



User Testing Policy on Patient Information Leaflets for Parallel Importers June 2019

1. BACKGROUND

Patient Information Leaflets (PILs) have been a legal requirement in the UK since 1999 for all medicines. Survey findings tell us that patients want more information than they currently receive and that they value the PIL which comes with the medicine more highly than any other source of information except doctors and pharmacists. The statutory PIL is both available and authoritative and for many patients this is the only written information they will have about the medicines which they are taking.

Good information helps patients to participate fully in concordant decision-making about medicines prescribed for or recommended to them by healthcare professionals. Self-care a key government objective relies heavily on patients having sufficient high-quality information on which to base their decision-making.

This guidance is to be read alongside the legislative requirements which are set out in Title V of Council Directive 2001/83/EC (as amended).

In addition to the provisions in article 59(1) concerning the content and order of the PIL article 59(3) requires applicants to provide evidence that the leaflet proposed for marketing reflects the results of consultation with target patient groups.

2. COMPLIANCE WITH ARTICLE 59(3) – USER TESTING

The legal basis for user testing is set out in article 59(3) of Council Directive 2001/83/EC. This states:

“The package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use.”

User testing or other form of patient consultation ensures that patients' views on the content and design and layout are taken into account so that the final leaflet which is submitted as part of the Marketing Authorisation enables most medicine users to take safe and accurate decisions about their medicines.

Both national and EU guidance is available concerning mechanisms for demonstrating compliance with article 59(3) of the directive [user testing].

MHRA will not require any particular method of testing to have been used but will look for evidence that people who are likely to rely on the leaflet can find and appropriately use the information.

Parallel importers have three options to demonstrate compliance with Article 59(3):

- 2.1. Full user test
- 2.2. Bridging studies
- 2.3. Compliance to the UK PIL

These are described in further detail below.

2.1. Full User Test

A full user test describes where a patient leaflet has been subjected to testing for readability by target patient groups. A full user test would be expected if a Company wishes to use their own 'house style'. They are required to complete a full user test on their chosen leaflet(s) so that they can bridge to this in the future.

As the PI licence holder, you are advised to ensure that you have:

- Clearly defined before the test what the most important information is – for example, what the medicine is for, the dosage and any significant side effects and warnings. This will vary depending on the active substance in the medicine in question. The questions asked of the participants should cover the key messages for safe use. These key messages for safe use are most likely to come from sections 1 – 4 of the leaflets, but the distribution and spread of questions will vary from one medicine to another. Although for some medicines there may be a need to ask a question from sections 5 or 6; this would not be usual. Make sure you cover all the key messages for safe use in the questionnaire to be sure of a successful outcome.
- Reflected in the test sample populations who are particularly likely to rely on the leaflet for the medicine in question (these may include carers). It will not be essential to reflect all patient populations in every circumstance – it will be sufficient that those involved can imagine having the condition for which the product is indicated. Healthcare professionals and other staff/people who routinely work with medicines information must be excluded to avoid bias. People who are familiar with the medicine would not normally be appropriate, although they can be a useful source of advice in the design stage.
- Ensure the test sample fulfils the sample size requirements. For a user test where both content and layout (style/design) are being evaluated, we would require at least two rounds of testing (depending on the results) and each round should have a minimum of 10 people. Where only a particular aspect of the leaflet is being tested, such as the wording of a discrete section or the layout, we would accept a “focus test”, where a lesser number of participants can be used. **However, since all PILs for parallel import licences must follow the text of the cross-referenced UK leaflet exactly, and this has already been tested and it is only the layout requiring validation; we would accept a minimum of two cohorts of 5 participants each.**
- Provided credible evidence that test participants can find and appropriately use the information. The questions included in the protocol will be assessed to ensure that they reflect the key safety messages identified. Questions must be open, allow the participant to imagine themselves in a particular scenario and must not lead them to the answer within the PIL. The questions should be designed to ensure that the user is able to understand what to do with the information they find, not just locate the information. It is important to note that the key messages will be different for different therapeutic products, therefore it is not possible to use a standard set of questions for every leaflet. Each question must perform satisfactorily. It is not appropriate for data to be accumulated and for one or more key messages not to be found and understood by participants. Assessors will be looking for relevant questions to be asked of participants and for each question to individually meet the success criteria determined prior to testing.

