Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

ZNF – CARL FRIEDRICH VON WEIZSÄCKER-ZENTRUM
FÜR NATURWISSENSCHAFT UND FRIEDENSFORSCHUNG

Strategies for the Risk Analysis of Genome Editing

Mirko Himmel, Eva Oellingrath, Nancy Connell, Piers Millet

BTWC Meeting of Experts MX2
Geneva, 31 July 2019

Outline

- **Dr Mirko Himmel:** Introduction / Strategies for the Risk Assessment of Genome Editing Technologies
- **MSc Eva Oellingrath:** Risk Analysis of Genome Editing: Laboratory Based Studies
- **Prof Nancy D. Connell, PhD:** Studies of Governance and Risk in Human Genome Editing
- **Dr Piers Millet:** Work of the WHO Expert Advisory Committee on Human Genome Editing

Strategies for the Risk Assessment of Genome Editing Technologies

SPONSORED BY THE
Federal Ministry of Education and Research

Genome Editing: Definitions

Genome: All genetic material of an organism or virus (coding DNA („genes“) + non-coding DNA; RNA of RNA viruses)

-> The term “Genom” was introduced in 1920 by H. Winkler, University of Hamburg.

Gene: A defined segment of DNA which contributes to a biological function

Genome editing: Genetic engineering technique which allows the targeted manipulation of a genome

Genome Editing: A New Era?

Genome Editing: BWC context

- **Genetic engineering** is perceived as powerful **enabling technique** for research and development of biological weapons

- **Historical evidence** highlights relevance of the misuse potential of genetic engineering for the BWC (eg., activities in former state-driven BW programmes)

- **Genome editing** may proven even more powerful due to certain biological and technical features of this technology

Genome Editing: BWC context

BWC MX2 2018 report:

"It was noted that genome editing, particularly techniques such as CRISPR, is opening new avenues in many scientific fields. [...]

The security implications of genome editing are uncertain and difficult to predict [...]

Gene editing could make the acquisition, development, and production of biological weapons easier; it could also help to counter such risks"

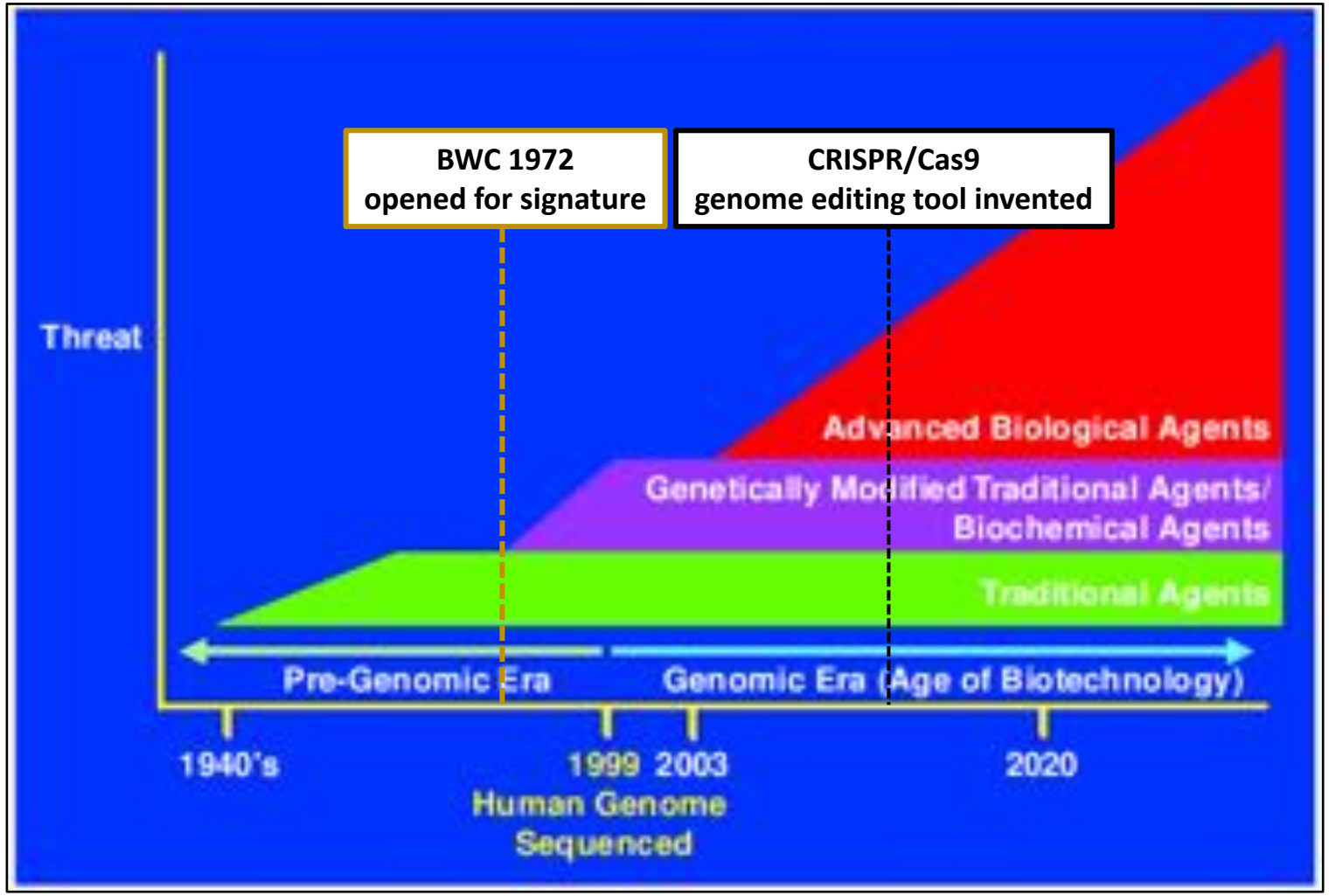
(BWC/MSP/2018/MX.2/3; p. 9)

