

Berlin | October 7, 2022

# DNA Synthesis Screening & the International Common Mechanism

G7 Global Partnership Conference on  
Current Biosecurity Challenges



NTI:bio

# Overview

- I. Technology advances & emerging biorisks
- II. DNA synthesis & screening
- III. The Common Mechanism
- IV. Benchtop synthesis
- V. An international home for the Common Mechanism
- VI. Discussion



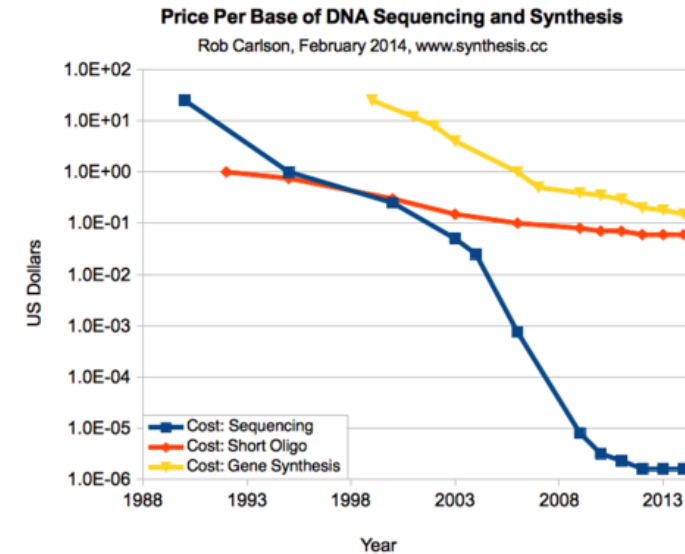
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# | **Technology Advances & Emerging Biorisks**

# Technology Advances & Emerging Biorisks

## Technology advances offer tremendous opportunities ...

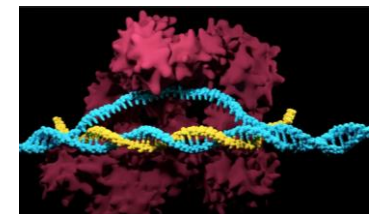
- Easier to read, write, edit DNA & RNA - Blueprint for all living organisms
- AI & robotics enable automation & experimentation at scale
- Cloud labs
- Emerging protein engineering capabilities



TWIST  
BIOSCIENCE

华大基因  
BGI

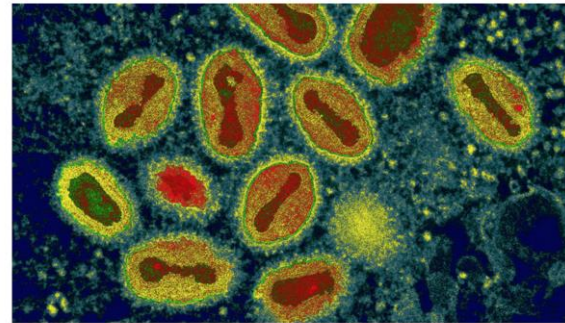
IDT  
INTEGRATED DNA TECHNOLOGIES



# Technology Advances & Emerging Bio-Risks

## ... but these advances also create potential risks

- Easier to generate pathogens from scratch or modify existing pathogens to make them more dangerous.
- Some researchers are using new tools to synthesize and modify pathogens.



An unpublished study suggests that making variola, the virus that causes smallpox, is neither expensive nor difficult. EYE OF SCIENCE/SCIENCE SOURCE

How Canadian researchers reconstituted an extinct poxvirus for \$100,000 using mail-order DNA

**nature**  
International journal of science

Letter | OPEN | Published: 02 May 2012

Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets

Masaki Imai, Tokiko Watanabe, Masato Hatta, Subash C. Das, Makoto Ozawa, Kyoko Shinya, Gongxun Zhong, Anthony Hanson, Hiroaki Katsura, Shinji Watanabe, Chengjun Li, Eiryo Kawakami, Shinya Yamada, Maki Kiso, Yasuo Suzuki, Eileen A. Maher, Gabriele Neumann & Yoshihiro Kawaoka ✉

