Points to Be Noted Regarding Notification

I. Points to be noted regarding notification

A notifier attaches necessary supporting data according to the form of Attachment 3-1 or Attachment 3-2 of the Guidelines, and submits them to the Ministry of Agriculture, Forestry and Fisheries (MAFF) with data that shows that 4. or 5. below is satisfied.

1. The name and contact (address, telephone number, e-mail address, etc.) of the person in charge of inquiry concerning notification forms are written in the format remarks column.

2. The name of notified item is written to clearly describe characteristics of the notified feed and feed additive.
(ex.) ***-enhanced *** strain (name of feed), anti-*** *** (name of feed)
(ex.) *** produced using *Escherichia coli* *** strain (name of feed additive)

3. It should be noted that the entries in the Publication Form are published on the website of the MAFF.

4. For genome edited feed, the following should be noted.

1) Names of item and breed and summary (usage and intended use) of the developed feed
- The names of the item and breed indicate the information and strain name which can identify the item. Also, the strain name alone is acceptable.
- When the intended use and usage are different from those of the existing feed, their summaries are described.

2) Details on method of genome editing technology and genetic modification used
- The type of genome editing technology used and the operation which was actually performed are described.
- The name of the target gene and its function are specified.
- The breeding process such as selection for producing the developed feed breed shall be described in the order of generations so that the breeding operations such as self-fertilization and cross-fertilization is clear.
- It is confirmed and described that intended changes in the target gene and the resulting transformation have been achieved in an appropriate stage of the breed selection process. The intended changes in the target gene are confirmed using a sequencer, etc. The transformation is confirmed by the method selected by a developer, etc. on a specific case-by-case basis.

- When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.

3) Information on confirmation that there are no remaining foreign genes or their parts
- When a foreign gene is transferred in the use of genome editing technology and subsequently removed, it is confirmed that no foreign gene or its parts remain using appropriate methods, including Southern blot, next-generation sequencer, and PCR.
- When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.
- When a foreign gene is present or valid data to determine that the foreign gene has been removed are not submitted, the technology is regarded as recombinant DNA technology and the process of safety assessment has to be gone through in accordance with the Procedures for Safety Assessment of Feeds and Feed additives Derived from Recombinant DNA technology (MAFF Notification No. 1780 of 2002, hereinafter referred to as "Procedures for Safety Assessment" based on the Ministerial Ordinance on the Specifications and Standards of Feed and Feed Additives (MAFF Notification No. 35 of 1976, which is hereinafter referred to as "Ministerial Ordinance on the Specifications and Standards.".

4) Information on confirmation that confirmed changes in DNA do not cause adverse effects on livestock health and human health through livestock products or increase of known toxic substances
- Sequences which are presumed to have a high probability of off-target effect occurring are confirmed, as appropriate, by a combination of several appropriate search tools, such as CRISPRdirect, and then checked by searching homology with existing toxic substances and the results are submitted. The names and versions of search tools used, etc. are specified.
- The fact of confirmation results showing no corresponding substances is mentioned.

5) Information on changes in major components (nutrient components only) related to the target metabolic system for items which modification affecting the metabolic system was performed in order to increase or decrease specific components.
- Information on increase or decrease of other substances associated with modification of the metabolic system (list of substances related to the target metabolic system (ex. Table of fatty acid composition, metabolic pathway map, etc.) is submitted.
- When specific substances accumulate due to modification of the metabolic system, the toxicity and the accumulation of such substances are estimated from the existing information and then the information indicating that they do not affect livestock health and human health through livestock products (ex. Data on risk of excessive supply to livestock collected by a developer, etc. based on the literature) is submitted. When the toxicity of the substances cannot be confirmed, further information is not required.
- In a feed analysis, multiple samples are analyzed and the name of analysis method used, instruments used, testing conditions, detection limits, etc. are specified.

6) Year and month of marketing (*Notify the MAFF of it after marketing according to the form of Attachment 4 of the Guidelines)

- The year and month when the feed which was first commercialized out of the notified genome edited feeds or feeds obtained using such feeds was marketed are reported.

5. For genome edited feed additives, the following should be noted.

1) Name of the developed feed additive

- The name of the item indicates the information which can identify the item.

2) Details on method of genome editing technology and genetic modification used

- The type of genome editing technology used and the operation which was actually performed are described.
- The name of the target gene and its function are specified.
- It is confirmed and described that intended changes in the target gene and the transformation have been achieved by microorganisms used in manufacturing. The intended changes in the target gene are confirmed using a sequencer, etc. The transformation is confirmed by the method selected by a developer, etc. on a specific case-by-case basis.
- When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.
- The safety of microorganisms used in manufacturing and the summary of manufacturing process are specified.
- The summary to be published includes major genome editing technology used and clear description of effects of modification of the target gene on the metabolic system.

3) Information on confirmation that there are no remaining foreign genes or their parts

- When a foreign gene is transferred in the use of genome editing technology, it is confirmed that the foreign gene and its parts do not remain using appropriate methods, including Southern blot, next-generation sequencing, and PCR.
- When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.
- When a foreign gene is present or valid data to determine that the foreign gene has been removed are not submitted, the technology is regarded as recombinant DNA technology and the process of safety assessment is gone through based on the Procedures for Safety Assessment.

4) The fact that the additive complies with the compositional standards specified in the Ministerial Ordinance on the specifications and Standards.

- It is confirmed that the obtained feed additive complies with the compositional standards specified in the Ministerial Ordinance on the specifications and Standards. Submission of the information confirmed is not required.

- When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.
- It should be noted that non-compliance with the compositional standards specified in the Ministerial Ordinance on the specifications and Standards. is subject to the penalty based on the Act Concerning the Safety Assurance and Quality Improvement of Feed (Act No. 35 of 1953).

5) Year and month of marketing (*Notify the MAFF of it after marketing according to the form of Attachment 4 of the Guidelines)
- The year and month when the feed additive which was first commercialized out of the notified genome edited feed additives was marketed, are reported.

II. Others
- Prior to the notification, consult with the Animal Products Safety Division, Food Safety and Consumer Affairs Bureau, MAFF according to Attachment 1-1 or Attachment 1-2 of the Guidelines.