United States Department of
Health & Human Services
Office of the Assistant Secretary for Preparedness and Response (ASPR)

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Screening Framework Guidance for Providers of Double-Stranded DNA

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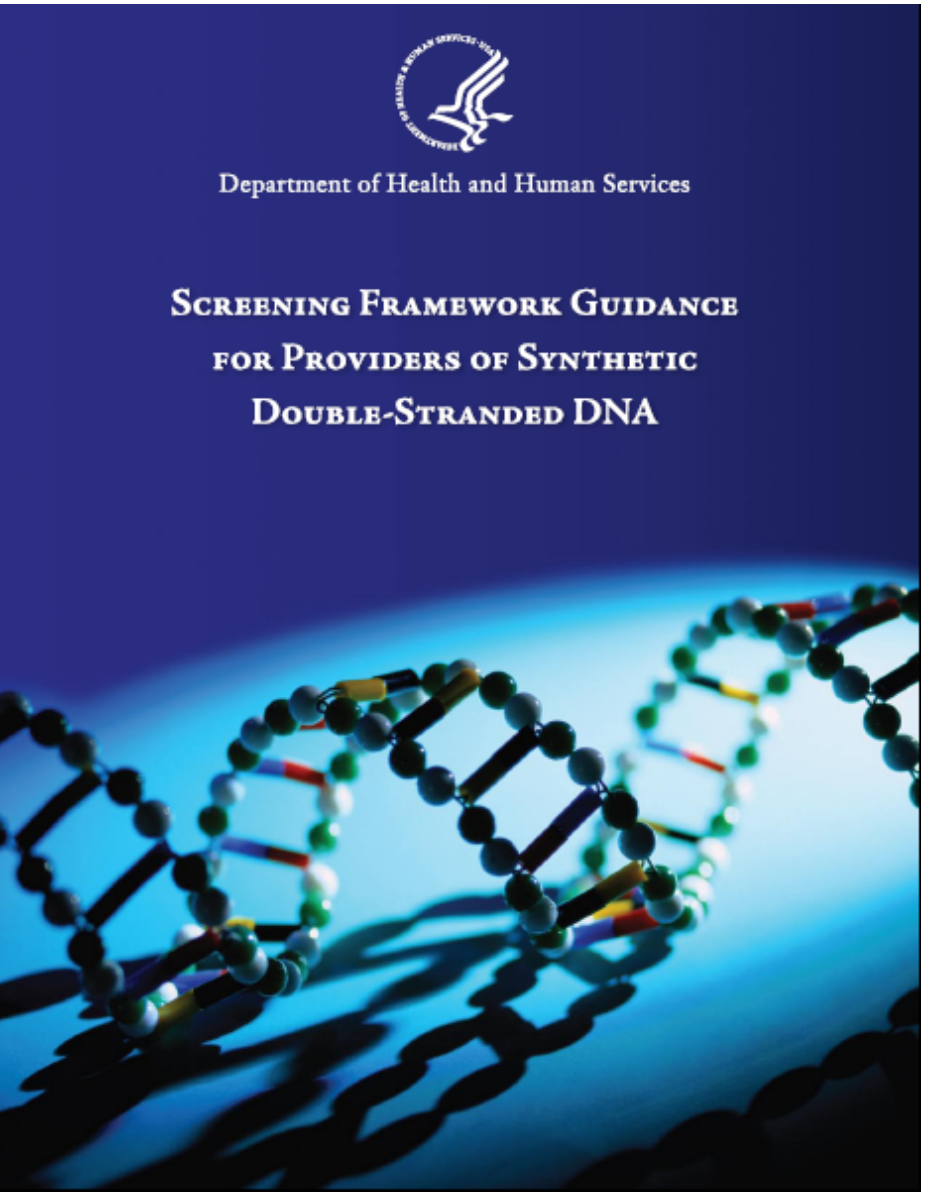
NSABB Public Meeting
October 19, 2010

Balancing Potential Benefits and Risks

- Synthetic biology and the underlying technologies can provide significant scientific, health, and economic benefits.
- Nucleic acid synthesis technology is a potentially enabling technology for the *de novo* reconstruction of dangerous pathogens, either in part or in whole.
  - *De novo* synthesis of naturally-occurring pathogens.
    - Evasion of current regulatory and physical access controls.
  - *De novo* synthesis of novel biological agents.
    - Pathogens with unique properties.
- Development of any oversight mechanism must…
  - balance the need to minimize the risk of misuse with the need to ensure that science and innovation are encouraged; and
  - involve engagement of the synthetic nucleic acid providers, the scientific community, and other stakeholders.

Screening Framework Guidance for Providers of Synthetic dsDNA



- **Primary Goal:**
  - Minimize the risk that unauthorized individuals or individuals with malicious intent will obtain “toxins and agents of concern” through the use of nucleic acid synthesis technologies.
  - Simultaneously minimize any negative impacts on the conduct of research and business operations.

Process Summary

- Draft Guidance was posted for public comment in the Federal Register on November 27, 2009 for a period of 60 days.
- Public comments were reviewed and incorporated.
  - *Response to Public Comments* was drafted.
- Final Guidance and Response were published in Federal Register on October 13, 2010.
- An interagency group has been convened by the White House to consider ways to implement and evaluate the Guidance.
- Stakeholder engagement regarding the Guidance will continue.

