Medicines Evaluation Board

Explanatory notes for completing the electronic application form

Application for permission to conduct experiments on feed additives in accordance with Article 3(2) of Regulation (EC) No 1831/2003

https://www.formdesk.com/collegeterbeoordelingvangenees/aanvraagTPT

Veterinary Medicinal Products Unit

Version 1.2 – 13 juli 2026

Table of contents

1. Introduction

To obtain permission to conduct a experiment with an unauthorised feed additive, a dossier (application form with annexes) shall be submitted together with the application form. This dossier contains reports from which it can be concluded that the requested experiment can be carried out safely and responsibly.

This dossier shall clearly show that the main purpose of the experiments is to determine the effectiveness and/or safety of the additive. The experiments may be carried out in specialised research institutes or in practical establishments.

When applying for a permission, you must provide all the important data that is available. These data are necessary for the assessment of safety for humans, animals and the environment. On the basis of this information, it can be decided to take certain precautions. These precautions may be required during the processing of the product or feed under investigation. They may also concern the use of the animal product for human consumption after a possible withdrawal period.

For more information, see:

- Regulation (EC) No 429/2008
- EFSA guidelines:
  - Guidance on the identity, characterisation and conditions of use of feed additives
  - Guidance on the assessment of the safety of feed additives for the target species
  - Guidance on the assessment of the efficacy of feed additives
  - Guidance on the assessment of the safety of feed additives for the environment
  - Guidance on the assessment of the safety of feed additives for the users
  - Guidance on the assessment of the safety of feed additives for the consumer
  - Guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use

➔ Please note: for the application for permission to conduct experiments on feed additives, the Working Conditions Act and the Animal Experiments Act also apply.

Your request and the data provided by you will of course not be disclosed to third parties.

Because situations in which permission to conduct experiments is requested may vary and are often not standard, the overview below is an indication, which cannot be exhaustive. Once the application form has been received, the data will be validated and assessed. It is possible that you will receive additional questions before your application can actually be approved. These questions will be asked by e-mail. It is important that these additional answers are included in the original application form. You do this by making the changes in the fill-in fields of the copy application form that you received with the application. When you forward this original e-mail, you can complete or change the fields you have filled in.

The signatory is responsible for the entire experiment covered by this application.

General instruction:

- The use of other non-authorised substances (such as inert substances) is not covered by the permission to conduct experiments on feed additives. A licence for the use of veterinary medicinal products, feed or other substances in a experiment must be applied for on the basis of Article 2.1(1) of the Decree on veterinary medicinal products 2022. You can submit this license application to the NVWA via erkenningen@nvwa.nl;
- The legal deadline for assessing the application will only start when all necessary documentation has been received. When it appears in the meantime that additional information is needed to

assess the content of the application, the assessment period will be stopped until you have provided all additional information;

- During the validation phase, you may be asked once to provide additional information in response to questions asked. Further information may also be requested once during the assessment phase. In some cases, additional information may be requested again during the assessment phase. After this, a decision will be taken on the application on the basis of the data available at that time;
- When a new application partially contains the same information as a previously submitted application, you can cut and paste the information from the previously submitted application into this new application;
- Does the Dutch application relate to activities in more than one EU Member State? Then we would like to receive the complete application and authorisation(s) from the other Member State(s). In this way, we can quickly check whether we need information from the other Member State.
- You can save the form in the meantime if you want to continue filling in the application at a later time. You will then receive a code by e-mail with which you can fill in the application at a later time. When several people within the organization have to fill in a part of the application, you can share this code with your colleague, after which he can continue to fill out the form;
- After submitting the application, you will be kept informed by e-mail about the status of the application.

2. The electronic application form

The electronic application form (hereinafter **eAVF**) consists of several sections:

- Contact and address details
- Additive description
- General information about the experiment
- Substantive aspects of the experiment
- Appendices
- Confidential information
- Contact person
- Signing

Each question of the eAVF contains a short explanation under the  sign. This instruction provides extensive information about filling in the eAVF and providing information.

2.1. Contact and address details

Fill in the details of the applicant and trial coordinator/researcher. Please also fill in the details of the manufacturers of experimental feed and/or premix. Under ‘Locations where the experiment is carried out’, indicate where the experiment takes place. ‘If there are more pilot sites, the list can be expanded. Under ‘Other participating institutes/companies in the experiment’ you can fill in additional

institutes/companies. Explain clearly the role of the institution/company. If there are more participating institutes, the list can be expanded.

