EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Frequently asked questions about parallel distribution

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1. General information

1.1. What is parallel distribution?

Centrally authorised medicinal products ("CAPs") put on the market of one Member State can be marketed in any other Member State by a distributor, independently of the marketing-authorisation holder ("parallel distribution"). Parallel distribution (hereinafter also "PD") pertains to all centrally authorised products and is checked by the European Medicines Agency (hereinafter "the Agency").

Centrally authorised products are marketed in all Member States under the same name and must comply with the Community Marketing Authorisation. The task of the European Medicines Agency is to check compliance of products distributed in parallel with the conditions laid down in Community legislation on medicinal products and in the marketing authorisation of the product. In this case the parallel distributors must send an initial notification for parallel distribution to the Agency.

Parallel import on the other hand concerns only nationally authorised products and is authorised by the national competent authority of the Member State of import based on the similarity to the product distributed in the Member State of destination by the marketing-authorisation holder (hereinafter "MAH").

1.2. What are the procedures of parallel distribution? Rev. May 2024

The Agency fulfils its obligation to check the conditions of parallel distribution by means of five procedures.

Initial Notification

An initial notification is a parallel distributor's notification to the Agency, informing of their intent to source, repackage and distribute a centrally authorised medicinal product from one or more Member States to one or more Member State(s). The Agency checks compliance of the particulars of this notification with the marketing authorisation and EU legislation on medicinal products and issues a PD notice (regulatory entitlement) when the check confirmed that for the medicinal product distributed in parallel, the conditions laid down in the EU legislation on medicinal products and in the marketing authorisation were observed at the time of issuance. For further information on how to submit an initial notification, please refer to the section Initial notification.

Safety Updates

Urgent safety updates to the originator product information are notified to the parallel distributor by EMA on a monthly basis. The resulting safety update by the parallel distributor to verify the update to their product information shall be submitted within a three-month timeframe of the notification by the Agency of the urgent safety update having occurred, otherwise the notification will be invalidated. Urgent safety update is not subject to any fee and it does not affect the duty to submit an annual update. One or more EU presentations of the same product with the same Member State of Destination can be included in a single submission. No other scopes of changes can be added to such notifications.

From 1 July 2024, the submission of urgent safety notifications will no longer be required. Parallel distributors will still be requested to implement safety-related changes to the product information within three months of the publication of the updated annexes, and within six months for non-safety-related changes. These changes will be reviewed as part of the annual update procedure. The discontinuation of the safety update notifications does not affect the timelines of the annual update nor the birthday date of the product.

For further information please refer to the section Safety updates/bulk changes/annual updates.

Bulk Change (change of manufacturer, change of name and/or address, reassignment of notices for parallel distribution)

A bulk change is a notification of changes that affect all parallel distributor's notices, at any point in time after the approval of the initial notification. The scopes of change are limited to changes in the-Re-packager's information, Update of parallel distributor's name and/or address, and Reassignment of PD notices. The procedure aims to provide the possibility of implementing a scope of change for all notices held by one company.

Update of parallel distribution notice status

The purpose of this procedure is to allow the parallel distributor to update the status of their notice to 'dormant', 'active' or 'withdrawn' in a simplified procedure. The update of the status does not incur a fee nor require a regulatory check and is therefore merely confirmed following receipt based on a declaration that parallel distributors are aware of the obligations/consequences related to the activation of dormant presentation, or request to withdraw a notice.

Annual Update

The purpose of the annual update is to combine all scopes of changes occurring within one year to one pharmaceutical form of a medicinal product with one Member State of destination in one application. It is aimed at maintaining an up-to-date database.

For further information please refer to the section Safety updates/bulk changes/annual updates.

1.3. Are the Agency parallel distribution notification procedures mandatory? Rev. Apr 2022

Yes, since entry into force of Regulation (EC) No 726/2004 on 20 May 2004, notifications of parallel distribution of centrally authorised medicinal products have become mandatory throughout the EU.

Article 57(1)(o) of Regulation (EC) No 726/2004 (amended by Article 1(22) (a) (iii) of Regulation (EU) 2019/5) foresees the following task for the Agency:

"Checking that the conditions laid down in Union legislation on medicinal products for human use and on veterinary medicinal products and in the marketing authorisations are met in the case of parallel distribution of medicinal products for human use and on veterinary medicinal products authorised in accordance with this Regulation or, as applicable, Regulation (EU) 2019/6."

Moreover, Article 76 (4) of Directive 2001/83/EC confirms the applicability of a fee to be paid:

"In the case of medicinal products which have been granted an authorisation pursuant to Regulation (EC) No 726/2004, the distributor shall submit the notification in accordance with paragraph 3 of this Article to the marketing authorisation holder and the Agency. A fee shall be payable to the Agency for checking that the conditions laid down in Union legislation on medicinal products and in the marketing authorisations are observed."

The obligation of notifying the Agency allows it to check compliance of the medicinal product to be distributed in parallel with the conditions laid down in the EU legislation on medicinal products and in the marketing authorisation. The outcome of the check is shared with the parallel distributor. Additionally the MAH and NCA will be notified when a letter of non-compliance is issued or the product is re-branded.

If the medicinal product is distributed in parallel, in the absence of the Agency's check or despite the Agency's letter of non-compliance, the national competent authorities may take regulatory actions regarding the said parallel distributor.

1.4. What is the parallel distribution notice?

The parallel distribution notice ("the PD notice") is a document issued as a result of the Agency having conducted its check of the parallel distributor's initial notification and the Agency having confirmed that for the medicinal product distributed in parallel the conditions laid down in the EU legislation on medicinal products and in the marketing authorisation were observed at the time of issuance.

Following the issuance of the PD notice, updates and changes shall be notified to the Agency by a safety update, a bulk change, an update of parallel distribution notice status and an annual update. The notice of safety update, the notice of a bulk change and the notice of an annual update confirm that for the medicinal product distributed in parallel the conditions laid down in EU legislation on medicinal products and in the marketing authorisation were observed at the time of issuance.

The PD notice, the notice of a safety update, the notice of a bulk change, and the notice of an annual update are cumulatively referred to as the Notices for PD.

1.5. What if a Notice for PD cannot be issued?

It may happen in any procedure (initial notification, safety update, update of the notice status, bulk change and annual update) that the Agency's check will establish that for a medicinal product the conditions for parallel distribution laid down in the EU legislation on medicinal products and in the marketing authorisation are not observed. In such cases the Agency will issue a letter of non-compliance.

The letter of non-compliance will be sent to the parallel distributor and an email will be sent to the MAH of the product concerned, and to the relevant national competent authorities ("NCAs"). The letter will confirm that for the medicinal product distributed in parallel the conditions laid down in the EU legislation on medicinal products, and in the marketing authorisation, were not observed at the time of issuance.

1.6. What is IRIS?

IRIS is a secure online platform for submitting and managing parallel distribution notifications.

IRIS provides a single space for parallel distributors to submit and manage information and documents related to their notifications. This reduces the time needed to prepare and submit notifications and ensures better data quality through integration with other EMA systems. It allows applicants to check the status of their notifications from any device, and to receive automatic status-update notifications.

For more information please refer to the IRIS User Guides to the portal for Parallel Distribution Industry users.

1.7. What to do when my organisation details have changed? NEW Aug 2023

Organisation information is maintained in EMA's Organisation Management Service (OMS) – which is part of SPOR system – that is consumed by other EMA systems, including IRIS. To change the organisation details, the steps below should be followed:

Firstly, a request to update your organisation details in OMS should be sent, following the IRIS User Guide.

Secondly, a follow-up regulatory submission should be completed in IRIS to update organisation details on your notices for parallel distribution. See Section 5.3 and Section 5.4 on bulk change submissions.

1.8. What is the public register of parallel distribution and what is its purpose?

The Public register of PD notices (hereinafter "the PD register") is a public register of the Agency's most current list of medicinal products checked to be in compliance with the marketing authorisation and EU legislation.

Once the PD notice is issued, the Agency will record this fact in the PD register. The record will be updated with a note when the letter of non-compliance regarding the particular product for the particular parallel distributor is issued as an outcome of annual update or safety update.

If the notice for a medicinal product/parallel distributor does not appear in the PD register this means that either no PD notice was issued at all or a communication of non-compliance for initial notification was issued at a later stage because for the medicinal product distributed in parallel the conditions laid down in EU legislation on medicinal products and in the marketing authorisation were not observed.

