22/06/2022
EMA/405782/2020 Rev. 3
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. 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.

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	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. In order to determine the correct version of the annexes to the relevant marketing authorisation. • 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) To determine the correct annex date, please refer to the date next to the procedure number (e.g. 04/06/2020, IB/49). As a rule of thumb, please use the most recent approved annexes. 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.	☐	☐
2. Package leaflet	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. 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. 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.	☐	☐

Regulatory check	Comments	Yes	N/A
	Ensure that the colour scheme of the annexes is adhered to in your package leaflet if the Annex requires this. 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).		
3. Text comparison report	A text comparison report mentioned in the submission form and included with an annual update will incur a reduced fee for the procedure. The text comparison report aims to serve as a proof that your package leaflet is in line with the annex used. IMPORTANT: Please ensure that you **justify** any deviations between the annex and the package leaflet in your report. Any discrepancies found between the annex and the package leaflet during random checks that have not been marked, or justified in the report, will lead to an invalidation of the procedure. The fee will remain fully payable. You will be asked to re-submit the annual update with a correct report and package leaflet. Guidance on the text comparison report can be found further below. 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 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. 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.	☐	☐

Regulatory check	Comments	Yes	N/A
	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:** **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 one in the package leaflet;* **Insertion**: Text found in the leaflet which is not in the annex, e.g.: *parallel distributor and repackager's details, internal code.* **Deviation**: Text found in the leaflet that is not identical to the one in the annex, e.g.: correction of *typos or grammatical mistakes;* **Size**: Changed font size – please make sure to follow the readability guidelines; *font size must be equivalent to at*		

Regulatory check	Comments	Yes	N/A
	least 'Times New Roman 9' or the package leaflet. Any other deviations will be considered as mistakes.		
4. Outer and inner labelling	A notification of an annual update has to be supported with **all** the following documentation (one set of colour copies **and** one set of mock-ups): • **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 scope of change. If the originally sourced product has a colour code related to safety, parallel distributors should follow the same style. As this is an annual update, please provide us with images of the product **as it is currently brought to market.** • **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). In case the annual update includes multiple presentations (e.g. EU-numbers), please provide us with only one set of colour copies and mock-ups of one presentation. *Exception:* in case different EU-numbers have a different immediate packaging (i.e. syringe/pen/vial), then **one set of colour copies and mock-ups of each** of these should be submitted.	☐	☐

Regulatory check	Comments	Yes	N/A
	Ensure that the images correspond to the product presentation indicated in IRIS and that the text is in the language of the MSD. The text on the labelling should match the information in the annexes apart from: • Manufacturer responsible for the release of the sourced product batch. • Parallel distributor and/or repackager(s) details. • Blue box, which should bear the name of the MSDs and any other information required by the MSD; 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. 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). 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 safely implications. If the colour scheme is part of the annex this has to be implemented in the new labelling as well. 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. For further requirements on labelling, please refer to the regulatory check section on the FAQs on parallel distribution published on the EMA website: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/frequently-asked-questions-about-parallel-distribution		
5. Annex IV (educational material & controlled	Ensure that any particular conditions for distribution of the product are met before placing the product on the	☐	☐

Regulatory check	Comments	Yes	N/A
distribution system), patient alert cards and biological products specifics	market, liaise with the relevant National Competent Authorities in the EU/EEA, as needed. In cases where labelling information is included as a result of national requirements but not included in the annexes, please provide valid justification for such inclusion with the submission.		
6. Creation of scopes of change	When creating a new scope of change please ensure the following: • 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 *add* 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).	☐	☐
7. Addition or removal of MSO or MSD	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. In case only one MSD is left after removal of others, ensure that it is not included also as MSO. Please tick only those MSOs you wish to *add* to the regulatory entitlement. To see the MSOs for which you are already authorised, please consult the 'Public Register'.	☐	☐
8. Prior letter for the specific mechanism	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: • Parallel distributor name;	☐	☐

