Matters to Set Out the Procedures for Safety Assessment of Feeds and Feed Additives Derived from Recombinant DNA Technology Based on the Provisions of the Ministerial Ordinance on the Specifications and Standards of Feeds and Feed Additives

Ministry of Agriculture, Forestry and Fisheries Notification No. 1780 of November 26, 2002

Ministry of Agriculture, Forestry and Fisheries Notification No. 361, partially revised on February 28, 2005

Ministry of Agriculture, Forestry and Fisheries Notification No. 1006 of July 23, 2014

Ministry of Agriculture, Forestry and Fisheries Notification No. 970 of June 20, 2025

Based on the provisions in 1 (1) Q and R of Appended Table 1 and provisions in 2 of Appended Table 2 of the Ministerial Ordinance on the Specifications and Standards of Feeds and Feed Additives (Ordinance of the Ministry of Agriculture and Forestry No. 35 of 1976), the procedures for safety assessment of feeds and feed additives derived from recombinant DNA technology shall be established as follows.

(Application)

Article 1 Procedures for confirmation on the provisions in 1 (1) L and M of Appended Table 1 and provisions in 2 of Appended Table 2 of the Ministerial Ordinance on the Specifications and Standards of Feeds and Feed Additives (Ordinance of the Ministry of Agriculture and Forestry No. 35 of 1976) (hereinafter simply referred to as “confirmation”) shall be governed by the provisions of this public notice.

(Application for Confirmation)

Article 2

1 An application for confirmation shall be filed by submitting a written application in Appended Form to the Minister of Agriculture, Forestry and Fisheries.

2 The documents listed in Appended Form 1, 2, or 3 shall be attached to the written application set forth in the preceding paragraph.

(Confirmation)

Article 3

1 The Minister of Agriculture, Forestry and Fisheries shall make a confirmation when they find that there is no risk of the production of hazardous livestock products, or the production of livestock products being hindered by damage to livestock, etc., in connection with the use

of feeds or feed additives pertaining to the application set forth in paragraph (1) of the preceding Article.

2 The Minister of Agriculture, Forestry and Fisheries shall hear the opinions of the Agricultural Materials Council when making confirmation.

(Publication)

Article 4 The Minister of Agriculture, Forestry and Fisheries shall, when they have made confirmation, publicize to that effect without delay.

(Revocation of Confirmation)

Article 5

1 The Minister of Agriculture, Forestry and Fisheries may, in cases where they have obtained new scientific knowledge or in other cases, revoke the relevant confirmation when they find there is a risk of the production of hazardous livestock products, or the production of livestock products being hindered by damage to livestock, etc., in connection with the use of feeds or feed additives for which the confirmation has already been obtained.

2 As to the revocation of confirmation set forth in the preceding paragraph, it shall proceed as directed in the provisions of Article 3, paragraph (2) and the preceding Article.

Appended Form (Re: Article 2, Paragraph (1))

Month Date Year

To the Minister of Agriculture, Forestry and Fisheries

Address (location of principal office
in the case of a corporation)
Name (name of the corporation and its representative
in the case of a corporation)

Based on the Procedures for Safety Assessment of Feeds and Feed Additives Derived from Recombinant DNA Technology (Ministry of Agriculture, Forestry and Fisheries Notification No. 1780, November 26, 2002), we will apply for the confirmation of the safety of the following items in the attachment:
Feeds derived from recombinant DNA technology
Feed additives derived from recombinant DNA technology

(Notes)
1 The paper size shall be Japanese Industrial Standards A4 size.
2 Characters shall be clearly written in standard style using ink, etc.

