

Microbial Products of Biotechnology Summary of Regulations under the Toxic Substances Control Act

EPA regulations for implementing its review program for new intergeneric microorganisms under section 5 of the Toxic Substances Control Act (TSCA) are found in the Code of Federal Regulations at 40 C.F.R. Part 725. The regulations define a number of exemptions and codify EPA's approach to research and development (R&D) for microbial products of biotechnology. These rules are designed to ensure that EPA can adequately identify and regulate risk associated with microbial products of biotechnology. This fact sheet summarizes the key components of the regulations. For more details, please refer to 40 CFR Part 725 and the Federal Register Notice announcing the regulations, published April 11, 1997 (62 FR 17910).

Microorganisms Subject to These Rules

Microorganisms subject to this rule are "new" microorganisms used commercially for "TSCA purposes," such as production of industrial enzymes and other chemicals; agricultural practices (e.g., biofertilizers); biosensors; production of biofuels, and breakdown of chemical pollutants in the environment. (See §725.8(c)(1)). According to EPA's rule, new microorganisms are those "intergeneric" microorganisms (including bacteria, fungi, algae, viruses, protozoa, etc.) formed by combining genetic material from organisms in different genera. (See §725.1(a) and 725.3.) The term for this definition is intergeneric. A genus (pl. genera) is a level in a taxonomic classification system based on the relatedness of organisms. EPA believes that intergeneric microorganisms have a sufficiently high likelihood of expressing new traits or new combinations of traits to be termed "new" and warrant review. Microorganisms that are not intergeneric are not considered "new", and thus are not subject to reporting under section 5 of TSCA. For the same reason, EPA also considers microorganisms formed with synthetic DNA not from the same genus to be new under TSCA and thus within the intended scope of this rule. EPA strongly encourages any manufacturer of a new microorganism using synthetic DNA to contact the Agency.

Reporting Requirements

The TSCA Section 5 notification specifically required for microorganisms is the Microbial Commercial Activity Notice (MCAN)(40 CFR Part 725 Subpart D). Persons intending to manufacture or import intergeneric microorganisms for commercial purposes in the United States must submit an MCAN to EPA at least 90 days before such manufacture or import. EPA has 90 days to review the submission in order to determine whether the intergeneric microorganism may present an unreasonable risk to human health or the environment. If EPA makes that determination, EPA may impose appropriate regulatory restrictions on the microorganism.

The regulations also cover intergeneric microorganisms used in R&D for commercial purposes. The TSCA Section 5 notification required for R&D testing of new microorganisms that are released in the environment is the TSCA Experimental Release Application (TERA)(40 CFR Part 725 Subpart E, §§725.250-.288). A TERA must be submitted to EPA at least 60 days prior to initiating such field trials. The TERA is designed, in recognition of the needs of researchers, to provide a high measure of flexibility and a shorter review period (60 days). R&D for commercial purposes are those activities which are funded directly, in whole or in part, by a commercial entity, regardless of who is actually conducting the research, or which will obtain for the researcher an immediate or eventual commercial advantage.

Exemptions¹

Certain intergeneric microorganisms are exempt from the requirement to submit a MCAN, if the manufacturer meets criteria defining eligible microorganisms and specified use conditions. This exemption is most applicable to the use of microorganisms to manufacture specialty and commodity chemicals.

Intergeneric microorganisms used for R&D in contained structures are exempt from EPA reporting requirements, if researchers maintain records demonstrating eligibility. Researchers are exempt from this record keeping requirement when the researcher or institution is in mandatory compliance with the National Institutes of Health (NIH) "Guidelines for Research Involving Recombinant DNA Molecules". Those researchers voluntarily following the NIH Guidelines can, by documenting their use of the NIH Guidelines, satisfy EPA's requirements for R&D use in contained structures. Alternatively, researchers can utilize the exemption by documenting that they meet eligibility criteria in the regulations.

Biofuels

The new chemicals regulated under TSCA by EPA includes certain biofuels and certain microorganisms used in the production of biofuels. Some biofuels and synthetic fuels may be new chemicals, and thus, would be subject to Premanufacture (PMN) reporting requirements, and as described above, there are analogous rules requiring MCAN submission for "new" microorganisms (including bacteria, fungi, algae, viruses, protozoa,

¹ EPA's biotechnology rule contains several exemptions. Exemptions for research and development (R&D) are contained in Subpart E. There is an R&D exemption for activities conducted inside a structure (§§725.234 and .235) and outside a structure (§§725.238 and .239). A test market exemption is provided in Subpart F. Subpart G provides two exemptions limited to specified recipient microorganisms and introduced genetic material that is limited in size, well-characterized, poorly mobilizable, and free of certain sequences. The "Tier I" exemption requires certain certifications and recordkeeping while the "Tier II" exemption requires certain certifications and a notification to EPA and EPA review of specific physical containment and control technologies.

etc.) which are ‘intergeneric’ genetically-engineered microorganisms.

Several prominent areas in the biofuels supply chain employ new chemicals and microorganisms. Success of many of the advanced fuel production technologies often depends on enhanced metabolic capabilities of microorganisms used in those technologies. Genetic engineering of microorganisms, using either traditional or synthetic biology approaches, may be necessary to achieve these enhancements. Since issuing the Biotechnology Rule, EPA has received numerous notifications, including for microorganisms critical in different parts of the fuel production processes for cellulosic ethanol manufacture. EPA has engaged companies regarding TSCA requirements for developing cellulosic ethanol and algal biofuels production and anticipates more notifications as these technologies mature in the next few years.

For More Information

For more detailed information on TSCA regulations concerning microbial products of biotechnology, refer to <http://www.epa.gov/oppt/biotech>