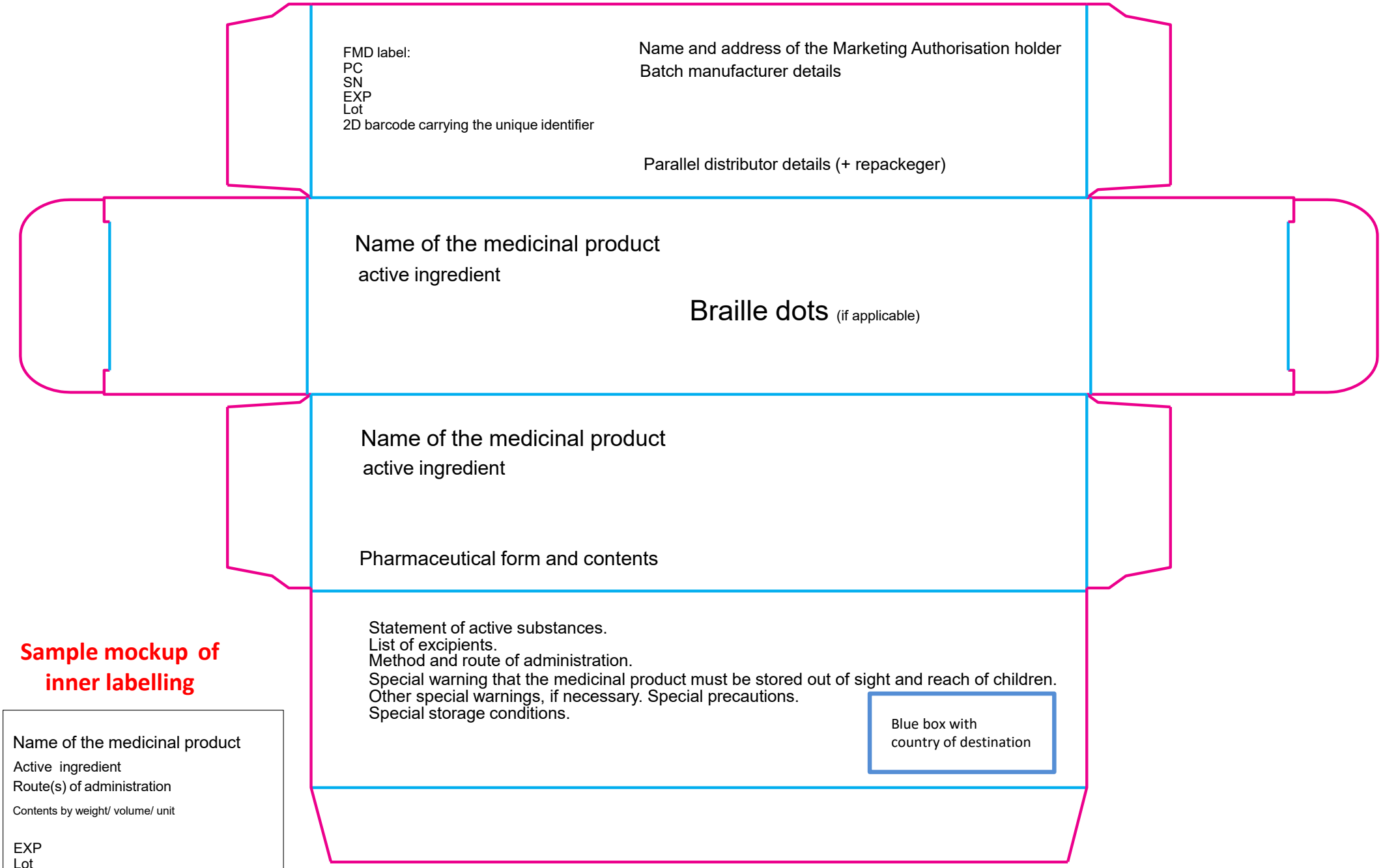
Regulatory check	Comments	Yes	N/A
	• Product name/active substance; • Member States of Origin; • Member States of Destination. The prior notice letter is to be signed and sent either by the parallel distributor or by another company on behalf of the parallel distributor. Further information on the specific mechanism can be found on the FAQs on parallel distribution published on the EMA website: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/parallel-distribution/frequently-asked-questions-about-parallel-distribution		
9. Addition/removal of repackaging method	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….'. Documents required when adding **re-boxing**: • **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 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. Documents required when adding **relabelling**: • **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	☐	☐

Regulatory check	Comments	Yes	N/A
	refer to Annex I at the end of this checklist for more information. The omission of colour copies is only accepted in case the new repackaging method has not yet been marketed *and* provided they comply with EMA requirements as laid down in the FAQs on parallel distribution published on the EMA website. For multipacks with intermediate packaging the repackaging method of the outer packaging containing the 'Blue box' defines the repackaging method of the presentation. 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…'.		
10. Addition of a repackager(s)	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 Provide reference number of the relevant "Manufacturing and Importation Authorisation" (MIA) for the company responsible for relabelling and/or re-boxing. 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/ In case the relevant MIA is not available in EudraGMDP, please include colour copies in your IRIS submission.	☐	☐
11. Addition of sourced presentations	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. In general, the sourced and the parallel distributed EU presentation should be identical except in pack size.	☐	☐
12. Introduction of bi- or trilingual packs	Please notify the Agency of the creation of a bilingual or trilingual pack through the cover letter. Simultaneously,	☐	☐

Regulatory check	Comments	Yes	N/A
	please submit an annual update/s for all presentations and MSD involved.		

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



Sample mockup of inner labelling

Name of the medicinal product

Active ingredient

Route(s) of administration

Contents by weight/ volume/ unit

EXP

Lot