➤ **Suitable questions:**

- *If you had started to take these tablets and you noticed some unusual aches and pains in your legs, what would you do?*
- *Imagine you are already taking ciclosporin. Are these tablets suitable for you?*

➤ **Suitable questions for some products only:**

- *Are there any special storage requirements for this medicine?*
- *Question on lactose content only if more serious warnings already covered*

➤ **Unsuitable questions:**

- *Can you show me where the information on [.....] is?*
- *Please list four side-effects.*
- *Who makes this medicine?*
- *What do the tablets look like?*

Interpretation of the Success Criteria

Success criteria state that 90% of literate adults should be able to find the information and of these 90% should be able to understand the information. Over two rounds of 5 participants on the final proposed leaflet we would expect 8/10 participants to have both found and understood the information. Where results fall below this level, we would expect revisions to the PIL to be made and further testing to be carried out. Where alternative test methods are proposed, different success criteria may be appropriate. Nevertheless, whatever success criteria are proposed, each question must satisfy the criteria individually.

Preparing the report for submission

The report should take into account guidance already published and available from Heads of Medicines Agencies (HMA) website. In addition, it is helpful to include the following sections in the report:

- Key messages for safe use.
Identify these up-front for the particular medicine
Discuss how the questions have been derived based on the key messages for safe use
- The questionnaire used should be submitted as part of the overall report.
- Participant selection and demographics
Discuss how the participant population chosen reflects the likely patient population for the medicine in question, both in sex and age spread.
Discuss exclusion criteria and educational level of participants to ensure bias is removed.
- Report each round of testing
Graphical representation works well but if graphs are used, they must be clearly labelled and easy to interpret.
Each question must pass the success criteria. Indicate which questions participants have problems with. This may in terms of location or understanding or both.
If you use subjective criteria such as “easily”, “with difficulty” etc to describe how participants find information, please be aware that we would consider those responses stating “with difficulty” or “with lots of difficulty” to be unsuccessful and that you should discuss how ease of finding the information can be improved by making changes to the PIL.
Propose changes to the PIL to address the difficulties
Retest and report further rounds
- Discuss and general feedback from the participants on the leaflet and propose changes to address any concerns of a general nature.
- Include all versions of the leaflet
- We do not need the original data obtained from the interviews – a summary of the verbatim responses will suffice. If we feel we need more information we will ask you for it during the assessment.
- You should not submit data on how each participant performed during the test. The leaflet is being tested, not the participants, and therefore these data are not relevant.
- Provide confirmation that the leaflet presented to the participants in User Testing is an exact replica (mock-up) of the leaflet that will appear in packs, with details of exact dimensions, page breaks and whether the leaflet will be printed on one or both sides. Although the paper weight used for the PILs in the User Test does not have to be identical to the paper used in production runs, the expectation is that it should be as close as possible. Companies should ensure that the paper type used is of suitable quality such that readability of the PIL on both sides of the paper is not impaired (where applicable).

General Points on Full User Tests

- You should not use the same participants within 6 months of them being involved in another user test, because otherwise they may get used to knowing where to find information and are no longer representative of patients who do not use leaflets regularly. You may however use the same people on the same day to test two leaflets if they are for very different products/layouts, as long as the demographics (age, sex etc) are appropriate for both products.
- It is useful to have a measure of how easy or difficult it was for the participant to find the information - an experienced interviewer can make a record of this without actually timing, as long as the criteria used for deciding whether it was easy or difficult is defined in the report.
- Written questionnaires alone are unlikely to provide sufficient evidence to demonstrate that participants can find and understand the required information. Our survey of user test houses indicates a need for written questionnaires of this sort to be supported by formal user testing protocols in order to provide robust data. Information obtained from the face-to-face interviews provides an understanding of how participants navigate the information which is not available in the remote setting.
- It is not sufficient for participants to simply identify appropriate headings and where information can be located in the leaflet.
- The headings used in the user tested UK PILs are the standard headings according to the European QRD (Quality Review of Documents) template and these headings should be used.
- If the UK leaflet combines the different strengths of the product, with differing indications/dosage instructions/ precautions for each strength and your PI PIL to be tested is for only one of the strengths, you should test the most complex version of the PIL, i.e. one with combined strengths or the strength(s) with the most complex information, which is usually the highest.
- Parallel importers can perform their own user tests; however, it may be advisable to obtain the help of a User Testing House with experience in this field and with a successful record of approved User Tested PILs. Please note that we are unable to give recommendations.

