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Post-authorisation Evaluation of Medicines for Human Use

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EMEA POST-AUTHORISATION GUIDANCE ON PARALLEL DISTRIBUTION

RELEASE FOR CONSULTATION (6 weeks)	1 July 2006 (Until 10 August 2006)
IMPLEMENTATION OF COMMENTS	
RELEASE OF FINAL DOCUMENT	

Updates and amendments introduced in this revision are identified respectively as "UPDATE" and "NEW" throughout the document.

Comments should be provided to the Parallel Distribution Secretariat luc.vansantvliet@emea.eu.int, fax: +44 20 7523 7051, by 10 August 2006

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EMEA POST-AUTHORISATION GUIDANCE – PARALLEL DISTRIBUTION (PD)

This guidance document addresses a number of questions, which parallel distributors or marketing authorisation holders (MAH) may have on the PD notification procedure. It also provides an overview of the EMEA position on issues.

This guidance is intended to give clarifications on the current handling of PD notifications in accordance with the "Procedure for notifications of parallel distribution of Centrally authorised Products" (EMEA/H/30313/98 Rev 2)".

Procedural changes are identified as "NEW" or "UPDATE" throughout the document.

This document will be updated regularly to reflect new developments/revisions resulting from accumulated experience in this field.

This guidance information and pre-notification dialogue between a parallel distributor and the EMEA should enable the parallel distributor to submit notifications, which are in conformity with the legal and regulatory requirements and which can be validated and processed speedily.

To obtain the information on a certain topic, simply **click** on the **highlighted key word**. We trust that the information, linked to the key word, answers most of your queries. However, in case of doubt after reading this guidance, we strongly encourage a parallel distributor in such cases to contact the EMEA Parallel Distribution Secretariat.

Update

- For issues related to an ongoing PD notification for a specific product or request for latest texts of a Commission Decision: please send your queries/requests to paralleldistribution@emea.eu.int.
- For more detailed queries on regulatory/legal and procedural matters related to PD notifications, you will be directed to the Scientific Administrator responsible for Parallel Distribution in the Regulatory Affairs and Organisational support Sector.

Update

In order to improve the EMEA service of providing pro-actively the latest texts of a Commission Decision to parallel distributors and to ensure that information regarding Commission Decisions and notifications is received by the relevant staff member of the parallel distributor, please inform the Parallel Distribution Secretariat of the contact point within the company and any updates (including: name, address, telephone number, fax number and email address) by sending an email to the Parallel Distribution Secretariat (paralleldistribution@emea.eu.int) or contact one of the team members of the Secretariat directly.

Please click here to enter into the list of questions.

Note:

Please note that this document has been produced for guidance only and should be read **in conjunction** with relevant Community legislation and the Commission Communication on the relevant Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998.

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Parallel distribution notifications

1. Is it possible to distribute a centrally authorised medicinal product from one EU Member State into another?

A Community Marketing Authorisation is valid throughout the European Union and a centrally authorised medicinal product is therefore by definition identical in all Member States. In addition, for centrally authorised medicinal products, the Community marketing authorisation encompasses all linguistic versions of the labelling and package leaflet of all authorised pack sizes. As a consequence, products put on the market in one Member State can be marketed in any other part of the Community by a 'parallel distributor', independent of the marketing authorisation holder (MAH).

The only changes that parallel distributors may introduce to the packaging of a centrally authorised medicinal product are those which are strictly necessary to market the product in the Member State of destination (use of different language version(s) of labelling and package leaflet; change in the package size provided the proposed pack-size falls within the scope of the Community Marketing Authorisation).

This context is different from the parallel importation of medicines authorised nationally because of differences, which can exist between the marketing authorisation granted by the Member State of origin and the one granted by the Member State of destination.

One of the consequences of the automatic extension of the Community Marketing Authorisations as of 1 May 2004 is that the nationally authorised marketing authorisations that are in conflict with centrally approved medicinal product become invalid. In order to avoid any unnecessary stock-outs or shortfalls, there may be a transitional period during which both nationally authorised and centrally authorised products will co-exist on the national market.

Any importation of a previously nationally authorised medicinal product, which has become centrally approved after the accession date of 1 May 2004, would qualify as illegal parallel importation and not as parallel distribution. National competent authorities should deal with such importations.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- PERF III Acquis Working Group, Reflection Paper on organisational aspects of Phasing in of Commission decisions concerning centrally authorised products in new Member States.

2. Is the EMEA Parallel Distribution (PD) notification procedure mandatory?

Regulation 726/2004 (EC) of the European Parliament and the Council laying down Community procedures for the supervision of medicinal products and establishing the EMEA determines the following task for the EMEA:

"Checking that the conditions laid down in Community legislation on medicinal products and in the marketing authorisations are observed in the case of parallel distribution of medicinal products authorised in accordance with this Regulation".

By the entry into force of this Regulation on 20 May 2004, notifications of parallel distribution of centrally authorised medicinal products have become mandatory throughout the Community. Therefore, on that date, all parallel distributed medicinal products on the market in the Community need to comply with the mandatory requirement involving notification to the EMEA.

References

- Regulation 726/2004 (EC) of the European Parliament and of the Council of 31 March 2004 laying down Community Procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136 30.04.2004), Article 57(o).

3. How shall I present my PD initial notification?

In order to facilitate the handling and the validation, PD notifications should be presented as follows, preferably in a plain plastic sleeve, not stapled, one notification per sleeve:

- Cover letter clearly indicating in the subject the name of the medicinal product, the strength, the pharmaceutical form and the pack-size.

Update

- The completed "Notification of parallel distribution of a centrally authorised medicinal product" form signed and dated by the official contact person.
  Information relating to the proposed PD notification, in particular:
  - Details of the parallel distributor (i.e. name, address, telephone and fax number, general e-mail address)
  - Details of the contact person in case of quality problems and defective batches, including a 24 hour contact number
  - Details of the medicinal product (i.e. invented name, active substance, strength, pharmaceutical form, packaging, pack-size) and authorisation number in the Community register of medicinal products (i.e. EU number)
  - Details of the MAH (i.e. name and address)
  - The Member State(s) of origin (choose from: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, The Netherlands, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom) (See also 'Can I distribute a centrally authorised product to and from Iceland, Norway and Liechtenstein?')
  - The Member State(s) of destination (choose from: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom) (See also 'Can I distribute a centrally authorised product to and from Iceland, Norway and Liechtenstein?')
  - Indication if the 'Specific Mechanism' is applicable to the notification or not (See also "Does the 'Specific Mechanism' agreed upon by the EU and the acceding countries apply to parallel distribution?")
  - Details of the Repackager(s) (See also: "Can I identify more than one repackager in the initial PD notification for a centrally authorised product?")
  - Nature of the repackaging
  - Certification that the condition of the product has not been affected
  - Statement that the product information remains in conformity with the latest Commission Decision and that the parallel distributor will submit a notification of a change to the EMEA should the product information and/or any other aspect of the notification be amended

- Annexes to the form:
  - Mock-ups[1] of the package leaflet of the medicinal product as proposed by the parallel distributor (2 copies), or if available, 2 printed package leaflets[2] of the medicinal product[3], clearly mentioning the date of the Commission Decision texts used.
  - Mock-ups[1] of the outer and inner packaging of the medicinal product as proposed by the parallel distributor (2 copies, in colour) or, if available, 2 colour copies[2] (e.g. scan, photocopy or photograph) of the repackaged medicinal product[3] (including outer and inner packaging). (See also "Do I need to submit colour copies and printed package leaflets of the repackaged presentation in my initial notification?")

