The views expressed in this presentation do not represent the opinions of the U.S. Department of Health and Human Services, or any U.S. government entity.

Screening Framework Guidance for Providers of Double-Stranded DNA

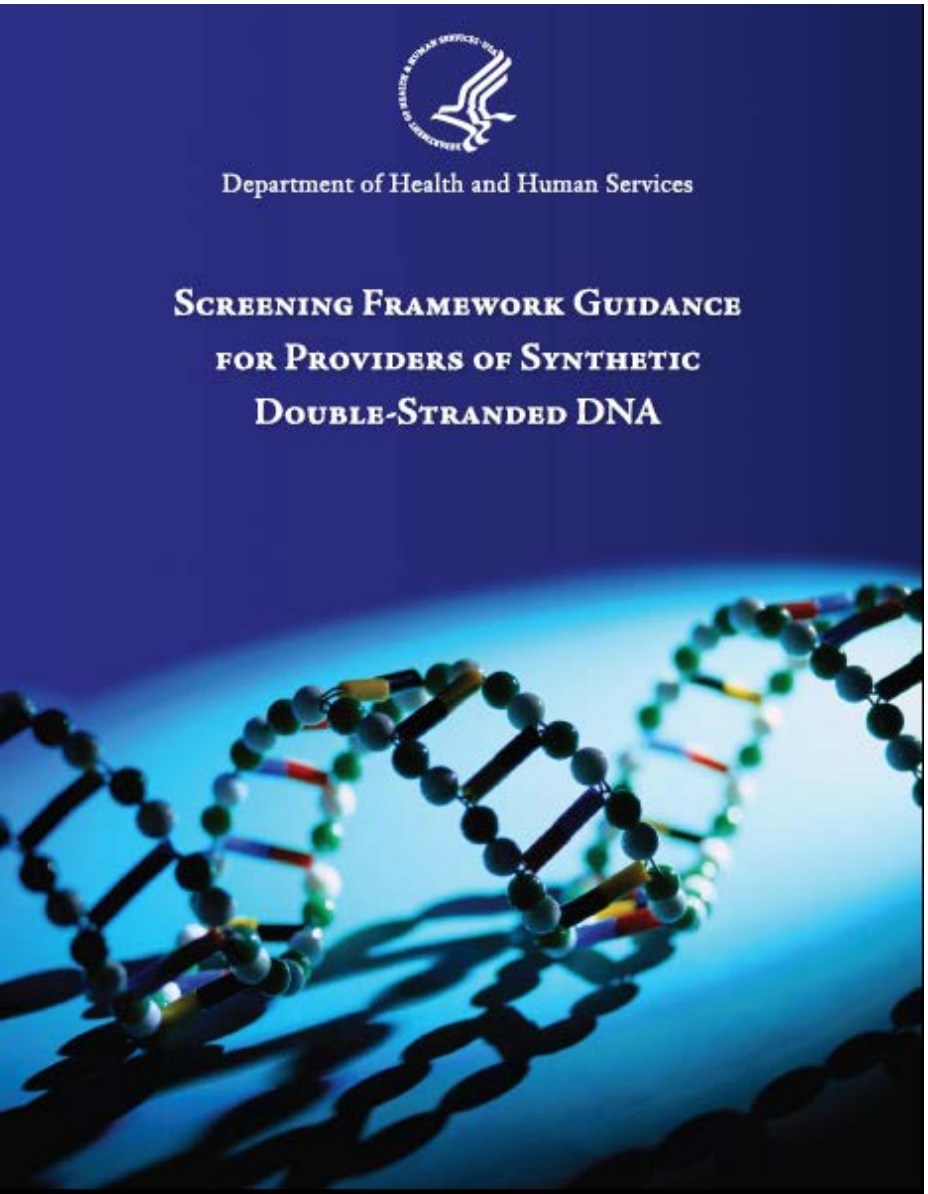
Jessica M. Tucker, Ph.D.
Senior Policy Analyst/Contractor
Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services

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- Draft Guidance was posted for public comment in the Federal Register on November 27, 2009 for a period of 60 days.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

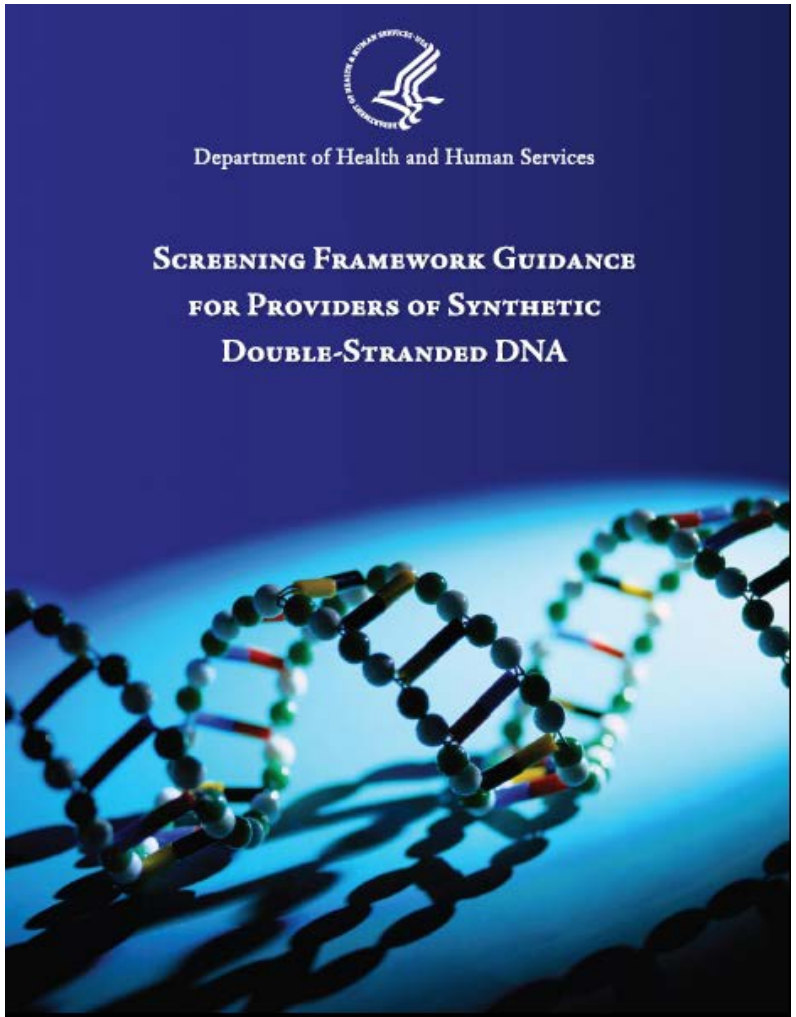
- *Sequence Screening Software and Expertise*
  - The U.S. Government recommends that:
    - Providers select a sequence screening software tool that utilizes a local sequence alignment technique.
    - Providers have the necessary expertise in-house to perform the sequence screenings, analyze the results, 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.