**nature**

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nature > articles > article

Article | Published: 04 May 2020

## Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform

Tran Thi Nhu Thao, Fabien Labrousseau, [...] Volker Thiel ✉

Nature 582, 561–565(2020) | Cite this article

93k Accesses | 13 Citations | 1086 Altmetric | Metrics

### REPORT

## Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets

Sander Herfst<sup>1</sup>, Eefje J. A. Schrauwen<sup>1</sup>, Martin Linster<sup>1</sup>, Salin Chutinimitkul<sup>1</sup>, Em...  
+ See all authors and affiliations

Science 22 Jun 2012:  
Vol. 336, Issue 6088, pp. 1534-1541  
DOI: 10.1126/science.1213362





# Deliberate & Accidental Release Risks

## Democratized access enables a wider range of actors to engineer pathogens

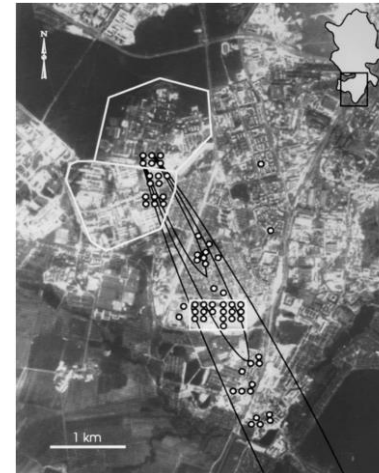
- Increased risk of non-state actor attack
- Increased risk of accidental release of engineered pathogen
- Might shape state bioweapons risks



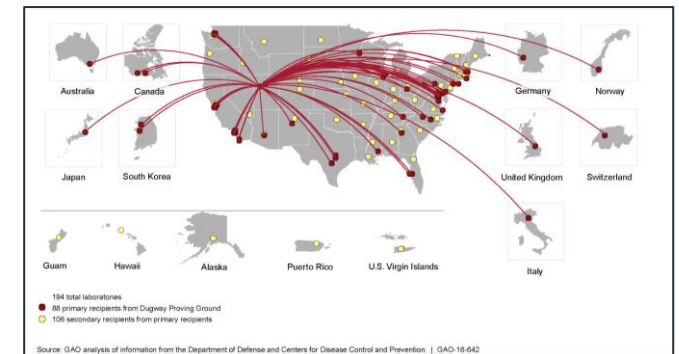
Aum Shinrikyo



2001 Anthrax Attacks



Sverdlovsk Accidental Anthrax Release



Shipment of insufficiently inactivated anthrax spores to 194 labs.



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## II **DNA Synthesis & Screening**