[1] A "Mock-up" is a copy of the label or flat artwork design in full colour, providing a replica of both the outer and immediate packaging and labelling text or a copy of the package leaflet text of the medicinal product. It is generally referred to as a "paper copy" or "computer generated version".
[2] A colour copy is a colour photocopy, a digital scan (colour print out of the scanned item) or a colour photograph of the (repackaged) sale presentation of the medicinal product as it will be put on the market in the Member State of destination. The printed package leaflet must be representative (content and format) of the sale presentation.
[3] If not available at the time of notification, the printed package leaflet and colour copies of the repackaged product will need to be provided to the EMEA before issuance of the notice.

- A full copy of the original Wholesale distribution license (within the meaning of Article 77 of Directive 2001/83/EC or Article 65 of Council Directive 2001/82/EC) for the parallel distributor
- A full copy of the original Manufacturing Authorisation (within the meaning of Article 40 of Directive 2001/83/EC or Article 44 of Council Directive 2001/82/EC) of the parallel distributor or the repackager is different from the parallel distributor

NEW

The Annexes to the Community Marketing Authorisation may mention several MAH manufacturers, as the MAH has to mention all its authorised manufacturers in the Annexes. The parallel distributor should provide only one mock-up or colour copy of the outer and one mock-up or printed version of the package leaflet mentioning one MAH manufacturer when submitting an initial notification (e.g. the manufacturer of the first batch that the parallel distributor will distribute). After the Notice has been granted, it is the responsibility of the parallel distributor to indicate the MAH manufacturer responsible for the release of the concerned, parallel-distributed batch on the outer labelling and in the package leaflet. A notification of a change is not necessary to change the MAH manufacturer (See also: "Do I have to mention the manufacturer on the outer labelling and in the package leaflet?")

The licenses should be submitted with the first notification to the EMEA and then again, whenever these are updated/amended.
It is also recommended to enclose an English translated version of the authorisation(s) in addition to the copy of the original one to facilitate their review and validation by the EMEA Inspection Sector.

NEW

It is allowed that a parallel distributor is located in a Member State different form the Member State of destination. The parallel distributor should hold a valid wholesale-distribution licence in the Member State where it is located.

It should be noted that the responsibility for the quality of the submitted documentation lies with the parallel distributors and is crucial to the overall process. In doubt, parallel distributors are advised to contact the EMEA Parallel Distribution Secretariat.
Similarly, deficient and missing documentation can lead to a 'Request for missing information' letter, and ultimately to the non-validation of the notification. (See "How shall my initial PD notification be handled (timetable)?")

NEW

The "Notification of parallel distribution of a centrally authorised medicinal product" form can be downloaded from the EMEA website: http://www.emea.eu.int under parallel distribution or under human medicines/parallel distribution/guidance and templates. Also explanatory notes how to fill in the forms are available.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of parallel distribution of a centrally authorised medicinal product form
- Notification of parallel distribution of a centrally authorised medicinal product form with explanatory notes

4. How and to whom shall I submit my initial PD notification?

Parallel distribution notifications should be addressed and sent for the attention of the Parallel Distribution Secretariat at the following address:

EMEA - Human Post-Authorisation Unit (or Veterinary Unit – *as appropriate*)
Parallel Distribution Secretariat
7, Westferry Circus
Canary Wharf
London E14 4HB
UK

Two paper copies of the PD notification form and supportive documentation should be submitted to the EMEA.

Update

Notifications of parallel distribution for veterinary medicinal products are handled by the Veterinary Unit and not by the Parallel Distribution Secretariat.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

5. When shall I submit my initial PD notification?

Parallel distributors must submit their initial notification to the EMEA in advance of commencing distribution of a specific product to allow for the procedure to be completed. (See "How shall I present my PD initial notification?" and "How shall my initial PD notification be handled (timetable)?")

Update

Until the procedure is finalised and EMEA has issued a notice, it cannot be determined if the proposed repackaged medicinal product complies with the terms of the Community Marketing Authorisation and the pharmaceutical legislation. A parallel distributor should therefore ensure that a notice is granted before initiating parallel distribution

Update

Experience has shown that the average overall handling time necessary for parallel distributors to obtain the Notice is 3 to 6 months. However, nothing precludes a faster review.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

6. How shall my initial PD notification be handled (timetable)?

Validation

Upon receipt of an initial PD notification, the EMEA will check its validity within 5 working days and inform the parallel distributor of the start of the regulatory check or of any missing or incorrect information with a 'Request for further information' letter.

The PD Secretariat will check compliance with the date of latest Annexes to the Community Marketing Authorisation for the concerned medicinal product at validation stage. In case the date on the proposed package leaflet (PL) is not corresponding with the date of the latest marketing authorisation, the relevant annexes will be provided together with the 'Request for further information' letter.

Receipt of PD notification	Day x
Start of EMEA validation	Day x+1
EMEA validation	Day x+5

In case of missing information, this period will be extended until receipt of all relevant information.
The parallel distributor is requested to send replies to the concerned staff member of the Parallel Distribution Secretariat within the set time frame, indicating clearly in the subject of the cover letter the name of the medicinal product, the strength, the pharmaceutical form and the pack-size and to send a separate reply for each notification.

Regulatory Check

The EMEA will check the conformity of the proposed labelling and package leaflet with the text of the latest annexes to the Community Marketing Authorisation within 30 working days after validation of the notification and will notify the parallel distributor of any objections or comments.

EMEA validation	Day y
Regulatory check	Day y+30

In case of objections or comments, the procedure will be suspended (Clock Stop) until receipt of revised proposals for labelling and/or package leaflet.
The parallel distributor is requested to send replies to the concerned staff member of the Parallel Distribution Secretariat within the set time frame, indicating clearly in the subject of the cover letter the name of the medicinal product, the strength, the pharmaceutical form and the pack-size and to send a separate reply for each notification.

A new cycle of 30 working days applies each time the parallel distributor (re)submits updated labelling and/or package leaflet proposals in accordance with the latest annexes to the Community Marketing Authorisation and with the EMEA comments.

The EMEA will ask the parallel distributor to provide 2 printed package leaflets[1] and 2 colour copies of the repackaged product[1] (including outer, inner packaging) before issuance of the EMEA notice in case these were not available at the time of the notification.

[1] The printed package leaflet must be representative (content and format) of the sale presentation. The colour copy is a colour photocopy, a colour print out of a digital scan or a photograph in colour of the (repackaged) sale presentation of the medicinal product.

EMEA Notice

When there are no objections/comments or when objections/comments have been completely addressed by the parallel distributor, the EMEA issues a Notice and sends it to the parallel distributor informing that the regulatory check has been completed and indicating that the product proposed for parallel distribution complies with the terms of the Community Marketing Authorisation of the concerned centrally authorised medicinal product.

The EMEA also sends a copy of the Notice to:

- the National Competent Authority of the Member State of destination
- the marketing authorisation holder (MAH) of the medicinal product
- the National Authority of the Member State where the parallel distributor is located, if different from the Member State of destination

NEW

- the Official Medicines Control Laboratory (OMCL) of the Member State of destination, in the case the medicinal product is a vaccine or a blood product.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of parallel distribution of a centrally authorised medicinal product form

7. Where can I obtain the latest texts for labelling and package leaflet for a given centrally authorised product?

Parallel distributors must ensure that the proposed labelling and package leaflet is in conformity with the latest Annexes to the Community Marketing Authorisation for a given centrally authorised product.

Relevant Annexes to the marketing authorisation for centrally authorised products can be obtained from the EMEA Parallel Distribution Secretariat upon written request to the attention of: paralleldistribution@emea.eu.int. The Parallel Distribution Secretariat will provide such texts within 5 working days.