It is important that the addresses provided are complete and correct. This is in connection with a possible review by the Dutch Food and Consumer Product Safety Authority (NVWA). During this review, physical visits shall be made to the sites where the experimental feed is produced and where the animals are kept.

2.2. Additive description

This section is expected to provide a sufficiently comprehensive and specific description of the additive. Certificates of analysis, declarations, specifications, etc. must be dated. *These documents may not be older than 3 years .*

2.2.1. Additive description

- Full and unambiguous ***name of the additive .***
- ***Category and registration number*** from the existing registration or a proposal for classification.
- Numbers of EFSA ***opinions*** present , if the additive has already been assessed by EFSA.
- Any ***other authorisation*** as a feed or food additive, veterinary medicinal product or other type of authorisation of the active substance shall be specified.
- ***Form of the product*** (powder, granules, solution, suspension, etc.) and ***intended administration*** (feed or water).
- ***Identity and composition*** of the whole additive: the active substance(s)/medicinal products and all other ingredients of the additive shall be indicated. Specify the concentration or amount of the active substance and the proportion by weight of all constituents (**up to 100%**) in the final product (for details see 2.2.1.1 and 2.2.1.2 in Annex II to Regulation (EC) No 429/2008). Please note the following:

    - ***For micro-organisms:*** the number of cells or spores expressed as CFU per gram.
    - ***For modified (production) organisms:*** detailed description of the origin of the organism and the nature of the modification.
    - ***For enzymes:*** each activity declared must be described and the number of units of each activity in the final product.
    - If the active ingredient of the additive is a ***mixture of substances,*** clearly indicate for each substance what it is (and the amount present). You should also mention the proportions in the mixture.
    - ***Other mixtures,*** e.g. plant extracts, should be clearly defined and the substances responsible for the action of the mixture and/or its main constituents should be identified. All reasonable efforts are expected to be made to document the composition of the mixture as fully as possible. The constituents, including any substances of concern, shall be fully and reasonably described. Justify that the product derived from the plant(s) concerned is not considered a prohibited product in any legislation. Extracts, tinctures and other processed forms are generally considered as additives. If they are complete parts of plants, they are usually considered as feed material. Safety must be demonstrated.

2.2.2. Absence of contaminants

Information about chemical contaminants (heavy metals) must always be provided. Information on microbial contaminants should be provided for microorganisms (probiotics), fermentation products, plant products and animal products. Substances with toxic or other undesirable properties that have not

been intentionally added and do not contribute to the activity of the additive shall be identified and quantified by the applicant.
This can be done by means of a certificate of analysis or the product specifications. In the absence of contaminants, reference may be made to this analysis.