1.9. What are the post-PD notice obligations of a parallel distributor? Rev. Apr 2022

Updates

The medicinal product distributed in parallel must always be in compliance with the latest version of the marketing authorisation and EU legislation on medicinal products. This may require introducing changes to the labelling and the package leaflet.

Changes concerning the medicinal product distributed in parallel or concerning the parallel distributor have to be checked by the Agency. This is done during the post-PD notice procedures which comprise: notification of safety update, update of status, bulk change, and annual updates.

Quality Defects and Rapid Alerts

If a parallel distributor identifies a quality defect of the product when sourcing it, or as a result of subsequent handling in the distribution chain, the parallel distributor is accountable and must report this to the Agency and to their national competent authority.

For further information regarding the procedure of reporting, please see the section Post-PD notice guidance.

Pharmacovigilance

According to Title IX of Directive 2001/83/EC and Section 5 of Regulation (EU) 2019/6, the responsibility for pharmacovigilance lies with the Member States and the marketing-authorisation holder. The Agency does not request any information regarding pharmacovigilance or the responsible person for pharmacovigilance from the parallel distributor during the notification procedure. For more information on the Article 57 Database, please refer to the Agency's website:

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/data-submission-authorised-medicines-article-57

Should the parallel distributor receive a notification of an adverse drug reaction from a patient, a doctor or any other source, the parallel distributor should inform this person that the adverse drug reactions should be reported directly to the marketing-authorisation holder of the medicinal product. The parallel distributor should do the same immediately.

1.10. Are parallel distributors allowed to open the packaging? Can the medicinal product distributed in parallel be repackaged?

In principle, **the only changes** to the medicinal product which can be required in order to allow parallel distribution are changes in the language of the labelling and package leaflet to comply with requirements of legislation on medicinal products. Thus, in general, repackaging shall not be allowed.

However, replacing the packaging of a medicinal product is sometimes objectively necessary if, without such repackaging, effective access to the market concerned, or to a substantial part of that market, would be hindered. The necessity of repackaging must be justified by the parallel distributor during a notification procedure.

The request to repackage medicinal products is thoroughly assessed on a case-by-case basis, to ensure compliance with the marketing authorisation of the medicinal product and EU legislation on medicinal products for the safety of patients. In particular, the repackaging cannot adversely affect the original condition of the product. The concept of adverse effects on the original condition of the products refers to the condition of the product inside the packaging. It is accepted that the condition of the product is not adversely affected when repackaging affects only the external layer, leaving the inner packaging intact.

The removal of blister packs from their original external packaging and their insertion with one or more original packages into new external packaging, or their insertion in another original package, the fixing of self-stick labels on original external packaging or blister packs, or the addition to the packaging of new user instructions or information is considered as an activity which shall not affect the condition of the medicinal product inside the packaging.

The justification of the parallel distributor must be taken into account. The operations should take place in a site with a manufacturing authorisation issued by the relevant national competent authority and in compliance with the principles and guidelines of GMP. Please also refer to Chapter 5 Question 5 'What are the requirements for batch numbers appearing on the packaging of medicinal products subject to parallel trade?' of the Guidance on good manufacturing practice and good distribution practice: questions and answers.

For additional guidance on safety features, please refer to Question 1.24 of this FAQ.

1.11. Who assesses the concept of the effective access to the market?

Some changes to the packaging (e.g. repackaging) of the medicinal product may be allowed if this is necessary for the medicinal product distributed in parallel to have effective access to the market.

It is for the Agency to check the compliance of the medicinal product distributed in parallel with the latest version of the marketing authorisation and the EU legislation on medicinal products.

When conducting the compliance check, the Agency takes into account the parallel distributor's justifications for particular repackaging activities and consults concerned Member States as regards effective access to the particular marketplace.

1.12. Are any deviations/differences from the text of the latest marketing authorisation allowed?

The Agency checks if the package leaflet and the labelling (inner and outer) of the medicinal product are in compliance with the EU legislation on medicinal products and with the marketing authorisation in the language of the Member State of destination. **No deviations/differences** are allowed because in principle, the medicinal product distributed in parallel shall be identical to the medicinal product distributed by the

MAH. However, some minor deviations are allowed due to parallel distribution specifics. For further details please refer to the exceptions as listed in the section What are additional requirements reflecting that the product is distributed in parallel?.

1.13. Can centrally authorised products be rebranded?

In principle, the rebranding of one centrally authorised product to another centrally authorised product is **not permitted**. Such cases will be assessed on a case-by-case basis.

In cases where the notice for parallel distribution includes rebranding, the NCAs and MAH will be notified by email.

1.14. Can centrally authorised products be sourced from Norway, Iceland and Liechtenstein?

Yes, the principles laid down in section D of European Commission Communication 98/C 229/03 on the Community marketing-authorisation procedures for medicinal products apply. The Agency notification procedures for parallel distribution will also apply for parallel distribution from Iceland, Norway and Liechtenstein, provided the products have been previously harmonised with the Union marketing authorisation. A parallel distributor can therefore source batches of a centrally authorised product in Norway, Iceland and Liechtenstein for parallel distribution in one or more EU Member States.

1.15. How does the Protocol on Ireland / Northern Ireland affect parallel distribution?

For more information on the effects of the Protocol on Ireland / Northern Ireland on parallel distribution, please refer to section 15 of the guidance document Questions and answers to stakeholders on the implementation of the Protocol on Ireland / Northern Ireland.

1.16. Is it possible to source a product from one Member State and parallel distribute it in the same Member State?

As parallel distribution is the distribution across European borders, sourcing a medicinal product from and distributing it to the same Member State market **does not** constitute parallel distribution.

1.17. Does the 'specific mechanism' apply to parallel distribution? Rev. May 2022

The specific mechanism is provided for in Accession Treaties with some of the new EU countries joining from 2004 onwards, and reads as follows:

"*With regard to the Czech Republic, Estonia, Latvia, Lithuania, Hungary, Poland, Slovenia or Slovakia [now also Bulgaria, Romania and Croatia], the holder or beneficiary of a patent or supplementary protection certificate for a pharmaceutical product filed in a Member State at a time when such protection could not be obtained in one of the above-mentioned new Member states for that product, may rely on the rights granted by that patent or supplementary protection certificate in order to prevent the import and marketing of that product in the Member State or States where the product in question enjoys patent protection or*

supplementary protection, even if the product was put on the market in that new Member State for the first time by him or with his consent.

Any person intending to import or market a pharmaceutical product covered by the above paragraph in a Member State where the product enjoys a patent or supplementary protection shall demonstrate to the competent authorities in the application regarding that import that one month's prior notification has been given to the holder or beneficiary of such protection."

It follows that the specific mechanism applies to the **medicinal products covered by a basic patent or SPC** (according to the Judgment of the Court of Justice in Case C-681/16, this also applies to paediatric extensions of SPCs) relying on it, if the patent application had been filed in the old Member States (now the Member State of importation) prior to the introduction of equivalent protection in the new Member State (now the Member State of export). The maximum possible duration of protection is **25 ½ years** (20 years basic patent, 5 years maximum validity of SPC and 6 months paediatric extension of SPC).

1.18. Can a centrally authorised product be parallel distributed in a Member State where the marketing-authorisation holder has not yet placed the relevant product presentation on the national market concerned?

When a medicinal product has been authorised at EU level, the marketing-authorisation is valid throughout the EU. A parallel distributor may therefore distribute a particular presentation of a centrally authorised product on the market after obtaining a PD notice from the Agency even if the MAH has not yet placed this presentation on the market in this Member State.

1.19. Is the Agency involved in any trademark issues?

No, the Agency is not involved in any trademark issues and only checks the compliance of the medicinal product distributed in parallel with the terms of the EU marketing-authorisation of the concerned centrally authorised product and EU legislation on medicinal products.

It is up to the trademark owner to check if the repacked product does not damage the reputation of the trademark and otherwise complies with the legislation and case-law related to trademarks, while the Agency is responsible for checking compliance of the submitted specimens with the terms of the EU marketing-authorisation and EU legislation on medicinal products.

The Agency does not take decisions or provide guidance on the use of registered trademark symbols.

