

Committee on Microbiological Safety (COMS)

Frequently Asked Questions Regarding Synthetic Nucleic Acid Research

FAQ 1: What has changed with respect to the scope of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*?

The scope of the *NIH Guidelines* has been modified to cover explicitly certain types of basic and clinical research with nucleic acid molecules created solely by synthetic means. These changes are effective March 5, 2013.

FAQ 2: What is the new definition of recombinant and synthetic nucleic acids in the *NIH Guidelines*?

In the amended *NIH Guidelines*, recombinant and synthetic nucleic acid molecules are defined as:

- (i) molecules that a) are constructed by joining nucleic acid molecules and b) can replicate in a living cell (i.e. recombinant nucleic acids);
- (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e. synthetic nucleic acids); or
- (iii) molecules that result from the replication of those described in (i) or (ii) above.

FAQ 3: What institutions are subject to the amended *NIH Guidelines*?

Institutions that receive NIH funding for any research involving recombinant or synthetic nucleic acids.

FAQ 4: What research is exempt under the amended *NIH Guidelines*?

In keeping with the exemptions for recombinant DNA molecules described in Section III-F of the previous version of the *NIH Guidelines*, certain synthetic nucleic acid molecules are exempt from the amended *NIH Guidelines* because:

- their introduction into a biological system is not expected to present a biosafety risk that requires review by an IBC, or
- the introduction of these nucleic acid molecules into biological systems would be akin to processes of nucleic acid transfer that already occur in nature, so that the appropriate biosafety practices would be the same as those used for the natural organism.

Specifically, research that is exempt under the *NIH Guidelines* includes the following.

A. An exemption was made for research with certain low-biosafety-risk synthetic nucleic acid molecules. . For example, use of oligonucleotides (e.g., for PCR and microarrays) might be exempt and so would not require COMS registration. Synthetic nucleic acids that meet all three

of the following criteria do not registration with COMS. Synthetic nucleic acids that meet the following criteria are exempt:

- can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., Oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and
 - are not designed to integrate into DNA, and
- do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight.**B. Synthesis of nucleic acids that are solely the exact sequence of a nonchromosomal or viral DNA source. The source (organism or virus) must exist contemporaneously in a natural (non-laboratory) setting.**

C. Chemical synthesis of nucleic acids that are not placed in a biological system. If the synthetic nucleic acids are placed in a biological system, the research might not be exempt.

FAQ 5: What clinical research with synthetic nucleic acids is covered under the amended *NIH Guidelines*?

Section III-C-1 of the amended *NIH Guidelines* covers human gene transfer experiments, i.e., research that involves the deliberate transfer into human research participants of either:

- Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
- Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules, that meet any one of the following criteria:
 - Contains more than 100 nucleotides; or
 - Possesses biological properties that enable integration into the genome (e.g., *cis* elements involved in integration); or
 - Have the potential to replicate in a cell; or
 - Can be translated or transcribed.

Please consult with your BSO if you need assistance determining whether the synthetic nucleic acids require COMS registration or are exempt from the regulations.

References:

NIH OBA FAQs http://oba.od.nih.gov/oba/faqs/Synthetic_FAQs-Sept-2012.pdf

NIH OBA Guidelines http://oba.od.nih.gov/rdna/nih_guidelines_oba.html