HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Labels and Leaflets of Human Medicines

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

CONTENTS

1 SCOPE

The guidance in this document applies to the labels and package leaflets of medicinal products for human use, authorised nationally, through mutual-recognition (MR) or through the decentralised (DC) procedure. The guidance does not apply to medicinal products authorised through the centralised procedure.

2 LEGAL BASIS

The legal basis for the requirements relating to labels and package leaflets are in Directive 2001/83/EC on the 'Community code relating to medicinal products for human use' as amended by Directive 2004/27 EC. The Directives have been transposed into Irish law by the Medicinal Products (Control of Placing on the Market) Regulations 2007. The legal basis for the requirements relating to the safety feature appearing on the packaging of medicinal products is in regulation (EU) 2016/161.

For general guidance, the following EU guidelines are also applicable to labels and package leaflets:

- CMDh annotated QRD template for MR/DC procedures (CMDh/201/2005)
- Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017)
- EC Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use (ENTR/F/2/SF/jr (2009)D/869)
- Guideline on declaration of storage conditions: A: in the product information of medicinal products B: for active substances (EMEA/CPMP/QWP/609/96, 2007)
- Compilation of QRD decisions on stylistic matters in product information (EMA/25090/2002)
- Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017)
- Guideline on the warning on transmissible agents in summary of product characteristics (SmPCs) and package leaflets for plasma-derived medicinal products (EMA/CHMP/BWP/360642/2021)
- CMDh Best Practice Guide on Multilingual Packaging (CMDh/413/2019)
- CMDh position paper on the use of Mobile scanning and other technologies to be included in the labelling and PL in order to provide information about the medicinal product (CMDh/313/2014)
- Mobile scanning and other technologies in the labelling and package leaflet of centrally authorised medicinal products (EMA/493897/2015)
- QRD recommendations on pack design and labelling for centrally authorised non-prescription human medicinal products (draft) (EMA/275297/2010)
- Notice to Applicants (Volume 2C) Guideline on the packaging information of medicinal products for human use authorised by the Union
- "Blue-Box" requirements (CMDh/258/2012)

3 INTRODUCTION

Product labels and package leaflets play an essential part in the safe and effective use of the medicine by patients and healthcare professionals. Thus, approval of the information on labels and package leaflets is an intrinsic part of the authorisation process for all medicinal products.

The detailed requirements for the information to be included in labels and leaflets are specified in Articles 54 to 69 of Directive 2001/83/EC. Prior to placing a medicinal product on the market, a mock-up of the outer packaging and of the immediate packaging of the medicinal product must be submitted to the HPRA for review of the layout and design.

The EC guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use' provides a definition of a mock-up as 'A flat art-work design in full colour, presented so that, (following cutting and folding where necessary), it provides a replica of both the outer and immediate packaging and of the leaflet and clearly demonstrates the three-dimensional presentation of the label text and of the leaflet text'. The guideline also provides guidance on how best to present the printed label, e.g. font size, use of colours, layout, particulars for small immediate packaging, etc.

Label and leaflet designs should be prepared in line with Directive requirements and with the advice available in EU guidelines. Further additional advice is provided in this guidance document. General information on submitting mock-ups to the HPRA is followed by specific guidance on certain aspects of labelling and leaflets.

4 PROCEDURE FOR SUBMITTING AND APPROVING LABELS AND LEAFLETS

4.1 New applications

The product information texts (SmPC, label and leaflet texts) are agreed in the national procedure or MR/DC procedure for new applications. The registered product information comprises the text versions of the SmPC, package leaflet and package labelling approved by the HPRA at the end of a new application procedure. The following paragraphs detail the HPRA's product information requirements for registration of products.

Label mock-ups are not reviewed as part of new applications. An Article 61(3) notification is required to register the label design, and this is outlined further below. All new applications are approved on the basis of product information texts, regardless of marketing status. For products authorised through MR/DC procedures, the registered labels and leaflet text can be either the national text versions or the EU harmonised text versions agreed at the end of the EU assessment procedure, provided that there is no requirement for national warnings~~, or the national text versions.~~. For products that have national safety warnings, the national text versions containing the national warnings are required to be registered. The national text version of an MRP/DCP product consists of the EU harmonised text templates with the addition

of national elements such as name in Ireland, PA number and any national legislative requirements. For products authorised on a purely national basis, there is only a national text version of the product information and this is considered the registered product information.

For products to be marketed post-authorisation, a national Article 61(3) notification is required to register the design and layout of the label mock-ups.

For products approved on the basis of EU harmonised text only, the following documents should be provided with the Article 61(3) notification, which in this instance is also used to register the national labelling and leaflet text:

- Currently agreed EU harmonised labelling and leaflet text for MRP/DCP products
- Proposed national labelling and leaflet text for MRP/DCP products
- Colour mock-ups of the labelling and an indication of minimum font size
- A HPRA declaration of compliance for Braille (see section 8)

For products approved on the basis of national text, the text of EU harmonised or national labels and leaflets is not required with the Article 61(3) notification. The following documents should be provided with the notification:

- Colour mock-ups of the labelling, and an indication of minimum font size
- A HPRA declaration of compliance for Braille (see section 8)

A mock-up of the leaflet is not required as the layout and design have been supported by user testing during the application. The exception to this is where the leaflet is part of a combined label-leaflet presentation, in which case the combined mock-up should be provided.

For MRP/DCP products where multilingual packaging is proposed for Ireland, mock-ups may be submitted during the new application procedure. The HPRA can comment on the mock-up layout and design elements (see section 6.3 for further information on multilingual packaging). A national Article 61(3) notification will be required to register the national mock-ups post-authorisation.

4.2 Renewal applications

It is not necessary to submit product information at the end of the renewal procedure unless changes to product information are being introduced during the renewal (i.e. agreed minor changes). In that case, national text versions of the labels and leaflet can be submitted. EU harmonised text versions can be submitted if the product is not marketed and there are no additional national warnings. Mock-ups are not required to be submitted for a renewal. Significant changes to the product information, including changes to the labelling design and layout, must be introduced by variation or Article 61(3) notification, post-renewal.

4.3 Variations and Article 61(3) notifications

Proposed changes to the approved labels and leaflet must be approved by the HPRA either by way of variation or Article 61(3) notification. However, the HPRA has identified a number of amendments where prior notification is not required. These changes are outlined in section 4.3.1. If the changes are a consequence of changes to the SmPC, the revised labels and/or leaflet should be provided with the variation application to update the SmPC. All other proposed changes not connected to the content of the SmPC must be submitted to the HPRA as an Article 61(3) notification. Continued compliance with any previously submitted Braille declaration should be ensured by the applicant or updated Braille declarations should be submitted. It should be noted that for products authorised through MR/DC procedures, changes that impact the common label or leaflet text must be submitted through the RMS, e.g. via an MR Article 61(3) notification, rather than a national Article 61(3) notification.

