

## **SCIENTIFIC AND TECHNOLOGICAL DEVELOPMENTS RELEVANT TO THE BIOLOGICAL WEAPONS CONVENTION**

Submitted by Sweden

1. Since the 5<sup>th</sup> Review Conference in 2001, there has been a continuous, broad and diversified development in biotechnology, life sciences and related technologies. Advances in biotechnology and genetic engineering have provided the means to modify and design microbial agents in very specific ways. This area of research and development has through the years created tremendous knowledge concerning basic principles of life processes and found worldwide applications within public health, animal health and the agricultural and industrial sectors. However, this development could also be explored to create new types of biological threats. Micro-organisms can be genetically modified in many different and sometimes unpredictable ways for illicit purposes and thereby jeopardize the efficiency of traditional biodefense and medical countermeasures. Micro-organisms can be designed to produce toxins and bioregulators, circumvent detection, survive harsh physical conditions and express new specific properties like for instance drug resistance. The development within research areas like genetic modification, expression technology, production and dispersions techniques for biological agents have in the past been recognised as relevant to BWC and therefore been carefully monitored and assessed by the State Parties to the BWC every five years to judge the comprehensiveness of Article I of the Convention.

2. Outside the areas of research and development focusing more or less directly on biological agents and toxins, many additional areas that contribute to the growing understanding of different life processes are increasingly explored. Therefore, areas like drug design, synthetic biology, systems biology, aerosol technology, nanotechnology, microencapsulation and targeted delivery of drugs also need to be assessed. In addition, developments in areas like physics, chemistry, engineering sciences, computational sciences and material sciences have and will continue to have great impact on the rapid progress in biotechnology. The accelerating pace and wider approaches in life sciences and related research areas will fundamentally alter the threat spectrum and mandate a need to adopt a broader perspective in assessing the threat.

3. The rapid progress in life science research generates a strong incentive for increasing investments as the need for new drugs and other products is steadily growing. For instance, characterization of bioregulators, (which are small, biologically active organic compounds), and the search for new pharmaceuticals using different techniques will continue to identify and generate many potentially new pharmaceuticals. The most promising compounds for new pharmaceuticals will be scrutinized and tailored for optimal biological effects. Many highly toxic compounds will also be identified and characterized in this process and they may have potential as new biological as well as chemical weapons. Bioregulators are considered by many to pose a more serious risk of being used for illicit purposes than previously due to the increased understanding of inter- and intra-cellular processes. The growing understanding of how bioregulators and other compounds affect and control central biological processes of mammalian systems, including human, is therefore judged as an increased dual-use risk.

4. The techniques to deliver biologically active organisms or compounds to their target structures have evolved as a key technology for pharmaceutical industry as well as for biotechnology in general. These targeting technologies are driven by the demands of the pharmaceutical, agricultural and public health sectors. Advances in this field, including

aerosol delivery, is one of the reasons behind the increasing concern regarding the use of bioregulators for nefarious purposes. Potential delivery platforms include the use of bacterial plasmids or viral vectors for cloning the genes encoding bioregulators, transgenic insects for production and inoculation, nano-scale delivery systems, and liposomes or biodegradable microspheres for controlled release. The small particles used in these technologies make the delivery of the particulate matter to the enormous adsorptive surface of the lungs outmost effective.

5. One area of drug delivery where significant progress has been made recently is the use of large porous particles (LPP) for delivery of drugs through adsorption in the lungs. LPP are significantly larger than the size regarded as optimal for inhalation and deep deposition. But due to the low density the LPPs are inhaled and drugs are efficiently delivered. A key feature of LPPs is their large surface area that can be used to carry a large number of small particles, in the size range of 25 to several hundred nm. The concept frequently is used to coat LPPs with nanoparticles carrying drugs for optimised aerosol delivery. These techniques could also potentially be used to develop highly efficient aerosol delivery systems for micro-organisms (viruses and possibly also small bacteria), toxins or chemical compounds for nefarious purposes.

6. The scientific and technical development relevant to the BWC since the fifth Review Conference has continued to be fast, extensive and increasingly diversified. Some research areas have, more than others, added new dimensions to the risk of illicit use. One such area is, BioProspecting, and its relevance and consequences on the comprehensiveness of the BWC is important to assess. Here we use the term BioProspecting to cover the rapidly developing research area that explores the biological and chemical diversity in nature. Pharmaceutical companies have for several years been actively screening for compounds produced by living organisms in different environments to evaluate their potential for drug development. There is a strong incentive for this research as it holds great promise to identify novel compounds for use in medicine, agriculture and industry. This research is dominated by private companies that are global in nature and have extensive international collaboration in this area. Through the rapid progress of this field a large number of new compounds of biological origin and mostly produced by the microbial community have and will continue to be identified.