Appended Form 1 (Re: Article 2, Paragraph (2))

Documents attached to the written application for confirmation in cases where feeds contain organisms (excluding microorganisms) obtained by recombinant DNA technology

1 Information related to outline of the items subject to review

2 Information related to the properties of existing varieties (referring to the host (in recombinant DNA technology, referring to living cells and individuals into which a gene or DNA is transferred; the same shall apply hereinafter) and the whole variety which is of the same species as the host and is commonly distributed as food or feed; the same shall apply hereinafter) used for comparison in a safety review
   1 Information related to the taxonomic positioning of existing varieties
   2 Information related to feeding performance of livestock animals, etc., using existing varieties
   3 Information related to the method of using existing varieties
   4 Information related to genetic ancestors of existing varieties, the history of breeding and development, and related plant species
   5 Information related to component, etc., of existing varieties
   6 Information related to contamination caused by exogenous factors that adversely affect livestock animals in the cultivation and distribution process of existing varieties
   7 Information related to safe use of existing varieties
   8 Information related to parasitic and fixing properties of existing varieties

3 Information related to differences from existing varieties of recombinants (in recombinant DNA technology, referring to hosts into which the gene of interest or DNA is transferred; the same shall apply hereinafter)
   1 Information related to traits to be newly added or altered
   2 Information related to the purpose of use
   3 Information related to the method of use
      (1) Information related to cultivation methods, harvest time, seed production, and management methods
      (2) Information related to ingested (edible) parts for livestock animals, etc., and methods of preparation and processing
      (3) Information related to the amount of intake of livestock animals, etc.
   4 Information related to differences from existing varieties that need to be examined for safety
   5 Information related to reasons if those other than existing varieties are used for comparison

4 Information related to the construction of inserted DNA (referring to DNA inserted into a vector (referring to a nucleic acid molecule that carries the gene of interest or DNA to transfer into a host, propagate, or express in it; the same shall apply hereinafter); the same shall apply hereinafter), gene products (referring to RNA and protein derived from introduced gene (referring to a gene integrated into a vector or host; the same shall apply hereinafter); the same shall apply hereinafter) and construct (referring to a nucleic acid molecule constructed to appropriately express a new trait by an introduced gene or DNA or to provide a new function; the same shall apply hereinafter)
   1 Information related to names and origin of vectors
   2 Information related to properties of vectors
      (1) Information showing the number of bases of the vector and its sequence
      (2) Information related to not containing any base sequences which are known to be harmful
      (3) Information related to genes involved in the selection of recombinants (including antibiotic resistance marker genes; the same shall apply hereinafter)
      (4) Information related to transmissibility and autonomous mobility
      (5) Information related to existing varieties dependency
   3 Information related to the donor of inserted DNA
      (1) Information related to name, origin, and classification
      (2) Information related to safety
   4 Information related to the properties of introduced genes and their gene products
      (1) Information related to the function of introduced genes
      (2) Information related to antibiotic resistance marker genes among genes involved in the selection of recombinants
      (3) Information related to regions involved in the expression of introduced genes and genes involved in the selection of recombinants
         A. Information related to promoters
         B. Information related to terminators
         C. Information related to not containing any base sequences which are known to be harmful
         D. Information related to its origin and properties if any other base sequences involved in the regulation of the expression of the introduced gene are integrated
   5 Other information related to the function of introduced genes and the properties and function of expressed proteins
   6 Information related to the method of incorporating inserted DNA to the vector, etc.
   7 Information related to constructs
      (1) Information related to the number of bases and their sequence
      (2) Information related to insertion area
      (3) Information related to purity

5 Information related to recombinants and transgenic plant lines

1 Information related to gene transfer
   (1) Information related to the method of introducing genes into existing varieties
   (2) Information related to transgenic plant lines
   (3) Information related to the number of copies and the neighbor sequence of inserted genes
   (4) Information related to the stability of introduced genes in transgenic plant lines
   (5) Information related to the presence or absence of open reading frames (hereinafter referred to as “ORF”) and the possibility of transcription and expression thereof
2 Information related to the expression site, expression time, and expression level of gene products in transgenic plant lines
3 Information related to the amount of protein intake of gene products
4 Information related to the susceptibility of gene products (limited to protein) to physicochemical treatment
5 Information related to the effects of transgenic plant lines on metabolic pathways (including information related to the possibility to react with substrates contained in existing varieties, native species, and their related species)
6 Information related to differences from existing varieties
   (1) Information related to nutrients, harmful physiologically active substances, etc.
   (2) Information related to the composition or metabolic system of altered nutrients
   (3) Information related to the ability to survive and proliferate in the external environment
   (4) Information related to limiting factors on the ability to survive and proliferate
   (5) Information related to the inactivation method
7 Information related to the approval and use of feeds, etc., in foreign countries