Genome Editing: The Dual Use Dilemma

- In many cases biological agents, methods, scientific and technical knowledge can be used for the good or for creating great harm!
- Misuse of science for hostile purposes:
  - **Biological Warfare**
  - **Bioterrorism**
  - **Biocrime**
- Genome editing would be useable in all three scenarios; most likely in state-sponsored BW programmes (and in violation of the BWC!)

Genome Editing: A security threat?

Impact of biotechnology on biological warfare threat



BIOSECURITY AND BIOTERRORISM: BIODEFENSE STRATEGY, PRACTICE, AND SCIENCE. Volume 1, Number 3, 2003. Modified.

Genome Editing: A security threat?

„CRISPR—a weapon of mass destruction?“
Science. 11 Feb 2016.

MIT Technology Review (Feb. 2016):

Genome editing is a weapon of mass destruction.

That’s according to **James Clapper, U.S. director of national intelligence**, who on Tuesday, in the annual worldwide threat assessment report of the U.S. intelligence community, **added gene editing to a list of threats** posed by “weapons of mass destruction and proliferation.”


Bulletin of the Atomic Scientists

SUBSCRIBE | CURRENT ISSUE | ARCHIVES | FEATURES | MULTIMEDIA

Home › Features › Analysis › Can the bioweapons convention survive Crispr?

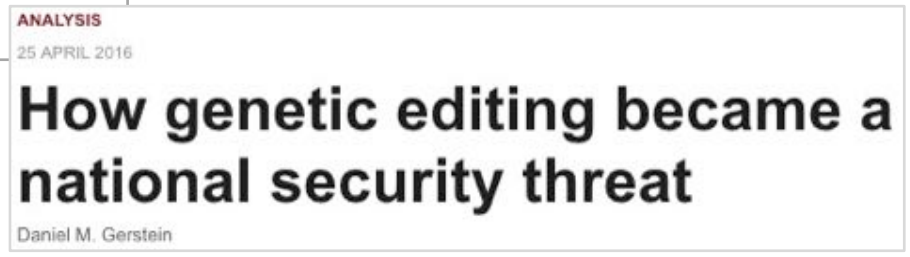
ANALYSIS

25 JULY 2016

Can the bioweapons convention survive Crispr?

Daniel M. Gerstein

When the Eighth Review Conference of the Biological Weapons Convention convenes in November, as it does every five years, to review the operations of the treaty and assess new developments in science and technology that might challenge its relevance, Crispr will be waiting for it. A revolutionary biotechnology that's making