The submission requirements for proposed variations and Article 61(3) notification of changes to the labelling and/or leaflet text, and label mock-ups are summarised in the table below as follows:

Nature of the change	Information to be provided in the submission
Change impacting the label and/or leaflet text only (See note 1 below)	- Approved label/leaflet text with proposed changes highlighted. - A clean version of the proposed label/leaflet text.
Significant change impacting only the layout or design of the label mock-ups (See notes 2 and 3 below)	- One copy of the currently approved mock-ups. - One copy of the proposed mock-ups.
Change impacting the label text with significant change to the design/layout of the label mock-ups (See notes 1, 2 and 3 below)	- Approved label text with proposed changes highlighted. - A clean version of the proposed label text. - One copy of the currently approved mock-ups. - One copy of the proposed mock-ups.

Notes:
The nature of all proposed changes should be clearly described in the application form.

1 As described in section 4.3, changes affecting the common label and leaflet text for products authorised through MRP/DCP may not be submitted via a national application.
2 If this is the first submission of label mock-ups, documentation as described in section 4.1 relating to the product information for marketed products is required. This information should be submitted by way of a national Article 61(3) notification.
3 A number of amendments that do not require formal assessment are outlined in section 4.3.1.

A mock-up of the leaflet is not required, except where significant design changes are proposed that require appropriate user testing and ~~thus~~ submission of a variation application (see section 9.2). The clean national text version of the leaflet is the version that will be published on the HPRA website. There is no requirement to include a date on a leaflet submitted to the HPRA. If a date (i.e. the submission date) is included on a leaflet submitted for publication, it will not be deleted. The HPRA website will clarify that this date is not necessarily reflective of the revision/approval date.

4.3.1 Amendments not requiring formal assessment

The HPRA has identified a number of amendments to the labelling and package leaflet that do not require formal assessment. The following changes do not require prior notification to the HPRA. Instead, the revised label and leaflet texts and label mock-ups should be submitted to the HPRA at the next regulatory activity involving a change in the product information.

Amendments impacting label mock-ups

- Minor amendments to the approved design or layout of the label, which do not affect the overall design and readability of the outer and immediate labelling. Amendments can be considered minor if the readability of the labelling is not impacted, the general location of the text remains the same, and the colour scheme used remains the same.
- Transfer of the entire text of a carton face to an opposing face, with no change to text, font size, layout, appearance or readability of text.
- Any change to a barcode, e.g. a number on the barcode that does not affect any other aspect of the labelling and does not change the location of the barcode.
- Change to the key line location on labelling, with no change to text, font size, appearance or readability of information.
- Addition, deletion or change in the administrative information for an EU member state (MS) or the UK placed within the 'blue box', which does not affect any other aspects of the layout and font size of packaging, labels and leaflet text.
- Change to the dimensions of a carton with no change in font size of text, or which leads only to an increase in font size.
- Relocation of Braille (with no change to text).
- Change to packaging code or the internal reference code on packaging.
- Reorientation of a pictogram without any changes to the content or meaning and with no impact on legibility.
- 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.
- Deletion of the MAH logo or trademark on the carton (but MAH still clearly identified).
- Placing a previously non-marketed pack size on the market, where the content, font size and appearance of the label text are identical to the marketed pack, apart from the contents by weight/volume/number of units.
- Addition of a quick response (QR) code or 2D barcode to product labelling and/or package leaflets for internal control purposes or as an anti-counterfeit measure, with no addition to or

impact on the approved product information and provided that the ~~conditions outlined in section 11.2 of this guideline and the~~ safety features labelling requirements outlined below and conditions outlined in section 11.2 are met.
- Change to the anti-tampering device, with no change in layout or font size of text.

Amendments impacting label and/or leaflet text
- Change to abbreviation for batch number and expiry date, provided the proposed abbreviation is one recommended in the EMA's 'Appendix IV Terms/Abbreviations for Batch Number and Expiry Date to be Used on the Labelling of Human Medicinal Products' (i.e. Batch number: Lot, Batch, BN; Expiry date: EXP).
- Addition, deletion or change in foreign MA numbers and/or foreign MA holder details, which does not affect any other ~~aspects~~aspect of the layout and font size of packaging, labels and leaflet text.
- Addition, deletion or change to the details for reporting of side effects in other member states not affecting the details for reporting of side effects in Ireland.
- Change/deletion of a product name in another member state in section 6 of the patient information leaflet (MRP products only).
- Change in the details of a distributor/wholesaler/local representative.
- Change to the trademark statement on a carton/leaflet, e.g. if a statement is changed from 'Product X is a registered trademark of Company Y' to 'Product X is a registered trademark'.

4.3.2 Preparation of mock-ups

The HPRA reviews colour label mock-ups to ensure user-friendly designs, readability and to avoid the arrangement of information in a format that could lead to confusion for the healthcare professional or patient. The HPRA does not review the text present on the label and package leaflet mock-ups. It is the responsibility of the marketing authorisation holder to ensure that the text on the labelling and in the leaflet mock-ups of the product on the marketplace is in line with the approved labelling and leaflet national text.
Mock-ups should comply with the following requirements:
- Mock-ups must be in colour.
- Where there is a range of pack sizes, only a representative mock-up of the smallest marketed pack size for each strength and dosage form should be provided (provided that there is no adverse effect on the readability of the text on other pack size labels).
- In the case of an additional product strength, a sample of the label of the existing strength(s) should also be submitted for comparative purposes.
- The particulars appearing on the label and the leaflet of medicinal products should comply with the minimum font size requirements outlined in the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use'. The font size should be stated on the mock-up.
- Label mock-ups are required for all immediate and outer packaging, including, for example, ampoules, vials, pouches, and blister strip labels.
- A colour code and an indication of scale are useful.

The mock-ups must be a true representation of the final packaging, and the readability of the text as required by the Directive must not be adversely affected by any print finishes used in the final packaging, e.g. the use of highly glossy or reflective surfaces or metallic print is strongly discouraged as such may adversely affect readability. Background colours or logos which adversely affect the readability of the text should not be used. Colour to highlight non-critical areas of product information, such as the number of tablets in a pack, could potentially be confusing and may detract from critical information such as the strength of the product. Colours should be chosen to provide a good contrast between the text and the background to assure maximum legibility and accessibility of the information. The use of different colours to distinguish different strengths is strongly recommended.

4.3.3 Submission of label mock-ups

To confirm that there are no readability issues with labelling, the HPRA needs to see label mock-ups:

1 Before initially marketing the product in Ireland, via a national Article 61(3) notification prior to marketing.
2 When significant layout or design changes are made to the labelling either through a variation or an Article 61(3) notification (e.g. introduction of a new corporate design of packs, changes to the colour scheme, significant changes to the layout and changes that impact the readability of the labelling).
3 At the next regulatory change involving a change to product information for those amendments outlined above (section 4.3.1).
4 When requested by the HPRA, the marketing authorisation holder should provide the current text or mock-ups without delay.

When the variation or Article 61(3) notification does not significantly impact the layout or design of the labels (see section 4.3.1) then no mock ups are required to accompany the submission and the submission of national text versions is sufficient.

4.3.4 Submission of package leaflet

If the product is to be marketed in Ireland, a national text version of the agreed package leaflet is required. A mock-up of the package leaflet is not required as the layout and design of the leaflet has been evaluated during the user testing assessment in the new application. Similarly a mock-up of the leaflet is not required to be submitted to the HPRA with a variation or Article 61(3) notification even if the design or layout is affected by the proposed change. However, the following notable exceptions apply:

Label/leaflet combination style package leaflet:
Where it is intended to market the product using a combined label/leaflet, a colour mock-up of this combined label/leaflet must be provided in addition to the text-only version of the package leaflet.