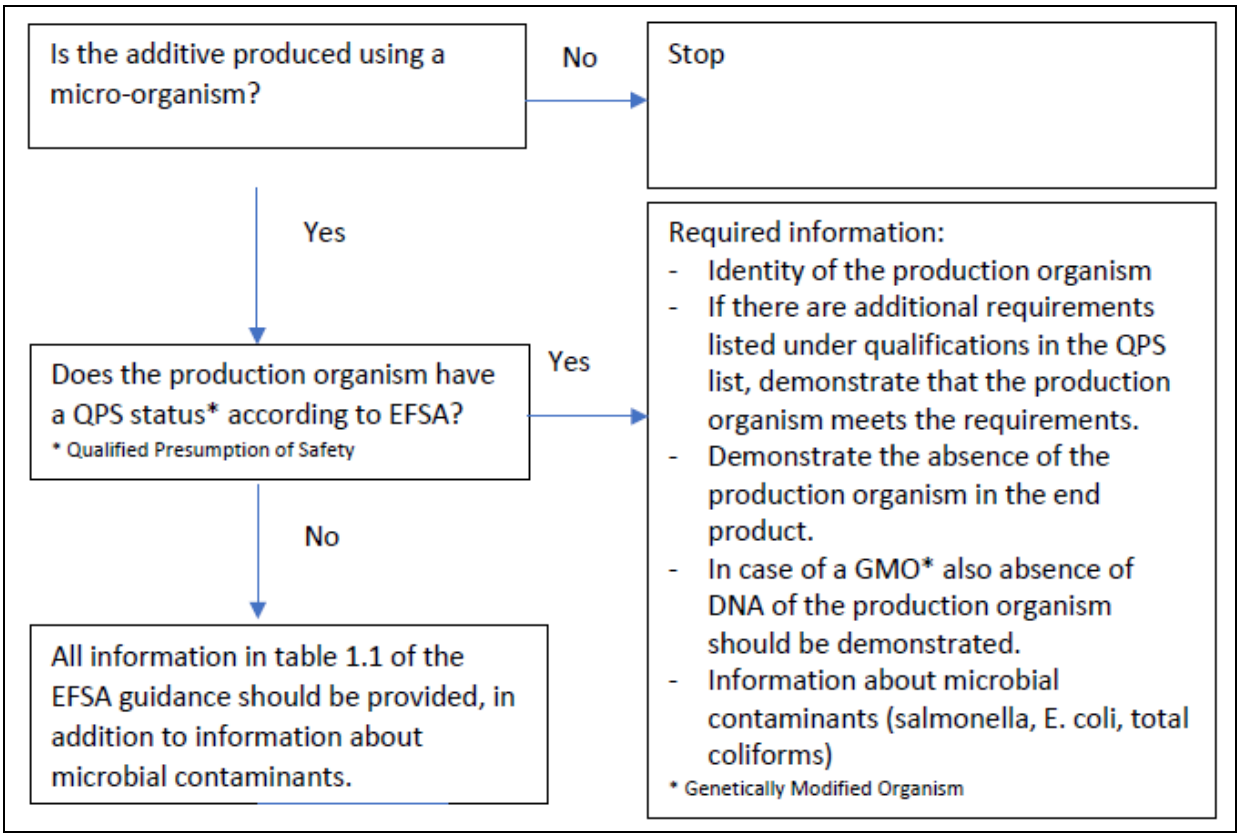
2.2.3. Microorganisms (probiotics) and production organisms (fermentation products)

Microorganisms may be present in products, such as probiotics. They can also be used as a production organism, for example for the production of enzymes or amino acids. The decision tree in Figure 1 indicates which information must be provided for fermentation products. This information is also explained in the text.

- ***Name of the (production) organism:*** the name and taxonomic classifications of the (production) organism.
- ***QPS status:*** A Qualified Presumption of Safety (QPS) status is the result of a pre-assessment that addresses the safety aspects for humans, animals and the environment. During this process, EFSA assesses the taxonomic identity of the micro-organism, its domain of knowledge and potential safety risks. Micro-organisms that are not well defined, for which some safety risks have been identified or for which it is not possible to conclude whether they pose a safety risk to humans, animals or the environment are not considered suitable for QPS status and must undergo a full safety assessment. Check here if the requested strain is on the QPS list (Appendix E Updated list of QPS recommended biological agents).
    - ***What is QPS: Does the (production) organism meet the requirements listed under the QPS qualifications?***
      Once you have found the strain in the table, look for the qualifications (Qualification 1,2,3..). Microorganisms only have QPS status if these qualifications are met. To substantiate the QPS status, this information should also be submitted.
    - ***Not QPS: Demonstrate that the (production) organism is safe***
      If microorganisms do not have QPS status, all information should be provided according to EFSA Guidance (see Table 1 of EFSA Guidance on the characterisation of microorganisms used as feed additives or as production organisms). The protocol used for the routine screening of production batches for contaminants and impurities shall be described. In the case of products produced by fungi, mycotoxins are important; For bacteria bacterial toxins are important.

- **In addition, for fermentation products,** the absence of production organisms in the additive shall be demonstrated.
- **For fermentation products produced by a genetically modified organism,** additional absence of the production organism **and** recombinant DNA of the production organism shall be demonstrated (see EFSA Guidance on the characterisation of microorganisms used as feed additives or as production organisms).

Figure 1. Decision tree for the information needed for the assessment of production organisms (based on EFSA Guidance on the characterisation of microorganisms used as feed additives or as production organisms).