7. New technologies have evolved with new opportunities to explore the biological and chemical diversity in nature that has been difficult to access by “natural methods”. The microbial community represents the largest source of genetic diversity on the planet. Many of these microbes produce compounds that have a large potential for use in medicine, agriculture and industry. Today it is possible to directly access large amounts of genetic material from these different environmental sources. The genetic material could encode an entire metabolic pathway to synthesize a specific compound or even be large overlapping fractions of microbial genomes that could be used to disclose entire genomes of previously unknown micro-organisms. Similarly, natural compounds can be extracted and characterized even if present in very low amounts and therefore BioProspecting research will rapidly generate a lot of novel information regarding biological and molecular diversity of our planet.

8. A combination of different technologies has contributed to the development in our increased understanding of biological and molecular diversity. Molecular biology has provided the tools to efficiently extract, clone and characterize genetic material from different environments even when present in very low amounts. Since the novel organisms identified by genetic techniques normally can not be grown, characterised and handled in the laboratory

there will be a strong demand to develop techniques for expression of the genetic information in various heterologous hosts to produce the new compounds of interest. These new host for production will not be restricted to micro-organisms but would for instance also include plants and insects. Vectors developed for cloning large segments into both bacteria and higher organism in so-called artificial chromosomes like BAC (bacterial artificial chromosomes) and YAC (Yeast artificial chromosomes) together with inexpensive DNA sequencing methods are key techniques that rapidly have contributed to identification and characterisation of previously unknown organisms.

9. Progress in bioinformatics, and accumulated information from the increasing number of organisms where the complete genomes have been sequenced and characterised, together with computational biology has made it possible to predict properties and complete metabolic pathways from sequence information generated from the genetic material isolated from different environments. This information can then be used to introduce the relevant genetic material into other hosts that can produce these compounds and thus in the laboratory mimic the natural organisms. Similarly, the technical developments in chemistry have made it possible to isolate and characterize compounds from very complex environments even when present in very low amounts.

10. High throughput screening (HTS) technology has become an increasingly important tool in the assessment of compounds with potential for drug development. The use of micro-organisms or higher cells in tissue culture genetically engineered to monitor a specific biological activity has made it possible to screen several thousands of compounds for the desired drug properties. Technical HTS platforms employing robot technology to screen libraries of compounds of chemical and/or biological origin are used by many pharmaceutical companies in their search for new drugs. The properties and biological activities of some of these compounds assessed will inevitably have activities that are toxic or affect animals and humans in harmful ways. These compounds will range from high molecular weight proteins to non-protein low molecular weight molecules.

11. Candidate drugs are optimised for specific biological activity, solubility, low toxicity etc. by chemical engineering techniques. The information on these novel compounds, with highly diverse but specific biological activities, will be collected and be readily available in different databases. These extensive data bases covering the chemical and biological properties of the compounds that have gone through various HTS protocols for specific biological activities will most likely be easily accessible through publications and the internet.

12. In summary, the rapid development in the area of BioProspecting will generate new insight into biodiversity of previously uncharacterised environments. An increasing number of organisms that until now not have been possible to study and characterise in the laboratory will be characterised and the compounds produced by these organisms will be the focus of extensive characterisation of their biological activities. The contribution of this research for drug development, agriculture and industry will most likely be very significant in the near future. On the negative side and of relevance to the BWC is that an increasing amount of information regarding the biological activity of a large number of compounds also those with severe effects and toxicity for humans will be available together with information on how to access and produce these compounds.

13. This development may also be judged as important to follow for defence purposes as it may have consequences on available measures of protection. The diversity of these new

biological active compounds screened and characterised is extensive and their effects may be lying outside the scope of existing protective measures. Many of these compounds will be modified by chemical means or even entirely synthesised by chemical methods and thus a concern of both BWC and CWC.

14. The rapid global dispersion of life science materials, knowledge and technologies are not limited to those with therapeutic and public health value. It is difficult to assess what kind of technological or scientific breakthroughs that may challenge the BWC and where in the world these innovations have and will appear. Many countries, today not commonly viewed as being technologically sophisticated, are rapidly gaining global prominence in these fields with increased contribution to the development. The task to assess emerging new threats is expanding and has to be continuous on both the national and international level. Frequent discussions among the State Parties about the implications of this development on Article I of the BWC will be needed to cope with the tremendous development and be able to judge the implication on the comprehensiveness of the Convention.

15. The diversified scientific and technical development involves a growing number of countries and both governmental and private enterprises all over the world. The creative power in this development is unprecedented and can not be directed. The tremendous speed and the creative power in the development is partly a result of the tradition of open exchange of research information. Restrictions in the exchange of information due to the risk that it may harbour unpredictable nefarious applications are unrealistic and will also hamper the scientific dialogue. Therefore it is important for the State Parties to take action to increase awareness of the dual-use dilemma and responsibility for improper use research results within the scientific community.

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