



21/07/2020
EMA/405782/2020
Human Medicines Division

Checklist for annual updates for parallel distribution

Guidance for industry

The European Medicines Agency (hereinafter 'the Agency') recommends that this checklist is used 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.

Please note that this checklist should not be included in the 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.

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/>



Regulatory check	Comments	Yes	N/A
<p>1. Annexes to marketing authorisation</p>	<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>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>	<input type="checkbox"/>	<input type="checkbox"/>
<p>2. Package leaflet</p>	<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>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<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>		
<p>3. Text comparison report</p>	<p>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.</p> <p>IMPORTANT:</p> <p>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.</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). <u>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:</u></p> <p>Change: Text found in the leaflet which replaces the text in the annex.</p> <p>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.</p> <p>Deletion: Text found in the annex which is not in the leaflet.</p>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<p>Insertion: Text found in the leaflet which is not in the annex.</p> <p>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.</p> <p>Case: Upper and lower case differences.</p> <p>Space: Change due to space inserted between characters vs. no space.</p> <p>Style changes:</p> <p>Bold: Changed font style (whether text is bold or not).</p> <p>Italic: Changed font style (whether text is italic or not).</p> <p>Underline: Change due to text being underlined or not.</p> <p>Size: Changed font size – please make sure to follow the readability guidelines (font equivalent to 'Times New Roman 9' for package leaflet).</p> <p>Sub/Super: Change between regular, superscripted, or subscripted text.</p> <p>The submitted report must not contain deviations with the exception of the date of the latest revision as well as the following:</p> <p>Acceptable deviations in the report:</p> <p>Revision date of the most recent published annex;</p> <p>Deletion: Text found in the annex which is not in the leaflet, e.g.: <i>more manufacturers in the annex, but one in the package leaflet</i>;</p> <p>Insertion: Text found in the leaflet which is not in the annex, e.g.: <i>parallel distributor and repackager's details, internal code.</i></p> <p>Deviation: Text found in the leaflet that is not identical to the one in the annex, e.g.: correction of <i>typos or grammatical mistakes</i>;</p> <p>Size: Changed font size – please make sure to follow the readability guidelines; <i>font size must be equivalent to at</i></p>		

Regulatory check	Comments	Yes	N/A
	<p>least 'Times New Roman 9' or the package leaflet. Any other deviations will be considered as mistakes.</p>		
<p>4. Outer and inner labelling</p>	<p>As this is an annual update, please provide us with images of the product as it is currently brought to market (i.e. no mock-ups and no computer-generated labelling but actual colour copies of the product as placed on the market).</p> <p>In case the annual update includes multiple presentations (e.g. EU-numbers), please provide us with only one set of colour copies of one presentation.</p> <p><i>Exception:</i> in case different EU-numbers have a different immediate packaging (i.e. syringe/pen/vial), then one set of colour copies of each of these should be submitted.</p> <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, which should bear the name of the MSDs and any other information required by the MSD; <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 this has to be implemented in the new labelling as well.</p>	<input type="checkbox"/>	<input type="checkbox"/>

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>		
<p>5. Annex IV (educational material & controlled distribution system), patient alert cards and biological products specifics</p>	<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 included as a result of national requirements but not included in the annexes, please provide valid justification for such inclusion with the submission.</p>	<input type="checkbox"/>	<input type="checkbox"/>
<p>6. Creation of scopes of change</p>	<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"/>
<p>7. Addition or removal of MSO or MSD</p>	<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>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<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>		
<p>8. Prior letter for the specific mechanism</p>	<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"/>
<p>9. Addition/removal of repackaging method</p>	<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. <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; <p>Mock-ups are only accepted in case the new repackaging method has not yet been marketed <i>and</i> provided they</p>	<input type="checkbox"/>	<input type="checkbox"/>

Regulatory check	Comments	Yes	N/A
	<p>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> <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>	<input type="checkbox"/>	<input type="checkbox"/>
<p>11. Addition of sourced presentations</p>	<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"/>
<p>12. Introduction of bi- or trilingual packs</p>	<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.