UNIVERSITY OF CALIFORNIA

Research Policy Analysis & Coordination

Guidance Memo

23-02

April 6, 2023

To: Procurement Offices
Biological Safety Officers
Contracts and Grants Directors
Research Compliance Offices

Subject: Guidance on Purchasing Gene Synthesis Equipment or Products

Purpose

This Guidance Memo informs the research community about Assembly Bill (AB) 1963 and provides guidance on purchasing gene synthesis equipment or gene synthesis products from gene synthesis providers.

The Research Policy Analysis and Coordination (RPAC) unit developed this Guidance Memo in coordination with UC Systemwide Procurement, Environment Health & Safety (EHS), Ethics, Compliance and Audit Services (ECAS) and representatives from the California State University (CSU) Office of the Chancellor.

Background

Gene synthesis is the process of designing and synthesizing sequences of nucleic acids, which allows individuals to create a gene from scratch. Synthetic genes are used for research to test genetic hypotheses, create advanced gene-editing systems, identify new drugs, and even develop life-saving vaccines. While gene synthesis is vital for research, there are biosecurity concerns associated with unauthorized access to potentially harmful biological agents.

The U.S. has made progress to reduce biosecurity risks associated with individuals with ill intent gaining access to harmful biological agents. In 2010, the US Department of Health and Human Services (HHS) published guidance for commercial gene synthesis providers that recommended screening sequence orders and customers. In addition, the industry-led International Gene Synthesis Consortium (IGSC) was formed in 2009 to share sequence and customer screening methods among its members. IGSC members commit to following specified gene sequence and customer screening protocols as well as record keeping and reporting requirements (see IGSC's Harmonized Screening Protocol, most recently updated in 2017). The federal government continues to evaluate biosafety concerns and provide updated guidance.

In August 2022, California passed AB 1963, which amends sections 66360 and 66361 of the Education Code to require CSU and to request that UC "develop systemwide guidance for purchasing gene synthesis equipment or gene synthesis products from providers who prevent

the misuse of synthetic genes and safeguard the benefits of gene synthesis technology while minimizing risk." The University is requested to consider including IGSC criteria in the guidance.

Guidance

Pursuant to AB 1963, UC is issuing this guidance to members of the University research community who may be involved in purchasing gene synthesis equipment or gene synthesis products for use in University research.

Prior to purchasing gene synthesis equipment or gene synthesis products, those placing orders, including researchers, lab managers, students, and local procurement offices, should ensure that the gene synthesis provider meets the IGSC criteria or that the provider applies protections commensurate to the IGSC criteria. An explanation of the IGSC criteria and commensurate protections are provided in the subsequent sections in this document.

Gene synthesis providers may complete an attestation form to demonstrate that they apply the IGSC criteria or commensurate protections. Alternatively, gene synthesis providers may present other written information demonstrating that they prevent the misuse of synthetic genes and safeguard the benefits of gene synthesis technology while minimizing risk. UC Systemwide Procurement has created a Smartsheet dashboard listing which gene synthesis providers have met the IGSC criteria. This Smartsheet dashboard includes an online tool for requesting provider attestations. In addition, a sample paper attestation form is provided in Appendix I of this guidance document.

UC purchasing offices should endeavor to keep gene synthesis providers' attestation letters or other written information on file within purchasing systems so that a gene synthesis provider will only have to provide this information once. Those purchasing synthesis equipment or gene synthesis products are encouraged to place orders from gene synthesis providers who have an attestation letter or other written information on file.

The IGSC Criteria

The IGSC is an industry-led group of gene synthesis companies and organizations formed to design and apply a common protocol to screen both the sequences of synthetic gene orders and the customers who place them.

The IGSC's "Harmonized Screening Protocol for Gene Sequence & Customer Screening to Promote Biosecurity" establishes five core components that IGSC companies must apply to promote the safe use of synthetic genes:

- **Gene Sequence Screening:** The complete DNA sequence of every synthetic gene order is to be screened against a Regulated Pathogen Database developed by the consortium and one or more of the internationally coordinated sequence reference databanks (i.e., NCBI/GenBank, EBI/EMBL or DDBJ). Amino acid sequences of possible translation products for each synthetic gene ordered will also be screened.
- **Gene Customer Screening:** A complete and thorough screening of each potential gene synthesis customer will be conducted to establish identity and clearance for delivery of genes ordered, in accordance with national guidelines. The screening protocol assigns special considerations to the ordering of Select Agent genes.
- **Record Keeping:** The IGSC companies will keep all screening, customer and order records for at least eight years.

