

# International Gene Synthesis Consortium (IGSC)

## - Harmonized Screening Protocol -

### Gene Sequence & Customer Screening to Promote Biosecurity

#### Preamble

This document outlines the standards and practices that IGSC gene synthesis companies apply to prevent the misuse of synthetic genes. By screening the sequences of ordered genes and vetting customers, IGSC companies help to ensure that science and industry realize the many benefits of gene synthesis technology while minimizing risk.

The ICGS companies together represent approximately 80% of commercial gene synthesis capacity world-wide.

#### 1. Gene Sequence Screening

IGSC companies screen synthetic gene orders to identify regulated pathogen sequences and other potentially dangerous sequences.

1. IGSC companies screen the complete DNA sequence of every synthetic gene order against the DNA sequences in a Regulated Pathogen Database, and against all entries found in one or more of the internationally coordinated sequence reference databanks (i.e., NCBI/GenBank, EBI/EMBL, or DDBJ). The IGSC is currently assembling a Regulated Pathogen Database that will include data from all organisms on the Select Agent list, the Australia Group List, and any other national list of regulated pathogens. Until this is deployed, each company is using its own database of pathogen sequences. At a minimum, IGSC companies screen for all pathogen and toxin genes from the US Select Agents and Toxins List and/or from the list specified in paragraphs 1C351-1C354 of European Union Council Regulation 428/2009.

2. IGSC companies translate all six reading frames of each synthetic gene into an amino acid sequence. This sequence is screened against the protein sequences derived from the databases described above.

3. IGSC companies use automated screening as a filter to identify pathogen and toxin DNA sequences. When automated screening identifies a potential pathogen or toxin sequence, the order is reviewed by a human expert and is either accepted, accepted with a requirement for additional customer review, or rejected.

## **2. Gene Customer Screening**

1. IGSC companies require identification data from all potential customers for synthetic genes, including at a minimum a shipping address, institution name, country, telephone number, and email address. We do not ship to PO Boxes.
2. Potential customers are screened against OFAC's SDN List, the Department of State's Debarred List, and BIS's Denied Persons, Entity, and Unverified lists, or the HADDEX list, and/or any other list required by applicable national regulations.
3. IGSC companies require additional customer screening before accepting orders for DNA sequences from regulated pathogens. Although the U.S. Select Agent Regulations and the European Commission regulations do not restrict access to all Select Agent genes, IGSC companies supply genes from regulated pathogens only to researchers in government laboratories, universities, non-profit research institutions, or industrial laboratories demonstrably engaged in legitimate research. Customers ordering Select Agent or Australia Group DNA fragments must provide a written description of the intended use of the synthetic product; we verify independently a) the identity of the potential customer and purchasing organization, and b) that the described use is consistent with the activities of the purchasing organization.

IGSC companies use the current recommendations from the U.S. CDC and/or the Department of Agriculture and/or the European Commission (CR42) to determine which DNA sequences are Select Agents as recombinant DNA fragments. We supply genes with such sequences only if the supplier and the customer are able to comply with all Select Agent regulations applicable to that gene.

In general, IGSC companies only sell DNA or fragments of regulated pathogens to bone fide end-users. We do not sell or ship such material to distributors or other resellers, unless those companies identify the end-user receiving the products and demonstrate their compliance with every requirement otherwise applicable to that end-user.

## **3. Record keeping**

1. Sequence Screen Results: IGSC companies retain records of every gene sequence screening result for at least 8 years.
2. Customer Screen Results: IGSC companies retain records of every customer screening result for at least 8 years.
3. Product & Delivery Information: IGSC companies retain records of every gene synthesized and delivered for a minimum of 8 years after shipping, including at least the following: (a) the synthetic DNA sequence; (b) the vector; and (c) the recipient's identity and shipping address.

#### **4. Order Refusal & Reporting**

1. IGSC companies reserve the right to refuse to fill any order and to notify authorities upon identifying potentially problematic orders.
2. IGSC companies have established relationships with local and national law enforcement and intelligence authorities with whom we can share information to report and to prevent the potential misuse of synthetic genes.
3. IGSC companies will report any request for a gene associated with the pathogenicity of an organism received from a suspicious potential customer and/or potential customer failing to establish its bone fides in application of the practices set forth in section 2.

#### **5. Regulatory Compliance**

1. IGSC companies comply with all applicable laws and regulations governing the synthesis, possession, transport, export, and import of gene synthesis and other products.
2. We comply with World Health Organization recommendations concerning the distribution, handling, and synthesis of Variola virus DNA.

#### **Consortium Collaborative Activities**

IGSC companies intend to work together in order to:

1. Develop and update a Regulated Pathogen Database to include all gene sequences identified as potentially hazardous by authoritative groups such as the CDC, the Australia Group, and the U.S. and European governments.
2. Ensure that we use the best and most effective algorithms to screen gene sequences against the Regulated Pathogen Database.
3. Collaborate with our respective national governments in support of effective oversight of gene synthesis technology, and to encourage international coordination.
4. Incorporate recommendations from the regulatory, scientific, and public interest communities into our screening and other biosecurity processes.

#### **Revisions to the Harmonized Screening Protocol**

This document represents an initial effort by a group of companies committed to the responsible use of gene synthesis technology. IGSC companies welcome comments and suggestions to improve the Harmonized Screening Protocol from scientists, regulators, and other interested parties. This document will be revised periodically in response to these suggestions and to changes in the scientific, technical, or regulatory environment.

## **Terminology**

**Gene Synthesis.** This document uses the phrase “gene synthesis” to refer to the production of double-stranded, recombinant DNA fragments from oligonucleotides. Synthetic genes are typically provided in plasmid vectors.

**Oligonucleotides.** Chemically-synthesized, single-stranded DNA fragments, typically supplied as a solution in a tube or a multi-well plate.

**Synthetic Gene.** A gene or other DNA fragment produced by gene synthesis, typically between 50 and 50,000 base pairs in length.

## **Related Links**

Select Agents and Toxins List

<http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html>

EU Council Resolution 428

<http://www.consilium.europa.eu/showPage.aspx?id=408&lang=en>

HADDEX

<http://www.ausfuhrkontrolle.info/ausfuhrkontrolle/de/arbeitshilfen/haddex/index.html>

OFAC’s SDN List

<http://www.treas.gov/offices/enforcement/ofac/sdn/>

Department of State’s Debarred List

<http://www.pmddtc.state.gov/compliance/debar.html>

BIS’s Denied Persons, Entity, and Unverified lists

<http://www.bis.doc.gov/complianceand enforcement/liststocheck.htm>

Current Recommendations from the U.S. CDC

<http://www.selectagents.gov/SyntheticGenomics.html>

Australia Group Listed Source Organisms

[http://www.australiagroup.net/en/biological\\_agents.html](http://www.australiagroup.net/en/biological_agents.html)

World Health Organization Recommendations Concerning the Distribution, Handling, and Synthesis of Variola Virus DNA

<http://www.who.int/csr/disease/smallpox/SummaryrecommendationsMay08.pdf>