Products without a separate package leaflet:
Where no separate package leaflet is produced because the required leaflet information is present on the packaging, a text-only version of the label is required in addition to the label mock-ups.

Changes requiring user testing:
These changes must be submitted via a Type IB C.I.z variation; refer to section 9 for further information.

4.3.5 Submitting amended product information during assessment

The following practical aspects apply for the assessment process. During an assessment, certain changes may be requested to the labels and package leaflet. Track-changed or annotated versions of the product information should be supplied to highlight these changes. When reviewing the amended texts or label mock-ups, the assessor will focus on the revisions that have been made. If other changes have been made that were not requested, the applicant should clearly identify them and bring them to the attention of the assessor separately. Applicants do not have to sign and date mock-ups or text-only versions of labels and package leaflets.

5 PRESENTATION OF THE PRODUCT NAME ON THE LABEL

The label must contain all elements required by Article 54 of Directive 2001/83/EC. For prescription medicines the invented name, the strength and the pharmaceutical form followed by the common name of the active(s) relevant to the strength in the name should appear in that order, as a cohesive unit and should not be separated by any interpolated text. The name should be consistent with SmPC section 1.

However, for OTC and general sale products containing two or more actives the following OTC format may be used:
- *'Invented name, pharmaceutical form*
- *INN 1, strength*
- *INN 2, strength*
- *INN 3, strength'*

Please note that where a company chooses this option for an OTC or general sale product, the entire text in italics above will be considered to be the product name. This product name must be listed as an integrated unit in section 1 of the SmPC, on all labels and leaflets and on all advertising related to that product.

The use of images as part of the invented name should be avoided as it can seriously impair the readability of the name. Images are acceptable only if the name can be easily read and, where relevant, is distinguishable from other names in a range. Font, mixture of upper and lower case

letters or other formatting techniques should not be used to highlight a section of the product name to the detriment of other parts of the product name.

An example of clear labelling would be:

Invented name x mg/y mg/z mg film-coated tablets Common name of active 1 Common name of active 2 Common name of active 3   28 film-coated tablets

6 SPECIFIC LABEL REQUIREMENTS

6.1 Space for dosage instructions

Article 54 of the Directive requires that space shall be provided on the labelling for the prescribed dose to be indicated.

This space should be large enough for a regular pharmacy dispensing label to be applied without obscuring the text required by the Directive, but need not be a designated box.

6.2 Labelling of perforated blisters

The packaging of products in individual perforated blisters allows for greater ease in dispensing to patients when the number of tablets to be dispensed is less than the number contained in the blister strip.

Each individual blister should preferably include the minimum label text for blisters: the name of the product, strength and pharmaceutical form, followed by the common name of the active substance, the name of the PA holder, the expiry date and batch number.

In section 6.5 of the SmPC, this presentation should preferably be described using the following text agreed by the EMA's Quality Review of Documents Working Group for centralised products: '[Number of tablets] x 1 tablets in <material, e.g. 'Aluminium/PVC'> perforated unit-dose blisters' (Compilation of QRD decisions on stylistic matters in product information (EMA/25090/2002)).

6.3 Multilingual packaging

Directive 2001/83/EC, Article 63(1) permits the use of multilingual text with the proviso that the same information appears in all the languages used. The exception to this is text captured within the blue-box. In this guide, multilingual packaging refers to a package which is designed for two or more European languages.

The HPRA actively encourages the use of multilingual labelling and package leaflets. The HPRA works closely with MAHs and other European regulators to help facilitate this and follows the principles of the 'CMDh Best Practice Guide on Multilingual Packaging'. An Article 61(3) notification is required to introduce Ireland into a 'cluster'. A 'cluster' is the group of member states who share multilingual packaging. For future language combinations where there is an impact on layout and/or design, this should be introduced by way of an Article 61(3) notification. This is to ensure the readability of the multilingual packaging is not compromised.

The HPRA accepts, by way of a 'blue-box', countries' national requirements as highlighted in the Notice to Applicants 'Guideline on the packaging information of medicinal products for human use authorised by the Union' and in the CMD(h) guidance on "Blue-Box" requirements, (CMDh/258/2012). The minimum requirements in the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use', ENTR/F/2/SF/jr, should also be followed.

Additional guidance can also be obtained in the EMA 'Compilation of QRD decisions on stylistic matters in product information', EMA/25090/2002.

A multilingual package must fulfil the following criteria:
- The name and the strength of the medicinal product is the same in all languages.
- The information in the SmPC is consistent with the information that appears on the labelling and the package leaflet.
- The information is clearly presented on the labelling and package leaflet, so that it can be understood by those who see it and patients can use their medicines safely and appropriately.
- The legal status (prescription or non-prescription) must be the same in both countries.

The HPRA is flexible specifically in relation to the following:
- **'mL' in Ireland (IE) vs 'ml' in other EU states:** The use of ml or mL is permitted.
- **Decimal point in product strength or volume - dot in IE vs comma in EU:** This can be overcome by repeating the invented name, the strength and pharmaceutical form as a cohesive unit in each language or by grouping information relating to the strength and pharmaceutical form, in the different languages, immediately next to the invented name.
- **Thousand separator in product strength or volume - comma in IE vs dot in EU:** This can be overcome by repeating the invented name, the strength and pharmaceutical form as a cohesive unit in English using the comma or a space as the thousand separator, or by expressing the composition on the side panel of the outer carton.

Note: The use of commas instead of dots can be accepted on multilingual immediate and outer packaging labels where absolutely necessary due to space constraints, where no risk of confusion exists and where the medicine is considered critical to the Irish market. Otherwise the above requirements apply. For centrally authorised products, prior agreement with the HPRA should be sought and the agreement email can be provided to the EMA.

- **Small immediate packaging units:** Small immediate packaging units are defined as containers sized up to and including 10 ml where only minimum particulars are required. On a case-by-case basis the minimum particulars could also be considered for other containers where it is not feasible to include all the information. As such, for multilingual labels where there are space constraints, the HPRA can accept minimum particulars on containers up to and including 50 ml where justified, particularly for more than two languages. Where product information is harmonised between MSs (e.g. via a mutual recognition procedure), applicants should ensure that minimum particulars are specified in the common texts for containers of the required size, referencing the need for reduced space for multilingual labelling for IE and other member states.
- **Use of one language:** In some cases, multilingual packaging in the EU have made use of one language for certain particulars in order to save space, e.g. English or Latin are commonly proposed for particulars such as INNs. The HPRA can accept English as a common language without further justification. The use of Latin will be considered where absolutely necessary due to space constraints, where no risk of confusion exists and where the medicine is considered critical to the Irish market.
- **Third country information:** Multi-country packs with the UK are acceptable on the condition that the product information is the same in the UK and Ireland and that additional UK administrative information is placed in a 'blue-box'. Examples of administrative information include the name and address of the MAH, the MA number and the UK site of batch release.
  Note: MAH and MA number information from other EU MSs is acceptable. It is acceptable to add, change or delete these details without prior notification to the HPRA.
- **Coordinating assessment with other MSs:** As multiple MSs are likely to be involved in the assessment of the mock-ups, the HPRA can be flexible on other aspects where justification is provided. Applicants can facilitate this by coordinating and sharing comments from different MSs. The HPRA can assist with aligning our approval times with any other MS as required once this information is imparted to us by the applicant. We can also assist in directly liaising with the other MSs if the other MSs is/are also agreeable to this.
  Note: The HPRA can work as part of the Nordic procedure if required.
- **Joint names:** When proposing an invented name, applicants should highlight to the HPRA, if it has been proposed to other MSs with which multilingual packaging are being developed.