1.20. What are the responsibilities of a parallel distributor regarding biologics (e.g. vaccines and blood products)? Rev. Jan 2020

Pursuant to Article 114 of Directive 2001/83/EC, Member States may impose additional requirements regarding live vaccines, immunological medicinal products and blood or plasma derived products. Parallel distributors are, in general, **obliged to notify** the national authority of the Member State of destination responsible for the parallel distribution of products which are subject to official control authority batch release such as vaccines or blood products.

1.21. Are a wholesale authorisation and/or a re-packager's manufacturing authorisation needed in order to allow parallel distribution?

Yes, a wholesale authorisation and/or a re-packager's manufacturing authorisation is needed in order to allow parallel distribution.

All parties (parallel distributor and re-packager) must hold the appropriate authorisations for the activities in which they are engaged, i.e. a wholesale distribution authorisation and/or manufacturing authorisation. Repackaging activities can be carried out either by the parallel distributor or another company, provided these companies have valid manufacturing authorisations. All authorisations should be available on the EudraGMDP website.

A copy of an up-to-date and complete (with attachments) original authorisation or a EudraGMDP reference should be submitted only with the first initial parallel distribution notification. It is also recommended to attach an English official translation of the authorisation(s) to facilitate the review and validation by the Agency when a copy of a paper authorisation is submitted. For more information please see the below link: http://eudragmp.ema.europa.eu.

1.22. Can a parallel distributor use more than one re-packager?

Yes, parallel distributors are allowed to identify more than one re-packager in their parallel distribution notification. The EudraGMDP reference number must be provided with every re-packager added, alternatively the copy of the manufacturing authorisation should be provided.

On the proposed outer labelling, the parallel distributor can only state **one re-packager** (and optionally the address), namely the one who is responsible for particular batch release. Only one colour copy with one re-packager has to be provided as an example.

1.23. Can the PD notice be transferred? Rev. Apr 2022

No, transferring a PD notice from one company to another is not possible.

Article 76 of Directive 2001/83/EC and Article 102 (5) of Regulation (EU) 2019/6 imposes the individual obligation on the distributor who intends to import a medicinal product from another Member State to submit the notification to the marketing authorisation holder and the Agency in case of medicinal products which have been granted an authorisation pursuant to Regulation (EC) No 726/2004.

However, if as a result of a merger/acquisition the parallel distributor is dissolved or if it changes the legal form, there is an assumption of continuity of the legal entity. In these situations, a notification of a bulk change ('Reassignment of notices for Parallel Distribution') would need to be submitted.

For more information, please see How to submit a bulk change?.

1.24. What are the requirements for parallel distributors in relation to the implementation of the Delegated Regulation on Safety Features?

Please refer to Commission Delegated Regulation (EU) 2016/161 and related Q&As. Please also refer to Chapter 5 Question 5 'What are the requirements for batch numbers appearing on the packaging of medicinal products subject to parallel trade?' of the Guidance on good manufacturing practice and good distribution practice: questions and answers.

2. Initial notification

2.1. How to access IRIS?

Please see the IRIS User Guides in the guidance section for detailed information on how to use IRIS as a logged-in user. You will need to complete a few registration steps to ensure that:

- You have an active EMA account in **EMA's Account management Portal**.

Allow up to two working days if you need to reset the password for an account for which you have not set up your security questions.

- Your organisation is registered in **EMA's Organisation Management Service (OMS)**.

Allow from five to ten working days to register a new organisation or update organisation data in OMS (one of the domains of SPOR master data).

- You have the appropriate user access role and affiliation to an organisation.

Allow up to two working days for EMA to approve the first "User Admin" role for your organisation.

- You have a valid EMA customer account number.

This is a unique reference number and should be quoted by applicants on each procedural submission and all correspondence related to financial matters. Information on how to set up a customer account and obtain the customer number can be found on the Agency's 'How to pay' page.

For technical support please **always liaise directly** with EMA Service desk.

2.2. How to contact Parallel Distribution Secretariat for general enquiries?

For general enquiries on parallel distribution, please send a question to the European Medicines Agency. Please indicate in the subject header that your question is related to parallel distribution.

2.3. How to apply for the PD notice? Rev. Apr 2022

The applicants should use the Checklist for initial notifications for parallel distribution: guidance for industry in advance of submission. In order to improve the quality of submissions, it is recommended to include the checklist with your submission.

Refer to the IRIS User Guides in the guidance section for detailed instructions on steps 1-5.

Step 1 Register organisation in Organisational Management Service (OMS)

Step 2 Set up an EMA account in EMA Account Management portal and request the necessary user access role including two managers in every submission

Step 3 Request EMA customer number

Step 4 Compile documentation including the below documents:

- a **cover letter (optional)** clearly indicating the name of the medicinal product, the strength, the pharmaceutical form, EU number and the pack-size, to be used for any other relevant information you may wish to provide;

- an **editable format** of the **package leaflet** in the final sales format (doc, pdf) in the language of the Member State of destination in compliance with the latest version of the EU marketing-authorisation;
- a **colour scan** of all sides of the re-labelled and/or re-packed outer packaging, as well as the re-labelled inner packaging, as they will be marketed in the Member State of destination compiled in a single document. Images must clearly show the braille text label if required according to the marketing-authorisation. Images of the relabelled inner packaging must be provided with every initial notification even if the original label contains text in the language of member state of destination. If the originally sourced product has a colour code related to safety, parallel distributors should follow the same style. In case of reboxing, and when the inner label fully covers the originally sourced product and this cannot be verified, parallel distributors must always include colour copies of the original product without the inner label attached for the Agency's assessment.
- **Mock-ups** in an editable format
    - in case of relabelling: please provide two separate documents: one document containing a mock-up of the outer label and another one of the inner label (not combined in one file).
    - In case of reboxing: please provide two separate documents: one document containing a mock-up of the outer carton and another one of the inner label (not combined in one file).
- other documents related to the submission (Ex.: patient alert card, etc.)
- In addition, please be aware that the responsible assessor may request images of the final product or, in exceptional circumstances, a physical sample at any point.

Note: When submitting the first initial notification for parallel distribution of a centrally authorised product, the parallel distributor will be requested to provide the Agency with images of the final repackaged product. Mock-ups do not suffice in this instance. The Agency reserves the right to request images of the finalised product at any time.

Step 5 Log into the IRIS platform using the address (location LOC-ID) which corresponds to the **address on the Wholesale Distribution Licence**.

Step 6 Follow the guide on submission via IRIS to fill the on-line form, upload the above documents and submit the notification.

Please note that the address of the re-packager(s) on the submission form must correspond to the manufacturing site address on the Manufacturing Importation Licence. Please ensure that you select the correct Location-ID for the repackager in IRIS.

It is strongly recommended that new parallel distributors submit only one notification when applying for a notice for parallel distribution for the first time and wait for the outcome of the parallel distribution notification check in order to avoid the repetition of errors when submitting subsequent notifications.

Should a parallel distributor submit a notification by mistake or discover an error in the submitted package, it should be **removed within 24 hours**. The fees will be payable following that period.

Updates to the information included in the IRIS form after submission of any notification for parallel distribution are only possible in exceptional cases, so the applicants should review the information included in the form carefully before submitting. Changes impacting fees would not be possible after submission. Only changes requested by the assessor would be possible and only by exception when properly justified.

Step 7 If all supporting documentation is satisfactory, the Agency will finalise the parallel distribution notification check and issue a PD notice. If necessary, the parallel distributor will be contacted by a parallel distribution assessor. Please note that all communication regarding a particular application should be conducted only through IRIS.

2.4. What file formats are acceptable?

All documentation should be submitted using file formats that facilitate the assessment of the file on screen. If the type of file you plan to upload is not included in the list below, please convert the file to an acceptable file type.

Data	**xls** (Microsoft Excel Spreadsheet)
Image	**bmp** (Bitmap Image) **gif** (Graphics Interchange Format) **jpg** (Joint Photographic Experts Group) **pdf** (Portable Document Format) **tif** (Tagged Image File Format)
Text	**doc** (Microsoft Word Document) **docx** (Microsoft Word Open XML Document) **pdf** (Portable Document Format)

PDF documents submitted as scans should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. Normally 300 dpi gives good results without compromising file size for text. Parallel distributors should ensure that the quality of the renditions is adequate for regulatory review.