# DNA Synthesis is a Key Enabling Technology

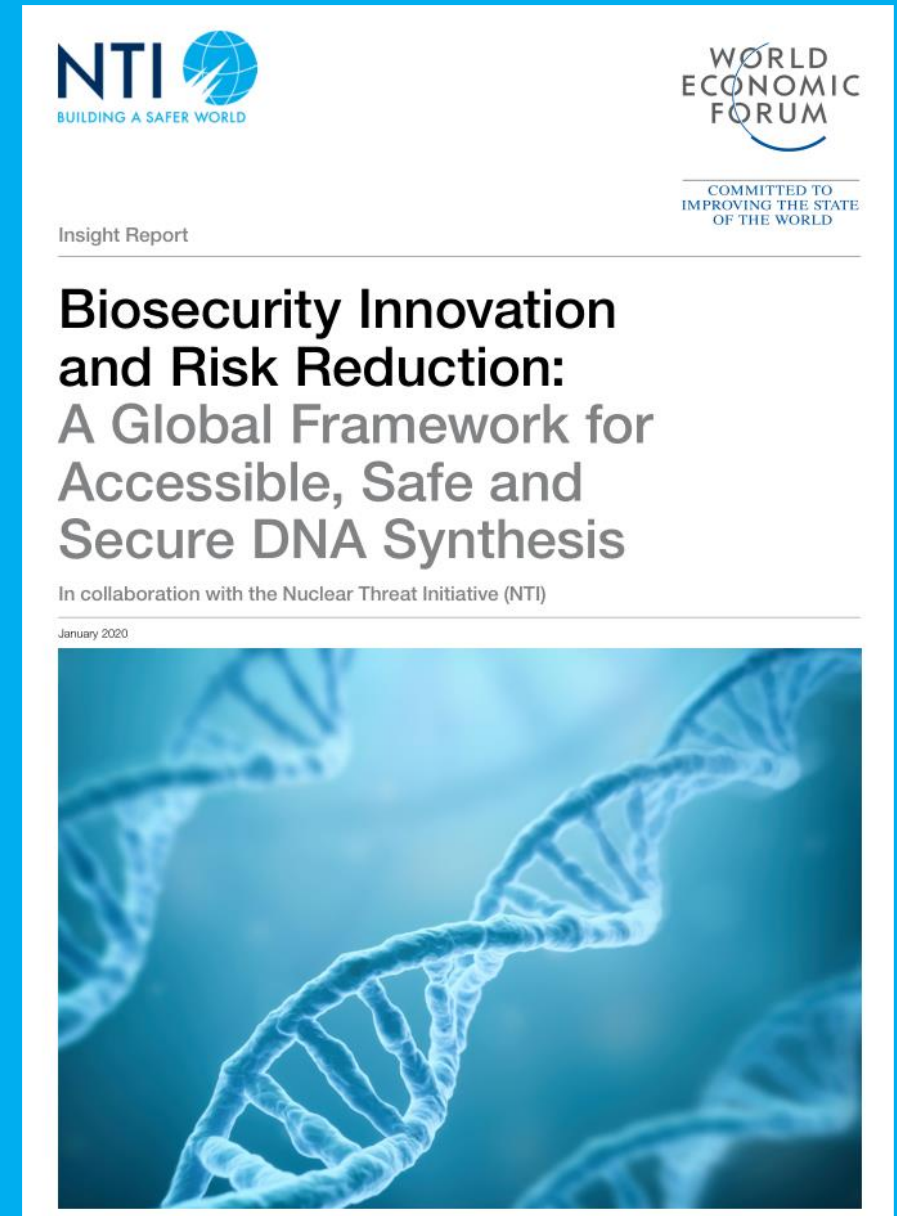
- **DNA synthesis is getting faster, cheaper, and more accessible**
- **DNA synthesis screening is voluntary**
  - An estimated 80% of global market share is screened
  - International Gene Synthesis Consortium of providers that screen orders
  - Not legally required in any country
- **Commercial availability of benchtop synthesis**
  - Likely to expand in next 2-5 years
  - Biosecurity safeguards for devices?





# Our work in this area: The Technical Consortium

- **NTI-WEF Working Group report, Jan 2020**
  - Establish a Technical Consortium to develop a DNA screening tool
  - Establish a normative entity to strengthen global norms and guidelines
- **Launch of Technical Consortium, May 2020**
  - Industry and international representation
  - IGSC collaboration and representation
- **Ongoing Technical Consortium Activities**
  - Development of Common Mechanism
  - Customer Screening Framework
  - Ensuring Integration with Benchtop Devices



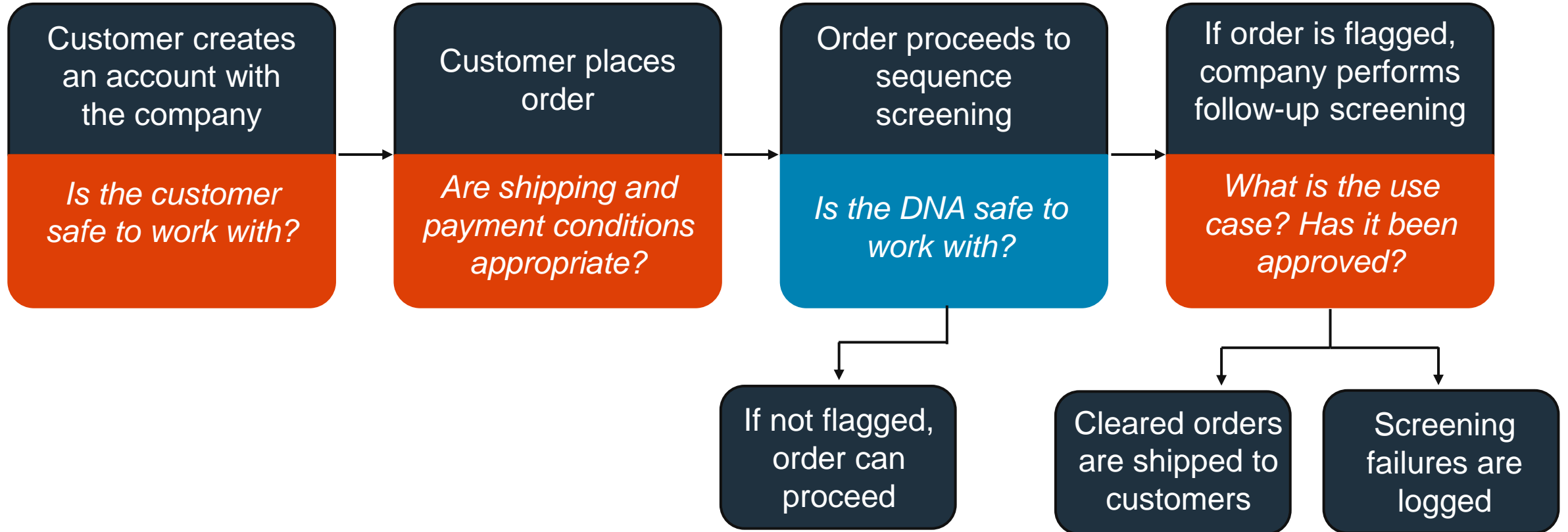
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III

