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EMERGING DUAL-USE TECHNOLOGIES IN THE LIFE SCIENCES: CHALLENGES AND POLICY RECOMMENDATIONS ON EXPORT CONTROL

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I. INTRODUCTION

Advanced biotechnologies such as synthetic biology, genome editing or nanobiotechnology are frequently categorized as 'emerging technologies'. Emerging technologies are often described as technologies that have disruptive potential but have not yet been developed to their fullest potential.[1] These technologies are usually rapidly growing with implications already discernible but their full range of practical uses is yet to be determined. However, there is no common agreement on the definition of such technologies. Emerging technologies may have great strategic value and the potential to be adopted for important military and non-military industrial purposes.[2] In principle, such technologies could be misused by states or non-state actors, such as terrorist groups, in the development of weapons of mass destruction (WMD). Therefore, at least some emerging technologies may pose a risk to national security and fall within the scope of international arms control treaties and non-proliferation measures.

The international treaties on biological and chemical weapons are the Geneva Protocol, the Biological and

[1] Brockmann, K., Bauer, S. and Boulanin, V., 'BIO PLUS X: Arms Control and the Convergence of Biology and Emerging Technologies', (SIPRI: Stockholm, 2019), p. 2.

[2] Brockmann, K., 'Drafting, implementing and complying with export controls: The challenge presented by emerging technologies', *Strategic Trade Review*, vol. 8, no. 6 (2018), pp. 5–28.

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SUMMARY

This policy paper addresses the challenges of regulating emerging dual-use technologies in the life sciences. Export control measures can be used as a key governance instrument to prevent the unwanted proliferation of dual-use technologies. However, emerging technologies present certain challenges for conventional export control mechanisms due to the rapid development of various technologies and uncertainties about their potential use. The paper describes key elements of the European Union export control system and provides examples of select dual-use technologies in the life sciences that challenge this system. Recommendations are made in order to improve current EU strategic export control.

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Toxin Weapons Convention (BWC) and the Chemical Weapons Convention (CWC).[3] The conventions prohibit the development and production of biological and chemical weapons, respectively, and require states parties to implement measures that prevent the proliferation of WMD. Biological and chemical dual-use technologies are covered by international export control regimes. The Australia Group (AG) focuses on both biological and chemical dual-use items.[4] The European Union (EU) is a member of the AG. EU member states also participate in the Wassenaar Arrangement (WA). [5] The WA lists items that could contribute to the development of military capabilities, including dual-use production technologies. However, there are no exact criteria or defined guidelines to clarify how technology assessments should be performed or export controls be put in place to deal with emerging technologies. Furthermore, there is no single, harmonized international framework available for the regulation of emerging dual-use technologies.

Generally speaking, biological agents, material, equipment, technologies or software used in the life sciences may fall into the category 'dual-use items' that can be used for both civilian and military applications as well as in the proliferation of WMD.[6] The implications of dual use are of particular interest in the life sciences since 'almost all biotechnology in service of human health can be subverted for misuse by hostile individuals or nations'.[7] Research in the life sciences may also lead to the generation of biological agents, material, knowledge or equipment that can be directly misapplied to cause great harm to humans, animals, plants or the environment. In the USA, many research activities are termed Dual-Use Research of Concern (DURC), which refers to a rather undefined subset of research with dual-use implications.[8] The classification of individual scientific work as DURC requires a case-by-case risk assessment. This concept is regarded as somewhat controversial by many arms control and biosecurity experts and has not been officially adopted in the EU.[9]

Export control measures can be used as a key governance instrument in order to prevent the unwanted proliferation of emerging dual-use technologies. However, emerging technologies present certain challenges for traditional export control mechanisms due to the speed of technological development and uncertainties about potential use. Examples of technology sectors that are of interest to export control and non-proliferation activities include additive manufacturing, advanced data science, advanced materials, artificial intelligence, biotechnology, nanotechnology, robotics and sensing technology.[10] All these sectors are useful to and can have an impact on the life sciences. Data science, for example, permits better analysis of biological data such as DNA sequences.[11] Nanotechnology or additive manufacturing contribute to the development of radically new applications for research results, such as in drug discovery and delivery. The convergence of cutting-edge biological research and emerging (bio-) technologies presents challenges for non-proliferation measures and arms control.[12] A unified classification of dual-use items would require a thorough understanding of their potential misuse, undesirable military

[3] Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases and of Bacteriological Methods of Warfare, opened for signature 17 June 1925, entered into force 8 Feb. 1928; Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, opened for signature 10 Apr. 1972, entered into force 26 Mar. 1975; and Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction, opened for signature 13 Jan. 1993, entered into force 29 Apr. 1997.

[4] The Australia Group was inaugurated in 1985. It is an informal group of countries sharing information on export controls and aiming to harmonize measures to prevent the proliferation of biological and chemical weapons of mass destruction. The group has 43 participants, including the European Union, see <https://australiagroup.net/>.

[5] The Wassenaar Arrangement on Export Controls for Conventional Arms and Dual-Use Goods and Technologies was established in 1996. Currently, 42 member states participate in the export control regime, see <https://www.wassenaar.org/>.

[6] The term 'biological agents' often refers to pathogens or toxins that can cause harm to human, animal or plant health or can degrade equipment or damage the environment.

[7] US National Research Council, *Biotechnology Research in an Age of Terrorism (The Fink Report)*, (National Academies Press: Washington, DC, 2004), p. vii.

[8] US National Science Advisory Board for Biosecurity, Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information (National Academies Press: Washington, DC, 2007). For a full-text definition of DURC, see National Institutes of Health (NIH) Office of Science Policy, 'Dual Use Research of Concern', [n.d.].

[9] US National Academies of Sciences, Engineering, and Medicine, *Dual Use Research of Concern in the Life Sciences: Current Issues and Controversies* (National Academies Press: Washington, DC, 2017).

[10] Hart, J. and Trapp, R., *Science and Technology and their Impacts on the Biological and Toxin Weapons Convention: A Synthesis Report on Preparing for the Seventh Review Conference and Future Challenges*, Technical report (SIPRI: Stockholm, 2011).

[11] DNA or deoxyribonucleic acid is the molecule that carries the genetic information in all cellular forms of life and some viruses.

[12] Brockmann, Bauer and Boulanin (note 1).

applications or even hostile use by state and non-state actors. At the same time, freedom of research is of critical importance and essential for scientific progress, which means that export control measures have to be carefully balanced in order to avoid negative impacts on science.

Section II provides an overview of the key EU non-proliferation measures currently in place to control the spread of emerging dual-use technologies. Section III discusses select emerging technologies in the life sciences that could be misused for the generation of biological or chemical weapons. Section IV analyses the future challenges for EU export control measures presented by emerging dual-use technologies in the life sciences. Section V summarizes the key findings and conclusions, and makes policy recommendations to the EU on how to cope with the challenges identified. The overarching aim of the paper is to provide the reader with a balanced analysis of the challenges facing EU export control measures linked to emerging technologies in the life sciences from the perspective of a natural scientist.