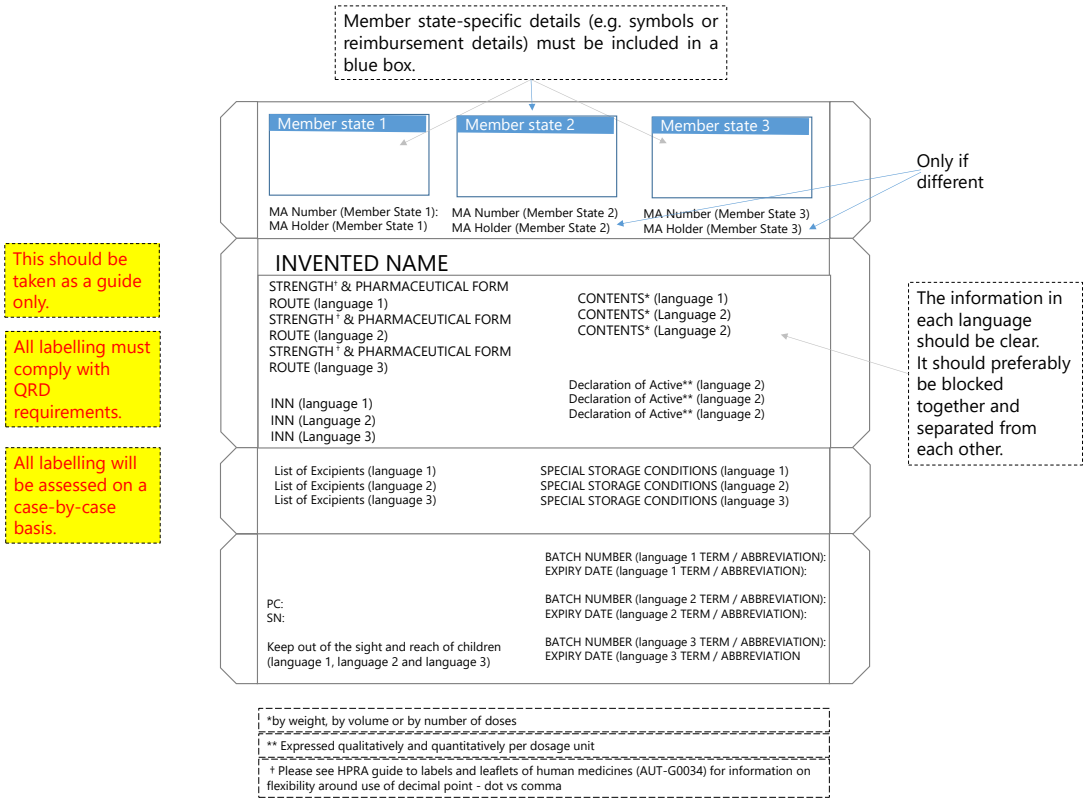
Additional recommendations to be taken into consideration:

- Information in English should be blocked together where possible.
- Where a number of countries share a common pack, list the 'blue-box' requirements for all countries on the same panel/side.
- Country-specific requirements, such as 'blue-box' text, must specify the country to which this applies, e.g. 'IE' or 'Ireland' before the text.

- For the package leaflet: a clear indication that the text following applies to Irish patients, e.g. a two-letter language code in an oval before the English language text:
  EN
- It is acceptable for perforated sections to be present on the pack, provided that the removable information is not the English language section. This should be indicated in the submission.

For further assistance, an example of multilingual labelling is displayed below. Note this is an example of trilingual labelling where it may not be possible to keep English language text together. It is acknowledged that this is only an example and that other layouts are acceptable. For further advice on the design of multilingual labelling, including those authorised via the centralised procedure, or joint UK/IE labelling where prior discussion with the HPRA may be necessary, please contact the HPRA's Customer Services section at info@hpra.ie.

An example of multilingual packaging is shown in the image below.



6.4 Labels of vaccine products and plasma-derived medicinal products

The labels of vaccine/plasma-derived medicinal products should contain peel-off label(s) on the immediate packaging to allow a record of critical information to be retained. This facilitates the

traceability of administered doses of vaccines/plasma-derived products and the recording of batch numbers and expiry dates.

The peel-off label(s) should contain, at a minimum, the following information:
- Invented name of the vaccine/plasma-derived medicinal product
- Batch number
- Expiry date

The overall readability of the statutory information displayed on the fixed part of the label should not be affected by the inclusion of the peel-off part. The information provided on the peel-off label should always remain available on the fixed part of the label once the peel-off part is detached.

Any exceptions to these requirements should be discussed in advance with the HPRA and will be considered on a case-by-case basis.

6.5 Label/leaflet combinations

Label/leaflet combinations present greater challenges in ensuring that the information is presented in a legible manner. For the package leaflet, a type size of at least 9 points as measured in font Times New Roman, not narrowed, with a space between lines of at least 3 mm, is considered as a minimum. The particulars appearing on the label should be printed in characters of at least 7 points leaving a space between lines of at least 3 mm.

The outermost face of the leaflet and the leaflet face in closest contact with the packaging (at the end of the leaflet) are both considered to be the immediate packaging label and the information that appears on each of these must be identical and meet all requirements of Directive 2001/83/EC for labelling and medicinal products. This is considered critical because in the event of the outer label and leaflet becoming detached from the product, the product must still be identifiable to the user.

Factors for manufacturers to consider when using these label/leaflet combinations include the quality of paper used (which must be sufficient to withstand handling during repeated opening and closing), the quality of adhesive used to attach the leaflet securely to the container and the ease with which the user can access the leaflet.

The point of opening of the leaflet should be clearly identifiable to the user by an arrow and/or helpful phrases such as ‘open here’ (or similar). It should be possible to open and reseal the label/leaflet combination.

It is the responsibility of the applicant to highlight the intention to use this label/leaflet combination at the time of submission of the application; in addition to the provision of mock-ups, a sample of the actual label and leaflet attached to the packaging may also be requested during assessment. In relation to the incorporation of Braille into label/leaflet combinations, if it

is intended to place the Braille on the outer most label it must be ensured that the Braille is readable and that the readability of the non-braille text is not compromised. In addition, applicants are required to conduct user testing of these leaflets as presented for use, i.e. attached to the immediate packaging.

6.6 Declaration of strength for liquid parenterals

The quantity per millilitre (ml) and the total amount per total volume should be listed on both the inner and outer label.