6 When safety cannot be confirmed based on information of 2 to 5 above, information related to the results of the necessary studies among the following studies:
1 Single-dose toxicity studies
2 Repeated-dose toxicity studies (short-term)
3 Repeated-dose toxicity studies (long-term)
4 Multi-generational breeding studies
5 Carcinogenicity studies
6 Mutagenicity studies
7 Developmental toxicity studies
8 Feeding trials using target animals
9 Other studies

Appended Form 2 (Re: Article 2, Paragraph (2))

Documents attached to the written application for confirmation in cases where feeds contain microorganisms obtained by recombinant DNA technology or where feeds are produced using microorganisms obtained by recombinant DNA technology

1 Information related to properties of hosts used for comparison in safety assessments and the differences from recombinants
   1 Information related to hosts and inserted DNA
      (1) Information related to the taxonomic positioning and origin of host species (scientific names), strain names, etc.
      (2) Information related to the taxonomic positioning and origin of species names, strain names, and line names of DNA donor
      (3) Information related to the properties of inserted DNA and the method of introduction
   2 Information related to the record of the use of hosts in the manufacture of feeds or the history of their use in feeds
   3 Information related to the components, etc., of hosts
   4 Information related to the method of using hosts and recombinants in feeds and their differences
      (1) Information related to the methods of manufacturing and storage
      (2) Information related to the intended uses and patterns of use
      (3) Information related to the amount of intake of livestock animals, etc.
      (4) Information related to the methods of preparation and processing
   5 Information related to differences between recombinants and hosts that need to be examined in safety assessments

2 Information related to hosts
   1 Information related to the taxonomic positioning of species names (scientific names), strain names, etc.
   2 Information related to pathogenicity and production of harmful physiologically active substances, etc.
   3 Information related to parasitic and fixing properties
   4 Information related to not being contaminated by foreign pathogenic factors (such as viruses)
   5 Information related to pathogenicity and production of harmful physiologically active substances of related strains of the host

3 Information related to vectors
   1 Information related to names and origins
   2 Information related to properties

(1) Information showing the number of bases of the vector and its sequence
(2) Information related to not containing any base sequences which are known to be harmful
(3) Information related to drug resistance
(4) Information related to transmissibility
(5) Information related to host dependency

4 Information related to inserted DNA, gene products, and construction of constructs
1 Information related to donor of the inserted DNA
(1) Information related to name, origin, and classification
(2) Information related to safety
2 Information related to the properties of inserted DNA or an introduced gene and its gene products
(1) Information related to the methods for cloning or synthesizing inserted DNA
(2) Information related to the number of bases and their sequence, and a restriction map with a restriction enzyme
(3) Information related to the functions of introduced genes
3 Information related to regions involved in the expression of introduced genes and antibiotic resistance marker genes
(1) Information related to promoters
(2) Information related to terminators
(3) Other information related to its origin and properties if any other base sequences involved in the regulation of the expression of the introduced gene are integrated
4 Information related to the method of incorporating inserted DNA to vectors
5 Information related to constructs
6 Information related to the method of introducing DNA into the host

5 Information related to recombinants
1 Information related to gene transfer
(1) Information related to the number of copies and the neighbor sequence of inserted genes
(2) Information related to the presence or absence of ORF and the possibility of transcription and expression thereof
2 Information related to the expression levels of gene products in the recombinant
3 Information related to the safety of antibiotic resistant marker gene
4 Information related to the stability of genes introduced into the recombinant
5 Information related to the effects of gene products on metabolic pathways
6 Information related to differences from the host
7 Information related to the inactivation of the recombinant

8 Information related to the methods of handling, storage, and management of the recombinant

6 Information related to confirmation of the absence of live recombinants

7 Information related to conventional feeds used for comparison in a safety assessment of feeds produced using recombinants

8 Information related to the method for manufacturing feeds produced using recombinants, and their nutrients, etc.
1 Information related to the method of manufacture
2 Information related to macronutrients
3 Information related to the safety of ingredients derived from production
4 Information related to the effects on other microorganisms coexisting in the production process
5 Information related to the approval and use of feeds, etc., in foreign countries