II. EU NON-PROLIFERATION ACTIVITIES

EU Legislation

In the European Union, a combination of EU regulations and national laws has been put in place to prevent the proliferation of WMD.[13] Council Regulation 428/2009 sets the legal framework for export controls by implementing a Community regime for the control of exports of dual-use items and corresponding technologies.[14] The lists of dual-use goods and technologies in the annex constitute an important export control instrument. These currently consist of the dual-use items listed in the international control regimes mentioned above. The regulation is usually updated on an annual basis in order to add new dual-use items and delist others. This legislation is directly applicable in all EU member states and may be complemented by additional national export control provisions. The licencing of exports and the dual-use classification of products and technologies remain within the competence of the EU member states.[15] Dual-use items that could potentially be used for military purposes outside the EU require an export licence from a national authority responsible for export matters. A licensing requirement also applies to unlisted dual-use items that may be used in connection with a biological, chemical or nuclear weapon or for a military end-use in an embargoed destination. The concept of this catch-all control mechanism relies on the cooperation of industries or suppliers with licensing authority in order to enable end-use-related export controls. While the addition of the technical expertise of companies is beneficial, in some cases it can be difficult to determine the intentions, or 'end-use', of customers abroad.

The EU Dual Use Coordination Group (DUCG) is composed of experts from EU member states and chaired by the European Commission. Its main tasks are to undertake technical consultations in order to prepare the Commission Delegated Regulation, updating the EU Control List and to develop guidelines on EU export controls. The DUCG supports further development of the Dual-Use Electronic System (DUeS), which assists information exchange between the national authorities responsible for export control matters and the European Commission. In addition, Article 13(1) of the regulation requires EU member states to notify each other and the Commission of export denials. The Commission reports to the European Parliament and the Council of the European Union on an annual basis on the implementation of the EU Dual-Use Regulation. In 2016, about 690 export denials were issued and exports of controlled dual-use items represented 2.6 per cent of the total volume of EU exports.[16]

The EU export control regime is currently under review.[17] In 2016, the Commission adopted a proposal to modernize the EU export control system. The

[13] Bauer, S., 'WMD-related dual-use trade control offences in the European Union: Penalties and prosecutions', *EU Non-proliferation Paper*, no. 30 (SIPRI: Stockholm, 2013).

[14] European Council Regulation (EC) 428/2009 of 5 May 2009 setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items, *Official Journal of the European Union*, L134, 29 May 2009; as amended by Commission Delegated Regulation (EU) 2017/2268 of 26 Sep. 2017, *Official Journal of the European Union*, L334, 15 Dec. 2017. This is a recast of European Council Regulation (EC) 1334/2000 of 22 June 2000 setting up a Community regime for the control of dual-use items and technology, *Official Journal of the European Union*, L159, 30 June 2000.

[15] For more details see European Commission, 'Dual-use trade controls', Updated 28 May 2018.

[16] Report from the Commission to the European Parliament and the Council on the implementation of Regulation (EC) 428/2009 setting up a Community regime for the control of exports, transfer, brokering and transit of dual-use items, COMM (2018) 852 final, 14 Dec. 2018.

[17] European Commission, Proposal for a Regulation of the European Parliament and of the Council setting up a Union regime for the control

proposed recast of the EU dual-use regulation is aimed at achieving: (*a*) modernization of existing control provisions; (*b*) optimization of EU licencing architecture; (*c*) convergence of catch-all controls; (*d*) re-evaluation of intra-EU transfers; (*e*) an initiative to control exports of cyber-surveillance technologies; (*f*) enhanced cooperation on implementation and enforcement; (*g*) enhanced transparency and outreach/private sector partnership; and (*h*) export control dialogue with third countries.[18]

EU Policy Strategies

The 2003 EU Strategy against Proliferation of Weapons of Mass Destruction states that 'the proliferation of weapons of mass destruction and their means of delivery such as ballistic missiles are a growing threat to international peace and security. [...] WMD and missile proliferation puts at risk the security of our states, our peoples and our interests around the world'.[19] On biological weapons proliferation, the strategy states that:

> [A]lthough effective deployment of biological weapons requires specialised scientific knowledge including the acquisition of agents for effective dissemination, the potential for the misuse of the dual-use technology and knowledge is increasing as a result of rapid developments in the life sciences. Biological weapons are particularly difficult to defend against (due to their lack of signature). Moreover, the consequence of the use may be difficult to contain depending on the agent used and whether humans, animals, or plants are the targets. They may have particular attractions for terrorists. Biological weapons, as well as chemical weapons, pose a special threat in this respect.

Enhanced detection and defence methods mean that views on biological threats may have changed since 2003, but the key assumptions are still valid today.

The 2003 WMD strategy was expanded on in the 'Council Conclusions and new lines for action by the European Union in combating the proliferation of weapons of mass destruction and their delivery systems' of 2008.[20] These new lines for action (NLA) call for intensified efforts 'to impede proliferation flows and sanction acts of proliferation'. One aim is to promote 'a security culture in the [chemical, biological, radiological and nuclear] CBRN area'. In particular, the NLA argue for 'a coordinated and complementary approach to biosafety and biosecurity problems guaranteeing optimal management in particular of biological risks and threats'. Knowledge of the requirements for such a coordinated approach to fostering biosafety and biosecurity needs to be better spread among scientists in research institutions.[21] Unfortunately, there is no internationally standardized teaching or training programme available for academic institutions.[22] Modern textbooks on the life sciences do not refer explicitly to dual-use issues or the mitigation of misuse of biology and medicine for hostile purposes. Exceptions can be found in textbooks on medical microbiology when it comes to biological threat agents, but the level of information on legal frameworks and individual responsibilities in the fight against WMD proliferation is still rather low.

EU Capacity Building Programmes and Outreach

Since 2006, the EU has provided assistance with strengthening the BWC and promoting the non-proliferation of WMD through its Common Foreign and Security Policy (CFSP) budget.[23] This instrument was renewed in 2008 and further supported by Council Decisions in 2012, 2016, and 2019.[24] Since 2006 the EU

of exports, transfer, brokering, technical assistance and transit of dual-use items (recast), COM (2016) 616, 2016.

[18] Eur-Lex, European Commission, COM(2016) 616 final, 28 Sep. 2016.

[19] Council of the European Union, Fight against the proliferation of weapons of mass destruction: EU strategy against proliferation of Weapons of Mass Destruction, 15708/03, 10 Dec. 2003.

[20] Council of the European Union, Council Conclusions and new lines for action by the European Union in combating the proliferation of weapons of mass destruction and their delivery systems, 17172/08, 17 Dec. 2008.

[21] Smith, D., Martin, D. and Novossiolova, T., 'Microorganisms: Good or evil, MIRRI provides biosecurity awareness', *Current Microbiology*, vol. 74, no. 3 (2017), pp. 299–308.

[22] In Germany, the Leopoldina-German National Academy of Sciences together with the German Research Foundation established a Joint Committee on the Handling of Security-relevant Research. The Joint Committee recommends the implementation of courses on dual-use issues in the life sciences and other research disciplines.

[23] Council Joint Action 2006/184/CFSP of 27 Feb. 2006 in support of the Biological and Toxin Weapons Convention, in the framework of the EU Strategy against the Proliferation of Weapons of Mass Destruction, *Official Journal of the European Union*, L65, 27 Feb. 2006.

