



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Division

Checklist for Annual Updates for Parallel Distribution

Guidance for industry

The European Medicines Agency (hereinafter 'the Agency') asks its applicants to use this checklist in advance of submission of an annual update for parallel distribution. You should be able to answer "Yes" to every item listed below unless a specific point is not applicable ("n/a") to the application in question. In order to improve the quality of submissions, it is recommended to include the checklist with your submission.

Points 6 – 12 refer to the creation of scopes of change within an annual update. In case you are only updating the package leaflet and labelling and are not creating any additional scopes of change, please refer to **points 1 – 5 only**.

Upon receipt of an annual update for parallel distribution, the procedure manager proceeds to validate the documentation submitted in accordance with the checklist included below.

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.

Reference documents for further information

- Parallel distribution regulatory and procedural guidance:
<https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/parallel-distribution-regulatory-procedural-guidance>
- Frequently asked questions (FAQs) about parallel distribution:
<https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/frequently-asked-questions-about-parallel-distribution>
- Public register of parallel distribution notices:
<https://iris.ema.europa.eu/registerpd/>

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Regulatory check	Comments	Yes	N/A
1. Annexes to marketing authorisation	<p>The annual update is a DO and TELL procedure. Therefore, the product has to be shown as it is currently being marketed. Please note that parallel distributors have six months to implement a new annex and three months for urgent safety updates. Please ensure this is reflected in your submission.</p> <p>Human medicines:</p> <p>In order to determine the correct version of the annexes to the relevant marketing authorisation:</p> <ul style="list-style-type: none"> • Check the EMA website: (https://www.ema.europa.eu/en/medicines) • and European Commission (EC) website: (https://ec.europa.eu/health/documents/community-register/html/index_en.htm) <p>To determine the correct annex date, please refer to the date <u>next to the procedure number</u> (e.g. 04/06/2020, IB/49). As a rule of thumb, please use the most recent approved annexes.</p> <p>Please note, that published yearly updates may not include the latest approved variation (i.e. the variation published above the yearly update on the EC website does not contain "updated with the decision of ABCD of DD/MM/YYYY"). In those cases, please refer to the information published on the European public assessment report (EPAR), which should contain the latest approved variation.</p> <p>Veterinary medicines:</p> <p>In order to determine the correct version of the annexes to the relevant marketing authorisation:</p> <ul style="list-style-type: none"> • Check the Veterinary Medicines Information website: https://medicines.health.europa.eu/veterinary/en <p>To determine the correct annex date, please search for your product. Once on the product page, scroll down to the header "Documents". Here you will find the product information. Please download the annex in the correct language and determine the annex revision date from the naming convention of the downloaded PDF. The naming convention is as follows: ema-combined-vXX-PRODUCT NAME-vraXXX-YYYY-MM-DD-language code.</p>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	The highlighted date is the correct annex date that should be used for your submissions.		
2. Package leaflet	<p>When the annual update includes multiple EU-numbers with different package leaflets for the same type of immediate packaging, please submit only one package leaflet. Please see the FAQs for the exception to this requirement.</p> <p>Ensure that the revision date of the package leaflet matches the date of the annexes and the date indicated in the field 'Product Information date' in IRIS.</p> <p>Ensure that the relevant manufacturer is mentioned and matches the one mentioned on the outer packaging. In case of discrepancies between the annex and the package leaflet of the sourced product, please follow the advice provided in the FAQs on parallel distribution and provide justification for such discrepancy in your submission.</p> <p>Ensure that the colour scheme of the annexes is adhered to in your package leaflet if the Annex requires this.</p> <p>Ensure that the reference to 'Appendix V' is replaced with the current contact information of the reporting system in the 'Member State(s) of Destination' (MSD).</p>	<input type="checkbox"/>	<input type="checkbox"/>
3. Text comparison report	<p>Text comparison reports are optional and do no longer provide for fee reduction. Inclusion of a text comparison report is still recommended since it does facilitate the assessment of your annual update.</p> <p>The Agency does not recommend any particular text verification software. It should be a text comparison software that preserves data integrity of the documents (e.g. the software should not change the file formats for the text comparison). The created report should ideally juxtapose the deviations in table form. It should be designed to detect deviations between the package leaflet and the text of the annex. Deviations should be highlighted and justified in the report.</p>	<input type="checkbox"/>	<input type="checkbox"/>
4. Outer and inner labelling	A notification of an annual update has to be supported with all the following documentation:	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<ul style="list-style-type: none"> • colour copies of the outer and inner labelling of only one EU presentation per pharmaceutical form: <ul style="list-style-type: none"> ○ Each set of colour copies per pharmaceutical form should be 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 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 product has multiple pharmaceutical forms with different immediate packaging, colour copies and package leaflets of one EU presentation of each of these should be included in the submission. For example, if you hold notices for a product with pharmaceutical form: solution for injection with immediate packaging syringes, vials, and cartridges; then three sets of colour copies and package leaflets will need to be provided. ○ 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 the 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. ○ As this is an annual update, please provide us with images of the product as it is currently brought to market. 		