2.3. General information about the experiment

For a good picture of the experiment, this information must be filled in briefly and clearly:

- legal basis: whether the application complies with Regulation (EC) No 1831/2003 (e.g. product, purpose, documentation, etc.);
- purpose of the experiment;
- target animal (species, age, sex, etc.);
- content and design (is it a scientific experiment, e.g. negative control, experiment design and dosage, etc.);
- duration of the experiment in days;
- period for which you want to request permission: enter the period for which you want to request permission. The granted permission expires after the specified period or, in the event of completion of the experiment before that time, 7 days after its completion. Is the period for which you want to apply for permission longer than 12 months? Please explain why the requested permission period is longer than 12 months. Indicate the planned start date as precisely as possible.
- As an applicant, you are obliged to send the Veterinary Medicinal Products Unit a notification at least 14 days before the start of the experiment with the exact start and end date of the experiment, because this may deviate from the planned start date of the experiment. The start date is the day on which the animals receive the experimental feed and the end date is the day on which feeding is stopped. The delivery and removal of the animals can take place at a different time. This because the Food and Consumer Products Safety Authority (NVWA) may carry out checks. These checks are intended to confirm that the experiments are carried out in accordance with the conditions. You can start carrying out experiments on the date indicated. You do not need to wait for any checks. You send the notification by e-mail to diervoeders@cbg-meb.nl.

2.4. Substantive aspects of the experiment

2.4.1. Production and processing of experimental feed

Experimental feed production

Describe clearly how the feed is produced in the experiment (including any premix). Indicate the proportion of the premixture in the feed. This also applies to relevant aspects of transport, storage and administration to the animals (including any water application).

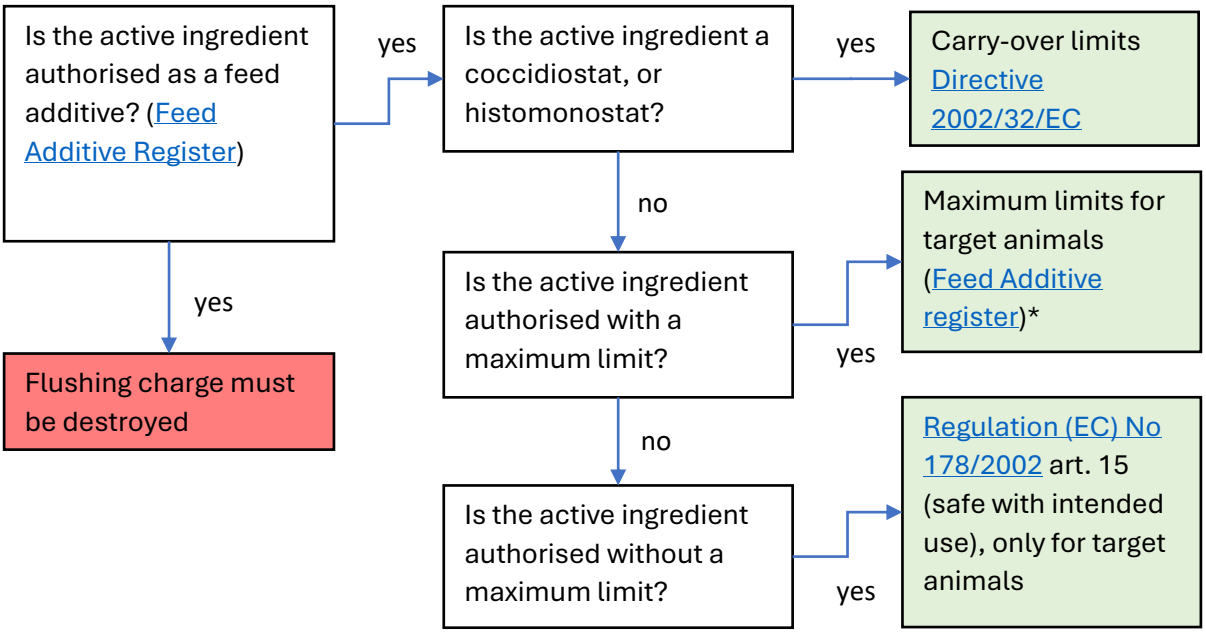
The feed business must have the correct registration/approval in accordance with the Hygiene Regulation (Regulation (EC) No 183/2005). In special cases, additional requirements apply. Because this Regulation has a wide scope, requirements may also be imposed in some cases on other types of (production) sites (e.g. the production of a premix or the processing of the additive via a feed mixer on a livestock farm, etc.).