6.7 Labelling of peel-off blisters

Peel-off blisters are often required for orodispersible tablets due to their fragility. For this reason, the HPRA recommends that clear information on how to remove the tablets from the blisters should be included in the SmPC, package leaflets and labels. Suggested approaches are as follows:

- Instructions on how to correctly remove the tablets from the peel-off blisters should be included in the SPC.
- Detailed instructions on how to remove the tablets from the peel-off blister should be provided in the package leaflet. The instructions should preferably be accompanied by pictograms where these are unambiguous/clearly interpretable.
- If space permits on the outer carton, a statement referring the user to the package leaflet for instructions on how to remove the tablets should be included. For example, 'See package leaflet for details on how to open the blister'.
- For blister labels, it is recommended that a pictogram indicating that the tablets should not be pushed through the blister is included on one side of the blister. On the other side, it is recommended that a distinctive arrow, indicating the point where the blister is to be peeled from, should be included.

Where such additional information is included in the product information, it should not affect the legibility of the other information as required by Articles 54-69 of Directive 2001/83/EC.

7 SPECIFIC PACKAGE LEAFLET REQUIREMENTS

7.1 Compliance of the package leaflet with the SmPC

In drawing up the leaflet, the name that appears at the top of the leaflet must correspond completely with Section 1 of the SmPC, i.e. name, strength and full pharmaceutical form followed by the INN. Applicants should note that all the information contained in the SmPC should be included; this applies especially to precautions, warnings and all listed undesirable effects.

7.2 Technical package leaflets

Technical package leaflets are not required for all products but are recommended (according to the QRD template) in the following instances:

- Practical information and/or instructions for administration of the medicinal product by the patient need to be provided when such information is too extensive for inclusion in Section 3 of the package leaflet (how to take/use X). A cross reference should be included in Section 3.
- For parenteral products or other products which are mainly used in hospitals, practical information on preparation and/or handling of the product can be included for healthcare professionals where relevant and a cross reference to Section 3 should be included.

If other information is to be included in the package leaflet for the healthcare professional, the applicant should provide the complete SmPC or appropriate sections of the SmPC as a tear off section at the end of the package leaflet, so that the information for the patient (the package leaflet) and the information for the healthcare professional (the SmPC) are clearly differentiated. The information for the healthcare professional should correspond fully with the SmPC.

8 BRAILLE AND ACCESSIBLE PACKAGE LEAFLETS

8.1 Introduction

To ensure improved access to information on their medicines for people with visual impairment, Article 56a has been introduced under Title V of Directive 2001/83/EC as amended by Directive 2004/27/EC. These requirements are implemented by S.I. 540 of 2007 Medicinal Products (Control of Placing on the Market) Regulations 2007. This requires that the name of the medicinal product must be expressed in Braille format on the packaging, allowing improved differentiation of medicines. It also requires that the marketing authorisation holder ensures that the package leaflet is available on request in formats which are suitable for people with visual impairment. The 'leaflet' provided should not be abridged in any way.

8.2 HPRA requirements

The HPRA takes the following approach to ensure compliance with this requirement:

A 'Braille Declaration Form', available from the HPRA website, must be provided by the applicant for all new applications, at renewal and for variations to update patient information in line with the provisions of Article 56a. Braille declarations are not required initially where a product is not to be marketed and text versions of labels and leaflets have been submitted, e.g. at the end of a DC procedure. The Braille declaration must then be submitted during the Article 61(3) notification to register the mock-ups prior to marketing.

The relevant sections 1a or 1b, **and** 2 must be completed and the declaration must be signed and dated by the applicant's authorised representative. HPRA assessors will assess that the

wording to be provided in Braille is in line with the requirements of the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use'.

Applicants must include ~~in Braille~~ the invented name, strength (where the product is available in more than one), and the pharmaceutical form (where a risk of confusion occurs), in Braille on the outer carton of medicinal products. Products which are for administration by healthcare professionals only are excluded.

Applicants should note that Section 2 of the declaration must always be completed, as package leaflets for all medicines must be available in formats suitable for blind or partially sighted people.

The Market Compliance section of the HPRA's Compliance department checks compliance with the labelling and other provisions of Article 56a. As part of this work, the Market Compliance section obtains samples of relevant medicinal products from the marketplace for checking, and also performs inspections, as necessary, in order to monitor compliance with the provisions of Article 56a and with the declaration provided.

All authorisations must be in compliance with labelling and leaflet requirements under Title V of the Directive. Applicants must meet the requirement to provide the leaflet in a format suitable for people who are blind or partially sighted ('patient accessible' leaflet).

Grade 1 Braille, which is uncontracted Braille, is the required type of Braille for use on medicinal packaging in Ireland.

Note that Unified English Braille (UEB) is the preferred type of contracted Braille for use in Ireland generally. Standard English Braille (SEB), another type of contracted Braille, has been previously in use. The change to UEB from SEB should have had no impact on most of the Braille applied to medicines packaging, with the exception of the Braille used for some mathematical symbols. Applicants should satisfy themselves that the Braille used for any mathematical symbols on its product packaging is in a format suitable for patients in Ireland, is easily readable and clearly comprehensible.

To date, several issues have arisen which have necessitated clarification and these are highlighted below.

- The timelines for implementation of variations affecting Braille follow current implementation timelines.

- The format of Braille to be used should be in line with the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use'.

- The Braille declaration form submitted must show exactly what information appears on the carton including units, backslashes, etc. Where applicable, a space should be present

between the strength and units of the product (i.e. 50 mg instead of 50mg). This space is important for Braille readers as the same Braille dots (up to the letter J) are used for both letters and numbers, and this space indicates that the Braille dots have changed from numbers to letters.

- There is no requirement for flat dot mock-ups to be provided at this time. Normal mock-ups should be provided along with the Braille declaration to indicate from which label version onwards the Braille declaration applies.

- Generally, one Braille declaration form should be provided per PA and will be kept on file (although multiple strengths of the same product form, e.g. tablets, could all be listed separately on the same declaration). For example, the Braille declaration form should be updated if there is a change in product name, if for PA5555/222/1, PA5555/222/2 and PA5555/222/3 the following text appears on the Braille declaration form:
  - 'Invented name x mg
  - Invented name y mg
  - Invented name z mg'

- If there is a change in packaging layout, e.g. an Article 61(3) notification, applicants must satisfy themselves that this does not affect the legibility of any text now underlying the Braille (e.g. indications, posology, strength), to maintain compliance with the Braille declaration on file.

- The Market Compliance section of the HPRA's Compliance department checks that the information provided in Braille on the carton is that which was stated in the Braille declaration on file and correctly interpretable.

- Where a product is for administration by the patient themselves, Braille must appear as per the recommendations of the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use'.

- The quality of the embossing mechanism and medium used must be carefully evaluated to ensure that the carton will still be readable at the end of shelf life. In particular, the height of the Braille dots is important to facilitate the readability of the Braille. Low dot height has frequently been an issue when compliance checks have been performed on Braille by the HPRA. Applicants are advised to consider I.S. EN ISO 17351:2014 'Packaging – Braille on Packaging for Medicinal Products' when ensuring that the Braille dots are of a sufficient height to enable one to read the Braille correctly. This standard sets out the Braille dot height criteria as follows:
  - The dot height target for the Braille cell should be 0.20 mm.
  - Not more than 5% of the Braille cell dot height measurements should be lower than 0.12 mm.
  - Not more than 1% of the Braille cell dot height measurements should be lower than 0.10 mm.