[24] Council Joint Action 2008/858/CFSP of 10 Nov. 2008, *Official Journal of the European Union*, L302, 13 Nov. 2008;

has allocated a budget of almost €10 million in support of the BTWC. European Council Decision 2010/430/CFSP established the EU Non-Proliferation (and Disarmament) Consortium as a collaborative network of European foreign policy and academic research institutions involved in the development and analysis of WMD non-proliferation measures.[25]

At the international outreach level, the EU CBRN Risk Mitigation Centres of Excellence initiative is a worldwide programme involving 56 partner countries in mitigation of risks related to CBRN materials.[26] It has a budget of €250 million for the funding period 2010–2020. This initiative is managed by the European Commission's Joint Research Centre and the United Nations Interregional Crime and Justice Research Institute (UNICRI). In addition, the EU partner-to-partner (P2P) export control programme on dual-use goods undertakes outreach activities on export control in partner countries in North Africa and the Middle East, south-east Europe, Eastern Europe and the Caucasus.[27] Council Decision (CFSP) 2019/97 also supports a number of instruments and programmes: (*a*) support for BWC universalization; (*b*) capacity development in support of BWC national implementation;
(*c*) fostering biosecurity networks in the Global South; (*d*) supporting the inter-sessional programme and preparations for the ninth Review Conference of the BWC; (*e*) enhancing the preparedness of states parties to prevent and respond to attacks involving biological agents; and (*f*) devising enabling tools for outreach, education and engagement. These instruments help to raise awareness of the implications of dual-use technologies and of export control measures in EU partner countries among developing life science and biotechnology sectors.

Section III provides examples of emerging dual-use technologies in the life sciences with clear misuse potential for the generation of biological and even chemical WMD.

III. EMERGING DUAL-USE TECHNOLOGIES IN THE LIFE SCIENCES

Historically, biological weapons have been successfully developed by several countries but militarily significant weapon arsenals have proved difficult to produce and stockpile.[28] Initially, these weapon programmes relied on classic microbiological techniques. By the late 1980s, however, genetic engineering was already being used in the Soviet Union's biological weapons programme for the construction of advanced biological warfare agents.[29] Genetic engineering was an emerging technology of the 1970s, and is therefore perceived as a classic example of establishing a technique that is useful for the generation of novel biological weapons.

Extensive studies have been published on more recent emerging bio-technologies.[30] A selection of emerging dual-use technologies is presented below. From a microbiological laboratory perspective, these

and Council Decision 2012/421/CFSP of 23 July 2012, *Official Journal of the European Union*, L196, 24 July 2012. In 2016 the Council of the European Union adopted Council Decision (CFSP) 2016/51 of 18 Jan. 2016 in support of the Biological and Toxin Weapons Convention (BTWC) in the framework of the EU Strategy against Proliferation of Weapons of Mass Destruction, Official Journal of the European Union, L12, 19 Jan. 2016. Furthermore, in 2019 the Council of the European Union adopted Council Decision (CFSP) 2019/97 of 21 Jan. 2019 in support of the BTWC, *Official Journal of the European Union*, L19, 22 Jan. 2019.

[25] European Council Decision (CFSP) 2018/299 extends the support for the EU Non-Proliferation and Disarmament Consortium until 2021, see <https://www.nonproliferation.eu>.

[26] For more details see European Commission, International cooperation and development, Updated 19 Aug. 2019.

[27] See Perry, T., 'Reducing proliferation risk through export control outreach: Assistance providers' use of maturity model-based approaches', *Strategic Trade View*, vol. 5, no. 7 (2019). These programmes began in 2004 with two pilot projects implemented by SIPRI and BAFA, see Bauer, S. and Mattiussi, J., 'Transforming the EU's approach to outreach and technical assistance in the area of export controls', ed. A. Ricci, *From Early Warning To Early Action? The Debate on the Enhancement of the EU's Crisis Response Capability Continues* (Office for Official Publications of the European Communities: Brussels, 2008); and Bauer, S., 'Arms trade control capacity building: Lessons from dual-use trade controls', *SIPRI Insights on Peace and Security* (Mar. 2013).

[28] Geissler, E. and Moon, J. E. v. C. M., *Biological and Toxin Weapons: Research, Development and Use from the Middle Ages to 1945*, SIPRI (Oxford University Press: Oxford, 1999); and Lentzos, F. (ed.), Biological Threats in the 21st Century: The Politics, People, Science and Historical Roots (Imperial College Press: London, 2016).

[29] Leitenberg, M., Kuhn, J. H. and Zilinskas, R. A., *The Soviet Biological Weapons Program: A History*, (Harvard University Press: Cambridge, MA, 2012).

[30] See e.g. Kirkpatrick, J. et al., *Editing Biosecurity: Needs and Strategies for Governing Genome Editing*, Technical report, George Mason University; and National Academies of Sciences, Engineering and Medicine, *Biodefense in the Age of Synthetic Biology* (National Academies Press: Washington, DC, 2018); Bajema, N. E., DiEuliis, D., Lutes, C. and Lim, Y.-B., *The Digitization of Biology: Understanding the New Risks and Implications for Governance*, Research paper no. 3 (2018), Center for the Study of Weapons of Mass Destruction, National Defense University, Washington, DC; and Inter Academy Partnership Biosecurity Working Group, *The Biological and Toxin Weapons Convention: Implications of Advances in Science and Technology*, Conference report, Global Network of Science Academies, 2015.

represent important upcoming technologies that have clear misuse potential.

Genetic engineering technologies

Since the 1970s, genetic engineering has been a powerful tool of both basic and applied research.[31] From the very beginning, there was a debate about potential biological risks and the misuse potential associated with these new techniques.[32] Conventional genetic engineering methods, for example for changing the biological traits of bacteria or mammalian cells, can be time-consuming and rather expensive. Therefore, new genetic engineering tools such as Clustered Regularly Interspaced Repeats/CRISPR-associated protein 9 (CRISPR/Cas9), which were introduced around 2012, have received great attention in both the life sciences and the biosecurity community.[33] CRISPR/Cas9 technology is based on the genetic principles of naturally occurring bacterial immune defence mechanisms against viruses and foreign DNA that can be used to modify the genetic information of a cell in a very convenient way—a process known as genome editing. Due to its simple molecular composition and straightforward use, CRISPR/Cas9-based genome editing is perceived as groundbreaking technology with a broad range of applications. Many possible uses have been proposed for CRISPR/Cas9. These include the elimination of genetic diseases by altering the human genome either transiently in the patient's body or permanently in the germ line, which would affect all offspring with consequences that are currently not well understood. Genome editing might help in the medium term to cure diseases that are currently untreatable. A lot of research effort and money is therefore being put into the development of genome editing.

CRISPR-Cas9 is thought to be superior to conventional genetic engineering tools due to its greater precision, speed and efficiency. In 2016, James R. Clapper in his capacity as US Director of National Intelligence made a statement on the worldwide threat assessment of the US intelligence community that highlighted genome editing as an upcoming technology with the potential to create harmful biological agents or products.[34] Genome editing is therefore a recent, prominent example of an emerging dual-use technology in the life sciences that requires better understanding of its risk potential as well as strategies for the mitigation of its misuse.

Export control lists should cover tangible and intangible items linked to CRISPR/Cas technology. However, preventing the proliferation of this technology through export control measures is hampered by the global spread of CRISPR/Cas9 tools, the abundance of its key molecular components in nature and its strong connection to basic scientific research. It would also be unwise to pursue preventive measures because interfering with scientific development poses the risk of erecting unnecessary barriers that could restrict scientific progress without necessarily increasing security. Therefore, experts recommend a focus on the aims of genetic engineering work and the resulting products, and assessment of dual-use implications from this perspective. Of course, in the case of any reason to suspect the intentions of the end-user, the exporter must react in compliance with EU and national export control legislation. Some biosecurity experts even challenge the view that CRISPR/Cas9 is a game changer at all, because of the many obstacles still in place that restrict its use by untrained actors.[35]

One application of CRISPR/Cas9 with clear dual-use implications is the use of so-called gene drives to change the genetic information of entire animal or plant populations in nature.[36] A gene drive is an

[31] It is a matter of debate whether there is a clear separation between basic and applied research. The EU Dual-Use Regulation 428/2009 defines basic scientific research as 'experimental or theoretical work undertaken principally to acquire new knowledge of the fundamental principles of phenomena or observable facts, not primarily directed towards a specific practical aim or objective'. Applied research is usually understood as being focused on specific practical uses. In the USA, fundamental research is defined as 'basic and applied research in science and engineering where the resulting information is ordinarily published and shared broadly within the scientific community, as opposed to research the results of which are restricted for proprietary reasons or by specific US Government access and dissemination controls' (US Code of Foreign Regulation, 22 CFR § 120.11(a)(8); 2019).

