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Updates to Variation Categories and Guide to parallel imports

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HPRA PPA webinar

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Introduction

- Changes to variation categories and the Variation application form
  - Changes and reduction to variation categorisations
  - Change in the layout of the form
- Updates to the Guide for Parallel Imports
  - Product information review frequency
  - Packaging changes not requiring variation

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Changes to variation categories and the variation application form

Variations

- Variations are required to update product information
- Currently there are three categories of variation based on their risk and impact to the product and patient
- Fees are set corresponding with the risk

Variation type	Risk level	Example
Type IA	Low	Change in the product authorisation number of a product in a source country
Type IB	Moderate	Updating product information to include new side effect (update in line with the Irish reference product)
Type II	High	Change in the excipients of the product

Changes to variation categories

Amount	Current	New
Total number of variation categories	26	18
Type IA (no fees)	13	11*
Type IB (fees)	12	7
Type II (fees)	1	0

* 5 **conditional** Type I variations

- A reduction in the total number of variations
- Merging of type IA categories
- A reduction in the number of variations requiring a fee
- Deletion of type II variations

Merging of Type IA's

- We have merged a number of type IA categories so that they fall under one variation number. Doing this enabled us to down grade certain variations.

Variation number	Variation	Previous Category	New single category
8	Replacement or addition of a manufacturer in a source country	Type IB	8. <u>Type IA:</u> Amendment to the details of the manufacturer of the product in the source country A. Replacement/addition of a manufacturer B. Deletion of a manufacturer C. Change in the name/address of the manufacturer
9	Deletion of a manufacturer in a source country	Type 1A	
10	Change of the name and/or address of the manufacturer of the product in a source country where the actual manufacturing site remains unchanged	Type 1A	

A reduction in the number of Type IB variations

- A reduction in the Type IB variations was achieved by re-categorisation of some variations and merging others.

Variation	Category	Category and new variation
Change to the labels and/or package leaflet of the PPA product which does not affect the approved SPC	Type IB	Type IB; Amendment of the SPC and Labels/Leaflet in line with the reference product or EU commission decision
Amend to bring the SPC, labelling and/or package leaflet in line with the reference product	Type IB	
Amend to bring SPC, labelling and/or package leaflet in line with EU Commission decision	Type IB	Type IB: Amendment of the labels and/or leaflet in line with the reference product where the SPC is not affected.
Update to any section of the SPC that is not covered by one of the previous categories	Type IB	

Changes to Variation form

- Bringing the form more in line with the variation form for national authorisations.
- The format of the variation listings in the form has been changed to now include documentation requirements of each variation and also to introduce the concept of conditional variations.

Documentation

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Can apply to multiple variations

1. Scan of source country packaging showing the change.
2. Scan of source country package leaflet showing the change.
3. A formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or new address is mentioned.
4. Revised product information.
5. Justification for the change.
6. Manufacturer's authorisation for the re-packager/assembler.
7. A scan/sample of the product with the differences clearly visible.

Changes to variation Application form: Documentation.

Variation number	Change description	Conditions to be	Documentation to be supplied	Fee code classification	
	product				
5	Deletion of a source country		4	☐	
6	Change in the name of the active substance	1	2, 4	☐	☐
7	Change in the product name	2, 3	4, 5	☐	☐

Documentation

1. Scan of source country packaging showing the change.
2. Scan of source country package leaflet showing the change.
3. A formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or new address is mentioned.
4. Revised product information (SmPC, package leaflet, labelling and Braille as applicable).
5. Justification for the change.
6. Manufacturer's authorisation for the re-packager/assembler.
7. A scan/sample of the product with the differences clearly visible.

Changes to variation application form cont.

8	Amendment to the details of the manufacturer of the product in the source countr				

Documentation

1. Scan of source country packaging showing the change.
2. Scan of source country package leaflet showing the change.
3. A formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or new address is mentioned.
4. Revised product information (SmPC, package leaflet, labelling and Braille as applicable).
5. Justification for the change.
6. Manufacturer's authorisation for the re-packager/assembler.
7. A scan/sample of the product with the differences clearly visible.

	c) Change in the name/address of the re-packager/assembler where the actual site remains unchanged		4, 6		

Changes to variation application form cont.