- **Order Refusal & Reporting:** The IGSC companies reserve the right to refuse to fill any order and to notify authorities upon identifying potentially problematic orders, coordinating efforts with local and national law enforcement and intelligence agencies.
- **Regulatory Compliance:** The IGSC companies comply with all applicable laws and regulations governing the synthesis, possession, transport, export and import of gene synthesis and other products.

Commensurate Protections

Gene synthesis providers who do not apply the IGSC criteria may attest to meeting protections commensurate to the IGSC specific to gene sequencing screening and gene customer screening.

In terms of gene sequencing screening, providers should have a way to screen requested sequences to identify if a request is a "sequence of concern."

The 2010 HHS Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA (PDF)[1] provides a set of recommended practices to companies synthesizing double-stranded (ds) DNA to encourage such companies to screen both their customers and requested sequences. HHS explains that "[t]he purpose of sequence screening is to identify when "sequences of concern" are ordered. Identification of a "sequence of concern" does not necessarily imply that the order itself is of concern. Rather, when a "sequence of concern" is ordered, further follow-up procedures should be used to determine if filling the order would raise concern. Sequence screening is recommended for all dsDNA orders."

HHS defines "sequences of concern" as sequences derived from or encoding select agents and toxins or items on the Commercial Control List (CCL), except when also found in unregulated organisms; or sequences that contribute to toxicity or pathogenicity, whether derived from or encoding regulated or unregulated biological agents.

As to gene customer screening, HHS explains that the purpose of customer screening is to verify the legitimacy of the customer and the principal user, to confirm that the customer and principal user placing an order are acting within their authority, and to verify the legitimacy of the end-use.

Resources for Compliance with AB 1963

As a resource for the UC and CSU community, UC Systemwide Procurement developed a Smartsheet dashboard listing which gene synthesis providers have met the IGSC criteria or attested to providing protections commensurate to the IGSC criteria. This tool may also be used to send requests to gene synthesis providers to complete an attest of either meeting the ICSC criteria or providing commensurate protections. Prior to purchasing gene synthesis equipment or gene synthesis products, those placing orders for these equipment or products are encouraged to use this tool to either check for compliance with AB 1963 or requesting attestation forms.

[1] In 2020 and 2022, HHS issued requests for information to update the 2010 Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA. To date of this RPAC Guidance Memo, the HHS Screening Framework has not been updated. Please refer to the HHS website for more information on these efforts.

Please also refer to the Smartsheet dashboard and tool for requesting provider attestations.

As an additional resource, a sample paper attestation form is provided in Appendix I of this guidance document. The attestation form may be used as a reference. Gene synthesis providers may also use this form to complete the attestation; however, UC recommends completing the attestation via the web tool instead.

Both the Smartsheet dashboard and web-based attestation form require UC or CSU email domains to access the information.

Additional General Information on Biosafety

While AB 1963 facilitates measures concerning the procurement of gene synthesis equipment or gene synthesis products, the research community is reminded that they must follow all applicable laws and policies regarding biosafety, including submitting a Biological Use Authorization if they are working with certain kinds of biological agents, such as recombinant DNA, synthetic nucleic acids, and pathogens.

Campuses Institutional Biosafety Committees (IBC) are responsible for enforcing policies and guidelines related to university-related use of all potentially hazardous biological agents, including but not limited to infectious agents, human and non-human primate materials (including established cell lines), CDC select agents, recombinant DNA and studies involving human gene transfer. The Committee ensures that research involving these agents is conducted in a manner that does not endanger the researcher, laboratory worker, human research subjects, the public or the environment.

UC has issued a systemwide Dual Use Research of Concern Policy (PDF) most recently updated in 2017. Each campus has a "Dual Use Research of Concern (DURC)" Administrator that researchers must contact if they plan to work with DURC agents/toxins identified by the U.S. Government, and campus Institutional Review Entities (IREs) are charged with oversight of, and education on, life sciences research involving the use of potential DURC agents. The DURC Administrator and IREs are not, however, specifically charged with reviewing or approving the procurement of DURC agents.

In addition, the NIH has in place Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules that applies to researchers who receive NIH funding. The NIH Guidelines provides details on safety practices and containment procedures for basic and clinical research involving recombinant or synthetic nucleic acid molecules, including the creation and use of organisms and viruses containing recombinant or synthetic nucleic acid molecules.

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