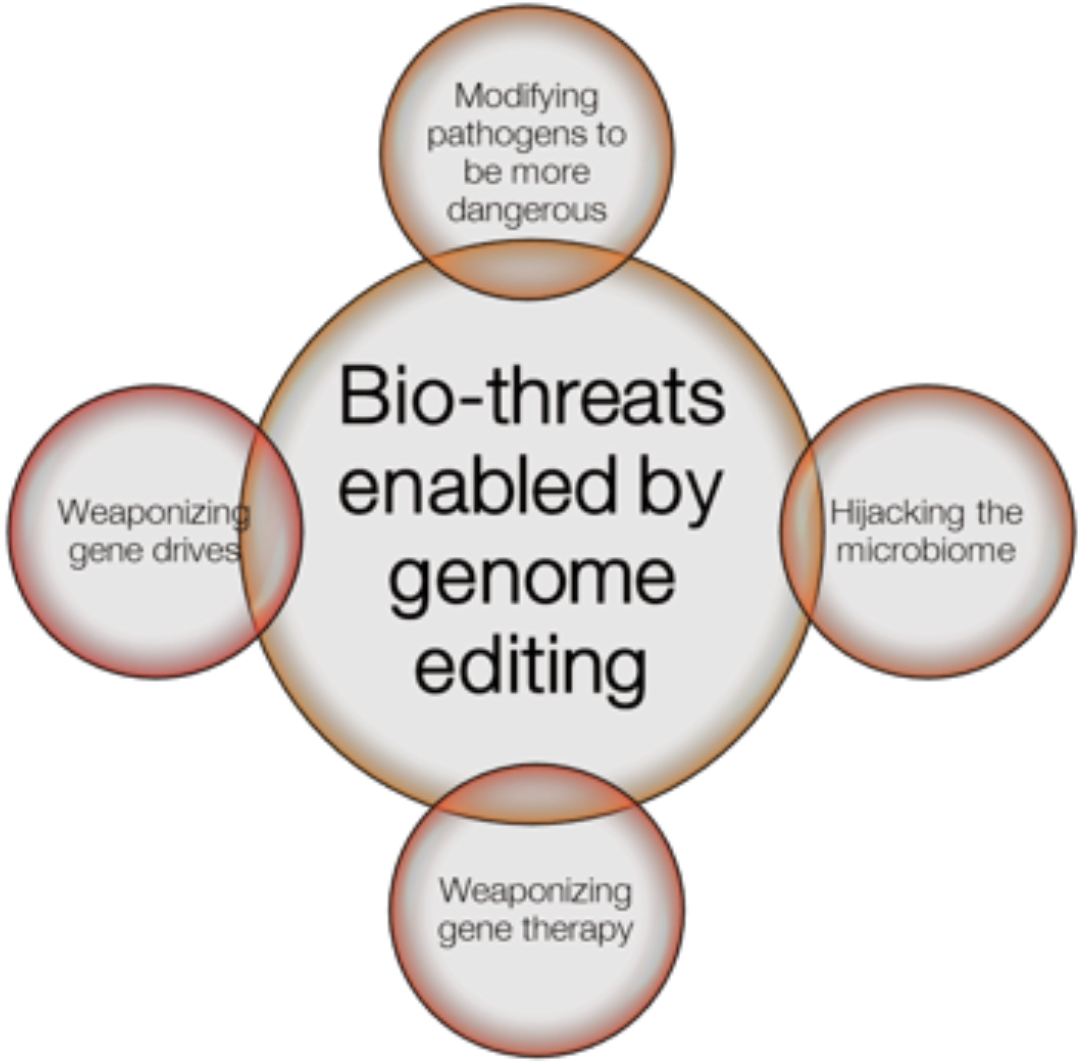

ANALYSIS

25 APRIL 2016

How genetic editing became a national security threat

Daniel M. Gerstein

Genome Editing: A security threat?