[32] Pennisi, E., 'The CRISPR craze', *Science*, 23 Aug. 2013, pp. 833–36.

[33] Ledford, H., 'Crispr, the disruptor', *Nature*, 3 June 2015, pp. 20–24; and Kirkpatrick (note 30).

[34] Clapper, J. R., 'Statement for the Record on the Worldwide Threat Assessment of the US Intelligence Community for the House Permanent Select Committee on Intelligence', Technical report, Office of the Director of National Intelligence, Washington, DC, 9 Feb. 2016.

[35] Vogel, K. M. and Ouagrham-Gormley, S. B., 'Anticipating emerging biotechnology threats', *Politics and the Life Sciences*, 23 Oct. 2018, pp. 1–17.

[36] Esvelt, K. et al., 'Emerging technology: Concerning RNA-guided gene drives for the alteration of wild populations', *eLife*, 17 July 2014.

artificial genetic element, which on introduction to a sexually reproductive species will autonomously spread from generation to generation overriding the natural Mendelian rules of inheritance. This gene drive technology could prove valuable in the elimination of pathogen transmitting vectors such as malaria mosquitoes. However, many questions remain unresolved in terms of biosafety, biosecurity and international regulation before such technology is ready for release into the environment.

Synthetic biology

The Engineering Biology Research Consortium defines synthetic biology as 'the design and construction of new biological entities such as enzymes, genetic circuits, and cells or the redesign of existing biological systems. Synthetic biology builds upon the advances in molecular, cell, and systems biology and seeks to transform biology in the same way that synthesis transformed chemistry and integrated circuit design transformed computing'.[37] Its major fields of application are in: (*a*) biocircuits [the artificial combination of genetic elements in an organism that have a special biological function] assembled with or without standard biological parts; (*b*) engineering cells to produce fine chemicals; (*c*) creating artificial life; (*d*) computer software for biocircuit design; (*e*) artificial ecosystems; (*f*) the use of an enlarged genetic alphabet; (*g*) engineering DNA with a chemically different backbone; and (*h*) the creation of a minimal genome.[38]

Synthetic biology could expand the opportunities for creating new biological threats.[39] In particular, the tools used in synthetic biology could be misused to make pathogens more harmful, recreate known pathogenic viruses through chemical synthesis, produce toxic biochemicals in genetically modified organisms by creating novel metabolic pathways or modulate human physiology by exploiting the research results of systems biology. A combination of using an enlarged genetic alphabet and the introduction of non-natural amino acids in proteins could produce completely new sets of chemically/biologically active protein molecules not found in nature.[40] The complexity of engineered metabolic pathways has steadily increased over the past two decades. For example, it is now possible to produce the anti-cancer drug noscapine in yeasts using an artificial biosynthesis route that involves 25 different enzymes.[41] It is even possible to produce opioids in bacteria such as Escherichia coli.[42] The progress of science and technology has made it clear that synthetic biology has biosecurity implications and requires careful assessment of potential DURC-type activity.[43] The development of appropriate export control measures that can keep pace with the rapid accumulation of novel technologies, materials and knowledge in synthetic biology, however, could prove to be exceptionally challenging.

There is also an important ongoing debate among security experts, social scientists and the promoters of synthetic biology on the extent to which this technology contributes to a deskilling of biology and thus increases the so-called dual-use threat.[44] Malicious actors could get access to biological agents and relevant technologies, but they might still lack the tacit knowledge of how to use the material in order to cause great harm. In sum, synthetic biology could become a key driving force for the widespread use of biotechnology in the medium term. Dual-use goods and technologies will include engineered organisms and blueprints for their generation, individual genetic elements ('BioBricks') for the construction of biocircuits as well as process manuals for the biotechnological production of biological or chemical substances.

[37] Engineering Biology Research Consortium, CA, USA.

[38] Pei, L., Gaisser, S. and Schmidt, M., 'Synthetic biology in the view of European public funding organizations', *Public Understanding of Science*, vol. 21, no. 2 (2012), pp. 149–62.

[39] National Academies of Sciences, Engineering and Medicine, *Biodefense in the Age of Synthetic Biology* (National Academies Press: Washington, DC, 2018).

[40] Jin, X., Park, O.-J. and Hong, S. H., 'Incorporation of non-standard amino acids into proteins: Challenges, recent achievements and emerging applications', *Applied Microbiology and Biotechnology*, vol. 103, no. 7 (2019), pp. 2947–958.

[41] Li, Y., Li, S., Thodey, K., Trenchard, I., Cravens, A. and Smolke, C. D., 'Complete biosynthesis of noscapine and halogenated alkaloids in yeast', *Proceedings of the National Academy of Sciences of the USA*, vol. 115 (2018), E3922–E3931.

[42] Nakagawa, A. et al., 'Total biosynthesis of opiates by stepwise fermentation using engineered Escherichia coli', *Nature Communications*, vol. 7 (2016), p. 10390.

[43] Gómez-Tatay, L. and Hernández-Andreu, J. M., 'Biosafety and biosecurity in synthetic biology: A review', *Critical Reviews in Environmental Science and Technology*, vol. 49, no. 17 (2019), pp. 1–35.

[44] Jefferson, C., Lentzos, F. and Marris, C., 'Synthetic biology and biosecurity: Challenging the "myths"', *Frontiers in Public Health*, vol. 2 (Aug. 2014), p. 115.

Digital biological data

In future, digital biological data could become one of the most important items in international trade. There are many types of digital biological data: (*a*) whole genome or individual DNA/RNA sequence data; (*b*) transcriptome, proteome or metabolome data describing the biological activity of a given cell or organism; (*c*) biomedical data from clinical tests; and (*d*) epidemiological data, among others. While knowledge is accumulating on the basic principles of life, there is still only a limited understanding of comprehensive biological data sets: 'chemistry is recognition, biology is still chaos theory'.[45] Quantum computing techniques could allow the identification of new drug candidates on the basis of huge biological data sets; for example, information on all active metabolic pathways combined with signalling activities in a particular cell type at any given point in time. The vast majority of this data is being aggregated and studied for purely civilian purposes and will contribute to a better understanding of the fundamentals of life. From the viewpoint of non-proliferation measures, however, this data might prove invaluable for hostile actors looking for new biological principles to cause harm to humans, animals, plants or the environment.