Note: the EMEA prospectively provides the latest Annexes to Community Marketing Authorisation for a given product to all parallel distributors that have validated Notification for that product. This service is provided to parallel distributors to help them to maintain the labelling and package leaflet of the repackaged medicinal products in conformity with the latest Annexes to the Community Marketing Authorisation. Parallel distributors who receive that information should save it upon receipt, as individual requests for the same information will not be processed by the EMEA. Please note that the last revision date is usually not mentioned in the electronic document of the Annexes itself. The European Commission when taking a Decision on the product determines this date. The last revision date is however always mentioned in the e-mail or Eudralink message accompanying the Annexes. The last revision date should be expressed in the package leaflet in the Month Year format, e.g. November 2005 (i.e. not in the 08/2005 format or adding the Day 25 November 2005).

Update

These annexes are also included in the European Public Assessment Report(s) (EPARs) available in all EU official languages on the EMEA website and in the Community Register of medicinal products for human use or in the Community Register of veterinary medicinal product on the website of the European commission:

Update

http://www.emea.eu.int under Human medicines/List of authorised products (EPARs).

http://europa.eu.int/comm/enterprise/pharmaceuticals/register/index.htm

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

8. Is there any deviation allowed to the texts of the Commission Decision for a certain product?

In respect of the package leaflet and labelling (inner and outer) the EMEA checks the strict compliance of the parallel-distributed product with the terms of the Community Marketing Authorisation for the centrally authorised medicinal product and in the language(s) concerned.

Apart from the mentioning of the 'parallel distributor', the 'repackager' and the 'MAH's manufacturer' on the outer labelling, the only additional flexibility given is in respect to the terms used for expressing the batch number and expiry date. (See "Do I have to mention the MAH's manufacturer on the outer labelling?" and "How and where shall I mention the parallel distributor and repackager on the medicinal product?") The parallel distributor is allowed to use the terms for batch number and expiry to be used for outer and/or inner labelling from Appendix IV to the QRD template for product information and any of the terms listed in the QRD document "Tables of Non-standard Abbreviations" (EMEA/27236-v7.0) for a certain Member State.

NEW

The parallel distributor is, however, allowed to make a reference to the registered trademark in the package leaflet and on the outer labelling (e.g. <Product X> is a registered trademark of <Company Y>) in accordance to trademark legislation.

NEW

Examples of additional text to the outer labelling or in the package leaflet, which will not be accepted by EMEA:

- 'Use as directed by doctor', if not mentioned in the Annexes to the Community Marketing Authorisation.
- 'Read the package leaflet before use', if not mentioned in the Annexes to the Community Marketing Authorisation.
- 'Procured from within the EU'. This sentence is not allowed particularly considering that parallel-distributed medicinal products by definition are sourced from within the EU.
- 'Imported by …'. Neither trademark law nor pharmaceutical law stipulates that the parallel distributor has to ensure that the word 'imported' appears on the outer packaging of medicinal product. This wording is not allowed particularly considering that it is no longer a question of 'importation', as parallel distribution only takes place within one market, i.e. the Community market.

NEW

Examples of minor changes to the text of the Annexes, which can be made by the parallel distributor, but only with the agreement of the EMEA or upon request of the EMEA:

- For medicinal products where a text is only visible after opening the packaging and the text is mentioned in the Annexes (e.g. 'Carton has been opened' under the lid of the carton box), this text has also be translated by the parallel distributor in the language(s) of the Member State of destination and added to the outer labelling of the parallel-distributed packs, if necessary in slightly modified form (e.g. 'After opening, the text <original text> will appear which means <text in the language of the Member State of destination>' or 'After opening, a foreign text in red letters will appear which means <text in the language of the Member State of destination>' on the label on the carton box).
- In case the composition or markings of a medicinal product changes, the parallel distributor must ensure that the formulation and markings mentioned in the leaflet of the parallel-distributed pack corresponds with the actual composition and markings in the pack. If simultaneous with the change of composition or markings other parts of the leaflet and/or labelling have changed, the parallel distributor should always use the latest version of the product information, but can change the composition or markings in the package leaflet to the concerned one. In this case, 2 proposals for the labelling and the leaflet should be submitted with the notification, i.e. one corresponding fully with the latest version of the product information and one corresponding also with the latest version of the product information with the exception of the concerned ('old') composition and marking.

If the local representatives of the MAH are mentioned in the Annexes, they form an integrated part of the product information and the parallel distributor should therefore add the local representatives of the MAH into the leaflet of the parallel-distributed packs.

References

- Tables of Non-standard Abbreviations (EMEA/27236-v7.0)
- Appendix IV to the QRD template for Product Information
- Council Regulation (EC) No 40/94 of 20 December 1993 on the Community trade mark
- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

9. Can I interchange multiple licenses in the context of parallel distribution?

The EMEA checks the compliance of the parallel-distributed product with the terms of the Community Marketing Authorisation for the concerned centrally authorised product in the language concerned.

Since this Community marketing authorisation is specific for a given centrally authorised product to be marketed under that particular invented name it is not acceptable for the parallel distributor to interchange them in the context of parallel distribution.

Parallel distributors wishing to distribute products which are available on the Community market under two or more invented names, need to submit to the EMEA a separate PD notification for each centrally authorised product.

Moreover, in accordance with Community legislation the name given to a medicinal product by the company may be either a) an invented name (brand name/trade name) or b) a common/scientific name together with the name of the manufacturer.

Since this means that the originator MAH is not allowed to interchange these, flexibility in this respect to a parallel distributor is also not allowed.

The same principle applies as to the use of the active substance description of the product.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended
- Guideline on the acceptability of invented names for human medicinal products processed through the centralised procedure (CMPM/328/98)

10. Can I propose a bundle-pack[2] of existing presentations in the context of parallel distribution?

The EMEA does not accept any proposals from parallel distributors to bundle existing presentations of a centrally authorised product to create a larger pack-size, even if this pack-size is covered by the Community marketing authorization of the concerned medicinal product.

The reason is that the different presentations are subject to separate central marketing authorisations.

Update

Only if there is a Community Marketing Authorisation for a bundle-pack with a particular EU registration number for a given medicinal product, also the parallel distributor can create this bundle-pack.

References

- ECJ (C-433/00) Aventis v Kohlpharma
- Notification of parallel distribution of a centrally authorised medicinal product form

[2] "Joining together of several packages of medicinal products, each leaving the necessary labelling in order to form a new retail unit"

11. How many PD notifications shall I submit for a given medicinal product?

The parallel distributor is only allowed to distribute presentations that are covered by the Community Marketing Authorisation for that particular centrally authorised medicinal product.

A separate notification should be submitted for each strength and pharmaceutical form of a given medicinal product (Several pack sizes for a given strength and form can be included in the same notification). (See also "How shall I present my PD notification/notification of a change")

References

- Notification of parallel distribution of a centrally authorised medicinal product form

12. What fee do I have to pay for an initial PD notification?

Update

A fee of 3,480 EURO for the administrative service of the regulatory check in the case of parallel distribution applies for each initial PD Notification.
This fee covers all pack-sizes of a particular strength and pharmaceutical form for a given medicinal product. In case, however, that a given medicinal product is available in a particular strength and pharmaceutical form, but has several presentations for administration (e.g. a solution for injection in a vial, a cartridge and a pre-filled pen presentation or a solution for injection in a pre-filled syringe and in an injection device presentation), a separate fee is applicable to the different presentations as the information on the labelling and the package leaflet is different.
The fee also covers the notification of parallel distribution for a given Member State of destination.

NEW

In the case of a PD notification for different Member States of destination with different official language(s) (e.g. Germany and Denmark), a separate fee for each Member State of destination will be charged, as the different languages have to be checked. In case of the same official language(s) in the different Member States of destination (e.g. United Kingdom, Ireland and Malta), only one fee is applicable.

For PD notifications submitted on or after 1 December 2005, the parallel distributor is no longer required to pay the fee in advance. EMEA will now issue an invoice on the date of receipt of the notification. The invoice is payable within 45 calendar days of the date of the invoice. The invoice is sent to the billing address indicated by 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. Where more than one notification is processed in a given month, a summary invoice will be issued at the end of each month indicating also the due date for payment of the invoice.