The key goal of this standard is to ensure sufficient Braille dot height is achieved to ensure the readability of the Braille. In this regard, a minimal Braille dot height of 0.12 mm is generally regarded as acceptable by the HPRA. Compliance with this ISO standard is not currently a GMP requirement. The GMP guide does not directly address Braille tests or checks at this time, and the HPRA recommends that medicinal product manufacturers consider this ISO standard as it can facilitate compliance with the legally binding company (MAH) Braille declaration for each product which commits to Braille text that is easily readable.

- Braille may be extended over more than one face of a carton, or oriented differently to the printed text. However, if this approach is taken it is the applicant's responsibility to ensure that the readability of the Braille text is not compromised.

- Hyphenation of long words in Braille may be carried out in line with the general rules for everyday Braille. It is the applicant's responsibility to ensure the Braille remains clearly comprehensible, and in a format suitable for Irish patients.

- The EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use' allows for contracted (Grade 2) Braille to be used for small containers with a capacity of less than 10 ml and also suggests that innovative packaging, e.g. tab label, should be used where space issues arise. To date the HPRA has accepted a justification for using the contraction 'o*t;t' for an ointment in a pack size less than 10 ml. The Braille declaration in such instances should include in English text an exact reflection of what appears in Braille on the carton and its explanation (ointment) for future reference.

- Braille may be included by the applicant on cartons or bottles via a permanent overlabel if necessary, providing the requirements of the Braille declaration are still fulfilled and no text on the cartons or bottles is obscured by the overlabel.

- It may be acceptable not to include Braille on bulk dispensing packs, where the applicant submits a justification that certain pack sizes are 'for administration by healthcare professionals only' as per the EC Guideline on the 'Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use'. The Braille declaration must be annotated to state to which pack sizes Braille is applied, and in all cases Section 2 must be filled out.

- Where the invented name of their product in Braille (accompanied by the strength and form if necessary) is too long to be displayed effectively in Braille on the carton, applicants should consider a variation to register a shorter invented name, as the invented name in Braille must match the invented name registered in Section 1 of the SmPC and on the patient leaflet, to avoid confusion and as per EU guidance.

- Braille declarations must also be submitted for existing products where Braille may have been historically included but never assessed for compliance with the current EU requirements.

- It is not considered necessary for PPA holders to overlabel Braille on cartons from other markets where they have checked and verified the following:
  - that the Braille shown matches the requirements for the Irish market with regard to inclusion of the Irish invented name and strength and/or form where required,
  - that the Braille is in a format suitable for Irish patients, is still easily readable, clearly comprehensible and does not interfere with the legibility of the underlying text or cause confusion for the patient, and they have signed and submitted a Braille declaration to that effect.

- Addition in Braille of an abbreviated pharmaceutical form, e.g. 'tablet' where the full pharmaceutical form is 'prolonged release tablet', should be avoided even if the preparation is only available in one form. Either the form should be omitted as per EU guideline or the full form added, to avoid any assumption that the product is immediate release.

8.3 'Accessible' leaflets

Marketing authorisation holders are required by Article 56a of Directive 2001/83/EC to provide patient information leaflets in formats suitable for blind or partially sighted people. Such formats could include Braille, audiotape, CD or large print. Choice of the appropriate medium should be made by the MAH in consultation with representatives of organisations for the blind and partially sighted. For new applications, renewals or variations to update in line with the provisions of Directive 2001/83/EC, a Braille declaration form to confirm compliance with the requirements of Article 56a must be supplied as described in 7.2 above.

These 'accessible' leaflets will not be assessed by the HPRA but must contain the same information in the order of the Directive as the approved leaflet and must not be abridged in any way. The Market Compliance section of the HPRA's Compliance department checks availability of suitable 'leaflets' and that the current version is being supplied.

The requirement for 'accessible' leaflets, i.e. leaflets to be available in formats suitable for people with visual impairment applies for all PAs.

The following should be noted:
- Applicants should ensure the 'patient accessible' leaflet is available promptly to the patient on request, especially considering situations where medicine is used for short-term illness, and ensure that the format used is such that the patient can consult the leaflet again at their convenience.

- Where no separate patient leaflet exists as the information required has been provided on the outer carton, the applicant must provide this information in a format suitable for blind or partially sighted patients, and submit a Braille declaration accordingly.

- The HPRA does not endorse any particular service provider for the production of patient accessible leaflets and Braille implementation. It is the responsibility of the applicant as per the Braille declaration they have signed, to ensure the Braille and patient accessible leaflet are suitable for Irish patients.

- PPA holders must also comply with the requirement to promptly provide the leaflet in a format suitable for blind or partially sighted people on request, and this must be suitable for patients in Ireland.

9 CONSULTATION WITH TARGET PATIENT GROUPS FOR THE PACKAGE LEAFLET

The purpose of this section of the guidance is to assist applicants in ensuring that the final package leaflet (PL) reflects the results of testing with patients so that it meets their needs and enables the patient to use the medicinal product safely and effectively. The guidance ~~will apply~~applies to applications for new marketing authorisations (MAs), significant variations to MAs, renewal applications, and applications where harmonisation of the PL is undertaken and which must be accompanied by data demonstrating compliance with Article 59(3) of Directive 2001/83/EC.

9.1 Background and legal basis

The legal basis for the submission and approval of user testing of package leaflets is detailed in Article 59(3) and Article 61(1) of Title V of Directive 2001/83/EC and S.I. No. 540 of 2007, Medicinal Products (Control of Placing on the Market) Regulations 2007.

Articles 59(3) and 61(1) of Directive 2001/83/EC require that the package leaflet ~~shall reflect~~reflects the results of consultations with target patient groups to ensure that it is legible, clear and easy to use and that the results of assessments carried out in cooperation with target patient groups ~~shall also be~~are provided to the competent authority.

Results of ~~such~~ a user test or justification for not providing it should be submitted in Module 1.3.4.

9.2 Circumstances where user testing is required

Submission of user testing of leaflets is required for all new applications and existing authorisations as follows:

National, mutual recognition, decentralised and centralised procedures:
- New applications submitted on or after 23 July 2007 (which was the date of transposition into Irish law of S.I. 540 of 2007) including line extensions if the original product in the series has not undergone user testing
- New products and new chemical entities

- Variations for change in legal supply status
- Inclusion of a novel presentation
- Addition of new indications with critical administration issues
- Medicines with critical safety issues
- New safety issues
- New leaflet format or layout

Changes to the format and layout which require user testing include:
- Change in font style used
- Change in typographical emphasis
- Change of colours used
- Change in style of writing and language used
- Addition/removal of pictograms
- Change in layout of critical safety sections of the package leaflet
- Switch to a fix-a-form leaflet

User test outcome reports should be submitted as Type IB ~~variation procedures~~variations under category C.I.z. This includes situations where the results of user consultation may indicate that no changes or only minor changes are required to the product information. Implementation of the approved leaflet and packaging will be six months after the variation approval date.

Changes to the format and layout which do not require user testing include:
- Change in font size (once not below minimum of 9 point)
- Change in orientation of the leaflet (text)
- Change in the number of columns/pages in the leaflet

9.3 Exemptions from user testing

The evidence from tests on similar package leaflets may be used where appropriate and accompanied by a bridging report identifying and justifying any differences. Bridging reports should be submitted as Type IB variations under category C.I.z.