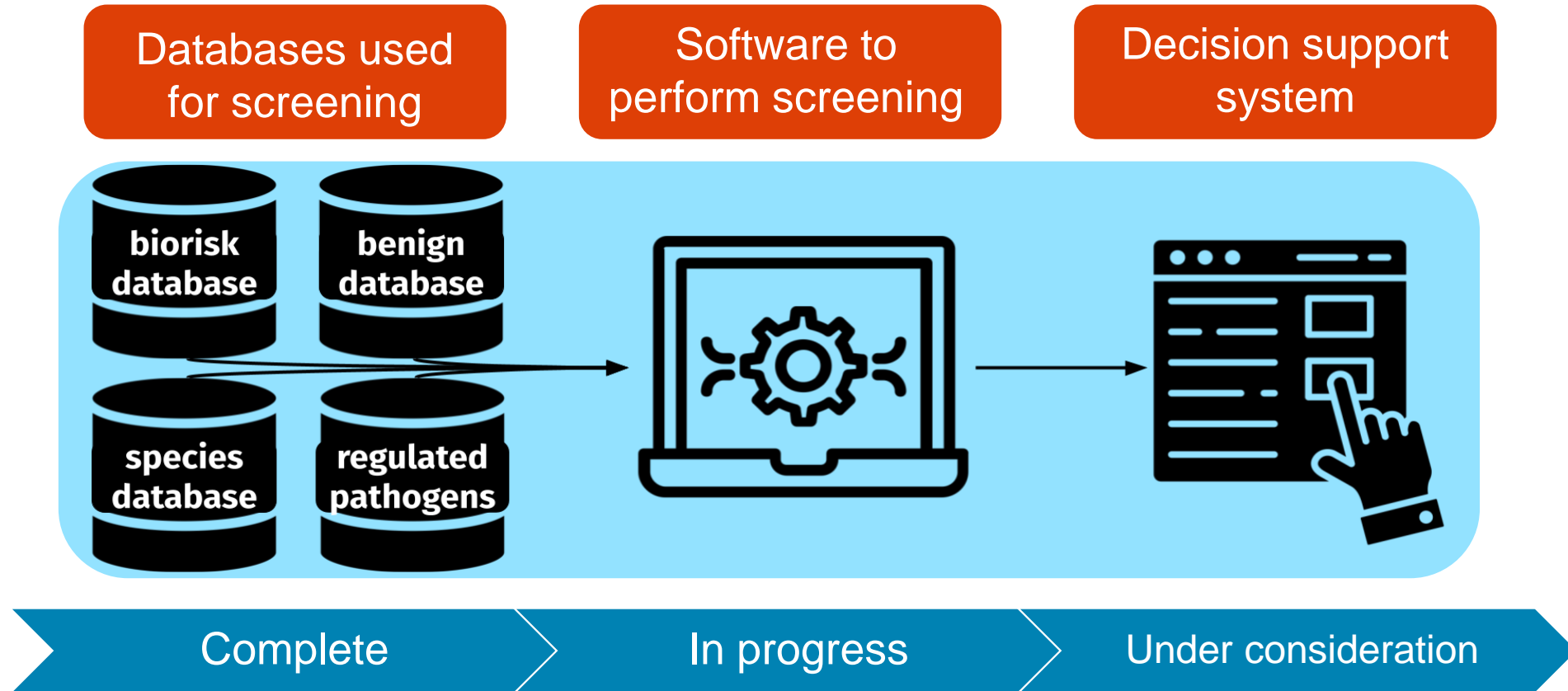
# **The International Common Mechanism for DNA Synthesis Screening**