NEW

In order for parallel distributors to be able to process these EMEA invoices in their payment system, they can quote a purchase order number or a similar reference in the cover letter accompanying the notification form. EMEA will include the quoted purchase order number or reference in the EMEA invoice.

Before the validation of a notification, the fee can be refunded after a written request from the parallel distributor to withdraw the notification. After the validation letter of a notification for parallel distribution has been issued, EMEA cannot refund the fee in case of withdrawal by the parallel distributor.

Update

EMEA will only issue the notice if the regulatory check has been completed successfully and if the payment of the invoice (fee) for a given PD notification has been received. In case of non-payment, the EMEA can decide not to provide the requested administrative service of the regulatory check of the parallel distribution notification or to suspend all services under way until the fee has been paid. EMEA can also decide to take the necessary legal actions. This means that a given notification for parallel distribution and/or all further received notifications will not be checked and that no notice will be issued.

For more information about fees and fee payment, please consult: http://www.emea.eu.int/htms/general/admin/fees/feesfaq.htm,

References

- Council Regulation (EC) No 1905/2005 of 14 November 2005 amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency
- Rules for the implementation of Regulation (EC) No 297/95 as amended on fees payable to the European Medicines Agency and other measures (EMEA/MB/356866/2005)
- Notification of parallel distribution of a centrally authorised medicinal product form
- EMEA Information on the revision of Parallel distribution Administrative Charges and clarification regarding the procedure to be followed when adding a country of destination (EMEA/Ho/13397/04)

13. Do I need to submit colour copies and printed package leaflets of the repackaged presentation with my initial PD notifications?

Update

At the time of submission of an initial PD notification, mock-ups of the package leaflet and of the outer and inner packaging of the medicinal product as proposed by the parallel distribution have to be annexed to the notification form. If available, colour copies of the outer and inner packaging, and a printed package leaflet of the repackaged sales presentation can be provided instead of the mock-ups. At the time of issuance of the Notice, however, colour copies of the outer and inner packaging, and a printed package leaflet of the repackaged sales presentation will be requested by the EMEA if not already available with the initial notification. Without the colour copies and the printed package leaflet, the EMEA cannot issue the notice. (See also "How shall I present my PD notification?")

Where the quality of the provided colour copies or printed package leaflet is not considered acceptable, the EMEA may request the submission of revised ones.

References

- Joined cases C-427/93, C-429/93 and C-436/93, *Bristol-Myers Squibb and others / Paranova (Rec.1996,p.I-3457), para. 79.*

14. Do I need a wholesale distribution and manufacturing license in the context of parallel distribution?

All parties need to hold the appropriate licences for the activities in which they are engaged i.e. a wholesale distribution authorisation and/or manufacturing authorisation.

The ECJ has defined operations such as “removal of blister packs from the original external packaging and their insertion into new external packaging” or “addition to the packaging of new user instructions or information or the fixing of self-stick labels”, as repackaging and will therefore always require a valid manufacturing authorisation.

These repackaging activities can be carried out by the parallel distributor or may be outsourced to another company, subject in either case to the holding of a valid manufacturing authorisation. In the case of human medicinal products a manufacturing authorisation may permit the wholesale distribution of products covered by that license.

A parallel distributor is normally engaged in activities defined as wholesale distribution and will need to hold a wholesale distribution authorisation.

A copy of the complete original authorisation(s) (with attachments) should be enclosed with the first PD notification. It is also recommended to enclose an English translated version of the authorisation(s) to facilitate their review and validation by the EMEA Inspection Sector. A copy of any update or amendments to these licences occurring after issuance of the Notice should be provided to the EMEA as soon as possible.

References

- Article 77 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended or Article 65 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended - Wholesale distribution license
- Article 40 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended or Article 44 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended - Manufacturing Authorisation
- Article 77(3) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended
- Case C-232/94, MPA Pharma / Rhône-Poulenc Pharma (Rec.1996,p.I-3671) Joined cases C-427/93, C-429/93 and C-436/93, Bristol-Myers Squibb and others / Paranova (Rec.1996,p.I-3457), para. 79. *C-71/94, Eurim-Pharm Arzneimittel / Beiersdorf and others (Rec.1996,p.I-3603)*
- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of parallel distribution of a centrally authorised medicinal product form

15. How and where shall I mention the parallel distributor and repackager on the medicinal product?

ECJ case law requires the repackager and the MAH manufacturer to be identified on the medicinal product. In addition, the EMEA recommends the mentioning of the 'parallel distributor' on the medicinal product as follows:

Outer labelling
On the outer labelling the following text should be added (in the language(s) of the member state of destination):

"Parallel distributed and repackaged by.... (name is mandatory, address is recommended but not compulsory)" - in case parallel distributor and repackager are identical.
"Manufacturer: ….(name is mandatory, address is recommended but not compulsory)"

"Parallel distributed by... (name is mandatory, address is recommended but not compulsory)"
"Repackaged by ..... (name is mandatory, address is recommended but not compulsory)" - in case parallel distributor and repackager are different.
"Manufacturer: ….(name is mandatory, address is recommended but not compulsory)"

Where the parallel distributor has notified more than one repackager in the notification, he should ensure to only mention on the outer label the repackager for the concerned batch. (See also: "Can I identify more than one repackager in the initial PD notification for a centrally authorised product?")

Update

Where the MAH has different manufacturers for the medicinal product, the parallel distributor should ensure to only mention on the outer label the manufacturer responsible for the release of the concerned batch or to mention all manufacturers if it is impossible for the parallel distributor to identify which is the concerned manufacturer (See also: "Do I have to mention the manufacturer on the outer labelling and in the package leaflet?")

Inner labelling
If practical, the name of the parallel distributor and repackager should preferably be included on the inner labelling as well, but it is not compulsory.

It is acceptable to only mention the name:

"Parallel distributed and repackaged by.... (name)" - in case parallel distributor and repackager are identical

"Parallel distributed by... (name)" and "Repackaged by ..... (name)" - in case parallel distributor and repackager are different

Where the parallel distributor has notified more than one repackager in the notification, he should ensure to only mention on the inner label the repackager for the concerned batch. (See also: "Can I identify more than one repackager in the initial PD notification for a centrally authorised product?")

Package leaflet
Reference to the 'parallel distributor' and 'repackager' is allowed in the package leaflet.
The manufacturer of the MAH is already mentioned in the package leaflet.

References

- Joined cases C-427/93, C-429/93 and C-436/93, *Bristol-Myers Squibb and others / Paranova (Rec.1996,p.I-3457)*
- Notification for parallel distribution of a centrally authorised medicinal product form

16. Do I have to mention the manufacturer on the outer labelling and in the package leaflet?

Community Law, as complemented by ECJ case law requires the parallel distributor to mention the manufacturer of the MAH on the medicinal product. The parallel distributor, therefore, should add the MAH manufacturer on the outer labelling of parallel-distributed packs. The manufacturer is already mentioned in the package leaflet, as it is a legal requirement for all medicinal products.

The parallel distributor should mention the manufacturer responsible for the release of the concerned batch, as it appears in the package leaflet of the original batch (i.e. member state of origin).

Note: The annexes to the Community Marketing Authorisation may mention several MAH manufacturers. This is because the MAH has to mention all its authorised manufacturers in the Annexes approved by the European Commission. However, in the printed package leaflet (i.e. package leaflet of the original batch of the member state of origin), the MAH has to specify the manufacturer responsible for the release of the concerned batch. Therefore, the parallel distributor should refer to the package leaflet of the original batch and not to the Annexes to the Community Marketing Authorisation to identify the relevant manufacturer to be mentioned on the packaging.