Examples of when this may be considered acceptable based on a sound justification by the applicant/marketing authorisation holder are:
- Reference to the PAR or EPAR of an identical package leaflet which has already been the subject of user testing (see CMD(h) Q & A Product information/Information on Medicinal Products), which also provides details of the documents which are required to be submitted, to qualify for this exemption.
- Line extensions. Bridging will generally be acceptable for package leaflets of the same active substance but with different strengths or routes of administration.
- Products which are not marketed in Ireland. If it is intended to market a product, then a user test must be performed, submitted and approved before the product can be placed on the market.

The expectation with respect to the holders of parallel import licences is to maintain the parallel import licence and, in this case, product information in line with the PA product.

9.4 Methods by which MAHs can meet the requirements

The options available to MAHs of licensed, marketed products in Ireland for meeting the user test requirements are:

1 To submit a stand-alone user test report on a package leaflet.
2 To submit a bridging report to another package leaflet(s) user tested and approved by another Member State.
3 Exemption from user testing (accompanied by appropriate justification).

A user test report of a package leaflet (termed 'parent' leaflet) can be used to fulfil the requirements of another leaflet (termed 'daughter' leaflet) if certain criteria are fulfilled. A bridging report comparing, contrasting and justifying the use of the parent user test report in support of the daughter leaflet must also be provided. In addition, the need for focus user testing should be discussed.

In some circumstances, it may be appropriate for some daughter package leaflets to rely on the results of testing for more than one parent package leaflet, i.e. a double bridge. For example, it would be possible to refer to the design and layout of one leaflet and to the content of the leaflet for another product.

The number of permissible bridging relationships should be limited to two or three.

9.4.1 Criteria for acceptable bridging

One or more of the following could be used as justification for bridging.

Medicines in the same drug class
Bridging ~~will~~is normally ~~be~~ acceptable for package leaflets for medicines in the same therapeutic class where the clinical information set out in the SmPC (and therefore the information in the PL) is similar.

Importantly the key messages for safe use with the related medicines should be similar. However, the format and layout of the package leaflets to be bridged should be identical. This means that the daughter package leaflet should be revised and drawn up in a design, layout and linguistic style which conforms to the parent package leaflet which will have been the subject of a successful user test.

A therapeutically similar product is defined as a group of medicines which have similar modes of action. The following examples are included but this list is not exhaustive.

Cardiovascular

- Thiazide and related diuretics
- Beta-blockers
- ACE-inhibitors

CNS

- SSRIs
- Tricyclic and similar antidepressants
- Antihistamines
- Benzodiazepines
- Opioid analgesics

Anti-infectives

- Penicillins, cephalosporins and macrolides
- Antifungals

Musculoskeletal

- NSAIDs

Endocrine

- Glucocorticoids

Malignant disease

- Alkylating cytotoxics

Nutrition

- Intravenous nutrition

Obstetrics/Gynaecology

- Oral contraceptives

Line extensions

Bridging ~~will~~is normally ~~be~~ acceptable for package leaflets of the same active moiety for different strengths or routes of administration. In these cases, the parent package leaflet should be the one which contains the more/most complex information for the patient. Where potentially similar products require the patient to understand significantly different methods of administration, different criteria will apply. Examples include but are not restricted to an inhalation device and a patch, where it will be important to ensure that the information in relation to the posology has been the subject of a successful user test. However, a daughter package leaflet could rely on user tests carried out on the package leaflets associated with more than one product. For example, a double bridge could be applied to the package leaflet for a salbutamol inhaler (daughter) which could be bridged to a successful user test for a package leaflet for an oral salbutamol preparation (covers information relating to the active moiety) and to the package leaflet for a beclometasone product with an identical inhaler device (covers information relating to delivery).

Same key messages for safe use

Where the key messages for safe use which have been identified for a range of medicines are similar and the package leaflets are designed, laid out and written in an identical manner, bridging here ~~will be~~is the easiest to justify.

Combination medicines

Generally, the package leaflet for the combination medicine should be considered as the parent package leaflet for the purpose of bridging to the individual component daughter package leaflets. It ~~will be~~is necessary to make sure that any key messages for safe use relating to the individual components have been addressed in the questionnaire for the combination package leaflet. It may be possible to use the individual component package leaflets as the parent package leaflets and bridge to the combination package leaflet as the daughter, provided any differences in layout and length of the combination package leaflet have been the subject of successful user testing within the company portfolio.

Short PLs for medicines with minor therapeutic actions and very low risk profile
Short PLs for such products are unlikely to need to be the subject of a specific user consultation. It ~~will be~~is sufficient to rely on the successful consultations carried out for other products within the portfolio even though these may not be in the same therapeutic class. Examples of such medicines are water for injection, aqueous cream, hypromellose eye drops.

Pictograms
Pictograms used within a company house style will need to be tested as part of a user test. For bridging to encompass pictograms successfully, the pictograms in daughter package leaflets should have the same design, dimensions and colours as those in the parent package leaflet.

9.5 Submission requirements

Applicants should present the results of user testing in English in a standardised 'User Test Outcome Report', including at least the following information, in Module 1.3.4 of the application:

Stand-alone report:
1. Cover letter
2. Application form
3. User test report to include (but not limited to):
   - Introduction/product description
   - Test details, such as:
     - Method used, test protocol
     - Explanation on the choice of test population
     - Language(s) tested
   - Questionnaire (including instructions and observation forms)
   - The original and revised package leaflets
   - Summary and discussion of results (i.e. subjects' answers, model answers, problems identified, and revisions made to relevant package leaflet section)
   - Conclusion

Bridged report:
1. Cover letter
2. Application form

3 Bridged report to include (but not limited to):
- Introduction/product description
- Justification for bridging
- Bridging procedure
- Comparison of package leaflet with bridging package leaflet(s) – see Table 1
- Package leaflet user testing methodology
- Summary of test results
- Discussion of results
- Any other relevant information
- Conclusions
- Focus user testing as appropriate

Table 1:
A tabulated illustration of the comparison/contrast and justification of the parent package leaflet to the daughter package leaflet would be beneficial. Below is an example of this type of table.

Package leaflet section	Parent package leaflet text	Daughter package leaflet text	Summary of differences	Comment on the effect on readability

9.6 The format of the assessment

9.6.1 Design and layout

The presentation of the information in the package leaflet is crucial to the way in which patients access the key messages for safe use. The following important aspects should be considered in both 'stand-alone' user test reports and bridged user test reports:
- Font and font size
- Headings and sub-headings including consistency of placement
- Package leaflet dimensions including whether the document is laid out in portrait or landscape format
- Use of colour and choice of colour
- Style of writing and language used
- Layout of critical safety sections of the package leaflet
- Use of pictograms
- Paper weight

The QRD template should be followed as much as possible. In exceptional cases, alternative headings may be acceptable, especially for those headings containing <take><use> or where a

different wording would be more appropriate for the product concerned, e.g. to better reflect the user of the product. This should not in any case impact on the content required for the section concerned. Applicants should justify the use of alternative headings referencing user testing results.

For ~~for~~ bridging to be successful, both the parent and daughter package leaflets should have a common design, layout and style of writing.

