

Additional Qs and As in relation to the new legal requirement to undertake consultation with target patient groups (Compliance with Article 59(3) of Council Directive 2001/83/EC)

This series of FAQs supplements those published by MHRA in June 2005 and should be read in conjunction with them. These are additional Qs & As drawn up following a number of enquiries to the agency. Earlier advice is not repeated here and remains in force. The MHRA has not set out particular requirements for the recording and submitting of data in compliance with article 59(3) of Council Directive 2001/83/EC (as amended) and applicants are free to provide the required information in a format to suit their current regulatory model. Any further questions not addressed here or earlier should be referred to jan.macdonald@mhra.gsi.gov.uk

Q1. How will my user test report be assessed by the MHRA?

A1. First of all the MHRA assessor will consider whether the PIL meets the legal requirements as set out in article 59(1) of Council Directive 2001/83/EC, including the order of the information. The assessor will then consider the design and layout of the leaflet, including the font style and size and the way in which the information is written and make a decision on the overall readability of the PIL as intended for marketing.

We will then consider which key pieces of safety information are essential for safe use of the medicine and judge whether or not the applicant has identified a similar set of key safety messages for inclusion within the protocol for the user test.

The user test (or other form of consultation with target patient groups) will then be assessed. The assessor will be looking for evidence that the participants in the test have been able to first find and then understand those key safety messages identified prior to undertaking the testing.

Q2. Who should I use to participate in the testing?

A2. Participants used will need to reflect those patients/carers who may be likely to rely on the information for safe use of the product. Although it is not always necessary to include real patients in the population used for testing the PIL, there may be good reasons why this may be necessary in certain circumstances. For certain products it may be sufficient for participants to imagine that they may need to use the medicine at some time in the future.

The suitability of subjects will be considered by the assessor and you will need to make sure sufficient detail is provided in the report concerning their background and their relevance to the target patient population for the medicine in question.

Participants should not be used more frequently than once every six months to take part in such testing. Healthcare professionals and other staff/people who routinely work with medicines information must be excluded to avoid bias. Care should be taken if using company employees to ensure the same exclusions apply.

Q3. How should my questions be worded?

A3. 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.

Q4. Should I report the overall total numbers of successful responses to the questions or should each question be reported individually?

A4. 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.

Q5. Are the success criteria flexibly applied?

A5. Yes. In general we would expect as a minimum for 18 out of 20 participants to find the information in the PIL and for a minimum of 16 out of 20 to be able to show that they can understand the information and to act appropriately. Even so, all questions must achieve the success criteria and it is not appropriate to sum the data. (See question 4).

Q6. Do I need to send in an expert supporting statement?

A6. Yes – the data you submit are your data. You must take ownership of these even though these may have been collected on your behalf by a contract test house. Where recommendations are made by the testing contractor you should address these in your supporting statement to avoid further questions from the assessor.

Q7. In what circumstances might the MHRA assessor seek additional information from you in relation to a user test?

A7. Certain key factors may give rise to concerns that appropriate information has not been collected and therefore we may consider that insufficient evidence had been provided to demonstrate compliance with article 59(3).

For example, if you fail to ask participants about the key safety messages in the PIL you may be asked to provide additional information to demonstrate that the PIL complies with article 59(3). Similarly, if the questions in the protocol are considered leading, closed, or irrelevant you may be asked to provide additional information to demonstrate that the PIL complies with article 59(3).

If during the test, recommendations are made about the design, layout, font and complexity of wording and you fail to take account of these and address the issues in the supporting documents you may be asked to provide additional information to demonstrate that the PIL complies with article 59(3).

If on assessment, the data from the study are found to be incorrectly reported you may be asked to provide additional information to demonstrate that the PIL complies with article 59(3).

Q8. How many rounds of testing do I need to do?

A8. Preferably you will need to make sure that if the PIL is revised as a result of user testing the final version of the leaflet submitted for assessment has been tested on two rounds each comprising 10 participants. Data from testing on previous versions of the leaflet should not be accumulated as this can skew the data.

