The IASB Code of Conduct for Best Practices in Gene Synthesis

Cambridge, MA. Nov. 3, 2009

1 Preamble

The field of Synthetic Biology is gaining momentum in the academic and commercial world and evolving rapidly. In parallel, a market for Synthetic Biology products and services has developed and grown rapidly over the past ten years.

The International Association Synthetic Biology represents a number of companies and organizations with a stake in Synthetic Biology, for instance as providers of double-stranded recombinant DNA synthesis (hereinafter "gene synthesis") or bioinformatics products. IASB has created this Code of Conduct in order to secure the foundations of this fledgling field against abuse and to bring Synthetic Biology to its full potential. It is aimed at all providers of gene synthesis services.

The most fundamental tools for the design of Synthetic Biology applications are synthetic genes and their intrinsic features of freedom of design and artificial biological function.

This Code of Conduct helps companies that provide DNA synthesis services and products and academic and public institutions that practice DNA synthesis to conduct their business in a sensible and responsible way.

Declaration:

The Undersigned herewith declare that they are in full agreement with the need for a safe and responsible use of synthetic DNA. They strictly follow all regulations and international standards designed to safeguard against intentional or unintentional abuse of synthetic DNA.

2 General Considerations

Synthetic Biology provides the means to accelerate the assembly of complex biological networks and to rapidly create biological entities with new properties. These powers will undoubtedly lead to a number of beneficial developments such as sustainable biofuels, new therapeutics, and biodegradable plastics.

However, the efficiency and potential power of Synthetic Biology can also create the risk of abuse. Through rapid DNA synthesis, biorisk-associated genes such as toxin genes or virulence factors become accessible to a large number of users.

In order to contain the risks of Synthetic Biology and to protect the field against misuse, the Undersigned have adopted this Code of Conduct which provides guidelines for safe, secure, and responsible commercial or non-commercial DNA synthesis.

One important consideration of any regulation for biosafety and biosecurity is the freedom of research: A lot of beneficial developments would be impossible without the freedom to explore organisms and genes that bear a certain environmental or health risk. It is our conviction that such a risk can be managed and contained in a secure manner, while at the same time ensuring the level of freedom that is necessary for desired scientific advancements.

It is our declared intention to raise barriers for malign attackers through a number of measures that will combine to protect Synthetic Biology from abuse. We aim at encouraging continued improvements and harmonization in this field, as well as adoption and further evolution of this Code of Conduct and the Best Practice Guidelines in the future.

The Undersigned will participate or otherwise reasonably contribute for regular scientific dialogue on the further evolution of screening, best practices and the topic of virulence factors and positive or negative lists of elements against which synthetic genes should be screened.

The Undersigned promise to develop a compliance plan for adherence to this Code of conduct.

This Code has been expressly designed to guide companies and other entities engaged in the synthesis of double stranded DNA of minimum 200 base pairs in length and multi-gene constructs. The Undersigned express no opinion about the extent to which the standards described herein may be applicable to the much shorter sequences known as “oligos.”

3 Risk assessment and risk management

Abuse of synthetic genes in hazardous applications is possible in two ways only: Intentionally, and by failures in risk assessment and management.

The technology of handling synthetic genes uses complex procedures which by their nature are self-contained and tightly controlled under existing standards of good practice.

For biosecurity, risk assessment entails the screening of DNA sequences for genes which can be intentionally abused, for example, in terrorist activities, whereas risk management entails the restriction of access to synthetic DNA to legitimate users.

4 Record keeping

- Records of suspicious inquiries and positive screening hits will be kept for at least 8 years.
- Statistics on biosecurity and biosafety related inquiries and orders will be kept for at least 8 years. Information to be retained shall include the total number of inquiries and orders for synthetic genes, the number of inquiries and orders with positive screening hits, and the number of orders with positive screening hits which have been respectively filled or rejected.

5 Cooperation with Authorities

Gene synthesis providers shall take reasonable steps to maintain communications with the government in the nation where they are headquartered. Gene synthesis providers shall promptly inform these authorities each time they encounter evidence which clearly suggests possible illegal activities. Such evidence will include, by way of example, inquiries and orders that strongly suggest illegal activities, such as attempts to conceal a non-business delivery address."