NEW

Only in the case the MAH includes more than one manufacturer in the leaflet of the original batch and if it is impossible for the parallel distributor to identify which is the concerned manufacturer, the parallel distributor should mention all manufacturers in the package leaflet. The parallel distributor, however, should then also indicate all manufacturers on the outer labelling.
In each case, the same manufacturer(s) should to be mentioned on the outer labelling as in the package leaflet.

(See also: "How and where shall I mention the parallel distributor and repackager on the medicinal product?")

References

- Article 54 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended
- ECJ cases.
  C-443/99, Merck, Sharp & Dohme (Rec.2002,p.I-3703)
  C-102/77, Hoffman-La Roche / Centrafarm (Rec.1978, p.1139)
  (GR1978/00351 P 1978/00391 ES1978/00317 SVIV/00107 FIIV/00107)
- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

17. Can I identify more than one repackager in the initial PD notification for a centrally authorised product?

Parallel distributors are allowed to identify more than one repackager in the initial PD notification provided they include separate sets of mock-ups for the outer and inner labelling and for the package leaflet, each clearly identifying the concerned repackager, and a copy of the Manufacturing Authorisation for each repackager.

For the proposed outer labelling on the medicinal product, the parallel distributor must state the name (and optionally the address) of the repackager responsible for the release of that particular batch.

For the proposed inner labelling on the medicinal product and in the package leaflet, the parallel distributor is allowed to only mention the name of the repackager responsible for the release of that particular batch. (See also*:* "How and where shall I mention the parallel distributor and repackager on the medicinal product?")

The parallel distributor may also submit a 'notification of change' in order to include an additional repackager.

References

- Notification of parallel distribution of a centrally authorised medicinal product form
- Notification of a change for parallel distribution of a centrally authorised medicinal product form

18. Can I distribute a centrally authorised product to or from Norway, Iceland and Liechtenstein?

The principles laid down in section D of Commission Communication 98/C229/03 on the Community marketing authorisation procedures for medicinal products apply.

The EMEA 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 Community marketing authorisation. A parallel distributor can therefore sourced batches of a centrally authorised product in Norway, Iceland and Liechtenstein for parallel distribution in one or more EU Member States.

Parallel distributors are strongly recommended to consult the EMEA prior to submission of a PD notification to ensure that the given product are effectively harmonised in these countries.

For parallel import of a centrally authorised product into Iceland, Norway and Liechtenstein, the national procedures for parallel import apply.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- EEA Joint Committee Decision 74/1999
- Guidance document for Industry, with regard to the extension of the centralised procedure, referral procedures, parallel distribution/import and pharmacovigilance requirements to Iceland and Norway (EMEA/8518/00 Rev 1)

19. When shall I submit a notification of a change?

Parallel distributors must ensure that the proposed labelling and package leaflet remain in conformity with the latest Annexes to the Community Marketing Authorisation for the product concerned. For this purpose, the EMEA will prospectively provide the latest Annexes to Community Marketing Authorisation for a given product to all parallel distributors that have already obtained a Notice for that medicinal product.

Where amendments have been made to the Annexes of the Community Marketing Authorisation for a centrally authorised medicinal product, or when the parallel distributor wants to change information submitted in the initial PD notification (e.g. change in repackager or parallel distributor details, addition of a repackager, addition of the statement regarding the trade mark, addition of the name of the parallel distributor and the repackager to the package leaflet), the parallel distributor should submit a "Notification of a change" form, stating the scope of change.

In addition, a notification of a change must be submitted when the parallel distributor wants to amend the Member State(s) of origin.

NEW

The "Notification of a change for parallel distribution of a centrally authorised medicinal product" form can be downloaded from the EMEA website: http://www.emea.eu.int/ under parallel distribution or under human medicines/ /parallel distribution/guidance and templates. Also explanatory notes how to fill in the forms are available.

Note: A Notification of a change can only be submitted after obtaining an EMEA Notice for the initial PD notification.

References

- Notification of change for parallel distribution of a centrally authorised medicinal product form
- Notification of a change for parallel distribution of a centrally authorised medicinal product form with explanatory notes

20. How shall I present my PD notification of a change?

In order to facilitate the handling, PD notifications of a change should be presented as follows, preferably in a plain plastic sleeve, not stapled, one notification of a change per sleeve:

- Cover letter

Update

- The completed "Notification of a change for parallel distribution of a centrally authorised medicinal product" form signed and dated by the official contact person.
  Information relating to the proposed PD notification, in particular:
  - Details of the parallel distributor (i.e. name, address, telephone and fax number, general e-mail address)
  - Details of the contact person in case of quality problems and defective batches, including a 24 hour contact number
  - Details of the medicinal product (i.e. invented name, active substance, strength, pharmaceutical form, packaging, pack-size) and authorisation number in the Community register of medicinal products (i.e. EU number)
  - Details of the MAH (i.e. name and addresse)
  - Scope of the change (i.e. changes resulting from amendments to the Commission Decision, changes proposed by the parallel distributor not related to the Commission Decision, changes concerning the Member State(s) of Origin) with details of the changes.
  - Indication if the 'Specific Mechanism' is applicable to the notification or not (See also "Does the 'Specific Mechanism' agreed upon by the EU and the acceding countries apply to parallel distribution?")
  - Certification that the condition of the product has not been affected

- Annexe to the form:
  - A printed package leaflet of the medicinal product as proposed by the parallel distributor, clearly mentioning the date of the latest Community Marketing Authorisation texts used. (if applicable)
  - One colour copy (e.g. scan, photocopy or photograph) of the repackaged presentation (including outer and inner packaging). (if applicable).
  - A copy of the Wholesale-distribution and/or Manufacturing licence should only be submitted in a notification of a change whenever they are updated/amended compared to the one submitted initially.

It should be noted that the responsibility for the quality of the submitted documentation lies with the parallel distributor and is crucial to the overall process. In particular, the notification of a change form must be duly completed, signed and dated. In doubt, parallel distributors are advised to contact the EMEA Parallel Distribution Secretariat.

Similarly, deficient and missing documentation can lead to 'request for missing information' letter, and ultimately to the non-finalisation of the notification of a change. (See "How shall my notification of a change be handled (timetable)?")

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of change for parallel distribution of a centrally authorised medicinal product form
- Notification of a change for parallel distribution of a centrally authorised medicinal product form with explanatory notes

21. How and to whom shall I submit my PD notification of a change?

PD notifications should be addressed and sent for the attention of Parallel Distribution Secretariat at the following address:

EMEA - Human Post-Authorisation Unit (or Veterinary Unit – *as appropriate*)
Parallel Distribution Secretariat
7, Westferry Circus
Canary Wharf
London E14 4HB
UK

One paper copy of the PD notification form and supportive documentation should be submitted to the EMEA.

Update

Notifications of a change of parallel distribution for veterinary medicinal products are handled by the Veterinary Unit and not by the Parallel Distribution Secretariat.

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of a change for parallel distribution of a centrally authorised medicinal product form

22. How shall my notification of a change be handled (timetable)?

Update

A Notice of a change is only issued for changes not related to the update of Annexes to the Community Marketing Authorisation.
The EMEA will check the conformity of the proposed changes (including a check of the labelling and package leaflet with the text of the latest annexes to the Community Marketing Authorisation, if applicable) within 5 working days and will notify the parallel distributor of any objections or comments. In case of objections or comments, the procedure will be suspended (Clock Stop) until receipt of revised proposals for labelling and/or package leaflet.
When there are no objections/comments or when objections/comments have been completely addressed by the parallel distributor, the EMEA issues a Notice of a change and sends it to the parallel distributor
The EMEA also sends a copy of the Notice of a change to:

- the National Authority of the Member State of destination
- the marketing authorisation holder (MAH) of the medicinal product,
- the National Authority of the Member State where the parallel distributor is located, if different from the Member State of destination
- the Official Medicines Control Laboratory (OMCL) of the Member State of destination, in the case the medicinal product is a vaccine or a blood product.