Regulatory check	Comments	Yes	N/A
	<ul style="list-style-type: none"> • Mock-ups in an editable format: <ul style="list-style-type: none"> ○ 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). <p>Ensure that the images correspond to the product presentation indicated in IRIS and that the text is in the language of the MSD.</p> <p>The text on the labelling should match the information in the annexes apart from:</p> <ul style="list-style-type: none"> • Manufacturer responsible for the release of the sourced product batch. • Parallel distributor and/or repackager(s) details. • 'Blue box' in accordance with national regulations of the Member State of destination. If there are no national requirements in place, the blue box is not mandatory. <p>In case of change of pack size, the sourced/original EU-number on the packaging has to be fully covered on both outer and inner labelling.</p> <p>Ensure that the product presentation corresponds to the description of the approved EU-presentation in its marketing authorisation (e.g. if according to the marketing authorisation, a product comes in a bottle without outer carton, an outer carton should not be created).</p> <p>Even if not included in the annex, it is recommended to adhere to the colour scheme of the packaging of the sourced product (e.g. warning text or colour code per strength) as this has correct use and patient safety implications. If the colour scheme is part of the annex, it has to be implemented in the new labelling as well.</p>		

Regulatory check	Comments	Yes	N/A
	<p>In case you are reboxing, and when the inner label fully covers the originally sourced product, please always include colour copies of the original product without the inner label attached for our assessment.</p> <p>For further requirements on labelling, please refer to the regulatory check section on the FAQs on parallel distribution published on the EMA website:</p> <p>https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/frequently-asked-questions-about-parallel-distribution</p>		
5. Annex IV (educational material & controlled distribution system), patient alert cards and biological products specifics	<p>Ensure that any particular conditions for distribution of the product are met before placing the product on the market, liaise with the relevant National Competent Authorities in the EU/EEA, as needed.</p> <p>In cases where labelling information is amended as a result of national requirements but not included in the annexes, please provide valid justification for such inclusion with the submission.</p> <p>It is noted that for pharmacovigilance reasons and traceability purposes, it may not be possible to deviate from the revision date on sourced Risk Minimisation Measures material.</p>	<input type="checkbox"/>	<input type="checkbox"/>
6. Creation of scopes of change	<p>When creating a new scope of change please ensure the following:</p> <ul style="list-style-type: none"> Consult the 'Public Register' to check what changes have been authorised in the past. For example, when adding Member States of Origin (MSO), please check which MSO you have already been authorised to source from and only tick those that you wish to <i>add</i> to the notice. Ensure EU-numbers are grouped per scope of change they are subject to (i.e. when two EU-numbers are subject to the same scope of change, for example the addition of reboxing, then please add both EU-numbers to the same scope of change. When you have a third EU-number that is subject to a different scope of change, for example addition of Romania as a MSD, then please create a second scope of change for this EU-number). 	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
7. Addition or removal of MSO or MSD	<p>As parallel distribution is the distribution across European borders, it is not possible to source a product from one Member State and parallel distribute it in the same Member State.</p> <p>In case only one MSD is left after removal of others, ensure that it is not included also as MSO.</p> <p>Please tick only those MSOs you wish to <i>add</i> to the regulatory entitlement. To see the MSOs for which you are already authorised, please consult the 'Public Register'.</p>	<input type="checkbox"/>	<input type="checkbox"/>
8. Prior letter for the specific mechanism	<p>Please ensure that if the specific mechanism applies, a prior notice letter containing, at least, the following details has been sent to the MAH at least 30 days before submission:</p> <ul style="list-style-type: none"> • Parallel distributor name; • Product name/active substance; • Member States of Origin; • Member States of Destination. <p>The prior notice letter is to be signed and sent either by the parallel distributor or by another company on behalf of the parallel distributor.</p> <p>Further information on the specific mechanism can be found on the FAQs on parallel distribution published on the EMA website:</p> <p>https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/frequently-asked-questions-about-parallel-distribution</p>	<input type="checkbox"/>	<input type="checkbox"/>