# The Common Mechanism

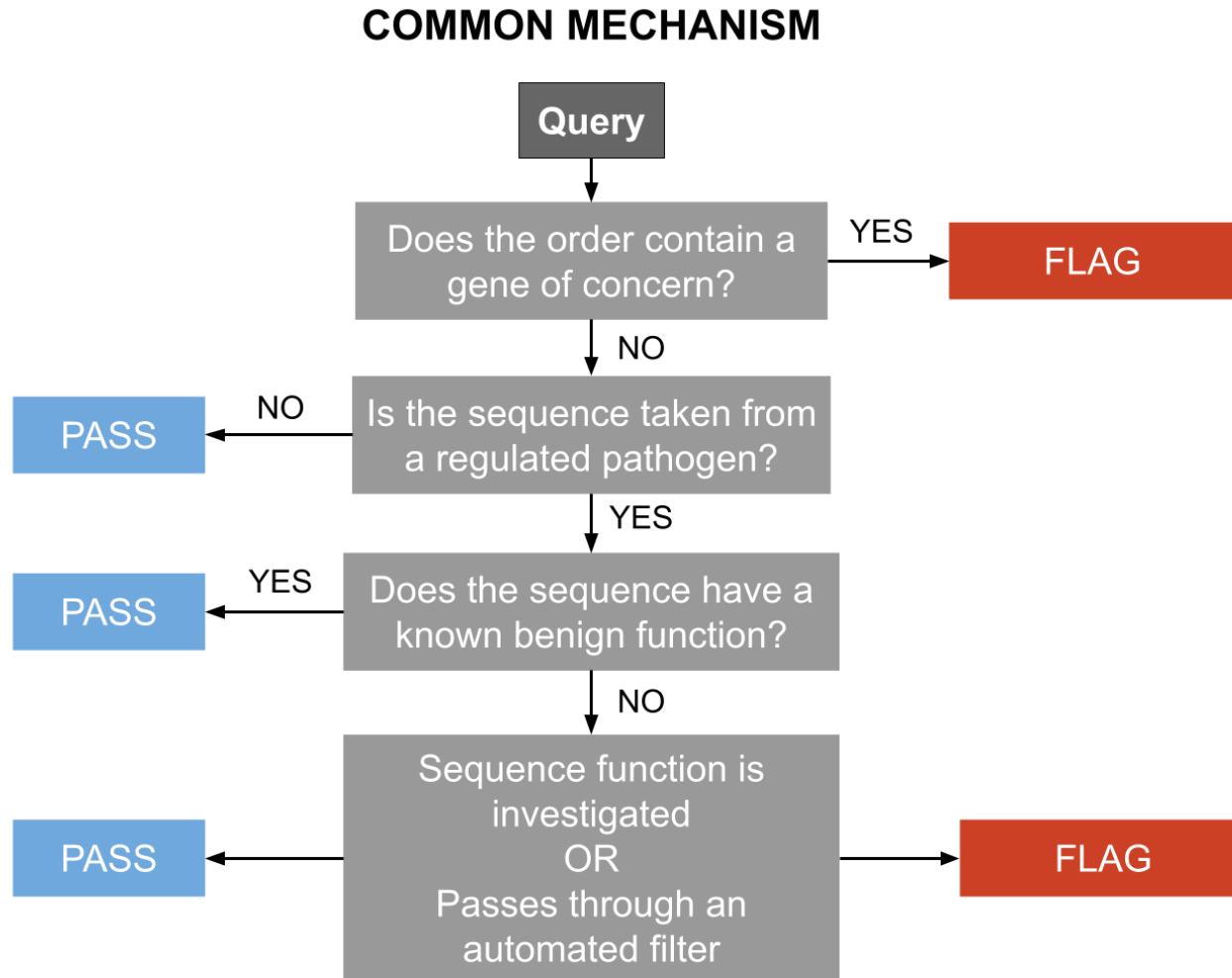
## Overview



# The Common Mechanism



# *Overarching approach*



# Biorisk screen

- **FLAG genes that pose an intrinsic threat**
- Criteria for identifying a “biorisk”
  - Genes that are regulated (e.g. toxins)
  - Genes that contribute to causing disease in regulated pathogens
- Build “sequence profiles” for each biorisk from publicly available sequences
  - Integrating many examples of the same sequence allows us to identify sequences designed to evade screening