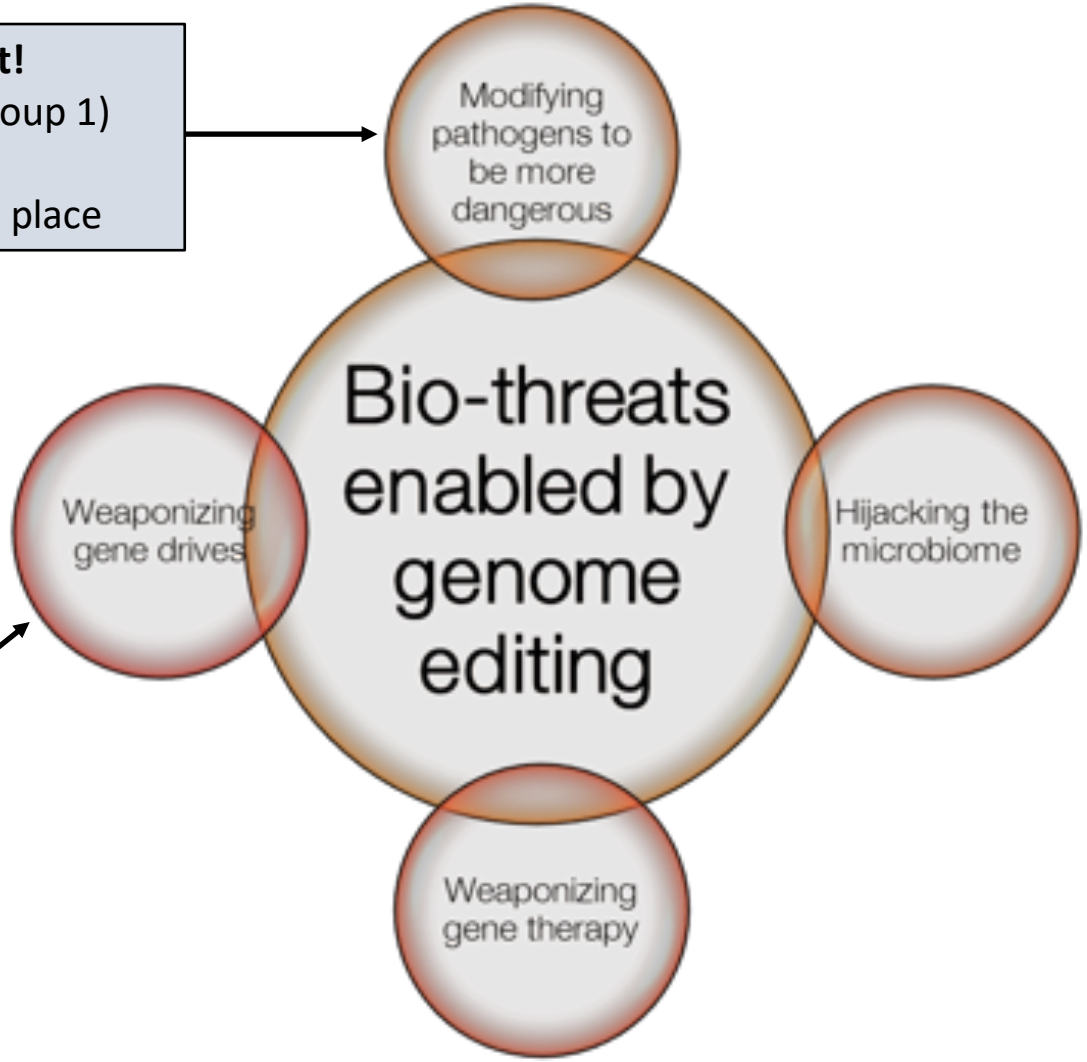
„Genome editing, and CRISPR in particular, poses a new set of challenges to biosafety, biodefense, and biosecurity!“

Kirkpatrick, J., Koblentz, G. D., Palmer, M. J., Perello, E., Relman, D. A., and Denton, S. W. (2018). **Editing Biosecurity: Needs and Strategies for Governing Genome Editing.** Technical report, George Mason University.

Genome Editing: A security threat?

Our approach: lab-based risk assessment!

- Non-virulent model organisms (risk group 1)
- Loss-of-function experiments
- Biosafety and biosecurity measures in place



„Genome editing, and CRISPR in particular, poses a new set of challenges to biosafety, biodefense, and biosecurity!“

More information on **Gene Drives**:
MX2 side event on Friday organised by Dr Guy Reeves, Max Planck Society, Germany

Kirkpatrick, J., Koblentz, G. D., Palmer, M. J., Perello, E., Relman, D. A., and Denton, S. W. (2018). **Editing Biosecurity: Needs and Strategies for Governing Genome Editing.** Technical report, George Mason University.