If additional conditions/data are required beyond the basic requirements as set out in the Hygiene Regulation, these must be provided (e.g. homogeneous mixing and carry-over for coccidiostats, etc.). More information on carry-over can be found on the NVWA carry-over page.

If the production line is flushed to reduce carry-over, describe how the flushing is carried out and the destination of the flush charge. To do this, use the diagram in Figure 2.

Figure 2. Diagram of processing conditions for experiment exemptions of feed additives.

Basis: the flushing charge can only be used outside of the experiment, under certain conditions, when the active ingredient is already authorised, for instance for another target animal, in a different concentration, or otherwise. The product containing the flushing charge has to comply with the regulations mentioned in the green boxes in the diagram as well as other applicable legislation.



* When processing the flushing charge, it must be checked whether the additive is authorised for the target animal and the maximum level applicable to the total ration of this target animal must be taken into account.

Explanation of the diagram

If the applicant wishes to process the flushing charge into feed, the test additive must be authorised in the EU and the product in which the flushing charge is incorporated must comply with the requirements in the right-hand side of the diagram (green blocks). For EU-authorised feed additives, a comprehensive safety assessment has already been carried out by EFSA. Therefore, the green part of the scheme is aligned with the already existing standards. Here a flushing charge with an authorised additive may be processed in a feed in which this additive is authorised, under the requirements that apply to it (e.g. standards, homogeneity, declarations and precautions).

If the trial additive is not authorised in the EU, the flushing charge should be demonstrably labelled as unfit for animal and human consumption and destroyed. The aim is to prevent the additive not authorised in the EU from entering the food chain or the environment.

Destruction means that the flushing charge must be incinerated or disposed of to a technical destination outside the feed chain (biogas production, fuel), provided that main or by-products remain outside the food chain or the environment. The use of the flushing charges for the production of animal feed (means, e.g. DDGS) or fertilising material (digestate) is expressly prohibited.

The collection of laboratory feed residues is subject to the same requirements as Article 18 of Regulation (EU) 2019/4.

Other types of processing

Authorisations may cover preliminary stages of the final product/studies. This means that different situations may be involved (e.g. tablets, dispensing over the feed, dispensing into the rumen/gut, etc.). Furthermore, there are additives for administration in drinking water. In these cases, information on the above cases, where applicable, should be provided in accordance with the adapted format.
Where applicable, how they are implemented and controlled shall be described for all of the above points.

Dosage and amount of additive

In this section, a complete and clear calculation of the amount of additive required is expected. Indicate which feed intake is used in the calculations, as well as the justification for the reserve amount of feed additive and experimental feed.

This table may be added as an annex:

Treatment	Description	# animals	Experiment duration, days	Dose			Required amount of experimental feed				Dosage per experimental feed	Required amount of addtitive		
				mg/kg DMI	mg/d	g/d	Intake, kg/head/d	Total, kg	Margin (10%)	Total, kg	mg/head/d	mg/kg product	mg/head/day	Total,mg
1	Control													
2	2x													
3														
4														
5														
	Total													

Assumptions:

2.4.2.Safety for the user

The safety for the user must be adequately ensured before the experiment is carried out. This should be indicated for all relevant situations, such as in the production of the experimental feed, administration to the animals in drinking water application, etc.

If any operator other than the one involved in the production of the feed is at risk, this should be described separately. Submitting an SDS is a good tool for this, but a different type of description can also satisfy.

2.4.3.Target animal safety

For certain additives, the safety for the target animals is taken for granted, without the need for specific information (see EFSA Guidance, Section 2). For other additives, safety for the target animals can be assessed through extensive literature reviews of studies on target animals, toxicity data (existing or new) from repeated dose studies in laboratory animals or tolerance studies in target animals.

In this section, all possible risks to the target animal (dosage, contamination, etc.) are expected to be considered when determining the posology.

Substantiate the chosen dose in the experiment with the literature data (e.g. NOAEL and BMDL) or the results from other studies. Use the information in the EFSA Guidance on the assessment of the safety of feed additives for the target species and/or the FACTS tool (The Feed Additives maximum safe Concentration in feed for Targets Species) to derive a safe daily concentration in the feed for the target species by applying an uncertainty factor (default 100 to cover intra- and interspecies variation).