2.5. How to name each file?

Standardisation of the electronic file names is necessary for easy identification of the content in the Agency's document system. The proposed naming is the following:

YYYY.MM.DD Product Name"_"last three digits of the EU number"_"Subject"

Possible subjects:

- 'cover' for cover letters;
- 'leaflet' for package leaflets;
- 'labelling' for inner and outer labelling;
- 'mock-ups' for mock-ups of the labels and outer carton in case of re-boxing;
- 'braille' for braille text labels;
- 'manufacturer' for the manufacturing authorisation of the parallel distributor or the re-packager;
- 'wholesale' for the wholesale distribution authorisation of the parallel distributor;

e.g. 2022.01.31_Stalevo_003 _Labelling

File names should be short and not exceed 100 characters to avoid technical problems. **File names should not contain characters such as "/" or "&"** which are known to cause problems. Files themselves must **not be password protected** or include security settings that may interfere with the process of handling by the reviewers.

2.6. How many initial notifications can be submitted per medicinal product?

A *separate* notification must be submitted for **each EU-number** and for **one Member State of destination** having one or more official languages, or for several Member States of destination having the same official language.

2.7. Where to find the latest published annex/EU marketing authorisation? Rev. May 2024

For human medicines:
To check the latest version of the annex of the centrally authorised product via the Agency website please visit the European Public Assessment Report (EPAR) section.

To check the latest version of the annex via the European Commission registry on medicinal products, please visit the Community Register.

Note that there **might be a discrepancy** between these websites; this could be due to one of the websites not yet having been updated. In that case, you should use the annex with the later publishing date.

If the medicinal product has been sourced from an old batch and some of the excipients/devices have changed, the parallel distributor should use the last annex where the old device or excipient was mentioned. In case further advice is needed on this matter, parallel distributors should consult their Quality and/or Regulatory Affairs specialists. In these cases, the specialists' advice should be attached to the notification for parallel distribution via IRIS.

For veterinary medicines:
To check the latest version of the annex of the centrally authorised veterinary product, please visit the Veterinary Medicines Information website.

For a detailed explanation, please refer to the Checklist for initial notifications for parallel distribution: guidance for industry and the Checklist for annual updates for parallel distribution: guidance for industry.

2.8. How to proceed if sourcing a product from a country where the language is the same as the language in the Member State of destination?

If a parallel distributor sources a product from a country where the official language is the same as the language in the Member State of destination (e.g. Ireland and Malta, or Austria and Germany) the parallel distributor is still required to provide complete labelling for the product.

2.9 What are some examples of grounds for invalidation, negative outcome and common mistakes often made? NEW May 2022

Incorrect submissions can be withdrawn free of charge only within 24 hours from the time of submission. A fee will be payable once the 24-hour window has passed. Applicants should therefore review the information on the form and supporting documents thoroughly prior to submission as mistakes could lead to invalidation or a negative outcome, while the fee will remain payable.

Examples that can lead to invalidation or the issuing of a negative outcome:

- Errors in the submission form, such as submission by an individual instead of an organisation, submission from an address (LOC-ID) which does not correspond to the legal address as per the WDA.
- Missing the response deadline given by the Agency.
- Not addressing all points following regulatory check or validation comments.
- Listing the same Member State of Origin (MSO) and Member State of Destination (MSD) on the submission form. The only exception allowed is when there are multiple MSDs that share the same official language.
- No MSOs selected at all.
- Wrong repackaging method(s) indicated in the form.
- Missing re-packager on the form or incomplete list of re-packagers. (e.g., the repackager listed on the product packaging does not correspond to any of the repackagers mentioned in the submission form).
- Repackager address on the form (LOC-ID) does not correspond to the manufacturing site address in the MIA.
- A bundle pack was created where this was not authorised in the MA.
- The EU presentation(s) proposed for distribution cannot be created from the proposed sourced one(s).

Most common mistakes:

General issues:

- IRIS user guide has not been respected (e.g., email attachments are not accepted, all files, screenshots etc must be uploaded to IRIS).
- Submitting an incomplete set of documents as listed in the FAQ and/or checklists.
- Steps for re-submission are not followed correctly.
- Public register was not consulted and information was not correctly referenced or reflected prior to submission.
- Only partial implementation of the requested changes and no further comments or clarifications were provided by the parallel distributor.

Product information:

- The font style in the package leaflet and on the labelling (bold, italic, underlined text when included in MA) does not meet readability guideline requirements.
- Only the "raw" format of the package leaflet was provided and not the "sales" version.
- Multiple manufacturers were listed in the package leaflet.
- Detailed images of the sourced product were not provided when the newly created label covered the product entirely, and therefore it was impossible to verify the actual product.

Note: Please note, that the above examples are not an exhaustive list and should be used as a guidance only. Each case is assessed strictly individually and therefore reasons for invalidation or a negative outcome may vary.

3. Parallel distribution notification check

3.1. What is the timeframe for the check? Rev. April 2020

The Agency finalises the check within 60 days after confirming the receipt of the notification. It will then issue either the appropriate Notice for PD or the letter of non-compliance. 60 days comprises 35 days for the Agency's assessment and 25 days for possible clock-stops.

The Agency conducts its check within 35 days from the day of confirmation of the receipt of the notification. Once the conditions laid down in the EU legislation on medicinal products and in the marketing authorisation are observed, the Notice for PD will be issued.

If there is any obstacle for the issuance of the Notice for PD, the parallel distributor will be informed thereof, and the time-limit of 35 days shall be suspended until the parallel distributor replies to the Agency's comments or maximum 25 days. A single list of comments will be provided, and the parallel distributor will be asked to address **all** comments in the reply to the Agency, supplement or change the parallel distributor's details, change or supplement the labelling or package leaflet or to provide clarification regarding the application.

The clock-stop may be granted once during the validation stage and once during the regulatory check. The total time of both clock-stops combined should not exceed 25 days. Should the parallel distributor fail to address all comments communicated in the regulatory check email and/or implement the requested amendment in a single submission response, the procedure may be invalidated or finalised with a negative outcome.

3.2. The parallel distributor should provide a response directly through IRIS. The time-limit is common for every procedure. You can check the status of your submission at any time in IRIS. Are there any exceptions allowed to the timeframe?

The extension of the time-frame is allowed **only exceptionally** and is possible only in the situations in which despite the good-will of the parallel distributor additional time is necessary to finalise the check. The exception to the timeframe has to be applied for by the parallel distributor and granted before the deadline and be thoroughly justified. For example, an updated annex to the marketing authorisation is published during the regulatory check.

3.3. Is it mandatory to include cover letters?

Cover letters are preferable to be provided but are optional.

3.4. What is the difference between relabeling and reboxing?

Reboxing / re-packing = creation of a new outer carton and affixion of inner labels on the immediate packaging.

Relabelling = affixion of an outer label on the original carton and affixion of inner labels on the immediate packaging.

Relabelling and Reboxing = both of the above activities, therefore 2 x sets of colour copies of the outer packaging are required.

For **multipacks** with intermediate packaging, the repackaging method of the final outer carton with the blue box determines the repackaging method.

3.5. Is it allowed to change the pack size of the sourced presentations?

Parallel distributors **can only place authorised pack sizes on the market**. Changes of the sourced pack sizes may be authorised but this is assessed individually on a case-by-case basis after provisions of a detailed justification and confirmation that the proposed pack size falls within the scope of the Marketing Authorisation. Mixing and matching of different batches and expiry dates in order to create one presentation is not allowed. Please also refer to Question 1.22 for more information on the safety features.

3.6. Is it allowed to resize or create bundle packs?

It is **not possible** to bundle two units of a presentation of a product so as to create a new presentation of a different size.

Bundle packs can only be created when bundle packs are explicitly listed in the packaging description of the marketing authorisation.

This needs to be distinguished from multipacks, which per marketing authorisation are presentations that consist of multiple units of size x, 'bundled together' to create size y.

Presentations that consist of one unit of size x can be used to create size y (resizing).

3.7. What is the difference between a mock-up and a colour copy?

A **mock-up** is a copy of the label or flat artwork design in full colour, providing a replica of both the outer and inner packaging and labelling text of the medicinal product. It is generally referred to as a paper copy or computer generated version.

A **colour copy** is a digital scan, a digital photograph or a colour photocopy of the (repackaged) sales presentation of the medicinal product.

3.8. What to do if the marketing-authorisation holder or the manufacturer of a particular centrally authorised product has changed?