3D printing

Advanced manufacturing techniques make 3D printing one of the key emerging technologies. A 3D printer allows the generation of complex 3D structures at high levels of spatial resolution. This is usually done by adding layer on layer of printable material such as solubilized plastics (or bioink). The range of applications for 3D printing is very broad in material sciences, weapon engineering, chemistry, biology and biomedicine. Among the most promising medical applications are printing material for reconstructive surgery or tissue engineering. The applications of 3D printing include not only the production of reaction vessels, but also the generation of chemically active surfaces within such devices.[46] This can assist the combination of several different catalytical activities for the production of chemicals or biopharmaceuticals. In combination with continuous flow production techniques, a batch of 3D printed microreactors could deliver significant quantities of highly toxic chemicals or biological toxins. In the long term, 4D printing could be relevant in the assembly of complex biochemical production units. This refers to '3D-printed objects that have the ability to evolve over time and under external stimulus by modifying their shape, properties or composition'.[47] Depending on the maturation grade of the 3D object, such an external stimulus could be used to change the essential properties of, for example, a biochemical reactor. This technology is still in its infancy and will probably take another 10 years to become mature. There are still huge obstacles to overcome, such as the ability to print mixed materials in a single run.[48]

In the biotechnology industry, bioreactors are used for the cultivation of bacteria, yeasts or eukaryotic cells under controlled conditions. Typical culture volumes range from lab-scale (up to 5 litres) to mass production scale (up to 15 000 litres). Depending on the biological production process and demand, several large-scale bioreactors can be operated in series. This results in a production capacity that is theoretically sufficient to feed an offensive biological warfare programme. Therefore, bioreactors fall into the category of dual-use goods in export control lists. First reports are emerging of proof-of-principle studies involving 3D printed bioreactors, but these still have fairly small cultivation volumes.[49] One example of the convergence of advanced cell cultivation techniques and additive manufacturing is the 3D printing of a yeast-laden hydrogel ink, which resulted in the construction of a 3D lattice of bioreactor compartments.[50] This study demonstrated the possibility of keeping yeasts alive in the 3D-printed bioreactors for a two-week period, enabling them to produce ethanol in a continuous batch process. The cultivation of mammalian cells might be more challenging but could prove valuable in

[45] Hodgson, J., 'Biotech's baby boom', *Nature Biotechnology*, vol. 37, no. 5 (2019), pp. 502–12.

[46] Hartings, M. R. and Ahmed, Z., 'Chemistry from 3D printed objects', *Nature Reviews Chemistry*, vol. 3 (2019), pp. 305–14.

[47] Mandon, C., Blum, L. and Marquette, C., '3D-4D printed objects: New bioactive material opportunities', *Micromachines*, vol. 8, no. 4 (Apr. 2017), p. 102.

[48] 4D printing technology is still in its infancy and currently under research and development. For further reference see e.g. Zhang, Z., Demir, K. G. and Gu, G. X., 'Developments in 4d-printing: a review on current smart materials, technologies and applications', *International Journal of Smart and Nano Materials*, 19 Mar. 2019, pp. 1–20.

[49] Qian, F. et al., 'Direct writing of tunable living inks for bioprocess intensification', *Nano Letters*, 20 Feb. 2019.

[50] Saha, A., Johnston, et al., 'Additive manufacturing of catalytically active living materials', *ACS Applied Materials & Interfaces*, vol. 10, no. 16 (2018), pp. 13373–380.

the production of therapeutic antibodies, vaccines or biochemicals.

The falling cost and increased availability of instruments and knowledge make the 3D printing of bioreactors in do-it-yourself (DIY) approaches more feasible.[51] Inexpensive 3D printing technology along with open-source platforms for electronic prototyping of bioreactors could change the way micro-organisms are cultivated for production purposes using new principles that are currently commercially unavailable.

Section IV considers the challenges facing EU non-proliferation and export control measures due to changes in the way science is conducted and the rapid emergence of new technologies.

IV. CHALLENGES FACING EU NON-PROLIFERATION ACTIVITIES

Strengthening provisions on the non-proliferation of WMD is essential to national and international security. Export controls on dual-use items are an essential tool in preventing the spread of agents, material, equipment, knowledge and technologies that can be misapplied for malevolent uses. A number of challenges for EU non-proliferation activities are set out below.

Disciplinary fragmentation and the growing body of scientific literature

The EU Dual-use Regulation excludes 'fundamental research' from export control requirements. However, there has been both uncertainty and controversy between the authorities in charge of export control and licencing and research professionals over discriminating between fundamental or basic research and the range of technologies and goods of relevance to export controls.

The fragmentation of scientific disciplines and the global diffusion of scientific technologies and knowledge make it increasingly complex to identify the most important actors working on sensitive research topics. Science is becoming increasingly trans- and interdisciplinary, and critical research results are no longer necessarily accumulating in one particular location.

A further challenge for those tasked with ensuring the non-proliferation of WMD is the rapidly growing accumulation of research results and scientific knowledge. Approximately 2.5 million scientific papers are published worldwide each year.[52] An unknown number of publications of research considered to be of dual-use concern are hidden in this impressive paper stack. In a literature survey of biological papers published in journals in the Nature Publishing Group in the period 2004–2008, 28 papers of the 74 000 total were found to deal with DURC.[53] In some cases redaction of part of the submitted manuscript containing DURC can be agreed.[54] For example, in 2013, researchers published their findings in the Journal of Infectious Diseases on a newly identified bacterial strain producing a previously unknown botulinum toxin.[55] In the paper, key information typically included in order to permit other scientists to reproduce and confirm the research was withheld until an effective treatment for the strain has been developed. Redaction of scientific data can only be an exception, however, as it interferes with freedom of research. Furthermore, a number of additional questions arise, such as who should gain access to the unpublished data and by what criteria. A lack of transparency can create new problems around certain types of work conducted in open research facilities.

Convergence of biology and chemistry

The increasing convergence of biology and chemistry could result in novel threats to national security. For example, new biotechnological production processes could be misapplied to the production of highly toxic chemicals, bioregulators or toxins.[56] Although the technical challenges are still quite large, in the medium term, new production strategies could appear for both biological and chemical agents.

[51] Pilizota, T. and Yang, Y.-T., '"Do It Yourself" microbial cultivation techniques for synthetic and systems biology: Cheap, fun and flexible', *Frontiers in Microbiology*, vol. 9 (30 July 2018).

[52] Plume, A. and Van Weijen, D., 'Publish or perish? The rise of the fractional author', *Research Trends*, vol. 38, no. 3 (2014), pp. 16–18.

[53] Satyanarayana, K., 'Dual dual-use research of concern: Publish and perish?', *Indian Journal of Medical Research*, vol. 133, no. 1 (Jan. 2011), pp. 1–4.

[54] Casadevall, A. et al., 'Redaction of sensitive data in the publication of dual use research of concern', *mBio*, vol. 5, no. 1 (Dec. 2013).

[55] Barash, J. R. and Arnon, S. S., 'A novel strain of Clostridium botulinum that produces type B and type H botulinum toxins', *Journal of Infectious Diseases*, vol. 209, no. 2 (2014), pp. 183–91.

[56] Organization for the Prohibition of Chemical Weapons (OPCW), *Convergence of Chemistry and Biology: Report of the Scientific Advisory Board's Temporary Working Group*, SAB/REP/1/14.

Transfer of intangible technologies

The regulation of intangible technology transfers (ITT) in the life sciences must also be taken into consideration.[57] One prominent case was the controversy surrounding influenza research in 2011.[58] Two research laboratories, one in the Netherlands and the other in the USA, independently conducted gain-of-function experiments with strains of the H5N1 influenza virus that were initially not transmissible between humans. These studies artificially generated critical gene mutations that changed the transmissibility of the modified virus from birds to mammals. This produced a potentially pandemic pathogen capable of causing great harm to human health in the case of a laboratory accident or the deliberate release of the genetically modified virus.