9 When safety cannot be confirmed based on information of 2, 3, 7, and 8 above, information related to the results of the necessary studies among the following studies:
1 Single-dose toxicity examination
2 Repeated-dose toxicity examination (short-term)
3 Repeated-dose toxicity examination (long-term)
4 Multi-generational breeding examination
5 Carcinogenicity examination
6 Mutagenicity examination
7 Developmental toxicity examination
8 Feeding trials using target animals
9 Other examinations

Appended Form 3 (Re: Article 2, Paragraph (2))

Documents attached to the written application for confirmation in cases where feed additives are produced using organisms obtained using recombinant-DNA techniques

1 Information related to the outline of the items subject to assessment

2 Information related to the properties of feed additives, hosts, etc., used for comparison in a safety assessment, and the differences from recombinant feed additives and recombinants
  1 Information related to the properties and use of conventional feed additives
    (1) Information related to names, origin and active ingredients
    (2) Information related to the method of manufacture
    (3) Information related to the intended uses and patterns of use
  2 Information related to hosts
    (1) Information related to the taxonomic positioning and origin of host species (scientific names), strain names, etc.
    (2) Information related to the record of the use of hosts in the manufacture of feed additives or the history of their use in feeds
    (3) Information related to the components, etc., of hosts
  3 Information related to inserted DNA
    (1) Information related to the taxonomic positioning and origin of species names, strain names, and line names of the donor of inserted DNA
    (2) Information related to the properties of inserted DNA and the method of introduction
  4 Information related to the properties and use of recombinant feed additives
    (1) Information related to product names and active ingredients
    (2) Information related to the method of manufacture
    (3) Information related to the intended uses and patterns of use
    (4) Information related to the properties of active ingredients and the amount of estimated intake of them compared with conventional feed additives
  5 Information related to the differences between recombinant feed additives and existing feed additives, and between recombinants and hosts, etc., that need to be considered in a safety assessment

3 Information related to the base sequence (inserted DNA, gene products, and construction of constructs) used for gene transfer
  1 Information related to the names and origin of vectors
  2 Information related to the properties of vectors
    (1) Information showing the number of bases of the vector and its sequence
    (2) Information related to not containing any base sequences which are known to be harmful
    (3) Information related to genes involved in the selection of recombinants
    (4) Information related to transmissibility
    (5) Information related to host dependency

3 Information related to the donor of inserted DNA
4 Information related to the properties of introduced genes and their gene products
5 Information related to the regions involved in the expression of introduced genes and genes involved in the selection of recombinants
   (1) Information related to promoters
   (2) Information related to terminators
   (3) Other information
6 Information related to the method of integrating inserted DNA into the vector, etc.
7 Information related to constructs
   (1) Information related to the number of bases and their sequence
   (2) Information related to insertion area
   (3) Information related to purity

4 Information related to recombinants
1 Information related to the purpose and method of using recombinants
2 Information related to differences from the host
3 Information related to gene insertion
   (1) Information related to the number of copies and the neighbor sequence of inserted genes
   (2) Information related to the presence or absence of ORF and the possibility of transcription and expression thereof
4 Information related to the safety of the genes involved in the selection of recombinants

5 Information related to the raw materials besides the recombinant and production equipment

6 Information related to recombinant feed additives
1 Information related to the approval and use, etc., in foreign countries
2 Information to rule out the mixing of recombinants
3 Information related to the safety of non-active ingredients derived from manufacturing
4 Information related to the method of purification and its effects
5 Information related to changes in ordinary components which suggest toxicity due to changes in content

7 When safety cannot be confirmed based on information of 2 to 6 above, information related to the results of the necessary studies among the following studies:
1 Single-dose toxicity examination
2 Repeated-dose toxicity examination (short-term)

3 Repeated-dose toxicity examination (long-term)
4 Multi-generational breeding examination
5 Carcinogenicity examination
6 Mutagenicity examination
7 Developmental toxicity examination
8 Feeding trials using target animals
9 Other examinations