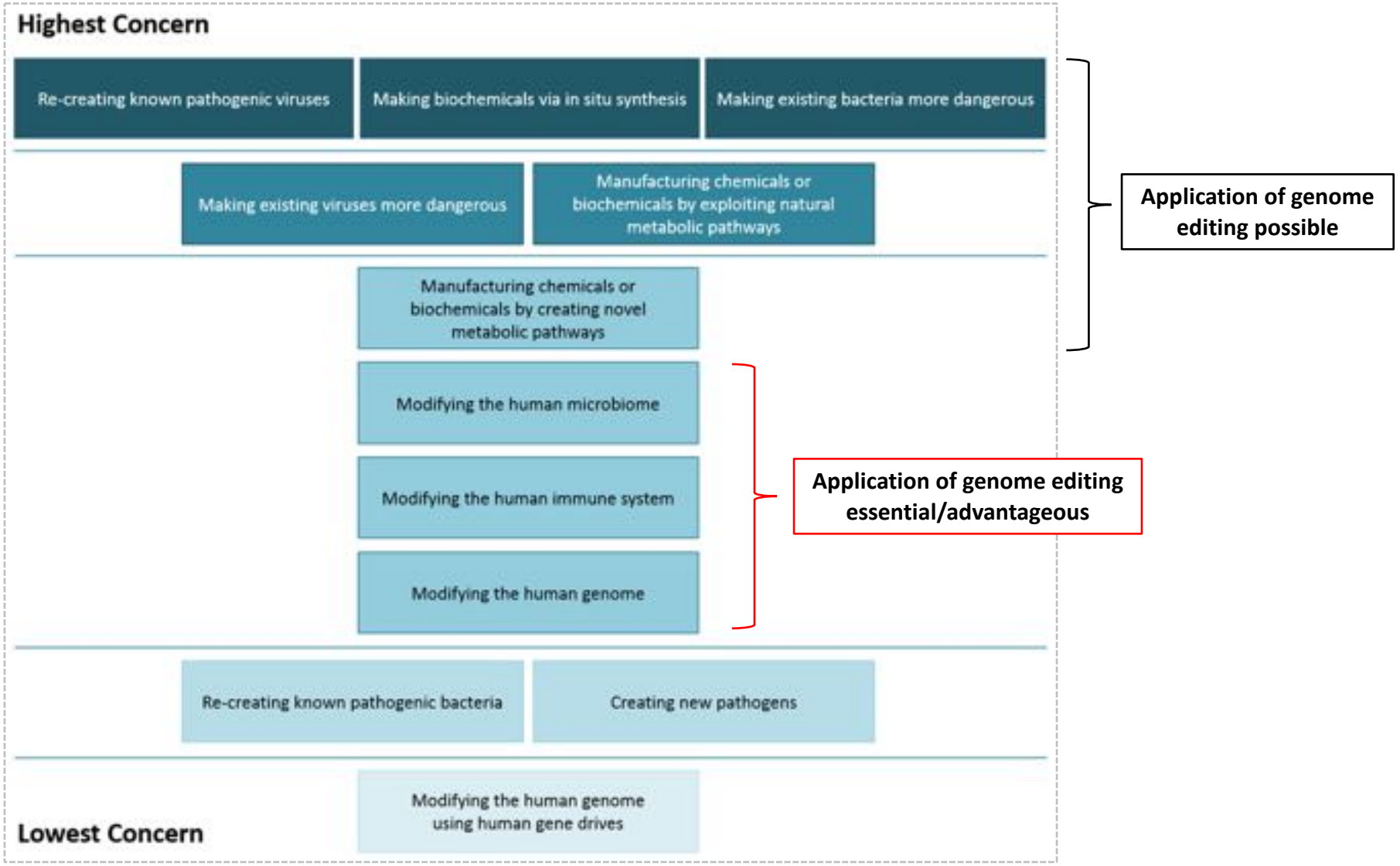
Synthetic Biology: Ranking of Concerns

Reminder:
Misuse for hostile purposes = violation of the BWC!

National Academy of Sciences (2018). **Biodefense in the Age of Synthetic Biology.** National Academic Press, Washington, USA.

