Information for perspective IGSC members:

The International Gene Synthesis Consortium (IGSC) was formed in 2009 to coordinate ongoing efforts in developing biosecurity "best practices," to work collaboratively with governments and others concerned with promoting the beneficial application of gene synthesis technology, and to safeguard and promote biosecurity in synthetic gene research. The IGSC is an issue and industry-specific association.

IGSC membership criteria comprise two qualifications:

1. Providing made-to-order gene synthesis services. To maintain its focus and perspective, the IGSC confines its membership to active practitioners of custom commercial gene synthesis, defined as organizations that manufacture and sell customer-specified, double- stranded DNA of lengths that might be functionally significant (currently defined as >= 200bp), using their own manufacturing facilities.

If an organization's manufacturing output consists of relatively short (< 200 nt) single-stranded products (such as PCR assays, NGS enrichment/capture baits), or other application-specific predesigned kits (even those that might contain genes), then the security concerns at the core of the IGSC's activities likely don't apply at all, and there's not much reason for such an organization to consider joining the IGSC. Biosecurity screening comes to the fore only when the customer is specifying what gets made. Note that *how* the customer specifies the desired product (e.g., by nucleoside or amino acid sequence, functional specifications, entry identifier in a genetic database, common gene nomenclature, etc.) is not relevant, only that they do.

Resellers and agents are encouraged to procure their products from an IGSC member organization, but are not themselves eligible for membership.

2. Willingness to demonstrate that your organization can and will abide by the IGSC's harmonized protocol, located at: http://www.genesynthesisconsortium.org/wp-content/uploads/2012/02/IGSC-Harmonized-Screening-Protocol1.pdf.

Bio-security screening itself consists of two parts: sequence screening and customer screening.

Sequence screening:
Sequences are screened to identify primary source species and function in order to determine whether the sequence is a "sequence of concern" (that is, a sequence with potential for dual use or of known pathogenic function). Sequence screening is really a two-step process. The standard for identification is "best match", so screening cannot be accomplished simply by looking for exact matches in a threat sequence database. Instead, potential order items are BLASTed for both nucleotide (NA) and amino acid (AA) composition against a major sequence identifier database such as the GenBank nr/nt database. The resulting closest-identified biological source(s) are then cross-referenced against a compilation of recognized and

regulated organisms and sequences to see if the requested sequences exist in the known-threat database.

“Sequences of concern” are gathered from multiple sources, chiefly:

1. Australia Group Common Control Lists: http://www.australiagroup.net/en/controllists.html
2. European Union Council Regulation (EC) No 428/2009:
    a. http://trade.ec.europa.eu/doclib/docs/2009/june/tradoc_143390.pdf
    b. http://ec.europa.eu/trade/import-and-export-rules/export-from-eu/dual-use-controls/index_en.htm
3. U.S. Commerce Control Lists: http://www.bis.doc.gov/index.php/regulations/commerce-control-list-ccl
4. U.S. Select Agents and Toxins Lists:
    a. http://www.selectagents.gov/
    b. http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html
    c. http://www.selectagents.gov/SyntheticGenomics.html

A primary procedural document for screening system implementation is the “Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA” published by HHS, and available at: http://www.phe.gov/preparedness/legal/guidance/syndna/Pages/default.aspx. This guidance sets the basic U.S. federally-recommended approach to customer and sequence screening and is the standard to which participants in the US market will want to adhere regardless of IGSC status.

Customer screening
A best-match hit to a sequence-of-concern obligates the manufacturer in addition to screen the customer for appropriate authority/credentials to handle the sequence identified in accordance with the applicable local and international agreements, regulations, and guidance documents. Customer screening issues (other than those already applicable to local, national, or international trade and shipments generally) are discussed in the “Screening Framework Guidance” reference mentioned above.

What the IGSC provides its members beyond this is fairly minimal--we maintain a consolidated controlled list (derived and updated in common from the sources listed above) and a performance standard--but the implementation of any sequence screening software or workflow automations is entirely up to each member organization.

Specific information for start-ups:
The IGSC recognizes that synthetic custom gene synthesis is a dynamic, evolving technology, and that new technical developments and approaches are likely, leading to new custom gene manufacturers. If your organization intends to engage in commercial custom gene manufacture but is not yet an active commercial custom gene manufacturer, then even though it's still too early to qualify for IGSC membership, the IGSC will be glad to provide you with mentor points of

contact on biosecurity procedures employed within the consortium so that you'll be ready once you do go into commercial production.