Publication of the research results as intended could have led to the release of sensitive information on how such gain-of-function experiments could be used to manipulate pathogens. Therefore, both research groups agreed to omit sensitive information prior to publication. In addition, in June 2012 the Dutch licensing authorities declared a corresponding scientific publication by the European research group subject to an export control licence for security reasons. In response to the incident, in 2014 the United States issued a moratorium on the funding of gain-of-function studies involving select pathogens and updated national regulations on such work. The moratorium was lifted at the end of 2017 but these two cases sparked a worldwide debate about security-relevant research in the life sciences. This debate is reflected, for example, in reports by the US National Science Advisory Board for Biosecurity and the German Ethics Council.[59]

Another striking example of the problem with control list-based approaches is the creation of the infectious horsepox virus by assembling synthesized virus DNA fragments in a Canadian laboratory, details of which were published openly in 2018.[60] In this case the genetic information required for the de novo synthesis of this virus was not controlled and the research group was acting in full compliance with domestic law.[61] The declared aim was to develop a smallpox vaccine. Critics of these experiments highlight the biosecurity implications of the published work because the published instructions could be applied to the artificial generation of the smallpox virus.[62]

Information sharing and legal harmonization

Non-proliferation measures require information on security-relevant developments within and outside the EU to avoid the risk of defocusing preventive action by law enforcement authorities. Classic export control approaches such as item-based lists may not be sufficient for the new technological developments in the life sciences mentioned above due to the time constraints involved in risk assessment procedures and the need to reach consensus among experts on the items to be added to the control lists. This problem can be addressed by the 'catch-all' clause on non-listed items, which requires the exporter to report any transaction if they are aware that the dual-use items may be intended to be used in ways contrary to the Dual-Use Regulation.[63]

Nonetheless, there is still a lack of legal clarity and harmonization within the EU, especially when it comes to the potential requirements of an export licence in cases of a reason to suspect that the end-user will misuse dual-use goods or technologies. Performing and documenting export control assessments for nearly all of the goods and technologies used in basic research represents a tremendous task for untrained personnel, even without looking into practical scenarios such as suspicious end-users or the context of the planned export. Can scientists at an academic research institution foresee malicious behaviour by a recipient? This could lead to uncertainties about the requirements of export licences.

Of course, there are due diligence requirements that a company's or an institute's legal department must fulfil together with the responsible scientist. In this

[57] See European Commission, 'Guidance note—Research involving dual-use items', [n.d.].

[58] Murdock, K. L. E. and Koepsell, D., 'Principals, agents and the intersection between scientists and policy-makers: Reflections on the H5N1 controversy', *Frontiers in Public Health*, vol. 2 (5 Aug. 2014), p. 109.

[59] German Ethics Council, 'Biosecurity: Freedom and responsibility of research', 2014.

[60] Noyce, R. S., Lederman, S. and Evans, D. H., 'Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments', *PLOS One*, vol. 13, no. 1 (Jan. 2018).

[61] Noyce, R. S. and Evans, D. H., 'Synthetic horsepox viruses and the continuing debate about dual use research', *PLOS Pathogens*, vol. 14, no. 10 (Oct. 2018).

[62] Inglesby, T., 'Important questions global health and science leaders should be asking in the wake of horsepox synthesis', *Bifurcated Needle*, 7 July 2017.

[63] See article 4, paragraph 4 of EU Dual-Use Regulation 428/2009.

respect, however, it is not entirely clear what these due diligence requirements include or to what extent investigative action by the exporter is required or even technically feasible.

Possible circumvention of export controls

Emerging technologies could support the circumvention of export controls. Cloud-based laboratories and biofoundries are examples of remote access to laboratory equipment such as DNA synthesis machines being provided to scientists. The idea is to share costly equipment and to use increasingly standardized protocols to improve reproducibility in synthetic biology.[64] This mode of operation increases the difficulties of understanding who is running which kind of process for what purpose. Here, export controls may not be able to keep pace with rapid technological developments, which could lead to evolving security threats for the EU.

New actors, such as the do-it-yourself biology community, have entered fields that may or may not fall within restrictive EU legislation.[65] These actors might not be sufficiently aware of their possible obligations under the export control regulations. Non-proliferation measures must therefore reach a wider audience and keep pace with technological and scientific advances that are not always obviously connected with dual-use implications.

Non-state actors such as bioterrorists could also present challenges for EU non-proliferation activities. Importantly, it is not just the export of dual-use items that is critical to European security, but also their import. This was demonstrated in a case of bioterrorism activity in Germany in 2018.[66] A single individual imported more than 3000 castor beans containing the highly potent ricin toxin. Following recipes posted on the internet by the Islamic State (IS) group, and presumably exchanged by electronic messenger services, he was able to purify a significant amount of the toxin.[67] In this case, analyses of trade flows involving toxic plant material triggered an alarm. The individual was stopped by the German law enforcement authorities before any damage was done.

Non-conventional trade flows

Monitoring the flow of dual-use items includes the export, transfer, brokering and transit of dual-use goods and technologies. The illicit trafficking of dual-use items through non-conventional trade flows organized over the darknet could become more relevant in the future. Law enforcement authorities and intelligence services are said to be monitoring the darknet extensively, but a key feature is the speed at which trade offers appear and disappear. Another level of complexity is the coded darknet language. Unless the technical language known to export control experts is checked against the more casual or coded descriptions of the material or equipment offered by criminals or hostile actors, sales transactions might proceed undetected. Although use of the darknet may not be as straightforward for non-professionals as is sometimes assumed, the higher the pressure to shield illicit activities, the greater becomes the level of sophistication in the use of non-conventional communications and exchange platforms.[68]

Section V draws conclusions and makes recommendations to policymakers, most notably at the EU level.

V. CONCLUSIONS

This paper analyses the challenges facing the implementation of export controls on emerging dual-use technologies in the life sciences. The relevant

[64] Lentzos, F. and Invernizzi, C., 'Laboratories in the cloud', *Bulletin of the Atomic Scientists*, 2 July 2019; and Jessop-Fabre, M. M. and Sonnenschein, N., 'Improving reproducibility in synthetic biology', *Frontiers in Bioengineering and Biotechnology*, vol. 7, no. 18 (Feb. 2019).

[65] The German legislation on genetic engineering, e.g., is quite strict. Running a genetic engineering laboratory requires a licence from the competent authorities, see German Federal Office of Consumer Protection and Food Safety, 'National regulations', [n.d.].

[66] This incident marks the first case of bioterrorism activity in Germany in which the suspect was able to acquire sufficient knowledge and material for the successful production of a toxic biological agent. The case was given broad media coverage, see for example, 'Cologne ricin plotters bought a hamster to test biological weapon', *Deutsche Welle*, 24 July 2018.

[67] Report by the Ministry of the Interior of the State of North Rhine-Westphalia, Germany, 29 June 2018, [in German]; 'Cologne ricin plot bigger than initially suspected', *Deutsche Welle*, 20 June 2018; and 'The new frontier in Jihadi bio-terrorism', *Daily Beast*, 5 Aug. 2018.