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Documentation

1. Scan of source country packaging showing the change.
2. Scan of source country package leaflet showing the change.
3. A formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or new address is mentioned.
4. Revised product information (SmPC, package leaflet, labelling and Braille as applicable).
5. Justification for the change.
6. Manufacturer's authorisation for the re-packager/assembler.
7. A scan/sample of the product with the differences clearly visible.

15	Replacement or addition of a new pack presentation (including re-boxing)		1, 4, 5		☐
16	Amendment of the SmPC, labels and/or leaflet in line with the reference product or EU Commission decision		4		☐
17	Amendment of the labels and/or leaflet in line with the reference product where the SmPC is not affected.		4		☐
18	Other (please specify):				☐

Conditional Type IA variations

- When defined criteria are met a variation may be categorised as a conditional type IA variation and not require a fee.
- Example:

Variation	Current	New	Conditions
Change in product description (including tablet markings and score lines)	Type IB	Type IB/Conditional Type IA	Type IA provided: The changes related to the product markings only (not the score line)

- If the conditions described are not met then the variation is automatically a type IB and will incur a fee

Conditions

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Are variation specific!

1. The proposed new name of the active substance must be in line with the Irish reference product. *(variation 6)*
2. The name is changing to the currently approved name of the Irish reference product. *(variation 7)*
3. The approved over-label already obscures the source country product name on both immediate and outer packaging. If the product is already re-boxed, the only change to the outer packaging is to the name on the re-box. *(variation 7)*
4. The proposed new manufacturer is listed in the current package leaflet for the reference product. *(variation 8.a)*
5. The new site must have a valid manufacturing authorisation/GMP certificate confirming that the site is authorised for secondary packaging. *(variation 9.a)*
6. The change relates to the product markings only. *(variation 11)*

Example

Variation number	Change Description	Conditions to be fulfilled	Documentation to be supplied	Classification	
				Type IA	Type IB
7	Change in the product name	2, 3 ✓✓	4,5 ✓✓	✓	

Conditions

2. The name is changing to the currently approved name of the Irish reference product.

3. The approved overlabel already obscures the source country product name or, if the product is already re-boxed, the only change is to the name on the re-box.

Documentation

4. Revised product information

5. Justification for the change

If the conditions are fulfilled this is a type IA, if not then it is a type IB

The documentation needs to be supplied in all cases

Example

Variation number	Change Description	Conditions to be fulfilled	Documentation to be supplied	Classification	
				Type IA	Type IB
7	Change in the product name	2,3 ✓✗	4,5 ✓✓		✓

Conditions

2. The name is changing to the currently approved name of the Irish reference product.

3. The approved overlabel already obscures the source country product name or, if the product is already re-boxed, the only change is to the name on the re-box.

Documentation

4. Revised product information

5. Justification for the change

If the conditions are fulfilled this is a type IA, if not then it is a type IB

The documentation needs to be supplied in all cases

Changes to the variation form

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Application for a Variation to a Parallel Import Licence

For details of the requirements, please see the Guide to Parallel Imports – Human Medicines. (For addition of a source country, use the form Application for Addition of a Source Country to a Parallel Import Licence.)

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CRN:

ALL SECTIONS MUST BE COMPLETED IN FULL

1 Name and address of the parallel import licence holder:

Name and address of the applicant, if different:

2 PPA Number:

Name of product: Active substance(s):

Pharmaceutical form: Strength(s):

3.

Variation number	Change description	Conditions to be fulfilled	Documentation to be supplied	Fee code classification IA	Fee code classification IB
1	Change in source country authorisation number (changes to a number of source country authorisation numbers for a single parallel import licence can be made under one Type IA variation)		1	☐	
2	Change in source country authorisation holder's name/address		1 and/or 2	☐	
3	Change in parallel import licence holder's name/address		3, 4	☐	
4	Change in PA number of the Irish-market product			☐	
5	Deletion of a source country		4	☐	
6	Change in the name of the active substance	1	2, 4	☐	☐
7	Change in the product name	2, 3	4, 5	☐	☐
8	Amendment to the details of the manufacturer of the product in the source country				
	a) Replacement/addition of a manufacturer	4	2, 4	☐	☐
	b) Deletion of a manufacturer		2, 4	☐	
	c) Change in the name/address of a manufacturer where the actual site remains unchanged		2, 4	☐	
9	Amendment to the details of the re-packager/assembler of the product				
	a) Replacement/addition of a re-packager/assembler	5	4, 6	☐	☐
	b) Deletion of a re-packager/assembler		4	☐	
	c) Change in the name/address of the re-packager/assembler where the actual site remains unchanged		4, 6	☐	
10	Change in product composition as stated in the SmPC, labelling or package leaflet		2, 4		☐
11	Change in product description (score-lines, colour, shape etc.)	6	4, 7	☐	☐
12	Change to the method of sale and supply or to method of promotion (following an approved change to the Irish reference product)		4,5		☐
13	Deletion or addition of a pack size where the pack size to be added is within the currently approved range for the PPA		4	☐	
14	Amend to add a new pack size (if outside the currently approved range for the PPA)		4, 5		☐
15	Replacement or addition of a new pack presentation (including re-boxing)		1, 4, 5		☐
16	Amendment of the SmPC, labels and/or leaflet in line with the reference product or EU Commission decision		4		☐
17	Amendment of the labels and/or leaflet in line with the reference product where the SmPC is not affected.		4		☐
18	Other (please specify):				☐