If the MAH (or the MAH's address or name), or manufacturer of a particular centrally authorised product has changed, parallel distributors must always use the latest version of the Annex for the details of the MAH but to indicate respectively the manufacturer responsible for the particular batch release as listed in the originally sourced package leaflet.

The details of the old MAH must be duly covered both on the outer and the inner packaging.

3.9. What to do if the composition of a product, its excipients or devices used have changed with new batches? Rev. Jan 2020

If the medicinal product has been sourced from an old batch and some of the excipients/devices have changed, the parallel distributor should use the last annex where the old device or excipient was mentioned. In case further advice is needed on this matter, parallel distributors should consult their Quality

and/or Regulatory Affairs specialists. In these cases, the specialists' advice should be attached to the notification for parallel distribution via IRIS.

3.10. What are the additional requirements reflecting that the product is distributed in parallel?

The following are additional **mandatory** requirements for the **outer labelling** (for multipacks, this refers to the outer carton with the blue box), even if they are not mentioned in the annex:

- manufacturer responsible for batch release (as mentioned in the original package leaflet of the concerned batch);
- the words 'parallel distributor/parallel distributed by' (followed by the name and optionally the address / logo) **OR** the words 're-packager/repackaged by' (followed by the name and optionally the address / logo);
- braille text (if mentioned in section 16 of the annex);
- 'blue box' (in accordance with national regulations of the Member State of destination).

Optional terms:

- <Product X> is a trademark of <Company Y>;
- internal reference number of the parallel distributor (for further information, please see section 'Parallel distribution notification check').

The following terms are **not allowed** to appear on the **outer labelling**:

- 'procured from within the EU';
- 'imported by';
- 'pack has been opened for parallel distribution purposes' or similar statement;
- more than one manufacturer responsible for batch release;
- any other text which is not part of the latest version of the annex (unless justified).

The following terms **are allowed** to appear on the **inner labelling** but are not mandatory:

- 'parallel distributor/parallel distributed by:' (followed by the name and optionally the address / logo) **OR** 're-packager/repackaged by:' (followed by the name and optionally the address / logo);
- <Product X> is a trademark of <Company Y>;
- internal reference number of the parallel distributor (for further information, please see section 'Parallel distribution notification check').

Mandatory terms to appear in the **package leaflet**:

- manufacturer responsible for batch release (same as the one on the outer labelling);
- local representatives if they are present in the annex.

Exceptions:

Minor changes are permitted to be introduced by the parallel distributor in the text of the labelling/package leaflet in the following situations and only with the agreement of an assessor:

- when the composition of a medicinal product changes the parallel distributor must ensure that the composition mentioned in the leaflet/labelling of the parallel distributed pack corresponds with the actual composition of the pack.

3.11. Can several languages be combined in one pack? Rev. Apr 2022

The EU pharmaceutical legislation mentions in Article 63(1) of Directive 2001/83/EC and in Article 102(2) of Regulation (EU) 2019/6 that all text shall appear in the official language(s) of the Member States where the product is placed on the market.

The labelling and the package leaflet should be in compliance with the text of the EU marketing authorisation for the concerned medicinal product in all official languages.

In the case of multilingual Member States of destination (i.e. Belgium, Finland, etc.), the parallel distributor must combine all languages of that particular country in the package leaflet and on the labelling.

A parallel distributor can create a multilingual pack provided that all particulars required by the marketing authorisation appear in all languages concerned. The outer carton should then contain separate blue boxes for each member state of destination.

3.12. What are the general requirements for the braille text labelling? Rev. Dec 2019

The **Guideline on the readability of the labelling and package leaflet of medicinal products for human use** as prepared by the European Commission (2009 D/869) sets out advice on the presentation of the content of the labelling and package leaflet and on the design and layout concepts meant to aid the production of high quality information.

The guideline clearly and unequivocally sets out how the requirements for braille text can be met.

As mentioned in the **Guidance concerning the braille requirements for labelling and the package leaflet** from the European Commission, these requirements are applicable to parallel distributors.

Further guidance on braille text can be found on national websites as well as:

European Blind Union website:

http://www.euroblind.org/

PharmaBraille website:

http://www.pharmabraille.com/

When submitting specimens or 'mock-ups', parallel distributors must declare, that the braille text presentation is submitted in the language of the Member State of destination, in compliance with the annex.

When the original braille text matches the braille text of the country of destination, the original braille text can be maintained provided that legibility and readability criteria apply.

According to Article 56a of Directive 2001/83/EC, the name of the medicinal product must be expressed in braille. This has to be in the language of the Member State of destination. As further clarified by the European Commission in above mentioned guidance the name should be followed by its strength, unless the medicinal product was only authorised in a single strength.

The Agency strongly advises parallel distributors to affix the new braille text on a different part of the outer packaging, and not on top of the original one.

The braille text is not mandatory on the immediate packaging (such as blisters, ampoules and bottles) unless required by the marketing authorisation.

The colour copy should make the braille text visible and readable. New braille text presentations must be submitted along with the indication where the braille text will be affixed on the outer packaging.

If the braille text is added on a separate label, a copy of this label should be added to the colour copy of the labelling or the documents submitted with the notification.

3.13. What are the special requirements for unit-dose blisters?

As a general note, when labelling unit dose perforated/peelable blisters, each segment of a perforated blister must be re-labelled individually following the same approach as that of the marketing-authorisation holder.

Please note that parallel distributors are not allowed to create a unit dose presentation from a non-unit dose presentation.

3.14. Is it allowed to cut blisters?

The cutting of blisters is **not recommended** by the Agency but may occasionally be permitted on a case-by-case basis, provided that it does not affect the original condition of the product and the proposals from the parallel distributor are in compliance with the conditions of the marketing authorisation. The assessment takes into account the necessity for the effective access to the market.

The parallel distributor should provide a valid justification for cutting blisters and a decision on whether this is acceptable will be made by the Agency.

3.15. How to re-label sterile and foil pack products?

As the original condition of the product may be altered by the opening of a sealed foil pack, a blister or a tray, when re-labelling the blister, syringe, cartridge or other primary packaging, the Agency strongly recommends:

- **not to open the tray** to re-label the syringe but instead to re-label the tray with all information required for the syringe and the tray preventing any possible contamination of the syringe or of the medicine itself;
- **not to open the aluminium wrapper/foil** as the foil provides protection and is important for the maintenance of the shelf life of these products.

3.16. How many manufacturers are allowed in the package leaflet and on the outer labelling? Rev April 2022

Article 59(1)(f)(vii) of Directive 2001/83/EC and Article 14(1)(a) of Regulation (EU) 2019/6 require that the marketing authorisation holder should always state **only one manufacturer** responsible for the batch release in the original package leaflet.

Please note that **only one manufacturer** shall be mentioned on the outer label, namely the manufacturer responsible for the release of the concerned batch as mentioned in the original leaflet. The manufacturer on the outer label should always correspond to the one in the package leaflet.

When more than one manufacturer is indicated in the sourced original package leaflet, the parallel distributor should contact the marketing authorisation holder to request that an investigation is conducted on the potential product defect and to obtain information on the manufacturer responsible for the particular batch release. If a response is not received within a reasonable timeframe (approximately 15 days), the PD should proceed to report a quality defect to the Agency.

It is advised that this information is obtained before the initial notification or annual update are submitted.

3.17. What are the requirements for the 'blue box'? Rev. Apr 2022

The 'blue box' is **mandatory** on the outer labelling of each centrally authorised human medicinal product as well as each parallel distributed product. The information required to appear inside the 'blue box' is specific to each Member State. Each 'blue box' must state the name of the Member State of destination and the information required by the Member State of destination as described in the Guideline on the packaging information of medicinal products for human use authorised by the EU.

The original 'blue box' should be completely covered. In principle the border of the blue box should be blue.

According to Article 57 of Directive 2001/83/EC, a Member State may ask for additional information to appear on the packaging concerning identification and authenticity of the product, the legal category for supply and the price. In addition, Article 57 of Directive 2001/83/EC states that Member States shall observe the detailed guidance referred to in Article 65 of Directive 2001/83/EC when applying Article 57 with regard to centrally authorised medicinal products, such as the Guideline on the packaging information of medicinal products for human use authorised by the EU. Such guidance has been prepared by the European Commission in consultation with the Member States and the parties concerned in order to describe how provisions of Directive 2001/83/EC, including Article 57 thereof, should be applied.