2.2. Bridging Studies

Although all PILs for medicines must reflect the results of consultation with target patient groups (user testing) not every leaflet needs to be the subject of a separate test. Bridging Studies which rely on testing applied to PILs for similar products can be used to demonstrate compliance with article 59(3) of Council Directive 2001/83/EC.

Minor changes to content or layout of a document can impact adversely on the readability. These differences can affect whether or not the resultant PIL is clear, legible and easy to use as required by law. The term bridging has been described to apply to leaflets which are sufficiently similar in both content and layout.

In bridging, a successful full user test on one PIL [the “**parent**” PIL] can be used as a justification for not testing other similar leaflets [“**daughter**” PILs]. Since the design and layout of the information is crucial to how the information is used and understood, “daughter” PILs should be of the same design, layout and writing style as the “parent” PIL in order for bridging to be successful.

The number of 'parent' leaflets approved will depend on the portfolio of the individual PI Company. Although generally for most Companies, 2-3 approved 'parent PILs' would cover most of the potential leaflet formats, sizes and complexities.

We do accept sharing agreements for "parent PILs" between different companies. You will need to submit written proof of this agreement with your bridging report.

The following points should be checked when deciding if it is acceptable to bridge the "daughter PIL" to the proposed "parent PIL".

	daughter PIL
Page Dimensions	width – same as parent length – may be different from parent (shorter or longer)
Layout (portrait or landscape)	Same as parent *
Column number	Same as parent
Column width	Same as parent
Font style	Same as parent
Font size (text and headings)	Same as parent or bigger (minimum for text is Arial 8pt)
Page Margins	Slight differences acceptable
Pharmaceutical forms	Can be a different pharmaceutical form to parent
Graphics	- Daughter PIL has diagrams – then parent PIL MUST have diagrams. - Daughter PIL does not have diagrams – then parent PIL may/may not have diagrams.

* The width of the parent and daughter leaflets must be the same. It is not acceptable to bridge an A3 daughter leaflet to an A4 parent PIL as the widths are different. In the same vein, the layout (portrait or landscape) of both leaflets must be the same. If the layout of the parent PIL is landscape, then the daughter leaflet must also be landscape. Bridging a portrait daughter leaflet to a landscape parent PIL is not acceptable.

PI companies may create their own template bridging report with all the necessary details below included:

- Product leaflets successfully user tested (PL number / Licensed Product name(s)) to which reference is being made (parent leaflet(s)):
- Confirmation that the same house style is used, *i.e.* in terms of font style and size for body text, headings and sub-headings, spacing, number and dimension of columns etc., with justification for any differences in layout between the 'parent' and 'daughter' leaflets.
- Confirmation that the UK leaflet text is followed exactly, including headings and diagrams, apart from product specific details.
- For a bridging report to a leaflet for the same product:
 - o Details of any differences in text, e.g. text added/amended due to variation to UK PIL since the user tested leaflet was approved.
- For a bridging report to a leaflet for other products:
 - o Justification for accepting the results of the previous user test based on similar product types and/or similar complexities of leaflet in terms of diagrams, tables, detailed instructions for use, extensive precautions or side-effects.

The following points for **BOTH parent and daughter PILs** must be stated in the bridging report submitted by companies. It is preferable to state these in a table format.

- Page dimensions
- Font style and size
- Column number
- Column width
- Orientation
- Printed single-sided, double-sided / flat sheet or booklet style

Note: Any differences between the parent and daughter PILs must be specified with a reason for the difference.

Some leaflets will be more complex than others due to the nature of the product, e.g. PILs for HRT/contraceptives are extensive; PILs for inhalers and transdermal patches contain diagrams and important administration instructions. It may be necessary to adapt the 'house style' to accommodate different lengths or complexities of leaflet, i.e. column numbers and widths, font size, etc. This will be assessed on a case by case basis.