2.4.4.Other safety aspects

Where permitted, situations involving additional risks shall be described and controlled in such a way that the risks are acceptable.

A challenge test in animal experiments is an experiment in which animals are artificially exposed to a specific microorganism (often pathogenic), to observe the animal's response and assess the safety or effectiveness of a particular treatment, additive or product. Such experiments are, for example, a requirement in the efficacy tests for coccidiostats.

Describe how safety for humans, animals and the environment is ensured during the challenge.

If a challenge with a pathogenic organism is carried out, it is possible that an additional questionnaire will be sent after submission of this form, if it appears that insufficient information has been provided to properly assess the challenge.

2.4.5.Destination of animals and animal products and residual experimental feed

Withdrawal periods

The possibility of residue formation in animal products (meat, milk, eggs) used for consumption from the experiment should be described. It shall be clearly described whether residues of the additive are expected in the animal products that become available for consumption and, if so, how high the level in the animal products is expected. This can be done, for example, by means of residue studies in meat, milk and/or eggs. It can also be described how the substance behaves in the target animal (absorption, distribution, metabolism and excretion).

In addition, the potential adverse effects of the substance in humans and the exposure levels at which these effects may occur should be described.

On the basis of the complete amount of information, it can be concluded whether a withdrawal period is necessary.

As a result, clearly justified withdrawal periods should be proposed.

Residual experimental feed and additive

Any residues of test feedingstuffs and/or additives shall not be used outside the experiment. It must be indicated how these are disposed of responsibly.

Describe the method by which the experimental feed is destroyed. A test food containing, for example, a living micro-organism (for example, probiotics) must be destroyed in a different way than a test food containing enzymes. Failure to properly destroy a food sample may affect the safety/health of other animals, humans and the environment.

2.5. Attachments and confidential information

- If you would like to refer to an annex to answer a question, please indicate which annex you are referring to. Provide the attachment with a name and number that clearly represents the content of the attachment. Never add the files as *zip. When forwarding the application after filling in, all attachments are archived.
- If you want to provide additional information with the application, for example an offer letter, you can add it in this section.
- Justification for the absence of data. If you consider that it is not necessary to provide certain data, you must provide a justification for this.
- If the supplier of the additive considers certain data to be confidential, it is possible to submit these data (without you as the applicant) directly to the Veterinary Medicinal Products Unit. The supplier must hereby authorise the assessment of this data.

- You can request a Secure transfer link for the supplier from the Veterinary Medicinal Products Unit. You can indicate this under the heading ‘Confidential information’.

2.6. Contact person and signature

Here you fill in the details and declare that you have filled in the application truthfully. As an applicant, you are personally responsible for the correct execution of all parts of the experiment.

3. Concluding remark

Be sure to complete the form completely and accurately to avoid delays in processing your application.

The application form is part of the decision on the permission to conduct experiments on feed additives.

In addition, the NVWA carries out the physical inspections (reviews) on the basis of the data in the latest version of the application form submitted. Incomplete or incorrect information may therefore lead to delays, additional questions or an incorrect assessment of your application.

The Veterinary Medicinal Products Unit strives to complete your application within 8 weeks after the application is complete. If this is necessary, the decision period can be extended once for a reasonable period (normally 6 weeks). If this is the case, we will inform you within the decision period of our decision to extend the decision period. Therefore, make sure that you submit your application well before the start of the experiment. When you are asked for additional information, this period ends. It is therefore important to provide additional information fully and quickly. This prevents your application from taking an unnecessarily long time.

For the processing of this application, assessment costs in accordance with Article 59(1) of the Feed Regulation (Regeling Diervoeders 2012) will be charged to you.

If you have any questions, please contact us at diervoeders@cbg-meb.nl.

4. Overview of changes

Main changes in version 1.2 compared to version 1.1 dated 11 March 2025:

- The general fill-in instruction, as also included in the application form itself, is included in the explanatory notes. This is because the explanatory notes are also available in English;
- It has been included that if the Dutch application relates to activities in more than one EU Member State, we would like to receive the complete application;
- Under 2.3 the period for which you want to apply for permission may now also be longer than 12 months. If this is the case, an argument must be made for this. It is explained what is meant by start and end date of the experiment;
- Under 2.4 dosage and amount of additive, here is shown in an example table how this data can be supplied;
- The text under withdrawal periods has been further clarified.