Synthetic Biology: Ranking of Concerns

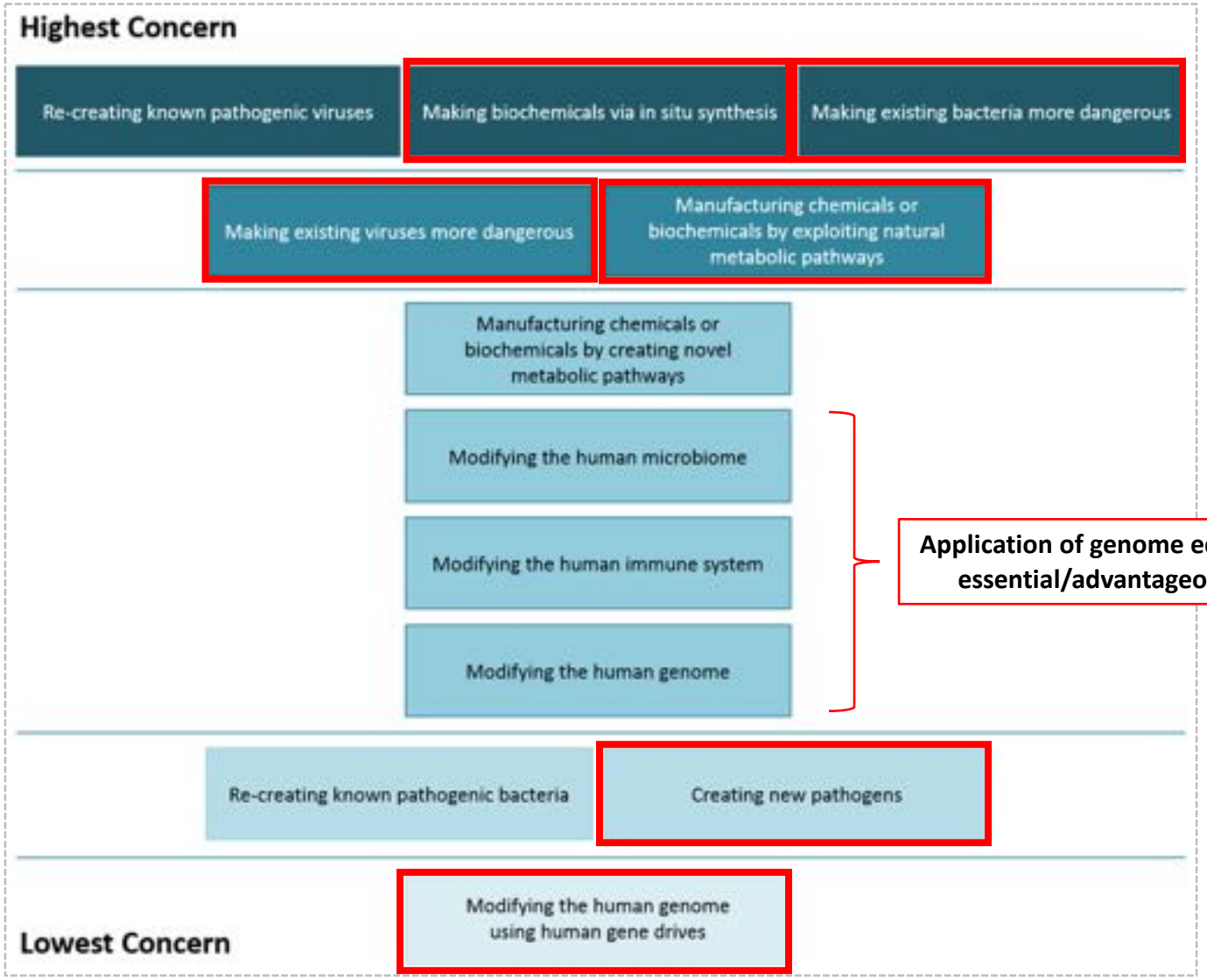
Reminder:
Misuse for hostile purposes = violation of the BWC!



National Academy of Sciences (2018). **Biodefense in the Age of Synthetic Biology.** National Academic Press, Washington, USA.

Synthetic Biology: Ranking of Concerns

Reminder:
Misuse for hostile purposes = violation of the BWC!



Application of genome editing possible

Application of genome editing essential/advantageous

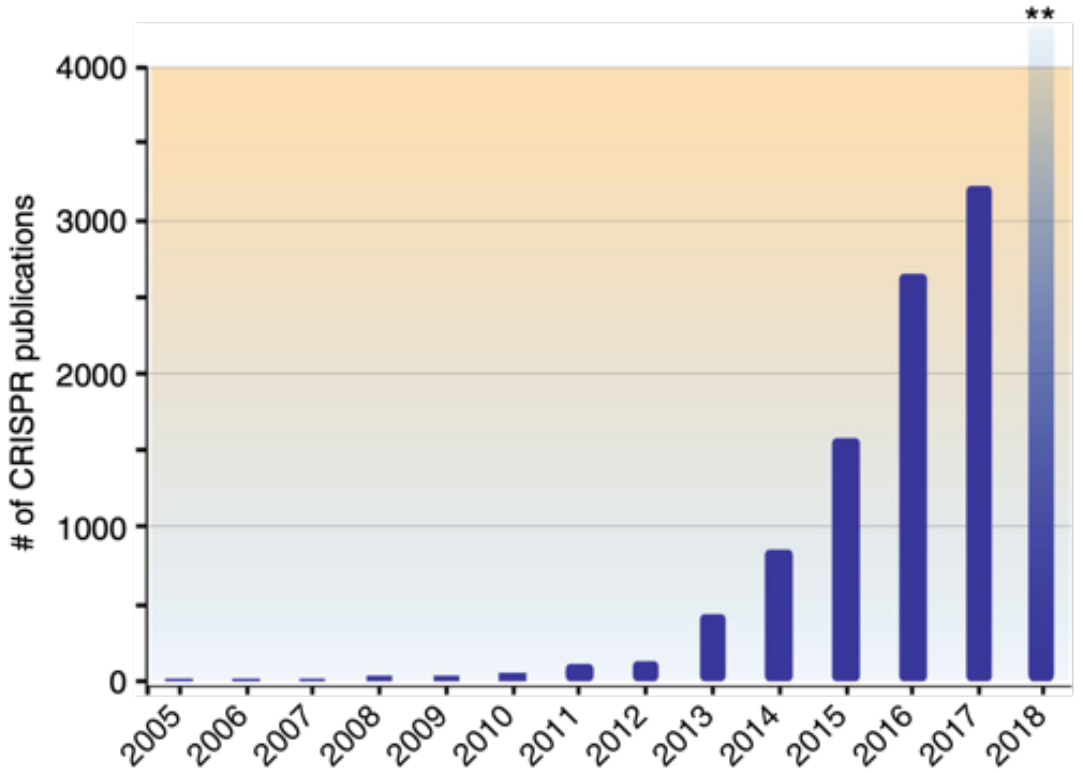
My own assessment: Application of genome editing could prove superior in mid-term future