For notifications of change solely related to the update of Annexes to the latest Community Marketing Authorisation, the EMEA will only acknowledge receipt of the notification of a change within 5 working days.
Nevertheless, parallel distributors have to file a notification of a change form and to provide a printed package leaflet and a colour copy of the repackaged specimen (outer/inner labelling). Instead of performing a detailed check of the updated labelling and/or package leaflet, the EMEA performs a “spot-check” system. Where the outcome of such spot-check is considered unsatisfactory, the notification of a change will be submitted to the full change review process.

Receipt of PD notification of a change	Day x
EMEA acknowledgement of receipt and/or notice of a change	Day x+5

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998
- Notification of a change for parallel distribution of a centrally authorised medicinal product form

23. Am I allowed to include several languages on the pack of a PD medicinal product?

The Community pharmaceutical legislation mentions that the particulars shall appear in the official language or languages of the Member State where the product is placed on the market.

This provision shall not prevent these particulars from being indicated in several (other) languages, provided that the particulars appear in all the languages used.

The labelling and package leaflet texts used by the parallel distributor should be in accordance with the texts of the Commission Decision granting or amending the Community Marketing Authorisation for the medicinal product concerned in all languages chosen.

If the Parallel distributor wishes to create multilingual packs suitable for distribution in different Member States of destination, this would require the submission of a separate notification per Member State of destination.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended - Title V. Labelling and Package Leaflet.

24. Does the EMEA accept combined package leaflet in a PD product?

The EMEA accepts parallel distributors to use combined printed package leaflet for their centrally authorised products provided that the originator product already includes a combined printed package leaflet.

A copy of the original combined package leaflet should be included in the initial PD notification or notification of a change.

The reason for the request of a copy of the original package leaflet is that combined printed package leaflet can only be acceptable if the three conditions described in the "Compilation of QRD decisions on stylistic matters in the product information" are met and the applicant of the centrally authorised product or the MAH submits a request to the Quality Review Documents (QRD) Group, together with a justification/rationale. A decision is then taken by the QRD on a case-by-case basis.

References

- Compilation of QRD decisions on stylistic matters in the product information (version 9.0, EMEA 12/2005).

25. Can I use a parallel distributor specific code to the proposed packaging material?

The addition of a parallel distributor internal code to packaging material is considered by the EMEA as good practice and therefore acceptable, provided it is not being presented as part of the core-text of the labelling and package leaflet. The original batch number must always be retained.

This includes the mentioning of a "re-pack batch" or the addition of a prefix or suffix to the original batch number to reflect additional repackaging activities.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended – Title V – Labelling and package leaflet
- Chapter 5 on Production of the Good Manufacturing Practices Guidelines

26. Can the EMEA request an inspection of a Parallel distributor?

The EMEA does not request inspections of parallel distributors.

The EMEA Inspections Sector will check the validity of the Wholesale-distribution and Manufacturing licenses submitted as part of the validation of a PD notification.

Where considered necessary, the EMEA Inspections Sector can inform the inspection services of the National Competent Authority on any issue that has been brought to its attention.

The responsibility for any actions, however, remains with the National Competent Authorities of the respective Member State(s).

References

- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

27. Is the EMEA involved in registered trademark matters?

The EMEA only checks the compliance of the parallel-distributed product with the terms of the Community Marketing Authorisation for the concerned centrally authorised product. The Annexes to the Commission Decision do not include any registered or trademark symbols.

Update

According to European Court of Justice of the European Communities - Case C-232/94 case law parallel distributors have the obligation to *"give notice to the trademark owner before the repackaged product is put on sale, and, on demand, supplies him with a specimen of the repackaged product."* It was suggested that a period of 15 working days seemed likely to constitute a reasonable time for this notice, but, the time being purely indicative, it remains open to the parallel distributor to allow a shorter time and to the trade mark owner to ask for a longer time to react than that allowed by the parallel distributor.

In accordance with ECJ case law it is up to the trademark owner to check if the presentation after repackaging is not such as to damage the reputation of the trademark.

NEW

The EMEA does not oppose nor impose the use of registered trademark symbols. The parallel distributor is allowed to make a reference to the registered trademark in the package leaflet and on the outer labelling (e.g. <Product X> is a registered trademark of <Company Y>) in accordance to trademark legislation.

References

- Case C-232/94, *MPA Pharma / Rhône-Poulenc Pharma (Rec.1996, p.I-3671)*
- Joined cases C-427/93, C-429/93 and C-436/93, *Bristol-Myers Squibb and others / Paranova (Rec.1996,p.I-3457)*
- Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03) OJ C 229 of 22 July 1998

28. Do I have responsibilities in the event of a quality defect?

In the case of products which have been subject to parallel distribution a defect may become apparent due to a problem with the original product as it left the manufacturer, or as a result of subsequent handling in the distribution chain, particularly where the packaging material, including the package leaflet, has been changed. In either case the parallel distributor has responsibilities.

1. A parallel distributor can make changes to the packaging materials of a product only if it holds a manufacturing authorisation issued by the relevant national competent authority. It is therefore bound to 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. Manufacturers are required to have a system for recording and reviewing complaints and for effective recall. A manufacturer is obliged to inform the competent authority of any defect it has become aware of that might result in a recall or abnormal restriction in supply and this applies equally to parallel distributors. The 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 procure product only from a holder of a wholesale distribution authorisation in the source member state. The supplier is consequently obliged to inform the parallel distributor of any recall activity originating with the supplier or earlier in the distribution chain including the original manufacturer that might involve products supplied to the parallel distributor. Such notifications must be handled within the parallel distributor's GMP/GDP (Good Distribution Practices) system to confirm whether the affected product was actually received, trace its utilisation and initiate recall procedures as necessary, including contacting the local competent authority.
   Marketing authorisation holders are encouraged to inform parallel distributors of any recall initiated by the marketing authorisation holder.

NEW

When a parallel distributor encounters a (possible) quality defect with a centrally authorised product, the EMEA should also be informed as competent authority. The procedure of notifying quality defects or product recalls from the EMEA Inspections Sector should be followed.

1. Complete the Defective Product Report form
2. Send the form by e-mail to qdefect@emea.eu.int or by fax to +44 20 74 18 85 90
3. Telephone the Inspections Sector to confirm that the form has been received
4. Keep the EMEA informed of any changes or additional information
5. Investigate, if applicable, the product defect/recall and send a report to the EMEA.

More information on this notifying procedure can be found on the EMEA webpage:
http://www.emea.eu.int/Inspections/Defects.html

References

- Article 44 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended, or Article 40 of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended
- Article 65 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products, as amended, or Article 77 of Directive 2001/83/EC of the European Parliament and of the Council

of 6 November 2001 on the Community code relating to medicinal products for human use, as amended

- Revised compilation of community procedures on administrative collaboration and harmonisation of inspections - Procedure for Handling Rapid Alerts and Recalls Arising from Quality Defects – September 2005
- Commission Directive 2003/94/EC, of 8 October 2003, laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use
- Commission Directive 91/412/EEC of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products

29. Does the EMEA provide information on notifications received to third parties?

Update

In the light of recent ECJ case law, the EMEA will, in accordance with its 'Procedure for notifications of parallel distribution of Centrally authorised medicinal products' (EMEA/H/30313/98 Rev 2), only send a Notice (of a change) to the parallel distributor, and a copy of the Notice (of a change) to the Member State of destination, to the Member State where the parallel distributor is located, if different, to the OCML of the Member State of destination in case of a vaccine or a blood product and to the MAH of the medicinal product, indicating that the regulatory check has been completed.