*NTI approach:  
compare to a sequence  
profile*



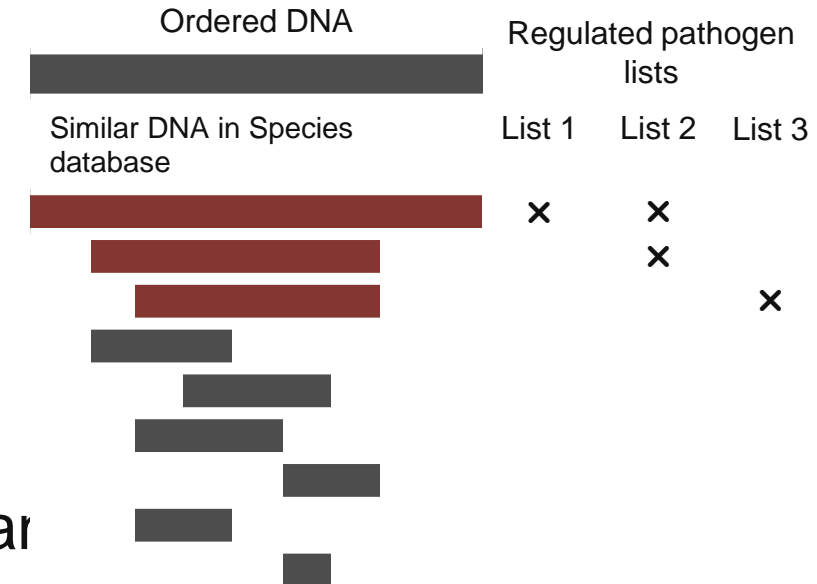
*Current approach:  
compare to individual  
sequences*





# Regulated pathogen screen

- **FLAG DNA/proteins from a regulated pathogen**
- Criteria for identifying sequences from regulated pathogens
  - Compare orders to publicly available DNA and proteins tagged with organism of origin
  - Cross-check organisms against recognized pathogen control lists
- Flag orders more similar to a regulated pathogen than any other organism



# Benign sequence exceptions

- **PASS regulated pathogen sequences if they have a known harmless function**
- Some regulated pathogen DNA can be supplied safely to a range of customers
- We pass pathogen genes if they are common to many living organisms – essential functions for life