National Academy of Sciences (2018). **Biodefense in the Age of Synthetic Biology.** National Academic Press, Washington, USA.

Genome Editing: How to access risk potentials?

- **Genome editing** is an **emerging technology** which full range of applications and risks for human/environmental safety and security is still not known

Growing number of published studies using CRISPR/Cas9



** >5,000 paper

Adli, M. (2018). The CRISPR tool kit for genome editing and beyond. Nat Commun, 9(1):1911.

Genome Editing: How to access risk potentials?

- Development of genome editing tools might also provide powerful countermeasures against biological threats

- Risk assessment of biotechnologies is dynamic process due to rapid development of science and technology and requires scientific input

- No standard analytical risk assessment approaches available covering all fields of applications > global harmonisation possible?

Genome Editing: How to access risk potentials?

The Decision Framework, suggested by J. Tucker (2012)

I. Risk assessment of misuse potential of (bio-) technologies:

(1) Accessibility ?
(2) Ease of misuse ?
(3) Magnitude of potential harm resulting from misuse ?
(4) Imminence of potential misuse ?

Three different levels: high, medium, low

Assumption: There is always an actor with malicious intent…!

Genome Editing: How to access risk potentials?

I. Risk assessment of misuse potential of (bio-) technologies:

(1) Accessibility ?

(2) Ease of misuse ?

(3) Magnitude of potential harm resulting from misuse ?

(4) Imminence of potential misuse ?

- **Theoretical methods:** expert interviews, literature survey,...

II. Determination of likelihood of misuse and feasibility of regulation

III. Selection of governance measures on cost-benefit-basis

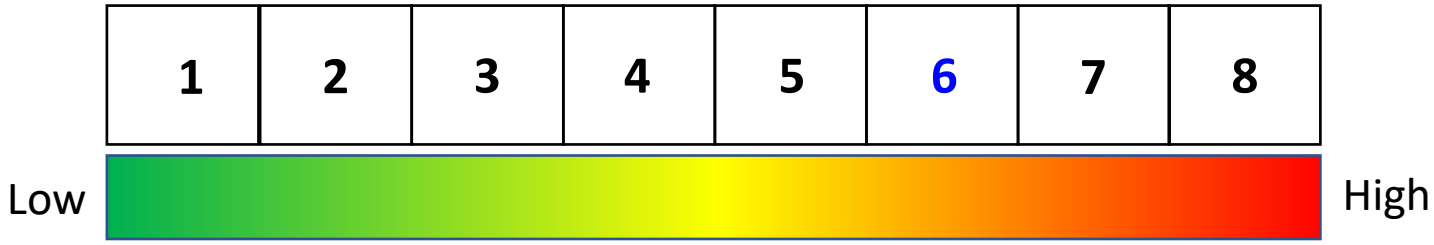
Genome Editing: How to access risk potentials?

I. Risk assessment of misuse potential of genome editing:

Misuse potential (points): High (2), Medium (2), Low (0)

(1) Accessibility	**High (2)**
(2) Ease of misuse	**High (2)**
(3) Magnitude of potential harm resulting from misuse	**High (2)**
(4) Imminence of potential misuse	**Low (0)**
	Sum: „High misuse potential“ (6 points)

Risk level for the misuse of a technology



Genome Editing: How to access risk potentials?

I. Risk assessment of misuse potential of (bio-) technologies:

(1) Accessibility ?

(2) Ease of misuse ?

(3) Magnitude of potential harm resulting from misuse ?

(4) Imminence of potential misuse ?

➢ **Theoretical methods:** expert interviews, literature survey,…

➢ **How to prove these assessments?** Experiments with dangerous microorganisms? -> Dual use dilemma! Safety & security concerns!

Genome Editing: How to access risk potentials?