Summary of Guidance Recommendations

- The U.S. Government recommends that all orders of synthetic dsDNA be subject to a screening framework that incorporates both *sequence screening* and *customer screening*.
- *Customer Screening*
  - The U.S. Government recommends that, for every order, synthetic dsDNA providers:
    - Verify the customer's identity.
    - Screen customers against several lists of proscribed entities.
    - Check for 'red flags.'
  - In any case where *customer screening* raises a concern, providers should conduct *follow-up screening.*

Summary of Recommendations, Continued

- *Sequence Screening*
  - The U.S. Government recommends that:
    - All dsDNA orders be screened against GenBank using a ‘‘Best Match’’ approach to identify sequences that are unique to Select Agents and Toxins (BSAT).
    - For international orders, dsDNA be screened using a ‘‘Best Match’’ approach to identify sequences that are unique to items on the Commerce Control List and sequences that are unique to BSAT.
    - *Sequence screening* be performed for both DNA strands and the resultant polypeptides derived from translations using the three alternative reading frames on each DNA strand (or six-frame translation).
    - Sequence alignment methods should permit the detection of hidden ‘‘sequences of concern’’ as short as 200 bps in length.
    - In any case where *sequence screening* raises a concern, providers should conduct *follow-up screening*.

Summary of Recommendations, Continued

- *Follow-up Screening*
  - When *customer screening* or *sequence screening* raises any concerns, the U.S. Government recommends that
    - Providers ask for information about the customer and principal user, including the proposed end-use of the order, to help assess the legitimacy of their order.
    - Providers take additional steps to verify the customer's and principal user's identity and need.
- *Domestic and International Orders*
  - The U.S. Government reminds providers to check against various lists of proscribed entities before filling every order; these lists vary for domestic and international customers.
- *Contacting the U.S. Government*
  - In cases where *follow-up screening* cannot resolve concerns raised by either *customer screening* or *sequence screening*, or when providers are otherwise unsure about whether to fill an order, the U.S. Government recommends that providers contact relevant agencies.

Summary of Recommendations, Continued

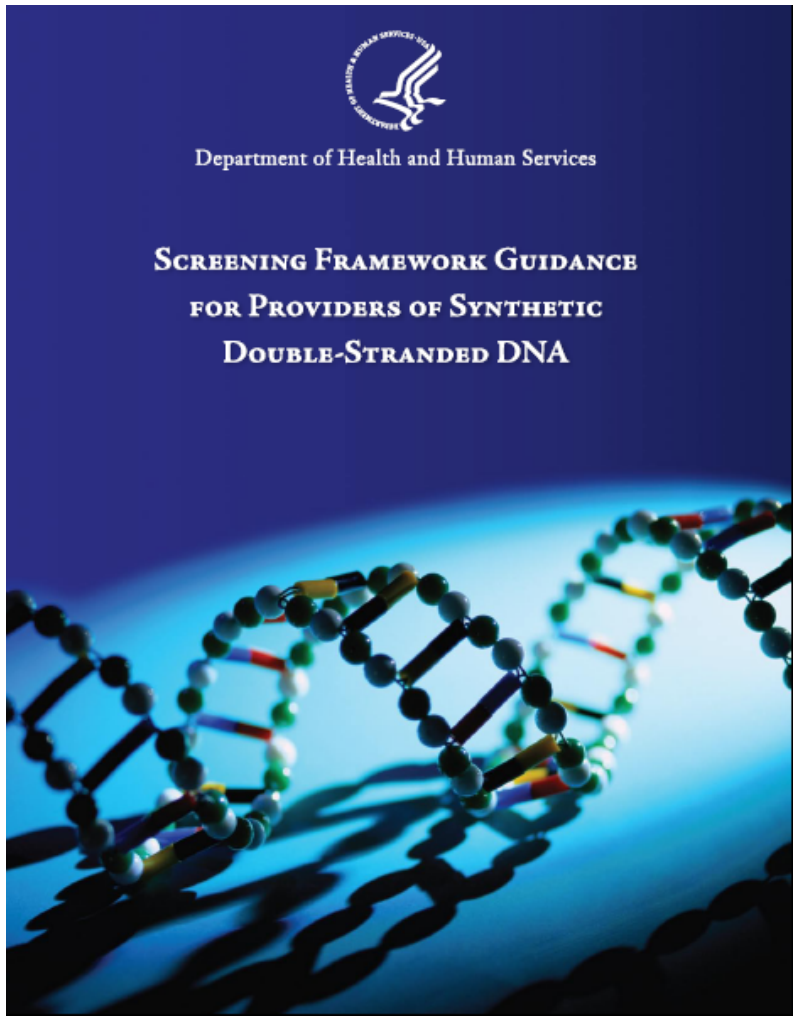
- *Sequence Screening Software and Expertise*
  - The U.S. Government recommends that:
    - Providers select a sequence screening software tool that utilizes a local sequence alignment technique.
    - Providers have the necessary expertise in-house to perform the sequence screenings, analyze the results, and conduct the appropriate follow-up research to evaluate the significance of dubious sequence matches.
- *Records Retention*
  - The U.S. Government recommends that providers retain records of customer orders for at least eight years.

Input from Public Comments

- Voluntary approach
- Length/Type of DNA to screen
- Identity of “sequences of concern”
- Methodology for *sequence screening*
- “End user” vs. customer
- Audience for Guidance
- Order in which screening is conducted

For Further Information

- www.phe.gov/syndna



Thank you.