[68] A case in Germany in 2018 involved illicit trade in Carfentanil, a narcotic drug and potential chemical warfare agent, as well as a botulinum toxin (BoTox) medical product and the most powerful toxin known so far, see Lahme, F., 'GSG 9 stoppt Brüderpaar aus Werries - Darknet-Dealer jetzt angeklagt' [Synthetic drugs delivered anywhere in the world - GSG 9 stops brothers from Werries - darknet dealer now charged], *Westfälischer Anzeiger*, 26 June. 2018.

technologies, such as genome editing, synthetic biology and 3D printing, are discussed in terms of security concerns. It is clear that the EU dual-use export control system is reliant on an integrated risk analysis procedure. The integration of several different types of information is essential for the corresponding governmental authorities to decide on approvals or denials for the planned exports. Rapid developments in emerging dual-use technologies in the life sciences challenge a control system that relies in part on relatively static export control lists. Production technologies in chemistry and biology tend to converge with many civilian/legitimate uses of biotechnology and biomedicine. Export control should therefore include the intended product or biological function behind certain research and developments activities.

A major conclusion is that emerging technologies require enhanced flexibility from EU export control measures. There is a need to develop unified criteria on export control-relevant categories of emerging dual-use technologies in the life sciences. The harmonization of national export control measures and extended information exchange should support EU member states in fulfilling their duties.

Most importantly, raising awareness among researchers working in biotechnology and the life sciences is a key element of strengthening the EU export control system. Approaches such as catch-all controls require a deep understanding of the proliferation risks associated with emerging technologies. Therefore, broad and continuous discussions about relevant technical and scientific developments would support the decision making of governmental export control authorities.

Recommendations

Develop a systematic science and technology review process

The amount of literature published each year and the lack of standardized risk assessment procedures make monitoring new developments in science and technology (S&T) of relevance to the non-proliferation of WMD a challenging endeavour. EU member states are actively contributing to the work of the BWC and the CWC. The EU has observer status in both treaty regimes. Therefore, the EU benefits from the S&T reviews that take place in the context of biological and chemical arms control. In the case of the CWC, a Science Advisory Board provides experts with knowledge about developments in S&T of relevance to the treaty. Some of this information can be useful for the mitigation of misuse in the life sciences as well. One example is a thorough analysis of the level of convergence between biology and chemistry and the possible impacts on the CWC.[69]

Unfortunately, the BWC lacks such an advisory body, although the August 2019 BWC Meeting of Experts saw renewed momentum for the creation of such a body. Nor has any verification mechanism been implemented. Other methods of compliance monitoring and trust building are therefore required, such as declarations by states parties of certain activities of relevance to the BWC.[70] There is also a lack of structured S&T review processes within the BWC or of concise reporting on potential challenges facing biological arms control.[71] It might be beneficial for the EU to set up EU-specific review mechanisms for the purpose of export control of dual-use items in the life sciences. This would require an institution equipped with sufficient financial and personnel resources to perform this task. A technical secretariat of five people could act as a nucleus for setting up an S&T review board. The head of this unit should be supported by three technical experts who specialize, for example, in infectious biology, nanobiotechnology and additive manufacturing, plus an administrator. A strong connection to the European Commission would be desirable. Experts from academia and industry should be included in the work of the review board, probably in temporary working groups.

Harmonize technical terms

Different interpretations of key technical terms such as 'biological agents' can lead to confusion between export control authorities, industry and academia over which items are covered by such terms. A revised definition of dual-use items in the life sciences could go beyond conventional military and state-centric approaches to security and could explicitly mention broader security implications such as the potential danger of human rights violations. For example, research results from neurophysiology would be likely to come under this dual-use category. In the

[69] OPCW Scientific Advisory Board, 'Convergence of chemistry and biology', Report of the Science Advisory Board's Temporary Working Group, SAB/REP/1/14, June 2014.

[70] Lentzos, F., '3D bio: Declare, document and demonstrate', *EU Non-Proliferation Paper*, no. 45 (Apr. 2015).

[71] Hart and Trapp (note 10).

light of the rapid evolution of biotechnology, synthetic biology and gene drive technology, in particular, it might be plausible to extend the technical definition of 'biological agents' beyond the rather conservative wording of the EU Dual-use Regulation's control list.[72] One possibility would be to adopt a modified version of the definition in the Biological Agents Ordinance published in the German Federal Law Gazette in 2013 (see box 1). In particular, the term 'technologically produced biological entities' could prove very valuable when it comes to risk assessments of novel developments in the life sciences such as gene drives. The concept of defining biological weapons *sensu lato* could even be used for biological arms control and non-proliferation measures.[73] The proposed category of 'biological weapons in the broader sense' is defined as: 'any tool of human aggression whose acting principle is based on disciplines of biology, including particularly microbiology, epidemiology, medical biology, physiology, psychology, pharmacology and ecology, but excluding those based on inorganic agents. Synthetically produced equivalents (not necessarily exact copies) and mock weapons are also included'. This definition is rather broad and more suitable for an academic discourse about dual-use technologies in the life sciences and other scientific disciplines. Obviously, there will be a continuing need to update the understanding of what biological weapons are and which fields of scientific and technical expertise might contribute to their development.

Establish an EU non-proliferation support unit

Together with national legislation on export controls, EU directives and regulations constitute key elements of EU non-proliferation activities. Digital resources such as DUeS are valuable tools for information sharing. However, there is a need to provide better assistance and guidance across all EU member states. In this respect, it would be advisable to establish an EU implementation support unit for non-proliferation activities in biotechnology. One task of this unit would be the aggregation of relevant information on dual uses, the practical experiences of export control of EU member states and on all excluded end-users. Not all of this information should be made publicly available. The support unit could help to identify best practices for regulating dual-use items in the life sciences, thereby contributing to the harmonization of non-proliferation measures within the EU. Equipped with appropriate technical and personnel resources, this support unit could advise the national authorities in charge of export matters as well as European research institutions working in a multinational environment. The EU Control List on dual-use goods and technology could act as a basis for collecting information on sensitive items. One major task of the EU non-proliferation support unit could be to 'translate' the technical export control terms and descriptions in the control lists of the EU into language that can be more easily understood by exporters and end-users in academia and industry. For example, in this context, the Missile Technology Control Regime (MTCR) provides a publicly available handbook that explains the technical details of the control lists in the MTCR annex.[74] Its key elements are a thorough description of technical terms and detailed photographs and illustrations of the items covered in the annex. A future EU support unit could build on this experience and use the structure of the AG control list to further expand on the relevant biological threat agents, dual-use technologies and critical state-of-the-art laboratory equipment. Furthermore, it would be of great interest to exporters for examples of intangible dual-use items to be included. This could also include examples of planned experimental procedures that have been categorized as DURC by oversight bodies. Finally, algorithms for risk assessment in export control would be of great help to the exporter. Together, these elements would promote a common understanding across the EU of the dual-use items and technologies in the life sciences that are subject to export control.

Increase awareness of export control measures in academia and industry

The recast of the EU Dual-use Regulation should be accompanied by an increase in the resources available for awareness raising and outreach activities within the EU. This could be achieved through harmonized education and training courses for the various stakeholder groups involved in dual-use activities in the life sciences, governmental research institutions, industry and the DIY/open science community.[75]

[72] Commission Delegated Regulation (EU) 2018/1922 of 10 Oct. 2018, *Official Journal of the European Union*, L319, 14 Dec. 2018.

[73] Rozsa, L., 'A proposal for the classification of biological weapons sensu lato', *Theory in Biosciences*, vol. 133, no. 3/4 (2014), pp. 129–34.

[74] Missile Technology Control Regime, *Missile Technology Control Regime: Annex Handbook, 2017.*

[75] Various industries would be relevant: the biotechnology industry, including suppliers of biomedical products and clinical diagnostics,

Box 1. Proposed extended definition of the term 'biological agents': Comparison between the EU Dual-use Regulation and the German Biological Agents Ordinance

European Commission Delegated Regulation (EU) 2017/2268 amending Council Regulation (EC) No 428/2009

'Biological agents' are pathogens or toxins, selected or modified (such as altering purity, shelf life, virulence, dissemination characteristics, or resistance to UV radiation) to produce casualties in humans or animals, degrade equipment or damage crops or the environment.