Practical methods for genome editing risk assessment:

- Generate “real numbers” (e.g., genome editing efficiency in certain applications) and identify possible risk mitigation measures
- Detection of indicators for genome editing of pathogens > identification and attribution of BW attacks?!
- Methods: genome analysis (transcriptomics, whole genome sequencing), proteomics, metabolomics; genetic fingerprinting

Conclusions

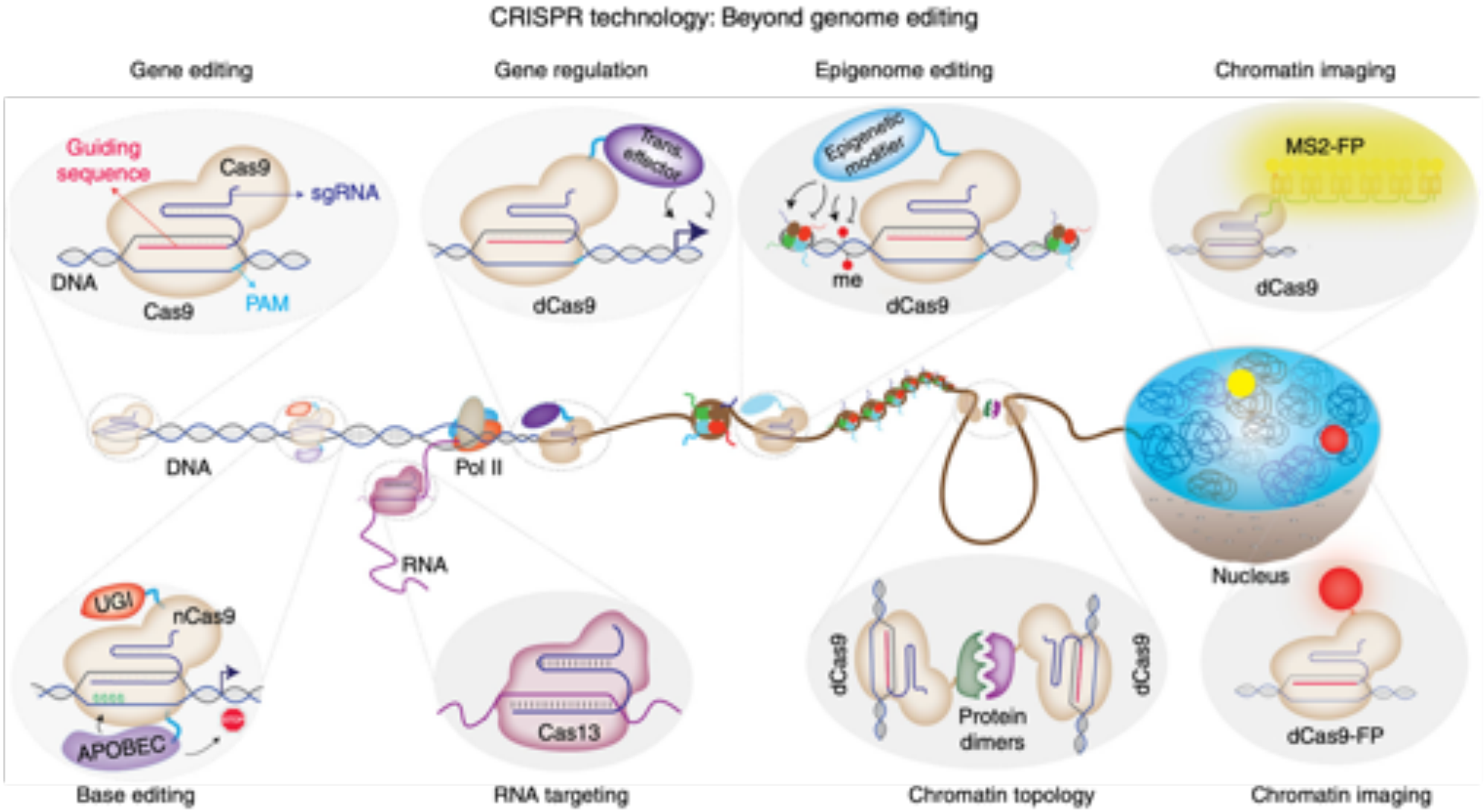
- Practical risk assessment will support informed debate about appropriate risk mitigation activities and governance of genome editing technologies

- BWC regime will benefit from research findings made public by individual labs and governmental bodies of Member States

- Lack of a structured review of developments in science & technology and results from various risk assessment studies

➢ BWC urgently needs a Science Advisory Board!

Development of CRISPR/Cas Tools



Adli, M. (2018). The CRISPR tool kit for genome editing and beyond. Nat Commun, 9(1):1911.


THANK YOU!
QUESTIONS?