Q9. Do the PILs for products administered by a healthcare professional need to comply with article 59(3)?

A9. Yes. All leaflets must be in the revised order and reflect the results of consultation with target patient groups, regardless of how the medicine is to be used. Not all PILs need to be subject to user testing however (see earlier guidance)

Q10. Do I need to print “actual” PILs for the user test?

A10. The leaflet used in the user test should be as close as possible to the final version which patients will find in the pack. It must include the actual size and colour of fonts intended for production and the design and layout, which are crucial to patients accessing the information, should be as intended in the market place. However, unless there are concerns that the paper quality could compromise the legibility of the information when printed we would not expect the final paper to be used in the testing environment. Should there be a complaint about the paper quality once the leaflet is in the marketed pack we would expect companies to take urgent and rapid steps to correct this deficiency.

Q11. What language do I need to work in for MR and DC procedure applications?

A11. You may choose to comply with the requirements of article 59(3) by user testing the full colour mock-up of the PIL in any official language of the EU. The RMS will offer advice on their particular requirements. The leaflet submitted with your application for harmonised approval and the dossier submitted in support of your application must, however, be written in English so that all CMS are in a position to assess the data. Where the UK is the RMS we recommend that all testing be carried out on the English language version of the full colour mock-up of the PIL on UK participants.

Q12. Can I change the harmonised leaflet text at the end of the procedure?

A12. At the end of the European procedure you will need to take rapid steps to prepare and submit to the all CMS the appropriate language version and any necessary mock-ups in order to conclude the procedure. In the UK it will be necessary to provide a full colour mock-up for inclusion in your application and this may require an element of translation into patient-friendly English. Assessors will be able to advise on specific requirements as the procedure progresses.

Q14. Do I need to follow the templates published by the Quality Review of Documents group?

A14. The templates are available for guidance. For MR and DC procedures the use of templates is recommended. Use of a template will result in a text version only which will

need to be formatted into the applicants house style for both the labelling and patient information leaflet. Use of template does not guarantee compliance with article 59(3) and you will still have to provide evidence on a full colour mock up of the PILS text that patients can find important safety messages and understand and act upon these to ensure safe use. Such testing may result in the need to use alternative forms of words from those published in the template which will be acceptable.

Q15. Can I change the order of the information and provide data to demonstrate compliance with article 59(3) at a later time?

A15. No. Compliance with both arms of article 59 [59(1) order and 59(3) consultation with target patient groups] must be undertaken concurrently.

Q16. When submitting a new application for assessment is it acceptable to provide a commitment to undertake user testing of the PIL post-approval?

A16. No. In order for your application to be considered valid you will need to provide data to demonstrate compliance with article 59(3) at the time of submission. Failure to do so will result in delays.

Q17. Can I refer to and use the recommendations in “Always Read the Leaflet” to improve the risk communication in my leaflets?

A17. Yes. MHRA is keen to see an uptake of the recommendations in respect of risk communication to improve the overall quality of the information provided. Headlines and the inclusion of benefit information can be used and should be subject to consultation with target patient groups to make sure the information is clear and adds value.

Q18. Once my leaflet has been updated to comply with the new requirements of articles 59(1) and 59(3) can I make changes to the information without undertaking further consultations with target patient groups?

A18. In general yes but there will be circumstances where the addition of significant safety messages by way of variation to a marketing authorisation may require either selected testing of key information or a full user test. You should discuss specific cases with assessors as they arise.

Q19. Can I add extra-statutory information to the leaflet and should this be subject to consultation with target patient groups?

A19. Yes. Information which includes detail about the disease being treated for example is helpful in setting the PIL in context for the patient. Separately you may wish to indicate the availability of alternative formats of the information for blind and partially sighted patients by way of a telephone number. Such alternative formats need not be the subject of formal consultations with target patient groups. However, you will need to make sure that the formats which are provided adequately meet patients' needs.

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