Conditions
1. The proposed new name of the active substance must be in line with the Irish reference product.
2. The name is changing to the currently approved name of the Irish reference product.
3. The approved over-label already obscures the source country product name on both immediate and outer packaging. If the product is already re-boxed, the only change to the outer packaging is to the name on the re-box.
4. The proposed new manufacturer is listed in the current package leaflet for the reference product.
5. The new site must have a valid manufacturing authorisation/GMP certificate confirming that the site is authorised for secondary packaging.
6. The change relates to the product markings only.

Documentation
1. Scan of source country packaging showing the change.
2. Scan of source country package leaflet showing the change.
3. A formal document from a relevant official body (e.g. Chamber of Commerce) in which the new name or new address is mentioned.

AUT-F0032-5.3 1/3

AUT-F0032-5.3 2/3

Changes to variation form

4. Revised product information (SmPC, package leaflet, labelling and Braille as applicable).
5. Justification for the change.
6. Manufacturer's authorisation for the re-packager/assembler.
7. A scan/sample of the product with the differences clearly visible.

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4. Background *(Please give brief background explanation for the proposed change to the product import licence)*

Specify the precise present and proposed details, using additional pages if necessary. If the change affects the SmPC, labelling or package leaflet, the changed words should be indicated by underline, strikethrough or highlight, and a clean version should be attached. Colour mock-ups must be provided where the change affects the labelling or leaflets.

Present	Proposed

5. I hereby apply to vary the parallel import licence. I confirm that no changes have been made to the

Send to: Receipts and Validation, Health Products Regulatory Authority, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2.
Tel. No. +353 1 676 4971 Fax No. +353 1 676 7836

Changes to variation form- section 4

- Examples of details that may be included in section 4:
  - What source countries the change relates to
  - What version of the Irish reference PL was used (date)
  - Is this variation being submitted in advance of an additional source country application?
  - Justification for the change (if required and clearly stated as such)
  - We do not require a repeat of the variation category discription
- What details need to go into present and proposed?
  - Pragmatic approach
  - If track changes are not being highlighted in documents supplied then list the changes here
- **NB! Only changes highlighted (either in the form or in tracked documents) are considered approved**

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Updates to the Guide for Parallel Imports

Updates to the guide for parallel imports

- Deletion of reference to type II variation
  - There is no longer a type II variation category for Parallel import products
- Appendix 4
  - Appendix 4 which used to list out specific documentation requirements for each variation has been amended to reflect the changes to the variation categorisation.
- Expansion of list of "non variation" changes to product labels
- Specified product review timetables

Label changes not requiring variation

- Change to the size, colour or font of a company logo or trademark on a carton that is similar in size to the currently approved logo/trademark and does not interfere with the legibility of the required text.
- Addition of a quick response (QR) code or 2D barcode to product labelling and/or package leaflets for internal control purposes or anti-counterfeit measures, with no addition or impact to the approved product information and provided that the conditions as outlined in section 9.7 of the HPRA guide to labels and package leaflets are met.
- Changing between overlabelling to overprinting on the immediate packaging, provided both options have been approved during the initial authorisation.

Variations- Specifying product review timelines

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- Current situation is that product information must be kept in line with the originator and the source country (quality and safety)
- Done on a batch basis
- Change to introduce product review timelines
- For marketed products full reviews should be done on a quarterly basis at a minimum
- For non-marketed products full reviews should be carried out over 6 months.
- Appropriate variations are to be applied for as necessary as a result of these reviews.

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Thank you