According to Regulation (EU) 2019/6, the 'blue box' is not required on the outer labelling of centrally authorised veterinary products.

3.18. What is the recommended font-size of the labelling and the package leaflet?

The Guideline on the readability of the labelling and package leaflet of medicinal products for human use gives recommendations on the font size of the text for the outer and inner labelling and the patient leaflet to ensure their legibility.

Concerning the package leaflet, the guideline states that 'The type size should be as large as possible to aid readers. A type size of 9 points, as measured in font 'times new roman', not narrowed, should be considered as a minimum.

With regards to the labelling, the guideline states that 'The particulars appearing on the label of all medicinal products should be printed in characters of at least 7 points (or of a size where the lower case "x" is at least 1.4 mm in height).'

3.19. Who receives Notices for PD and letters of non-compliance? Rev. Jan 2020

Notices for PD are sent to the parallel distributor only. The MAH, the national competent authorities in the Member State of destination, and in the Member State where the parallel distributor is registered can consult Public register of PD notices on a regular basis. In cases where a letter of non-compliance is issued, the parallel distributor, NCA and MAH will all be notified by email.

3.20. Do parallel distributors have to adhere to particular packaging design or/and colour code when repackaging the products? NEW May 2022

Packaging design of the products distributed in parallel must comply with the terms of marketing authorisation when the annexes of the marketing authorisation (Annex I, IIIA or IIIB) indicate a particular location of the text on the packaging, its colour and/or font type.

In addition, in case an originator's packaging contains product safety-related design elements which have been included to support the safe and correct use of the product (e.g. colours for strength identification, prominent fonts for "once daily", "oral use", etc.), parallel distributors are strongly advised to align with the originator's products on the design, colour and special fonts.

4. Post - PD notice guidance

4.1. What is the validity of the notice for parallel distribution and can it be revoked, suspended or annulled? Rev. Aug 2023

The PD notice is a document confirming that at the time of issuance, for the medicinal product distributed in parallel the conditions laid down in EU legislation on medicinal products and in the marketing authorisation were observed. If it is established that the medicinal product distributed in parallel is no longer compliant with the latest version of the marketing authorisation or with the EU legislation on medicinal products a letter of non-compliance will be issued for this product.

The Public register (PD register) provides the up-to-date information on the status of the notice letter (active, dormant, cancelled, etc). Thus, the PD register represents the Agency's most current list of medicinal products checked to be in compliance with the marketing authorisation and EU legislation.

In exceptional situations the PD notice may be cancelled. The cancellation of the PD notice may take place if the PD notice was issued due to an error or based on information which subsequently turned out to be incorrect.

PD notice can also be withdrawn following the submission of withdrawal request by parallel distributor via 'Update of Parallel Distribution Notice Status' procedure.

The notice for parallel distribution can be suspended in case of suspension of manufacturing authorisation of the re-packager responsible for re-packaging processes, when no additional re-packager has been authorised to perform the re-packaging activities.

4.2. Can a centrally authorised medicinal product continue to be distributed in parallel if the marketing authorisation is suspended, revoked or withdrawn?

The medicinal product distributed in parallel is covered by the central marketing authorisation. As a consequence, the scope and validity of the marketing authorisation determine the situation of the medicinal product. In case of a revoked, withdrawn or suspended marketing authorisation, no further batches can be released into the supply chain but the batches in the distribution chain can be used, except in case of a recall.

If the MA withdrawal is **not related to product safety**, the respective pack sizes will remain on the market until the last batch expires and these presentations 'naturally' leave the market. Until this happens, parallel distributors will have to re-package the product in line with the last annex which contained labelling for currently withdrawn presentations.

The parallel distribution secretariat **will not automatically cancel** notices for parallel distribution for those products where the MA was withdrawn for non-safety-related reasons, unless requested by parallel distributor.

The parallel distribution secretariat **will cancel** notices for parallel distribution for those products where the MA was withdrawn for safety-related reasons. The affected companies will be notified.

4.3. Can the Agency request the national competent authorities to perform an inspection of a parallel distributor? Rev. Apr 2022

Where considered necessary, the Agency shall inform the national competent authorities of any issues or non-compliance that have been brought to the Agency's attention which **may trigger** an inspection, in accordance with Article 111 of Directive 2001/83/EC and with Article 123 of Regulation (EU) 2019/6.

The responsibility for any further action remains within the remit of the national competent authorities of the respective Member State(s).

4.4. What are the parallel distributors' responsibilities regarding quality defects? Rev. Apr 2022

If a parallel distributor identifies a quality defect of the product when sourcing it, or as a result of subsequent handling in the distribution chain, the parallel distributor is accountable and must report this to their national competent authority as well as the Agency.

1. A parallel distributor can make changes to the packaging materials of a product only if they hold a manufacturing authorisation issued by the relevant national competent authority. They are bound by the provisions of that authorisation, which include compliance with the principles and guidelines of good manufacturing practice (GMP) that are laid down in Directives 2003/94/EC and 91/412/EEC, for human and veterinary products respectively.

According to Article 13 of Directive 2003/94/EC, manufacturers are required to have a system for recording and reviewing complaints and for effective recall. A manufacturer is obliged to inform the national competent authority of any defect they have become aware of that might result in a recall or abnormal restriction in supply. This applies equally to parallel distributors, as provided for by Article 80 of Directive 2001/83/EC and by Article 102 (6e) of Regulation (EU) 2019/6. The national competent authority will assist the parallel distributor in the recall process and will initiate the rapid alert system accordingly. A parallel distributor should ensure that the marketing authorisation holder is informed of any recall initiated by the parallel distributor.

2. Parallel distributors must only source products from companies which have a valid wholesale distribution authorisation in the Member State where they are located. The supplier is consequently obliged to inform the parallel distributor of any recall activities that might involve products supplied to the parallel distributor within the supply chain. Such notifications must be handled within the parallel distributor's GMP/GDP (good manufacturing/distribution practices) system to confirm whether the affected product was actually received, to trace its utilisation and to initiate recall procedures as necessary, including contacting the local competent authority.

When a parallel distributor encounters a quality defect or has any suspicion about the sourced product, the competent national authority as well as the Agency should be informed immediately.

The procedure of Reporting quality defects or product recalls is outlined on the Agency webpage.

4.5. Is it required to keep reference and retention samples of each product?

Annex 19 of the good manufacturing practice guideline for medicinal products gives guidance on the taking and holding of reference samples of starting materials, packaging materials or finished products and the retention samples of finished products.

A **reference sample** is a sample of a batch of starting material, packaging material or finished product which is stored for the purpose of being analysed should the need arise during the shelf life of the batch concerned.

A **retention sample** is a sample of a fully packaged unit from a batch of the finished product. It is stored for identification purposes (i.e. for identifying presentations, packaging, labelling, package leaflets, batch numbers or expiry dates) should the need arise during the shelf life of the batch concerned.

Where the product has been re-packaged (e.g. to replace the carton or package leaflet) one full retention sample per repackaging activity of each batch of finished product should be taken, as there is a risk of product mix-up during the assembly process. It is important to be able to identify quickly who is responsible in the event of a mix-up (i.e. original manufacturer or re-packager), as it would affect the extent of any resulting recall.

Reference and retention samples from each batch of finished product should be retained for at least one year after their expiry date. Records of traceability should be maintained and be available and accessible for review by the competent authorities at any time.

4.6. What is a product with special conditions for distribution imposed on the marketing authorisation holder?

A medicinal product with special conditions for distribution is a product which can only be distributed under specific conditions, such as the requirements for **educational materials, patient alert cards or controlled distribution system**.

If any specific conditions are mentioned in the annex of the marketing authorisation for the product, it is the responsibility of the parallel distributor to comply with these conditions and restrictions before making the medicinal product available in the Member State of destination. The parallel distributor is required to liaise with the marketing-authorisation holder, and the national competent authorities in the Member State of destination to discuss the requirements they may need to meet before distributing the medicinal products and to include the information required as per the annex (e.g. patient alert card) and/or relevant national legislation.

The marketing-authorisation holder and the national competent authorities are mainly responsible for agreeing the details of controlled distribution systems and the details of the operation of surveillance programmes. In case a parallel distributed product has not been first put on the market of the Member State of destination by the marketing-authorisation holder, the parallel distributor and the national competent authorities should ensure that there is a controlled distribution system, a surveillance programme as well as an educational programme in place (e.g. physician's pack, patient alert card, etc.), if appropriate, which achieves the aims of the systems required by the conditions of the marketing authorisation for parallel distributed medicinal products.

