(a) *Prenotice consultation.* EPA strongly suggests that for a TME, the applicant contact EPA for a prenotice consultation regarding eligibility for a TME.

(b) *When to submit a TME application.* Each person who is eligible to apply for a TME under this subpart must submit the application at least 45 calendar days before the person intends to commence the test marketing activity.

(c) *Recordkeeping.* Each person who is granted a TME must comply with the recordkeeping requirements of §725.65. In addition, any person who obtains a TME must retain documentation of compliance with any restrictions imposed by EPA when it grants the TME. This information must be retained for 3 years from the final date of manufacture or import under the exemption.

§725.355 Information to be included in the TME application.

(a) To review a TME application, EPA must have sufficient information to permit a reasoned evaluation of the health and environmental effects of the planned test marketing activity. The person seeking EPA approval must submit all information known to or reasonably ascertainable by the person on the microorganism and the test marketing activity, including information not listed in paragraphs (c), (d), and (e) of this section that the person believes will demonstrate that the microorganism will not present an unreasonable risk of injury to health or the environment as a result of the test marketing. The TME application must be in writing and must include at least the information described in paragraphs (b), (c), (d), and (e) of this section.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) Persons applying for a TME must submit the submitter identification and microorganism identity information required for MCANs in §725.155(c), (d)(1), and (d)(2).

(d) Persons applying for a TME must submit phenotypic and ecological characteristics information required in §725.155(d)(3) as it relates directly to the conditions of the proposed test marketing activity.

(e) Persons applying for a TME must also submit the following information about the proposed test marketing activity:

(1) *Proposed test marketing activity.* (i) The maximum quantity of the microorganism which the applicant will manufacture or import for test marketing.

(ii) The maximum number of persons who may be provided the microorganism during test marketing.

(iii) The maximum number of persons who may be exposed to the microorganism as a result of test marketing, including information regarding duration and route of such exposures.

(iv) A description of the test marketing activity, including its duration and how it can be distinguished from full-scale commercial production and research and development activities.

(2) *Health and environmental effects data.* All existing data regarding health and environmental effects of the microorganism must be reported in accordance with §725.160.

§725.370 EPA review of the TME application.

General procedures for review of all submissions under this part are contained in §§725.28 through 725.60. In addition, the following procedures apply to EPA review of TME applications submitted under this subpart:

(a) No later than 45 days after EPA receives a TME, the Agency will either approve or deny the application.

(b) A submitter may only proceed with test marketing activities after receipt of EPA approval.

(c) In approving a TME application, EPA may impose any restrictions necessary to ensure that the microorganism will not present an unreasonable risk of injury to health and the environment as a result of test marketing.

Subpart G—General Exemptions for New Microorganisms

§725.400 Scope and purpose.

(a) This subpart describes exemptions from reporting under subpart D of this part, and from review under this part altogether, for manufacturing and importing of certain new microorganisms for commercial purposes.

(b) Recipient microorganisms eligible for the tiered exemption from review under this part are listed in § 725.420.

(c) Criteria for the introduced genetic material contained in the new microorganisms are described in § 725.421.

(d) Physical containment and control technologies are described in § 725.422.

(e) The conditions for the Tier I exemption are listed in § 725.424.

(f) In lieu of complying with subpart D of this part, persons using recipient microorganisms eligible for the tiered exemption may submit a Tier II exemption request. The limited reporting requirements for the Tier II exemption, including data requirements, are described in §§ 725.450 and 725.455.

(g) EPA review procedures for the Tier II exemption are set forth in § 725.470.

(h) Subparts A through C of this part apply to any submission under this subpart.

§ 725.420 Recipient microorganisms.

The following recipient microorganisms are eligible for either exemption under this subpart:

(a) *Acetobacter aceti*.
(b) *Aspergillus niger*.
(c) *Aspergillus oryzae*.
(d) *Bacillus licheniformis*.
(e) *Bacillus subtilis*.
(f) *Clostridium acetobutylicum*.
(g) *Escherichia coli* K-12.
(h) *Penicillium roqueforti*.
(i) *Saccharomyces cerevisiae*.
(j) *Saccharomyces uvarum*.

§ 725.421 Introduced genetic material.

For a new microorganism to qualify for either exemption under this subpart, introduced genetic material must meet all of the criteria listed in this section.

(a) *Limited in size*. The introduced genetic material must consist only of the following:

(1) The structural gene(s) of interest.

(2) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(3) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(4) The nucleotide sequences needed for vector transfer.

(5) The nucleotide sequences needed for vector maintenance.

(b) *Well-characterized*. For introduced genetic material, well-characterized means that the following have been determined:

(1) The function of all of the products expressed from the structural gene(s).

(2) The function of sequences that participate in the regulation of expression of the structural gene(s).

(3) The presence or absence of associated nucleotide sequences and their associated functions, where associated nucleotide sequences are those sequences needed to move genetic material including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(c) *Poorly mobilizable*. The ability of the introduced genetic material to be transferred and mobilized is inactivated, with a resulting frequency of transfer of less than 10^{-8} transfer events per recipient.

(d) *Free of certain sequences*. (1) The introduced genetic material must not contain a functional portion of any of the toxin-encoding sequences described in this paragraph (d).

(i) For the purposes of this section, a functional portion of a toxin-encoding sequence means any sequence which codes for a polypeptide that has one of the following effects:

(A) It directly or indirectly contributes to toxic effects in humans. Directly contributes to toxic effects in humans means those sequences encoding polypeptides that have direct toxicity to target cells. An example of a sequence which directly contributes to toxic effects in humans is one which encodes the portion of diphtheria toxin, listed in paragraph (d)(2) of this section, capable of interacting with elongation factor 2, leading to inhibition of protein synthesis in target respiratory, heart, kidney, and nerve tissues. Indirectly contributes to toxic effects in humans means a sequence whose encoded polypeptide is not directly toxic to target cells, yet still adversely affects humans. An example of a sequence which indirectly contributes to toxic effects is the sequence