Although the MAH may request an overview of all EMEA Notices issued for their products at any time, these will not include information on ongoing procedures.

Exceptions to the above rules are made for any request for information on parallel distribution received from a National Competent Authority. Information as to the status of a particular notification in the process is also provided.

At the moment, the EMEA does not release or publish information on the parallel distributors or parallel-distributed products for which a Notice has been issued, but is considering to publish a list of Notices for PD issued on a monthly basis on the EMEA website.

30. Does the 'Specific Mechanism' agreed upon by the EU and the acceding countries apply to parallel distribution?

The following text has been included in the Act of Accession:

"With regard to the Czech Republic, Estonia, Latvia, Lithuania, Hungary, Poland, Slovenia or Slovakia, 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."

For a limited period after accession, some medicines on the market in the new EU Member States will not have the same level of intellectual property right protection found in the existing EU Member States. The Accession Treaties therefore introduced the above mentioned transitional period to the full application of the principle of the free movement goods to prevent parallel trade in pharmaceutical products that lack equivalent intellectual property right protection. The mechanism also introduces the requirement that parallel traders have to provide confirmation to the competent authority that they have informed the patent holder one month in advance of a notification for a parallel distribution. However, the legal responsibility for enforcing intellectual property rights will remain with the patent holder.

When submitting a notification (of a change) to the EMEA, parallel distributors are required to specify the Member State(s) of origin and of destination of the medicinal product they intend to parallel distribute and to specify whether the specific mechanism applies to the concerned notification. Parallel distributors are also requested to confirm that the patent holder or beneficiary has been given one month's advance notice in their application when the specific mechanism applies.

In case the specific mechanism does not apply, parallel distributors will commit to submit a Notification of a change should they subsequently initiate parallel distribution from countries where the specific mechanism applies. In addition, parallel distributor will commit to ensure that the patent holder or beneficiary will be given one month's advance notice in their application.

References

- Annex IV(2) of the Act of Accession signed on 16th of April 2003
- Notification of parallel distribution of a centrally authorised medicinal product form
- Notification of a change for parallel distribution of a centrally authorised medicinal product form

NEW

31. Are the Braille requirements applicable to parallel-distributed medicinal products?

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

The parallel distributor should add the name of the medicinal product in Braille to the outer labelling of parallel-distributed packs when this Braille requirement for the product name appears in section 16 of the labelling requirements of the Annexes to the Community Marketing Authorisation.

Usually only the (invented) name of the medicinal product followed by its strength is mentioned in section 16. For medicinal products authorised only in a single strength, often only the (invented) name is stated. However, the MAH can express further information (pharmaceutical form, and if appropriate, whether it is intended for babies, children or adults, etc) in Braille on a voluntary basis in section 16.

The Braille text on parallel-distributed packs should appear in the language or languages of the Member State of destination. The original Braille text of the Member State of origin, if present and if different than in the language(s) of the Member State of destination, should not cause confusion for the patient. If the original Braille text is the same in the language(s) of the Member State of destination, this original text should not be covered or replaced.

The Braille text does not have to be printed on the immediate packaging – such as blisters, ampoules and bottles - it only has to appear on the outer packaging, which is normally a carton. Concerning the location of the Braille on the outer packaging, there is no need to put the Braille dots on an empty space of the packaging, but the underlying printed text has to be easily legible.

EMEA will check the presence of the text in the language(s) of the Member State of destination, verify it and determine if the original text (if present) can cause confusion. The parallel distributor should indicate the text added in Braille on the colour copy. If possible, the colour copy itself should make the text visible. If the Braille text is added on a separate label, a copy of this label can be added to the colour copy or the documents submitted with the notification. If necessary, EMEA will request a specimen of the outer package for verification.

Parallel distributors, like the marketing authorisation holders, are encouraged to apply the provision for Braille to all medicinal products as soon as possible. If a parallel distributor prefers to add Braille text to the outer labelling before the marketing authorisation holders does, this will be accepted by the EMEA for new initial notifications or for notifications of a change.

Upon request of the patient, the parallel distributor should also provide the leaflet in a suitable print, taking into consideration all aspects determining the readability, for partially sighted people and in an appropriate format for blind people (e.g. in Braille or perceptible by hearing on CD-Rom, audiocassette, etc.).

References

- Guidance concerning the Braille requirements for labelling and the package leaflet (Article 56a of Directive 2001/83/EC as amended)

NEW

32. Are there special requirements in case of unit dose blisters?

When a medicinal product is presented in a unit dose blister and the MAH mentions all information for the blister packaging on each section of the blister containing a unit of the product (e.g. tablet, capsule), the parallel distributor should ensure that this information is also added in the language(s) of the Member State of destination on each section of the blister of the parallel distributed packs. In case of technical constraints with regards to addition of this information (e.g. insufficient space to add a label with all information), the parallel distributor should seek guidance from the Parallel Distribution Secretariat.

Although there is no real definition of a unit dose presentation in the pharmaceutical legislation, Article 55 of Directive 2001/83/EC defines the particulars which should at least appear on the immediate packaging which take the form of blister packs, i.e. the name of the medicinal product, the name of the MAH, the expiry date and the batch number. However, the style (dimensions, presentation and form) of the packaging (both inner and outer labelling) to be used for a medicinal product are determined and specified in the Annexes of the Community Marketing Authorisation. The parallel distributor should follow the same style as the MAH and add, therefore, the information for the blister in the language(s) of the Member State of destination to each section of the blister containing a unit of the product.

In case of insulin cartridges of prefilled syringes presented in blisters or trays, the parallel distributor should either label each cartridge or syringe individually with the product information for the immediate packaging or add a label with this information to each section of the blister containing a cartridge or the tray cover.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

33. Do I have to keep reference and retention samples of medicinal products repackaged for parallel distribution?

Annex 19 to the Guide to Good Manufacturing Practice for Medicinal products gives guidance on the taking and holding of reference samples of starting materials, packaging materials or finished products and 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 finished product. It is stored for identification purposes, e.g. presentation, packaging, labelling, package leaflet, batch number, expiry date should the need arise during the shelf life of the batch concerned.

The qualified person of the repackager or the parallel distributor, as defined in a written agreement between the two parties, should take and keep a retention sample of each batch of parallel-distributed products.

Where the secondary packaging of the original product is opened during the repacking process for parallel distribution, e.g. to replace the carton or package leaflet, then one full retention sample, per packaging operation, containing the product (i.e. a fully packaged unit) 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 repackager), as it would affect the extent of any resulting recall.

The samples from each batch of finished product should be retained for at least one year after the expiry date. Records of traceability of samples should be maintained and be available for review by competent authorities. The samples should be accessible at all reasonable times.

References

- Annex 19 on Reference and Retention Samples – EU GMP Guidelines.

NEW

34. How long is a notice for parallel distribution valid?

The notice for parallel distribution of medicinal product is valid as long as the Community Marketing Authorisation of the concerned product is valid. The parallel-distributed product, however, has always to be in conformity with the latest annexes to the Community Marketing Authorisation for the product. When the Community Marketing Authorisation is amended affecting the product information (packaging and package leaflet) or in case any other information that the parallel distributor provided to the EMEA has changed (e.g. change in repackager), the parallel distributor should submit a notification of a change. (See also "When shall I submit a notification of a change?")

In the case that the Community Marketing Authorisation of a medicinal product is expired (e.g. the Community Marketing Authorisation is not renewed after its first 5 year validity), also the notices for parallel distribution of the concerned product expire. The EMEA will inform the concerned parallel distributors accordingly. (See also "Can I parallel distribute a medicinal product for which the Community Marketing Authorisation has been suspended or revoked?")

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

35. Can I parallel distribute a medicinal product for which the Community Marketing Authorisation has been suspended or revoked?

