

(5) Sequences for toxins affecting membrane function.

Sequence Source	Toxin Name
<i>Bacillus anthracis</i>	Edema factor (Factors I II); Lethal factor (Factors II III)
<i>Bacillus cereus</i>	Enterotoxin (diarrheagenic toxin, mouse lethal factor)
<i>Bordetella pertussis</i>	Adenylate cyclase (Heat-labile factor); Pertussigen (pertussis toxin, islet activating factor, histamine sensitizing factor, lymphocytosis promoting factor)
<i>Clostridium botulinum</i>	C2 toxin
<i>Clostridium difficile</i>	Enterotoxin (toxin A)
<i>Clostridium perfringens</i>	Beta-toxin; Delta-toxin
<i>Escherichia coli</i> & other Enterobacteriaceae spp.	Heat-labile enterotoxins (LT); Heat-stable enterotoxins (STa, ST1 subtypes ST1a ST1b; also STb, STII)
<i>Legionella pneumophila</i>	Cytolysin
<i>Vibrio cholerae</i> & <i>Vibrio mimicus</i>	Cholera toxin (choleraegen)

(6) Sequences that affect membrane integrity.

Sequence Source	Toxin Name
<i>Clostridium bifementans</i> & other <i>Clostridium</i> spp	Lecithinase
<i>Clostridium perfringens</i>	Alpha-toxin (phospholipase C, lecithinase); Enterotoxin
<i>Corynebacterium pyogenes</i> & other <i>Corynebacterium</i> spp.	Cytolysin (phospholipase C), Ovis toxin (sphingomyelinase D)
<i>Staphylococcus aureus</i>	Beta-lysin (beta toxin)

(7) Sequences that are general cytotoxins.

Sequence Source	Toxin Name
<i>Adenia digitata</i>	Modeccin
<i>Aeromonas hydrophila</i>	Aerolysin (beta-lysin, cytotoxic lysin)
<i>Clostridium difficile</i>	Cytotoxin (toxin B)
<i>Clostridium perfringens</i>	Beta-toxin; Epsilon-toxin; Kappa-toxin
<i>Escherichia coli</i> & other Enterobacteriaceae spp.	Cytotoxin (Shiga-like toxin, Vero cell toxin)
<i>Pseudomonas aeruginosa</i>	Proteases
<i>Staphylococcus aureus</i>	Gamma lysin (Gamma toxin); Enterotoxins (SEA, SEB, SEC, SED SEE); Pyrogenic exotoxins A B; Toxic shock syndrome toxins (TSST-1)
<i>Staphylococcus aureus</i> & <i>Pseudomonas aeruginosa</i>	Leucocidin (leukocidin, cytotoxin)
<i>Streptococcus pyogenes</i>	Streptolysin S (SLS); Erythrogenic toxins (scarlet fever toxins, pyrogenic exotoxins)
<i>Yersinia enterocolitica</i>	Heat-stable enterotoxins (ST)

§ 725.422 Physical containment and control technologies.

The manufacturer must meet all of the following criteria for physical containment and control technologies for

any facility in which the new microorganism will be used for a Tier I exemption; these criteria also serve as guidance for a Tier II exemption.

(a) Use a structure that is designed and operated to contain the new microorganism.

(b) Control access to the structure.

(c) Provide written, published, and implemented procedures for the safety of personnel and control of hygiene.

(d) Use inactivation procedures demonstrated and documented to be effective against the new microorganism contained in liquid and solid wastes prior to disposal of the wastes. The inactivation procedures must reduce viable microbial populations by at least 6 logs in liquid and solid wastes.

(e) Use features known to be effective in minimizing viable microbial populations in aerosols and exhaust gases released from the structure, and document use of such features.

(f) Use systems for controlling dissemination of the new microorganism through other routes, and document use of such features.

(g) Have in place emergency clean-up procedures.

§ 725.424 Requirements for the Tier I exemption.

(a) *Conditions of exemption.* The manufacture or import of a new microorganism for commercial purposes is not subject to review under this part if all of the following conditions are met for all activities involving the new microorganism:

(1) The recipient microorganism is listed in and meets any requirements specified in § 725.420.

(2) The introduced genetic material meets the criteria under § 725.421.

(3) The physical containment and control technologies of any facility in which the microorganism will be manufactured, processed, or used meet the criteria under § 725.422.

(4) The manufacturer or importer submits a certification described in paragraph (b) of this section to EPA at least 10 days before commencing initial manufacture or import of a new microorganism derived from a recipient microorganism listed in § 725.420.

(5) The manufacturer or importer complies with the recordkeeping requirements of § 725.65 and maintains records for the initial and subsequent uses of the new microorganism that verify compliance with the following:

(i) The certifications made in paragraph (b) of this section.

(ii) All the eligibility criteria for the Tier I exemption including the criteria for the recipient microorganism, the introduced genetic material, the physical containment and control technologies.

(b) *Certification.* To be eligible for the Tier I exemption under this subpart, the manufacturer or importer must submit to EPA a document signed by a responsible company official containing the information listed in this paragraph.

(1) Name and address of manufacturer or importer.

(2) Date when manufacture or import is expected to begin.

(3) The identification (genus, species) of the recipient microorganism listed in § 725.420 which is being used to create the new microorganism which will be used under the conditions of the Tier I exemption.

(4) Certification of the following:

(i) Compliance with the introduced genetic material criteria described in § 725.421.

(ii) Compliance with the containment requirements described in § 725.422, including the provision in paragraph (a)(3) of this section.

(5) The site of waste disposal and the type of permits for disposal, the permit numbers and the institutions issuing the permits.

(6) The certification statement required in § 725.25(b). Certification of submission of test data is not required for the Tier I exemption.

§ 725.426 Applicability of the Tier I exemption.

The Tier I exemption under § 725.424 applies only to a manufacturer or importer of a new microorganism that certifies that the microorganism will be used in all cases in compliance with §§ 725.420, 725.421, and 725.422.

§ 725.428 Requirements for the Tier II exemption.

The manufacturer or importer of a new microorganism for commercial purposes may submit to EPA a Tier II exemption request in lieu of a MCAN under subpart D of this part if all of the following conditions are met:

(a) The recipient microorganism is listed in and meets any requirements specified in § 725.420.

(b) The introduced genetic material meets the criteria under § 725.421.

(c) Adequate physical containment and control technologies are used. The criteria listed under § 725.422 for physical containment and control technologies of facilities should be used as guidance to satisfy the Tier II exemption request data requirements listed at § 725.455(d). EPA will review proposed process and containment procedures as part of the submission for a Tier II exemption under this section.

§ 725.450 Procedural requirements for the Tier II exemption.

General requirements for all submissions under this part are contained in § 725.25. In addition, the following requirements apply to requests submitted under this subpart:

(a) *Prenotice consultation.* EPA strongly suggests that for a Tier II exemption, the submitter contact the Agency for a prenotice consultation regarding eligibility for the exemption.

(b) *When to submit the Tier II exemption request.* Each person who is eligible to submit a Tier II exemption request under this subpart must submit the request at least 45 calendar days before the person intends to commence manufacture or import.

(c) *Contents of the Tier II exemption request.* Each person who submits a request under this subpart must provide the information described in §§ 725.428 and 725.455, as well as information known to or reasonably ascertainable by the person that would permit EPA to determine that use of the microorganism, under the conditions specified in the request, will not present an unreasonable risk of injury to health or the environment.

(d) *Recordkeeping.* Each person who submits a request under this subpart must comply with the recordkeeping