German Biological Agents Ordinance (2013, 2017)

Part 1, Section 2: Definitions

(1) Biological agents shall mean

1. micro-organisms, [toxins], cell cultures and endoparasites including their genetically modified forms,

2. agents [such as prion proteins] associated with transmissible spongiform encephalopathy (TSE),

that may constitute a hazard to humans [animals, plants or the environment] as a result of infections, communicable diseases, toxin formation, sensitization or other effects which are harmful to human [animals or plants] health [or degrade equipment].

(2) The following agents shall be considered as equivalent to biological agents:

1. ectoparasites which may cause autonomous diseases in humans [animals or plants] or create sensitizing or toxic effects,

2. technologically produced biological entities with new properties that may pose a threat to humans [animals, plants or the environment] in the same way as biological agents'.

Note: Text in square brackets represents technical terms which were derived from the Council Regulation (EC) No 428/2009 and which should be added here.

Sources: European Commission, Commission Delegated Regulation (EU) 2017/2268 of 26 Sep. 2017, Official Journal of the European Union, L334, 15 Dec. 2017; and Ordinance on Safety and Health Protection at Workplaces Involving Biological Agents (Biological Agents Ordinance, BioStoffV) of 15 July 2013, Federal Law Gazette, Part I, p. 2514), as amended by Article 146 of the Law of 29 Mar. 2017 (Federal Law Gazette I, p. 626).

Outreach to academia and the biotechnology industry, including small and medium-sized enterprises, is essential in order to raise awareness of the key concepts of export control. For example, the German Federal Office for Export Control recently published a handbook on implementing export control measures and guidelines in German research institutions.[76] The handbook provides valuable hints, insights and information on the self-assessment of planned exports of what may be dual-use goods or technologies. Furthermore, the handbook gives the academic exporter some indication of how to separate fundamental or basic research from industry-sponsored research and development projects, which are not excluded from export control.

It is the responsibility of each individual researcher to perform an initial self-assessment of any planned transfer activities, ranging from obvious cases of the transfer of biological agents to rather exotic questions around planned exchanges of dual-use information by email or telephone. EU export control training for academics should therefore include specific examples for scientific disciplines such as the life sciences, the social sciences, computer science or psychology in order to shed light on the requirements of export licences. In the absence of such training, it is hard to imagine that the scientific community could cope adequately with the likely future challenges posed by export controls. Scientists will of course fulfil their legal obligations, but in some cases there might simply not be enough publicly available information to perform an adequate risk assessment where the question of a reason to suspect must be addressed. The situation might be slightly different for larger biotechnology companies with specialized personnel on hand to perform export control-related assessments on a regular basis. At some point, however, the national authorities must step into the export control process to provide clear indications of export risks. One possibility might be the use of EU-wide harmonized lists of excluded end-users. This information is in many ways sensitive but without having such information available to them, scientist exporters might have no reason to suspect a misuse.[77]

as well as bioprocessing equipment; companies working on additive manufacturing technologies; data handling service providers, including of cloud computing services for the life sciences; and publishers of scientific literature, among others.

[76] Federal Office for Economic Affairs and Export Control, Handbuch Exportkontrolle und Academia [Handbook on Export Controls and Academia], Feb. 2019.

[77] The Handbook on Export Controls and Academia clearly states that the exporter ('Ausführender', e.g. a researcher) has an obligation

Improved outreach and awareness raising activities would fit well within the EU's NLA-defined goal of fostering the development of a CBRN security culture across the EU. In this respect, it would be advisable to enable collaborations with academic research groups working in cutting edge fields such as synthetic biology, molecular infection biology, neurochemistry or nanobiotechnology. The work of the CBRN Risk Mitigation Centres of Excellence could be used as a model for such cooperation. Activities could include funding of awareness raising courses for European research institutions and biotechnology industries, as well as other relevant studies at universities across the EU. Funding could be provided from the EU research budget. Educational material and research findings should be made publicly available.

Include academia in the e-Licencing process

A model project is planned for the investigation of e-licencing as a new toolkit for EU-wide harmonized export control measures. The main idea is to reduce the bureaucratic burden on both exporters and export control authorities. The e-licencing instrument could prove invaluable for research institutions. In combination with electronic dual-use assessment tools and e-learning modules, this could create a completely new environment close to the vision of the 'CBRN security culture' proposed in the EU's NLA. For academia, one important factor would be a reduction in the bureaucratic burden when it comes to the electronic exchange of scientific and technical information with collaboration partners outside the EU. It is interesting to note that the European Commission has proposed changes to the current definition of when the transmission of software or technology by electronic means or media should be considered an export operation that requires a licence. This proposed revision would apply to transmissions to legal and natural persons outside the EU, which would remove uncertainty and administrative burdens on exporters such as academic institutions when it comes to the transfer of digital data.

The introduction of special e-licencing tools for academia could be complemented by the voluntary establishment of internal compliance programmes (ICP) in research institutions. Local export control advisers working on the ICPs of individual research institutions could support researchers in the life sciences to implement the Dual-use Regulation appropriately. In this way, a network of experts in export control of dual-use technology in the life sciences could be created across the EU.

In sum, emerging dual-use technologies in the life sciences pose challenges for existing EU non-proliferation and export control measures. Enhanced cooperation between academia, industry and the EU export control authorities will be required to cope with these challenges. Export control measures must be designed to prevent the proliferation of dual-use technologies but must also back freedom of research wherever possible.

to take note of all the sources of information ('Erkenntnisquellen') available to him or her that are accessible without special effort. In cases where a sensitive use for the goods is identified ('positive Kenntnis'), the exporter must initiate the export control process.

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A EUROPEAN NETWORK

In July 2010 the Council of the European Union decided to support the creation of a network bringing together foreign policy institutions and research centers from across the EU to encourage political and security-related dialogue and the long-term discussion of measures to combat the proliferation of weapons of mass destruction (WMD) and their delivery systems. The Council of the European Union entrusted the technical implementation of this Decision to the EU Non-Proliferation Consortium. In 2018, in line with the recommendations formulated by the European Parliament the names and the mandate of the network and the Consortium have been adjusted to include the word 'disarmament'.

STRUCTURE

The EU Non-Proliferation and Disarmament Consortium is managed jointly by six institutes: La Fondation pour la recherche stratégique (FRS), the Peace Research Institute Frankfurt (HSFK/ PRIF), the International Affairs Institute in Rome (IAI), the International Institute for Strategic Studies (IISS), the Stockholm International Peace Research Institute (SIPRI) and the Vienna Center for Disarmament and Non-Proliferation (VCDNP). The Consortium, originally comprised of four institutes, began its work in January 2011 and forms the core of a wider network of European non-proliferation and disarmament think tanks and research centers which are closely associated with the activities of the Consortium.

MISSION

The main aim of the network of independent non-proliferation and disarmament think tanks is to encourage discussion of measures to combat the proliferation of weapons of mass destruction and their delivery systems within civil society, particularly among experts, researchers and academics in the EU and third countries. The scope of activities shall also cover issues related to conventional weapons, including small arms and light weapons (SALW).

www.nonproliferation.eu

EU Non-Proliferation and Disarmament Consortium

Promoting the European network of independent non-proliferation and disarmament think tanks

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