It is clear that when the Community Marketing Authorisation of a medicinal product is revoked, the Marketing Authorisation Holder can no longer distribute the product.

In case of a revoked Community Marketing Authorisation, the EMEA will also revoke the parallel distribution notices issued and close down ongoing notifications for the concerned product.

In case of the suspension of a Community Marketing Authorisation, the EMEA will also suspend the parallel distribution notices and put on hold ongoing notifications for the concerned product. Once the suspension of the Community Marketing Authorisation has been lifted and the medicinal product is reintroduced on the market, the notices will be reissued, after a notification of a change if applicable, and the ongoing procedures can be resumed upon request of the parallel distributor.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

36. Do I have to inform other instances of the parallel distribution of vaccines and blood products?

In the case of parallel distribution of centrally authorised vaccines or blood products the normal parallel distribution notification procedure should be followed. However, the parallel distributor should also inform the Official Medicines Control Laboratory (OMCL) of the Member State of destination of the parallel distribution of the vaccine or the blood product and to provide this OMCL with the following information on each batch of the product distributed:

- name of the medicinal product
- strength and pharmaceutical dosage form
- pack size
- EU registration number
- name and address of the MAH
- name and address MAH manufacturer
- name and address of the parallel distributor
- Member State of origin
- batch number and expiry date
- batch size (number of packages to be parallel distributed

In case of a notification for parallel distribution of a vaccine or a blood product, the EMEA sends also a copy of the Notice the OMCL of the Member State of the destination.

A list of the addresses of the OMCLs in the EU (Human OCABR contact list) can be found on the website of the European Directorate for the Quality of Medicines (EDQM): http://www.pheur.org/site/page_611.php#

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

37. Is the sunset clause applicable to parallel distribution?

According to Directive 2001/83/EC as amended, the MAH should inform and notify the EMEA of the marketing and cessation of placing on the market of a centrally authorised product. This legal requirement is not applicable to the parallel distributor and therefore the parallel distributor does not have to provide the EMEA with marketing information. However, EMEA can request marketing information on a case by case basis from parallel distributors.

Also the sunset clause (i.e. a three-year period without marketing of the medicinal product leads to the invalidity of the Community Marketing Authorisation; this period can start counting from the granting of the Community Marketing Authorisation or from the last cessation of placing the product on the market) is only applicable to the MAH and not to the parallel distributor. The parallel distribution activity depends on the availability of the product on the market. As long as the product is available on the market, a parallel distributor can source it and distribute it. Therefore, there is no specific sunset timer (i.e. a tool used to monitor the overall sunset clause period) for parallel distribution. (See also: "Can I parallel distribute a medicinal product for which the Community Marketing Authorisation has been suspended or revoked?")

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

38. How shall I handle a notification of an adverse drug reaction?

According to Directive 2001/83/EC as amended, the MAH should have a pharmacovigilance system in place in order to collect all adverse drug reaction and to report them to the competent authorities. This legal requirement is not applicable to the parallel distributor.

However, in the case that the parallel distributor receives a notification of an adverse drug reaction from a patient, a doctor or another source, the parallel distributor should inform the person notifying that adverse drug reactions should be reported to the MAH of the medicinal product directly. The parallel distributor should also forward this adverse reaction notification immediately to the MAH.

References

- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, as amended.

NEW

39. Can I transfer a notice or an ongoing notification to another parallel distributor?

If a parallel distributor wishes to transfer a notice or an ongoing notification for parallel distribution to another, he should inform the EMEA of the transfer and submit a transfer of a parallel distribution notification of a centrally authorised medicinal product form. A notice or a notification can only be transferred to another authorised parallel distributor who will take over the full responsibility for the notice or notification of the product.

In order to facilitate handling, notifications of a transfer should be presented as follows:

- Cover letter

- The completed "Transfer of a parallel distribution notification of a centrally authorised medicinal product" form signed and dated by the official contact person of the transferor and transferee.
  Information relating to the proposed PD notification, in particular:
  - Details of the medicinal product (i.e. invented name, active substance, strength, pharmaceutical form, pack-size), authorisation number in the Community register of medicinal products (i.e. EU number), date of the notice if already granted
  - Details of the parallel distributors, i.e. transferor (parallel distributor transferring the notice or notification) and transferee (parallel distributor to whom the transfer is to be granted)
  - Details of the contact person of the transferee in case of quality problems and defective batches, including a 24 hour contact number
  - Date of the transfer
  - Certification that the complete and latest approved product information concerning the medicinal product has been transferred to the Transferee
  - Statement that no other changes have been made to the product information other than those related to the transfer application

- Annexes to the form:
  - A full copy of the original Wholesale distribution license (within the meaning of Article 77 of Directive 2001/83/EC or Article 65 of Council Directive 2001/82/EC) for the parallel distributor (transferee)
  - A full copy of the original Manufacturing Authorisation (within the meaning of Article 40 of Directive 2001/83/EC or Article 44 of Council Directive 2001/82/EC) for the repackager of the transferee
  - An updated printed package leaflet of the medicinal product mentioning the transferee, if applicable.
  - An updated colour copy of the outer and inner packaging of the medicinal product mentioning the transferee and the repackager. (See also "Do I need to submit colour copies and printed package leaflets of the repackaged presentation in my initial notification?")

It should be noted that the responsibility for the quality of the submitted documentation lies with the parallel distributors and is crucial to the overall process. In particular, the notification of a change form must be duly completed, signed and dated. In doubt, parallel distributors are advised to contact the EMEA Parallel Distribution Secretariat. Deficient and missing documentation can lead to 'request for missing information' letter.

An application of a transfer of a parallel distribution notification should be addressed and sent for the attention of the Parallel Distribution Secretariat at the following address:

EMEA - Human Post-Authorisation Unit (or Veterinary Unit – *as appropriate*)
Parallel Distribution Secretariat
7, Westferry Circus
Canary Wharf
London E14 4HB
UK

Instead of performing a detailed check of the updated labelling and/or package leaflet, the EMEA performs a “spot-check” system. Where the outcome of such spot-check is considered unsatisfactory, the application will be submitted to a full review process.

When there are no objections/comments or when objections/comments have been completely addressed by the parallel distributor, EMEA will issue a notice of transfer within 5 working days to the parallel distributor (transferee).
The EMEA also sends a copy of the Notice of a change to:

- the National Authority of the Member State of destination
- the marketing authorisation holder (MAH) of the medicinal product,
- the National Authority of the Member State where the parallel distributor is located, if different from the Member State of destination
- the Official Medicines Control Laboratory (OMCL) of the Member State of destination, in the case the medicinal product is a vaccine or a blood product.

Receipt of an application for transfer	Day x
EMEA Notice of transfer	Day x+5

References

- Transfer of a parallel distribution notification of a centrally authorised medicinal product form

NEW

40. Do I need to add a blue box to the outer labelling?

Member States may require the use of certain forms of labelling making it possible to indicate the price of the medicinal product, the reimbursement conditions of social security organisations, the legal status for supply to the patient or identification and authenticity. This information is specific to a Member State and should be accommodated on the label in a boxed area (the so-called 'blue box'), to appear on one side of the pack (outer carton or outer labelling). Each 'blue box' should only be presented in the official language or languages of the Member State concerned and should state the name of that Member State. The information required by the different EU Member States is described in the Guideline on the packaging information of medicinal products for human use authorised by the Community.

The parallel distributor should add a blue box with the information required for the Member State of destination in the concerned language(s) to the parallel-distributed packs. The original blue box should be covered as it mentions the Member State of origin and contains information which is only required for the Member State of origin. This information is usually not applicable for the Member State of destination and in order to avoid confusion, the original blue box should be covered completely.

In principle, the 'blue box' border should have a blue colour.

References

- Guideline on the packaging information of medicinal products for human use authorised by the Community.