5. Safety Updates/bulk changes/annual updates

5.1. What is a safety update? Rev. Nov. 2020

Mandatory changes due to the **urgent safety updates**: notifications of changes resulting from urgent safety updates to the product information shall be submitted within a three-month timeframe of the notification by the Agency of the urgent safety update having occurred. Notifications submitted due to an urgent safety update will not affect the "birthday date" of the annual update and the annual update should still be submitted in due time. No other scopes of changes can be added to such notifications. Therefore, the update of the package leaflet with the latest safety information does not exempt the parallel distributors from submitting annual update to report the update of the labelling and package leaflet and/or other changes.

Notifications of safety update received after the three-month deadline will be invalidated.

Notifications of safety update submitted for dormant product presentations will be invalidated. The presentation needs to be activated before safety update is submitted.

5.2. How to submit safety update? Rev. Apr 2022

A notification of safety update has to be submitted for every EU presentation of the affected product and must be supported with the following documentation:

- **an editable format** of the **package leaflet(s)** (doc, pdf) in the final sales format in the language of the Member State of destination in compliance with the version of the annexes to the EU marketing authorisation which introduced safety updates (indicated in monthly communication to parallel distributors);
- if applicable**, colour copies** of the outer and inner labelling compiled in a single document (if indicated in monthly communication to parallel distributors);
- if applicable**, mock-ups** in an editable format
    - in case of relabelling: please provide two separate documents: one document containing a mock-up of the outer label and another one of the inner label (not combined in one file).
    - In case of reboxing: please provide two separate documents: one document containing a mock-up of the outer carton and another one of the inner label (not combined in one file).
- a notification of safety update can contain more than one EU presentation of the affected product for one member state of destination (or more where applicable);

The above documentation should be submitted via the procedure form in IRIS. For guidance on the submission, please refer to the IRIS submission guide in the Guidance section.

Updates to the information included in the IRIS form after submission of any notification for parallel distribution are only possible in exceptional cases, so the applicants should review the information included in the form carefully before submitting. Only changes requested by the assessor would be possible and only by exception when properly justified.

5.3. What is the scope of a bulk change? Rev. Aug 2023

The scope(s) of changes that can apply to a bulk change are limited to:

- a change in the details of the parallel distributor ('Change of name and/or address' or 'Reassignment of notices for Parallel Distribution'),
- addition or deletion of a re-packager ('Change of manufacturer'),
- and/or a change in the name and/or address of a re-packager ('Change of manufacturer').

The change to the bulk may be implemented only once the bulk change procedure has been finalised.

5.4. How to submit a bulk change? Rev. Aug 2023

A notification of a bulk update ('Change of name and/or address', 'Change of manufacturer', 'Reassignment of notices for parallel distribution') must be supported with the following documentation:

- **new wholesale authorisation and/or a re-packager's manufacturing authorisation;**
- one set of **colour copies** of the outer and inner labelling compiled in a single document with the images of one repackaged product;
- **an editable format** of one **package leaflet** (doc, pdf) in the sales version in the language of the Member State of destination;
- in case of 'Reassignment of notices for parallel distribution', a **proof of merger/acquisition** where the parallel distributor is dissolved, or it changed the legal form as well as a **statement** confirming that the new parallel distributor has taken over all rights and obligations of the previous parallel distributor. See Can the PD notice be transferred?;

NOTE:

If as the result of 'Reassignment of notices for parallel distribution', the parallel distributor becomes the owner of duplicate notices, the parallel distributor should decide which notices for PD to keep and request the withdrawal of the duplicates by submitting an "Update of parallel distribution notice" notification.

In cases where the parallel distributor name/address changes, or where notices have to be reassigned to a new company, a notification of "Change of name and/or address" or "Reassignment of notices for parallel distribution" has to be submitted to update the details of the parallel distributor on the notices. Additionally, if the same company also acts as a re-packager, the new owner of the parallel distribution notices has to submit a "Change of manufacturer" to also update the details of the repackager.

The above documentation should be submitted via the procedure form in IRIS. For guidance on the submission, please refer to the IRIS submission guide in the Guidance section.

5.5. What is an annual update? Rev. May 2024

The annual update is the procedure that allows the Agency to have an overview of the medicinal products distributed in parallel. By the annual update the parallel distributor notifies the Agency of any changes introduced to the medicinal product through the last year. The annual update is mandatory for every medicinal product except for dormant products (see What are the requirements for dormant notices? below).

Products distributed for 12 months with no changes (no new annex, no new Member States of origin/destination, no changes of labelling, no new re-packagers etc.) still require a completed annual update form, indicating 'no changes' and a complete set of documents listed in How to submit an annual update, but will not be subject to a fee.

The annual update is a "DO and TELL" procedure. A parallel distributor can implement changes and only inform the Agency about these changes with the next annual update. Mandatory changes due to the urgent

safety update notified no later than three months before the submission of the annual update can be included in its scopes of changes. This way urgent safety update can be reported with the notification of annual update along with other changes.

1 application per product, pharmaceutical form & Member State of destination = 1 fee

Example: A company holds PD notices for all four pharmaceutical forms of 'product X':

- tablets;
- orodispersible tablets;
- oral solution;
- solution for injection.

This parallel distributor has to submit four annual updates for 'product X', one for each pharmaceutical form.

From 1 July 2024, mandatory changes due to urgent safety updates should be reported as part of the notification of annual update along with other changes. In case of multiple safety updates impacting the same product, only the latest version of the annex needs to be submitted.

5.6. What is the relation between the annual update and the bulk change?

The **annual update** procedure can be used to introduce changes to the parallel distribution notice for a particular medicinal product.

The annual update however needs to be submitted every year. Consequently, the annual update allows the Agency to have an overview of the medicinal products distributed in parallel. The Agency recommends that parallel distributors notify all of the changes made to a particular product within a year through the annual update.

The **bulk change** is a procedure of a different scope than the annual update.

5.7. What is the "birthday date" of an annual update?

The "**birthday date**" of an annual update is the date by when an annual update should be submitted. The first "birthday date" is counted from the date of the last PD notice issued for a certain pharmaceutical form of a particular product for each Member State of destination, prior to 01/05/2013. When no PD notice for a certain pharmaceutical form of a particular product for each Member State of destination had been issued prior to 01/05/2013, the birthday date is calculated from the date of the first PD notice issued after 01/05/2013.

Example: A parallel distributor holds the following PD notice for 'product X' tablets issued on: 5 March 2006, 27 July 2008, 22 December 2008 and 19 February 2013. The first "birthday date" is February 2014 and the company is required to submit an annual update before the end of February 2014.

The following "birthday dates" will remain the same for all subsequent annual updates. If the first annual update was submitted in February 2013, then the second "birthday date" will be February 2014. The "birthday date" can also be moved forward if the annual update is submitted before the set date. If the second "birthday date" is February 2014, but the annual update is submitted in January 2014 then the third "birthday date" will be January 2015.

5.8. When to submit an annual update?

An annual update should be submitted once a year before its "birthday date" only for those products which have been distributed in the last 12 months and/or for those products which will be distributed in the next 12 months.

ONE application per product AND pharmaceutical form AND Member State of Destination = 1 FEE

It is strongly recommended that the parallel distributors submit only one notification when applying for a notification of an annual update for the first time and wait for the outcome of the parallel distribution notification check in order to avoid the repetition of errors when submitting subsequent notifications.

5.9. How to submit an annual update? Rev. Apr 2022

The applicants should use the Checklist for annual updates for parallel distribution: guidance for industry in advance of submission. In order to improve the quality of submissions, it is recommended to include the checklist with your submission.