9. Addition/removal of repackaging method	<p>When requesting addition to the already approved re-packaging method, please select the option 'Relabelling and re-boxing' in IRIS and provide details of the new re-packaging method, for example, 'we are adding re-boxing to already approved relabelling option....'.</p> <p>Documents required when adding re-boxing:</p> <ul style="list-style-type: none"> • Colour images of the new outer packaging and images of the re-labelled inner packaging in one single file. • Mock-ups in case of reboxing: please provide two separate documents: one document containing a 	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<p>mock-up of the outer carton and another one of the inner label (not combined in one file). The text on the mock-up should be identical to the text on the colour copies and in compliance with the annex. Please refer to Annex I at the end of this checklist for more information.</p> <p>Documents required when adding relabelling:</p> <ul style="list-style-type: none"> • Colour images of the relabelled original outer packaging and images of the re-labelled inner packaging in one single file. • Mock-ups 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). The text on the mock-up should be identical to the text on the colour copies and in compliance with the annex. Please refer to Annex I at the end of this checklist for more information. <p>The omission of colour copies is only accepted in case the new repackaging method has not yet been marketed <i>and</i> provided they comply with EMA requirements as laid down in the FAQs on parallel distribution published on the EMA website.</p> <p>For multipacks with intermediate packaging the repackaging method of the outer packaging containing the 'Blue box' defines the repackaging method of the presentation.</p> <p>When requesting removal or change of the already approved re-packaging method, please select the option 'relabelling' OR 're-boxing' in IRIS and provide details of the new re-packaging method, for example, 'we are removing re-boxing as repackaging method and will only relabel the product...'</p>		
<p>10. Addition of a repackager(s)</p>	<p>Enter the repackager(s) that you wish to add to your presentations. If they are not available in the list, liaise with your repackager(s) to register themselves in OMS: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/iris-guide-registration_en.pdf</p> <p>Provide reference number of the relevant "Manufacturing and Importation Authorisation" (MIA) for the company responsible for relabelling and/or re-boxing.</p>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<p>MIAs can be found in the European Community of manufacturing authorisations and of certificates of good manufacturing practice database (EudraGMDP): http://eudragmdp.ema.europa.eu/</p> <p>In case the relevant MIA is not available in EudraGMDP, please include colour copies in your IRIS submission.</p>		
11. Addition of sourced presentations	<p>Please include all EU-numbers you wish to source. Please ensure you split the scopes of change to reflect the correct addition of sourced presentations for every EU-number you are distributing.</p> <p>In general, the sourced and the parallel distributed EU presentation should be identical except in pack size.</p>	<input type="checkbox"/>	<input type="checkbox"/>
12. Introduction of bi- or trilingual packs	<p>Please notify the Agency of the creation of a bilingual or trilingual pack through the cover letter. Simultaneously, please submit an annual update/s for all presentations and MSD involved.</p>	<input type="checkbox"/>	<input type="checkbox"/>

This checklist is published for transparency purposes and does not preclude that, during the actual validation of the submitted application, the Agency may identify other issues to be addressed by the applicant.

Sample mockup of outer packaging - computer-readable text, i.e. separate text parts can be highlighted

Top flap:

FMD label:
PC
SN
EXP
Lot
2D barcode carrying the unique identifier

Name and address of the Marketing Authorisation holder
Batch manufacturer details

Parallel distributor details (+ repackager)

Main body (two identical panels):

Name of the medicinal product
active ingredient

Braille dots (if applicable)

Bottom flap:

Name of the medicinal product
active ingredient

Pharmaceutical form and contents

Statement of active substances.
List of excipients.
Method and route of administration.
Special warning that the medicinal product must be stored out of sight and reach of children.
Other special warnings, if necessary. Special precautions.
Special storage conditions.

Blue box with
country of destination

Sample mockup of inner labelling

Name of the medicinal product
Active ingredient
Route(s) of administration
Contents by weight/ volume/ unit

EXP
Lot