9.6.2 Technical aspects

MAHs should ensure that the user test meets the following criteria:

- The most important information must be clearly defined, for example, what the medicine is for, the dosage and any significant side effects and warnings.
- The test sample populations who are particularly likely to rely on the leaflet for the medicine in question (these may include carers) must be reflected in the report.
- A clear protocol for the user test must be presented.
- Evidence that test participants can find and appropriately use the information must be provided.

Where it is intended to market a medicine in Ireland, any user testing undertaken should be on the English language version of the patient information leaflet.

9.6.3 Key issues to be addressed in a successful bridging report

- Identifying key messages for safe use (of both parent and daughter package leaflet, the differences should be addressed and/or risk assessed):
  - The key messages for safe use within daughter package leaflet should be discussed.
  - How these are covered within the test carried out on the parent package leaflet should be justified.
  - Where key messages are not identical, the bridging report ~~will need to~~must critically appraise these differences and address their relevance to the daughter package leaflet.
  - Synergies and similarities in the key messages should be discussed.

- Design and layout issues:
  - A critical comparison of the design and layout of both daughter and parent package leaflets should be presented.

- Complexity of message and language used:
  - A critical discussion of the complexity of the messages contained within the parent and daughter package leaflets should be presented.
  - The language used in both package leaflets should be discussed and compared.
  - Differences and similarities should be discussed.

10 SAFETY FEATURES

In accordance with the 'CMDh implementation plan for the introduction of the safety feature on the packaging of nationally authorised medicinal products for human use' (CMDh/345/2016), a unique identifier (UI) carried by a 2-D barcode and an anti-tampering device (ATD) is required on the packaging of prescription medicines and certain non-prescription medicines for the purposes of authentication and identification.

Medicinal products that have to bear a safety feature must comply with the revised QRD template, i.e. implement the standard statement on the unique identifier and its carrier under Section 17 and 18 of the particulars to appear on the outer packaging or the immediate packaging if the medicinal product has no outer packaging. The abbreviations for the human readable headers (product code and serial number) should in general comply with the provisions of the QRD template.

In the case of nationally authorised products where the QRD template may not be available, mock-ups can be provided.

In the case of medicinal products where the ATD is placed on the immediate packaging because there is no outer packaging and the ATD affects the container and its closure system(s), information on the ATD and how the ATD affects the container and its closure system(s) is required (Sections 3.2.P.2.4 and/or 3.2.P.7 of the Notice to Applicants Volume 2B).

~~An Article 61.3 notification including mock-ups, is required if the implementation of the safety features results in changes to the label not covered by section on changes above (see section 4.3.1), such as deletion of information or affecting the readability of the label.~~

11 PROVISION OF ADDITIONAL INFORMATION ON THE LABEL AND IN THE PACKAGE LEAFLET

Article 62 in Directive 2001/83/EC, states that the outer packaging or package leaflet may include '...symbols or pictograms designed to clarify certain information mentioned in Articles 54 or 59(1) or other information compatible with the SmPC which is useful for the patient, to the exclusion of any element of a promotional nature'. Therefore, symbols, pictograms or pictures or other text may only appear on outer labelling as long as they are in line with the SmPC, are not promotional nor misleading, and do not interfere with legibility. Guidance on the acceptability of certain additional information is given below.

11.1 General information on the medical condition

Information on the condition for which the product has been prescribed may be included in the leaflet, provided it is in line with the requirements of Article 62 of Directive 2001/83/EC.

11.2 Quick response (QR) codes or 2D barcodes on labelling and in package leaflets

The addition of a QR code or 2D barcode to product labelling or package leaflets is permissible in the following circumstances:

1 Where the QR code or 2D barcode is intended for internal manufacturing processing, stock control or anti-counterfeit measures and does not therefore provide information to patients about the medicine. The addition of the QR code or 2D barcode for this purpose should not affect any other aspect of the label or leaflet and should not affect the legibility of the approved label or leaflet text, otherwise an Article 61(3) notification is required for its inclusion.

2 Addition of a barcode to provide information to patients must follow the general principles and procedural rules for mobile scanning and other technologies in the labelling and package leaflet of centrally authorised medicinal products as published by the EMA (Mobile scanning and other technologies in the labelling and package leaflet of centrally authorised medicinal products, EMA/493897/2015) and the corresponding CMDh position paper (CMDh/313/2014). Addition of and changes to these technologies require an appropriate application (usually an Article 61.3) notification).

11.3 Websites

Website addresses are not permitted on the label or leaflet, whether they are sites related to the PA holder or to the particular product. References to websites, coupons, product-specific phone lines, mail clubs, etc., are considered to be promotional in nature and are not permitted. References to other websites, such as those for patient organisations or for medical conditions are not acceptable. The only exception to this is when including the URL of the platform hosting the content of an approved mobile technology feature (refer to EMA/493897/2015 and CMDh/313/2014 for further information).

11.4 Telephone numbers and email addresses

Telephone, fax numbers or email addresses for the PA holder are acceptable on the label and/or leaflet as long as they are accessible to Irish patients. They can also be included in the printed version of the SmPC used by the PA holder but will not be included in the SmPC which is part of the PA schedule. Emails linking to websites are not acceptable - see above.

11.5 Accreditation logos

Accreditation logos or statements, e.g. for 'organic', 'Kosher', 'Halal', 'Guaranteed Irish', are not acceptable on the label or leaflet~~, with the sole exception of the recycling symbol which may be used on the label or leaflet in line with EU requirements for recovery and recycling of packaging waste under Directive 94/62/EC~~.

11.6 Recycling symbols

The following may be added where space permits:

11.6.1 Identification system for packaging materials

The relevant marking and identification system as defined under Directive 94/62/EC may be included on the labelling or package leaflet.

11.6.2 MyWaste Recycling Labels

The inclusion of 'MyWaste Badges' can be accepted **only** on the labelling or package leaflet of medicinal products not subject to prescription. The positioning of such badges should not impair readability of information critical for the safe use of the medicinal product, as such it is preferential that they be included for example on a side panel or end of package leaflet. An Article 61(3) Notification is required to register the inclusion of such badges on the outer carton or package leaflet. The focus of the Article 61(3) Notification assessment is on the positioning of the badges and the potential impact on readability of the mandatory labelling information. It is the responsibility of the applicant to ensure the correct badge is used. Therefore, these badges will not be subject to review.

~~11.6~~11.7 Patient registration forms

Forms in the package leaflet or coupons which request patients to send their details to the PA holder for further information are considered promotional and not acceptable.

~~11.7~~11.8 Patient organisation details

Contact details for independent patient organisations may be included in package leaflets, e.g. phone or fax numbers (as long as they are accessible to Irish patients), email addresses, but not websites (as above).

~~11.8~~11.9 Use of 'New' on packaging or package leaflet

Statements such as 'New' or 'New product' may not be used for promotional purposes on product labelling.
'New' may be used on product labelling in order to alert pharmacists and patients to a change in an existing product of which they should be aware or which might give rise to concern in the absence of such comment (changes in the composition, appearance, colour, shape, flavour, markings, etc.). In these cases, 'new' must qualify the property which has changed, e.g. 'New markings', 'New formulation'. This statement should be included for a period of six months only.