A notification of an annual update has to be supported with the following documentation:

- **colour copies** of the outer and inner labelling of only one EU presentation of that particular pharmaceutical form compiled in a single document preferably showing the most complicated re-packaging option e.g. re-boxing or re- labelling of a product sourced from a Member States of Origin where non-Latin alphabets are in use; or the colour copies of the new re-packaging method when it is included in the form. Where the pharmaceutical form consists of presentations with different medical devices, colour copies of each of these should be included in the submission. If the originally sourced product has a colour code related to safety, parallel distributors should follow the same style. In cases where the language on the sourced product is the same as the language of the destination Member State, parallel distributors may be requested to provide additional labelling that they intend to use in case they source the product from a country where the language from the destination Member State does not feature on the cartons.
- **Mock-ups** in an editable format
    - in case of relabelling: please provide two separate documents: one document containing a mock-up of the outer label and another one of the inner label (not combined in one file).
    - In case of reboxing: please provide two separate documents: one document containing a mock-up of the outer carton and another one of the inner label (not combined in one file).
- **additional documents** relating to the particular scopes of changes (e.g. authorisations, mock-ups etc.);
- **an editable format** of the **package leaflet** (doc, pdf) in the final sales format in the language of the Member State of destination in compliance with the latest version of the EU marketing authorisation;
- a **report** extracted from text comparison software (if applicable).

Annual updates for bilingual packs (E.g. Member State of Destination Sweden and Denmark) should be submitted at the same time. Please provide clarifications in the cover letter or in the details of re-packaging method.

If in addition to revision of the product information (indicated in 'Annual update' submission) a parallel distributor wishes to notify the Agency about other changes, such as change in the re-packaging method, countries of origin/destination, product presentations should be grouped by scopes of change.

For example, EU005, EU001 additionally are now being re-boxed from different EU presentations – create first 'Annual update-scope of change' submission to report re-boxing and change of the sourced pack size.

EU002 is now created by sourcing EU001 - create second 'Annual update-scope of change' submission to report change of the sourced pack size.

The above documentation should be submitted via the procedure form in IRIS. For guidance on the submission, please refer to the IRIS submission guide in the Guidance section.

Updates to the information included in the IRIS form after submission of any notification for parallel distribution are only possible in exceptional cases, so the applicants should review the information included in the form carefully before submitting. Changes impacting fees would not be possible after submission. Only changes requested by the assessor would be possible and only by exception when properly justified.

5.10. What are the requirements for dormant notices? NEW May 2024

If the medicinal product has not been distributed in parallel for the last 12 months it should be updated to the 'dormant' status using the 'Update of Parallel Distribution Notice Status' procedure, which does not incur any fees. During the period of dormancy, the annual update does not need to be submitted.

The confirmed dormancy will be reflected in the public register of parallel distribution. An independent notice will not be sent.

The notices will remain 'dormant' until the Agency is notified otherwise.

If the parallel distributor wishes to re-introduce the medicinal product to the market in parallel, he shall submit an 'Update of Parallel Distribution Notice Status'. It is mandatory to simultaneously submit an annual update notification for that said product. The product can then be distributed in parallel once again, from the day of status update in IRIS, provided that the Agency has been made aware of the changes which have occurred since the product was dormant through the annual update procedure.

5.11. Text comparison software report

In cases where the check of the package leaflet has to be completed (i.e. when there is a change in the package leaflet), a text comparison report submitted with an annual update/notification of changes will attract a reduced fee. The report should serve as a proof that the submitted package leaflet is in compliance with the latest annex.

The Agency does not recommend any particular text verification software. It should be text comparison software that preserves data integrity of the documents (i.e. the software should not change the file formats for the text comparison). The created report should list the deviations in table form. It should be designed to detect the following deviations between the package leaflet and the text of the annex:

- **Change:** Text found in the leaflet which replaces the text in the annex.
- **Deviation:** Text found in the leaflet that is not identical to the one in the annex, e.g. typos, grammatical mistakes etc. Please note, if an error is found in the annex, the parallel distributor should inform the Agency by mentioning the error in the report.
- **Deletion:** Text found in the annex which is not in the leaflet.
- **Insertion:** Text found in the leaflet which is not in the annex.
- **Hyphenation:** Change due to a software-generated hyphen inserted at the end of the line or due to an addition or removal of a hyphen – the Agency software interprets a missing hyphen as a deletion.

- **Case:** Upper- and lower-case differences.
- **Space:** Change due to space inserted between characters vs. no space.

Style changes:

- **Bold:** Changed font style (whether text is bold or not).
- **Italic:** Changed font style (whether text is italic or not).
- **Underline:** Change due to text being underlined or not.
- **Size:** Changed font size – please make sure to follow the readability guidelines (font equivalent to Times New Roman 9 for package leaflet).
- **Sub/Super:** Change between regular, superscripted, or subscripted text.

The submitted report must not contain deviations with the exception of the date of the latest revision as well as the following:

Acceptable deviations in the report:

- The **revision date** of the most recent published annex;
- **Deletion**: Text found in the annex which is not in the leaflet: e.g. more manufacturers in the annex, but fewer in the package leaflet;
- **Insertion:** Text found in the leaflet which is not in the annex: e.g. parallel distributor and re-packager's details, internal code, trademark symbol or sentence;
- **Deviation:** Text found in the leaflet that is not identical to the one in the annex: e.g. correction of typos or grammatical mistakes should be listed and justified in the report;
- **Size:** Changed font size – please make sure to follow the readability guidelines; font size must be equivalent to at least Times New Roman 9 for the package leaflet.

Any other deviations will be considered as mistakes and will result in invalidation of the submitted notification, if not justified in the submitted report or in the cover letter.

6. Fees

6.1. What are the administrative fees payable to the Agency in relation to parallel distribution?

Pursuant to Article 8 (3) of Regulation (EC) 297/95 "a fee shall apply for administrative services where the information required in the case of parallel distribution has to be checked." In case of non-payment the Executive Director may refuse to perform the administrative service and return the notification to the parallel distributor or to suspend the service until the fee has been paid, including the relevant interest, Article 10 (3) of Regulation (EC) 297/95.

For further information on fees, see Fees payable to EMA.

6.2. How does the invoicing system work?

The fee due date is the date when the Agency determines the total fee amount that is due for an application or service. In the case of parallel distribution, the fee due date corresponds to the date of submission of the

notification and the parallel distributor's obligation to pay that fee starts on that date. An application for parallel distribution can be withdrawn without any charges within 24 hours from the day of the submission.

The Agency's terms and conditions for payment of fees stipulate that an invoice is payable 30 days from the invoice date. That represents the deadline for the parallel distributor to settle the payment.

The invoice is sent within 15 days of submission to the parallel distributor and contains clear details of the product(s) involved, the amount of the fee, the bank account to where the fee should be paid and the due date for payment.

For information and guidance on invoicing, terms and conditions of payment, and how to set up a customer account, see **How to pay**.

6.3. Fees for an initial notification

A **full fee** for the parallel distribution notification check is applicable to **each EU presentation** of a medicinal product per Member State of destination.

If the official language in different Member States of destination is the same (Germany and Austria; Greece and Cyprus, Belgium and Luxembourg, Ireland and Malta.), only one fee is applicable. The fee covers the parallel distribution notification check and any subsequent safety updates relating to the initial notification triggered and adopted by the Committee for Medicinal Products for Human Use.

6.4. Fees for an annual update

Each annual update is subject to a fee. This fee covers all EU presentations for one pharmaceutical form of a certain product per Member State of destination or for several Member States of destination having the same official language.

A reduced fee is applicable to each annual update if supported with a report generated through text comparison software which meets the specific conditions listed in the section about the Text comparison software report. The quality of the reports will be monitored by random checks of the package leaflets with the purpose of confirming their validity. The **reduced fee** only applies, where a parallel distribution notification check of the package leaflet is replaced by a valid text comparison report in addition to the package leaflet. The validity of the reports will be monitored by random checks of the package leaflet. If during regulatory check it is established that the text comparison report is not provided, although indicated otherwise in the submission form, or random check revels deviations from the annexes to the product information, the submission will be invalidated while the fee will remain payable.

6.5. Fees for a safety update

Safety updates are processed free of charge as they are covered by the fee for initial notifications.

6.6. Fees for bulk changes

Each notification of bulk changes is subject to a fee. This fee shall cover all of a parallel distributor's initial notifications approved by the date of submission of the notification of bulk changes. The scope(s) of the changes are limited to: a change in the details of a parallel distributor ('Change of name and/or address' or 'Reassignment of notices for Parallel Distribution'), addition or deletion of a re-packager ('Change of manufacturer'), and/or a change in the name and/or address of a re-packager ('Change of manufacturer'). For more information, see fee regulations.

6.7. Further information on the fee structure of the Agency and relevant EU legislation

Further information on the fees payable to the Agency is available in the Explanatory notes on fees payable to the European Medicines Agency and in the Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures.