect against pathogenic viruses, as well as efforts to improve how our immune systems function.[42]

6. Efforts to improve the immune system have included: building self-replicating killer cells from a disabled form of HIV-1 and human T-cells capable of killing target cells, multiplying inside the host and patrolling against relapses and subsequent infections (which has shown dramatic results in three patients to date);[43] building genetically-modified antibodies against specific pathogens by reprogramming human B-cells and assisted by engineered T-cells;[44] advances in our understanding of how the immune system uses antibodies to respond to viral infections after they enter host cells, opening up new opportunities for improving upon the natural process;[45] as well as through the modulation of

[33] http://pubs.acs.org/doi/abs/10.1021/ac200596f
[34] http://wwwnc.cdc.gov/eid/article/17/4/10-1726_article.htm
[35] http://www.eurekalert.org/pub_releases/2006-11/uog-sbu111506.php
[36] http://www.ncbi.nlm.nih.gov/pubmed/15893831
[37] http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0023400
[38] http://aem.asm.org/content/74/14/4309.full
[39] http://www.technologyreview.com/news/421253/a-long-lasting-universal-flu-vaccine/
[40] http://www.ncbi.nlm.nih.gov/pubmed/20439758
[41] http://www.plospathogens.org/article/info%3Adoi%2F10.1371%2Fjournal.ppat.1000921
[42] http://www.nature.com/nature/journal/v476/n7361/full/nature10356.html
[43] http://stm.sciencemag.org/content/3/95/95ra73.abstract
[44] http://hplusmagazine.com/2010/02/02/re-engineering-human-immune-system/
[45] http://www.ncbi.nlm.nih.gov/pubmed/21045130

the gut microbiome to both reduce the chances of infection and reducing the adverse side-effects of antibiotics.[46]

7. There have also been advances in delivering vaccines and prophylaxes, including through trans-dermal patches.[47]

IV. Therapeutics

8. Developing novel antibiotic capabilities remains a priority for the fight against disease. The last few years have seen the creation of novel classes of antibiotics, e.g. Ceftobiprole.[48] It has also seen the initiation of programmes to develop targeted antibiotics that sense and attack specific pathogens.[49] Researchers have also identified a range of new targets for antibiotics, including: manipulating the cell walls of multi-drug resistance bacteria;[50] disrupting flagella and motility;[51] structural elements in RNA polymerases;[52] as well as disrupting quorum sensing systems.[53] Papers published in the last few years have shown how previously uncharacterized antibiotic systems, such as the aminoglycosides, actually work.[54] This might enable the development of improved systems and conformationally similar drugs developed. Research has also identified additional mechanisms by which bacteria overcome antibiotics - both at the genetic level and functionally, such as through the use of nitric oxide-producing enzymes.[55] There have also been advances in new antibiotic discovery technology, for example, through nanotechnology cantilevers to enable high-throughput screening.[56]

9. Perhaps the most promising recent development in anti-viral therapy has been the possibility of developing a broad-spectrum antiviral drug that could kill any cell infected by a virus.[57] Researchers redesigned the enzyme that detects long strands of RNA (which is only produced during viral transcription and replication), which binds to the RNA blocking further production of viral proteins and initiates an extreme self-destruction response. Laboratories trials have shown these drugs to be effective against 15 human pathogens ranging from those that cause the common cold to haemorrhagic fevers. A range of more traditional anti-viral drugs have also been discovered, including: squalamine, a compound that protects sharks from viral infections; RNA interference (RNAi) therapies for Ebola in non-human primates;[58] as well as the identification of novel monoclonal antibody therapies for influenza infections.[59] Research over the last five years has also helped further our understanding of how viruses work, which in turn opens now opportunities for therapies. One group has published, for example, how Ebola infects cells. A second team used a more sophisticated understanding of Ebola to create a siRNA protocol designed not to cure Ebola

[46] http://www.ncbi.nlm.nih.gov/pubmed/18197175
[47] http://www.technologyreview.com/news/419880/a-flu-vaccine-without-the-needle/
[48] http://newswire.rockefeller.edu/2008/07/02/new-antibiotic-beats-superbugs-at-their-own-game/
[49] http://www.nature.com/news/2010/100414/full/464970a.html
[50] http://www.cbc.ca/news/health/story/2010/10/08/bacteria-cell-wall-trick.html
[51] http://www.ncbi.nlm.nih.gov/pubmed/20676082
[52] http://www.cell.com/abstract/S0092-8674(08)01190-2
[53] http://www.newscientist.com/article/dn16563-new-antibiotics-would-silence-bugs-not-kill-them.html
[54] http://www.cell.com/abstract/S0092-8674(08)01195-1
[55] http://www.sciencemag.org/content/321/5887/365.abstract
[56] http://www.newscientist.com/article/dn14912-nanolevers-could-speed-up-hunt-for-superbug-drugs.html
[57] http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0022572
[58] http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60357-1/fulltext
[59] http://www.cidrap.umn.edu/cidrap/content/influenza/panflu/news/feb2309monoclonal-br.html

but to hold its replication in check until the hosts immune system could begin to respond effectively, which in turn allowed a monkey to recover from the disease. In 2008, researchers discovered virophages - viruses which spread at the expense of other viruses. Such a discovery offers possibilities for the design of anti-viral virus therapies.[60]

10. There have also been relevant advances in developing therapies to deal with toxins, including: the identification of genetic sequences in hosts required for intoxication by ricin and Pseudomonas exotoxin (offering treatment opportunities by blocking the functionality of these genes);[61] nanocarriers designed to allow toxins to be flushed from the system;[62] nanoparticles designed to trap toxins and carry them to the liver for destruction;[63] compounds designed to prevent the uptake of toxins into certain cell types, such as botulinum toxin into nerve cells;[64] as well as small binding agents designed to latch on to toxins enabling them to be identified by antibodies, also allowing it to be flushed from the system.[65]

11. Several research groups have also been developing more unusual therapeutic approaches. Developments in the understanding of human metabolic network topology in disease have led to the development of multi-target drugs designed to disrupt disease-related molecular networks.[6667] Equally, advances in sequencing capabilities have enabled the use of comparative genome wide analysis to identify novel targets for drugs. One research group has developed non-biological nanofactories designed to prevent bacterial replication offering an entirely new approach for therapeutics via nanomaterials. Another group built a nanoparticle that disrupts bacterial cells walls and shows promise in treating bacteria that have become multi-drug resistant. There is also an ongoing research project to develop adjutants that help break up bacterial infections into single cells, making them more sensitive to existing antibiotics.[68]

V. Response capacity

12. Over the past five years there have been advances that improve capabilities to investigate if an attack has taken place and who might be responsible. Researchers are currently working on a way to identify cultured pathogens (as opposed to those that have evolved in nature).[69] This would help determine that a disease event has a deliberate or accidental origin, rather than being caused naturally. New statistical methods have also been developed to identify individual genotypes from samples comprised of mixed genetic data or from aggregate SNP data enabling better tracing of specific agents during investigations.[70] Perhaps most importantly, recent years have also seen the release of some of the microbial forensic procedures and practices used to investigate the use of B. anthracis filled envelopes as a weapon in the United States.[71]

[60] http://www.nature.com/nature/journal/vaop/ncurrent/full/nature10380.html
[61] http://www.asiaone.com/News/AsiaOne+News/Singapore/Story/A1Story20110724-290762.html
[62] http://www.ncbi.nlm.nih.gov/pubmed/18654405
[63] http://pubs.acs.org/doi/abs/10.1021/ja102148f
[64] http://www.ncbi.nlm.nih.gov/pubmed/21832053
[65] http://news.tufts.edu/releases/release.php?id=156
[66] http://www.pnas.org/content/105/29/9880
[67] http://www.ncbi.nlm.nih.gov/pubmed/18985027
[68] http://www.ncbi.nlm.nih.gov/pubmed/18985027
[69] http://news.rice.edu/2010/08/16/telltale-signs-of-bioterror/
[70] http://www.sciencemag.org/content/322/5898/44.1.full.pdf
[71] http://www.pnas.org/content/early/2011/03/01/1016657108.abstract

13. Data published since 2006 also has implications for restricting the spread of a disease event. A paper published in August 2010, for example, demonstrated that quarantine methods are effective in preventing secondary outbreaks. Although enforced quarantine is a traditional disease control measure, relevant legislation in many countries has not been updated recently and may be inconsistent with subsequent developments in rights and freedoms.[72]

14. There are also advances which will help clean up after a disease event. One group, for example, reported in 2011 having developed a decontamination foam capable of killing pathogens such as that which causes anthrax, using nothing more than chemicals found in common household materials. [73]

[72] http://wwwnc.cdc.gov/eid/article/16/8/09-1787_article.htm
[73] http://www.koat.com/print/29135497/detail.html