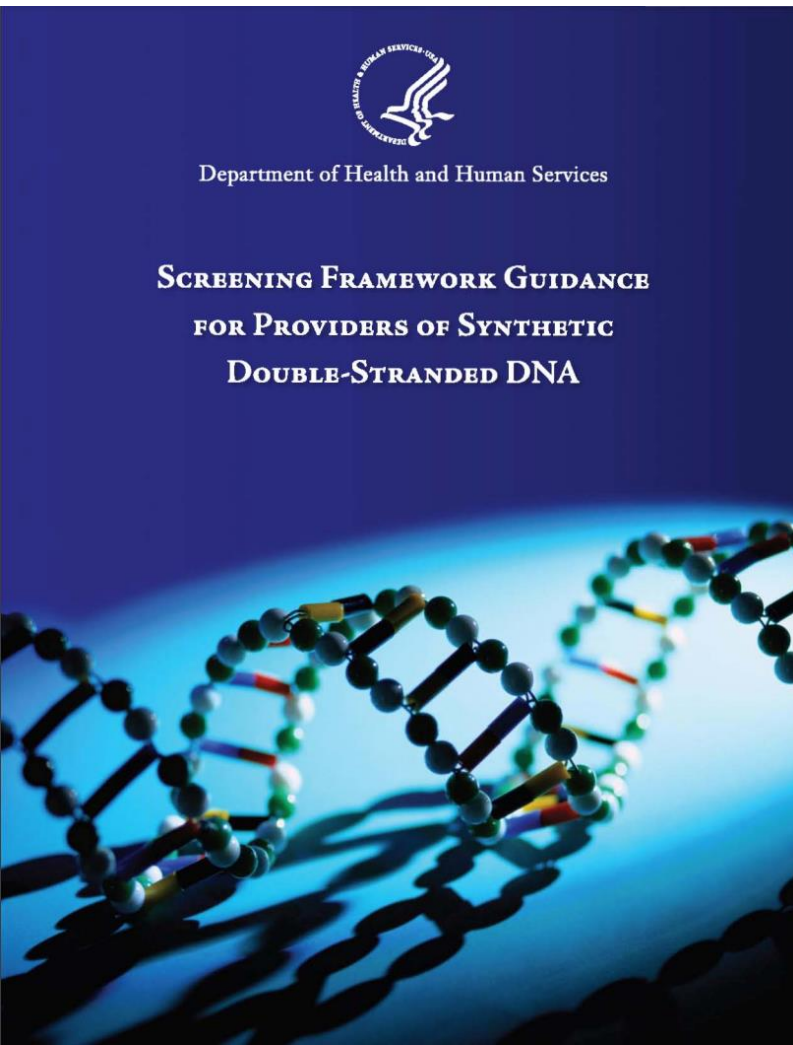
# Key considerations

- Which biorisks should fall under screening guidelines?
- Can screening tools be tested against an agreed-upon performance standard?
- What should companies do for pathogen DNA of unknown or poorly documented function?



# Guidance from Government

- The only guidance on DNA synthesis screening is from the US.
- Will other countries also provide guidance?
- Work toward globally agreed standards?



This image is a screenshot of a webpage. The top navigation bar is orange and contains the NTI logo (a globe with a lightning bolt) and several menu items: 'Nuclear', 'Biological', 'Science &amp; Tech', 'Get Involved', 'Impact', 'About', a search icon, and a 'DONATE' button. Below the navigation bar, the date 'NEWS — Jun 30, 2022' is displayed. The main headline reads 'NTI-WEF Technical Consortium for DNA Synthesis Screening Comments on Revised U.S. Government Guidance'. To the right of the text is a blue-tinted image of multiple DNA double helix structures, some appearing as solid models and others as wireframe or point-cloud representations.

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IV

**Benchtop Devices:  
Safeguarding Distributed DNA  
Synthesis**

# Benchtop Devices

- Enables distributed DNA printing
- Commercial availability likely to expand over next 2-5 years
- NTI conducted interviews with >30 experts
- Three Key Questions:
  - What are current and anticipated benchtop device capabilities?
  - What are the biosecurity implications?
  - What governance approaches can most effectively safeguard this technology?





# Benchtop Devices: NTI Report

## Findings

- Near-future capabilities: Devices will be easier to use and able to automatically synthesize DNA fragments up to 5,000–7,000 base pairs
- Biosecurity implications:
  - May increase the potential for misuse of synthetic DNA, including risks associated with pathogen engineering
  - Significant hurdles to pathogen engineering would remain
- Governance:
  - Many potential oversight mechanisms depend on device manufacturers to conduct customer and sequence screening
  - A range of incentives, including from governments, will be needed



# Benchtop Devices: NTI Report

## Recommendations

- Device manufacturers should:
  - Ensure rigorous customer screening
  - Ensure sequence screening directly by manufacturer, where feasible
- Governments should:
  - Provide guidance, incentives, and resources to support screening
  - Implement regulations requiring biosecurity practices for most devices
- Civil society, funders, and others should:
  - Develop resources, tools, and funding requirements to support screening
  - Explore other types of incentives, such as insurance and liability



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V

**An international home for the  
Common Mechanism**

# A NEW INTERNATIONAL INITIATIVE

**IBBIS**



International Biosecurity and  
Biosafety Initiative for Science

# MISSION & VISION

## MISSION

- IBBIS works collaboratively with global partners to strengthen biosecurity norms and develop innovative tools to uphold them.
- We undertake this work to safeguard science and reduce the risk of catastrophic events that could result from deliberate abuse or accidental misuse of bioscience and biotechnology.

## VISION

- A world in which bioscience and biotechnology can flourish, safely and responsibly

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# VI **Discussion**



# Discussion Questions

- I. What should governments do to safeguard DNA synthesis technology?
- II. Should the international community work toward globally agreed upon standards for DNA synthesis screening?
- III. How can governments, industry and civil society work together to strengthen biosecurity for DNA synthesis and other emerging biotechnologies?



# Thank you!



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