Documents to be submitted for a successful bridging study:

3 separate PDF files:

1. Cover letter
2. Mock-up of amended (proposed) PIL.
3. Bridging report AND parent PIL AND proposed daughter.

2.3. Compliance to the UK PIL

Parallel Import Leaflets can be judged to have met the requirement for consultation with target patient groups if they are sufficiently similar to the UK leaflet. Companies wishing to follow this route '**compliance to the UK PIL**' should provide the information detailed below for consideration and approval of their proposed leaflets.

A PI leaflet can be considered to reflect consultation with target patient groups if it is sufficiently similar to the UK leaflet. The leaflet can be judged as sufficiently similar if the following conditions are met:

Text: The PI leaflet must use the full text of the UK leaflet apart from product specific particulars.

Colour: We encourage PI leaflets to adopt a colour scheme which, if not the same, should at least be a similar shade to that used in the UK leaflet. It is however recognised that the colour portions of the UK leaflet may be replaced by grey scale or black & white equivalents provided the overall presentation remains clear. Any portion of the UK leaflet highlighted by means of colour should be appropriately highlighted also using the adopted colour scheme in the PI leaflet.

Column format: The column dimensions of the PI leaflet should give a line length (number of characters) similar to that of the UK leaflet. The PI leaflet will be expected to have the same number of columns as the UK leaflet though this may be different in exceptional cases, if satisfactory justification is provided. The text justification should be the same as the UK leaflet, i.e. left or fully justified. The gap between columns should preferably be at least 10mm and not less than 6mm. A vertical line may assist visual separation of columns where the gap is small.

Font: The font and font size used in the PI leaflet does not have to be the same as that used in the UK leaflet. The font chosen should have a readability at least equal to that of 8pt Arial (normal width) though it is preferable if a larger font is used, e.g. Arial 9pt.

- Line spacing:** This should normally be the same as that used by the UK leaflet and in any event should not be reduced to less than that which is normal for the font chosen.
- Headings:** These should be clearly emphasised, preferably in the same way as the UK leaflet, for example by use of a larger font size, bold text and/or reverse printed text.
- Sub-headings:** Should be distinguished from both headings and other emphasised text and should be similar in placement and design to the UK leaflet.
- Emphasis:** Emphasised sections of the UK leaflet (e.g. bold or boxed) should be appropriately emphasised in the PI leaflet. Inappropriate emphasis (e.g. product name in bold throughout the leaflet) is not allowed.
- Graphics:** The PI leaflet should include all graphics present in the UK leaflet. The UK leaflet graphics may be replaced by grey scale or line drawing versions providing that the content of the image is the same. The graphics should be at least 95% of the size of the equivalent graphic in the UK leaflet. The aspect ratio of the original graphic must be maintained and the relative sizes of multiple graphics should be maintained. They must be clearly legible.
- White space:** There should be good use of white space, e.g. to break up large sections of text. For example, there should be a small space between paragraphs and sections of the text. The general pattern of white space in the UK leaflet should be followed in the PI leaflet but large areas of white space in the body of the leaflet should be avoided if possible.
- Paragraphs:** These should be used appropriately to avoid large blocks of continuous text.
- Column breaks:** These should be in appropriate places in the text. Important paragraphs should not be split across columns unless unavoidable and appropriately justified.
- Page dimensions:** The page size and aspect ratio should normally be similar to the UK leaflet though they can be different in exceptional cases, if satisfactory justification is provided.
- Page margins:** Preferably 10mm and not less than 7mm.

If the leaflet is not in line with the above requirements, a full user test may be required. Any differences between the UK PIL and the PLPI PIL must be clearly identified in the '**statement of compliance**' with a valid justification for this. A template statement of compliance can be found below:

Statement of Compliance

The patient leaflet for the parallel import licence detailed below can be regarded as satisfying the requirement for consultation with target patient groups by virtue of its similarity to the UK leaflet.