6 Sequence Screening

- Gene synthesis companies should always take reasonable steps to determine the relationship of the requested sequences to risk-associated sequences before sending them to customers. The following procedure reflects IASB members' best collective judgment of how to achieve this goal within the framework of existing technology:

    - DNA sequences submitted as inquiries or orders for DNA synthesis by customers will be screened against GENBANK for reasonable sequence similarity to pathogens. Members may take further reasonable steps to determine the function and evaluate the associated biorisk associated with homologous genes following procedures to be defined by the Technical Experts Group on Biosecurity (hereinafter "TEGB"). Pending such procedures, providers shall determine and follow their own best practices.

    - In addition to determining biorisk, entities shall also comply with all national laws. This will include reviewing and comparing top homology hits against (a) all Australia Group biological dual-use organisms, (b) The US Select Agent and Toxins list, and (c) against national organism lists for export control or biological safety/security.

- The foregoing procedure establishes a benchmark capability for detecting threat sequences. However we expect researchers to develop new sequence screening technologies over time. Members shall be free to adopt such alternative technologies *provided* that the new methods have first been empirically shown to detect threat sequences at reliability levels that meet or exceed the benchmark methods described above, as elaborated by TEGB over time. IASB members pledge to promptly update this Code of Conduct to reflect such new (and potentially higher) standards as they appear.

- IASB members pledge to take ongoing, collective efforts to refine and improve today's screening technologies over time. These shall include:

    - Establishing a standing Committee to review and if necessary update and extend this Code of Conduct in light of changing threats and/or technology advances over time.

    - Regularly exchanging literature searches, virulence judgments, and other data needed to determine the function and/or threat potential of Genbank genes through a secure on-line collaboration to be hosted by the University of California's Goldman School of Public Policy (VIREP).

    - Regularly exchanging, discussing, and collaborating on best practices and ideas through person-to-person contacts and through a secure on-line collaboration.

- Providers which find that a requested gene may code for functions that pose a biosecurity risk shall not fill such orders unless and until they have conducted intensive customer screening at the highest levels provided for in Section 8 of this Code.

7 Response to Identified Threats

- Whenever any of the procedures described in Section 6 produce a “hit” as defined by the then-applicable TEGB guidance, the hit will be assessed by a molecular biologist or similar subject matter expert.

- When the hit is deemed authentic,

    - the customer will be notified and made aware of the perceived risk,

    - the order will be accepted only if the customer is a legitimate user (see section 8) and all national regulations that apply to the exporting/producing company have been met.

    - National authorities shall be contacted as to the extent provided for in Section 5.

8 Customer Screening

Gene synthesis providers should always take reasonable steps to confirm that their customers are who they say they are. Where customers seek risk-associated sequences, providers should take further reasonable efforts to confirm that the customer seeks the requested sequence for legitimate purposes, and has carefully considered any safety or security risks potentially associated with their use of the sequence. The following procedure reflects IASB members' best collective judgment of how to achieve these goals within the framework of existing technology:

- In a first step, which is to be performed for all orders independent of whether they are considered to be risk-associated:
    - A minimum set of identification data for the customer will be retrieved, including postal address, institution, country, telephone number, and email address
    - These data will be kept on record according to section 4.
- When an ordered synthetic gene is identified as a risk-associated sequence, the following steps are to be performed:
    - The legitimacy of the customer will be determined by a commercially-reasonable inquiry by the gene synthesis provider and the decision of legitimacy will be documented.
    - It will be ensured that the stated postal address is not a residential address nor a PO box or similar address with limited traceability.
    - The foregoing determination shall include, *inter alia,* verifying the addresses of businesses and institutions which placed the order, and ensuring that the address owner is a legitimate organization (such as a registered business or an internationally recognized academic institution).

The foregoing procedure establishes a benchmark capability for screening customers. However we expect researchers to develop new screening methods over time. Members shall be free to adopt such alternative methods *provided* that they meet or exceed the benchmark methods described above. IASB members pledge to promptly update this Code of Conduct to reflect such new (and potentially higher) standards as they appear.

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Where the provider's investigation reveals that its immediate customer of a risk-associated gene is not the intended end-user but will instead re-ship the risk-associated gene to a third party end-user, gene synthesis companies shall either (a) identify and investigate the end-user as provided for in this Code, or (b) take reasonable steps to confirm that its immediate customer has adopted and routinely follows procedures comparable to those provided for in this Code.

9 Cooperation on Biosafety and Biosecurity

- The Undersigned will participate in the formation of a Technical Expert Group on Biosecurity (TEGB). This group will review current design and implementations of biosafety and biosecurity measures, and will propose and initiate improvements.

- The TEGB shall develop an IASB operated seal of approval program to certify compliance with this Code. Providers will be encouraged to apply for seals whether or not they are currently IASB members.