PLPI No. :

PLPI Product Name(s) :

	UK PIL	PLPI PIL
PL No. / PLPI No.		
Font Type		
Font Size (title)		
Font size (headings)		
Font size (body text)		
Page size		
Page Orientation (portrait/landscape)		
Finished Format: Flat Sheet/ booklet, page no. Single / Double sided		
Column Number		
Column width		
Space between columns		

- The text of the leaflet exactly follows the text of the UK leaflet except for product specific differences. Yes / No (delete as appropriate).
- A 100% scale mock-up (i.e. exact replica of the leaflet which will be inserted into the patient packs) of the leaflet has been provided. Yes/No (delete as appropriate)
- A copy of the current UK PIL has been provided. Yes /No (delete as appropriate)
UK PIL date: -----
- The format of the PI PIL is identical to the UK PIL. Yes/No (delete as appropriate).
If No, please provide justification here:
Signed:
Name:
Date:

Documents to be submitted for a successful compliance study:

3 separate PDF files:

1. Cover letter
2. Mock-up of amended (proposed) PIL
3. Statement of compliance **AND** proposed PIL **AND** a copy of the current UK PIL.

Additional Points on Compliance

- i. When a product is no longer marketed in the UK and the UK licence is under Sunset Clause, the MA holder must still update the SPC and Patient information Leaflet. However, the MAH is not obliged to provide a mock-up leaflet.
This potentially poses a problem for PI companies, who wish to use Compliance to the UK PIL as a method of user testing of their leaflet.

In this situation:

- a) If you are submitting a variation to update your leaflet, follow the existing format of your granted leaflet but simply update the text.
- b) If you are submitting a new application, and do not have access to the previous granted leaflet you should:
 - i. If you have a suitable parent PIL approved within your Company portfolio, follow this format.
 - ii. Follow the style of the emphasised sections within the text version of the PIL (*i.e. section headers, bold, italics*).
Use one of the following standard formats, depending on which is more appropriate for the text length and content of the leaflet.
 - ❖ Custom size – portrait, 2 columns of equal width.
 - ❖ Custom size – landscape, 4 columns of equal width.
- ii) If the UK leaflet has a custom size width of less than 210mm (A4 portrait width), it would be acceptable for the width of the PI leaflet to be increased to a maximum of 210mm, however the format and style must remain the same.
- iii) When the UK PIL is of a format that would be extremely difficult to replicate, for example certain contraceptives and HRT products that are in a booklet style, the parallel importer may adopt one of the following two formats:
 - Custom size paper, landscape, 4 columns of equal width
 - Custom size paper, portrait, 2 columns of equal width

When the UK cross referenced leaflet changes in format, parallel importers are not required to repeat the user testing – the PLPI leaflets should be updated as usual via a type 64 leaflet variation, keeping the format and house style that is already user test approved.

General Points to Consider on User Testing

- Any leaflets for healthcare professionals that are to be inserted into medicinal packs are not required to be user tested. These can be attached to the user tested Patient Information leaflet as is the case with some UK cross-referenced leaflets.
- An updated user test will NOT be required when changes to the leaflet are to introduce a new word or phrase within a section which has previously been subject to testing or when changes to the design and layout do not impact on placement or size of the information presented. The user test report only needs to be updated when the paper size, format or style of leaflet is changed.
- When significant changes are introduced to the design and layout of a previously tested PIL such as changes in orientation and/or placement of text size of text and introduction of alternative formats (flat leaflet moving to booklet) will require supplementary bridging data, focus testing or in some cases a full user test to be carried out. These will be assessed on a case by case basis.
- With all PIL User Test applications, please provide confirmation that the leaflet presented to the participants in User Testing
 - is an exact replica (mock-up) of the leaflet that will appear in packs.
- The PIL should not exceed more than one sheet of paper. Larger leaflets should be printed on custom sized paper.
- Use of bold type or uppercase for the product name in the body of text should not be used as this can often reduce the impact of the bold type or uppercase used to highlight key messages within the leaflet.
- The minimum font size for the main body of the text should be Arial 8pt or equivalent.
- It is preferable to use the same pictures/diagrams as the UK leaflet (size and quality of the graphics should be maintained) however due to trademark issues PI companies may use their own providing the size and key messages that the pictures are portraying are consistent to the UK.