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**REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND
THE COUNCIL**

**in accordance with Article 59(4) of Directive 2001/83/EC of the European Parliament
and of the Council of 6 November 2001 on the Community code relating to medicinal
products for human use**

(Text with EEA relevance)

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1. INTRODUCTION

This report is prepared pursuant to Article 59(4) of Directive 2001/83/EC¹ according to which the Commission shall present to the European Parliament and the Council an assessment report on current shortcomings in the summary of product characteristics and the package leaflet and how they could be improved in order to better meet the needs of patients and healthcare professionals.²

2. REGULATORY FRAMEWORK

The summary of product characteristics (SmPC) the content of which is described in Article 11 of Directive 2001/83/EC and the package leaflet (PL) the content of which is described in Article 59 of Directive 2001/83/EC form an intrinsic and integral part of the marketing authorisation for medicinal products in the Union in accordance with Article 6 of Directive 2001/83/EC and Article 3 of Regulation (EC) 726/2004³.

Article 8(3)(j) of Directive 2001/83/EC and Article 6(1) of Regulation (EC) 726/2004 require that, in order to obtain a marketing authorisation, a SmPC and a PL must be included in the marketing authorisation application.

¹ Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

² This is a first Commission report under Article 59(4) of Directive 2001/83/EC. The initial deadline for submission of the report was 1 January 2013, but it was delayed due to the need to obtain additional evidence through an external expert study, to consult the Member States on the outcomes of the external study and to analyse the input received.

³ Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, OJ L 136, 30.4.2004, p. 1.

Detailed guidance on the correct implementation of the abovementioned legal requirements is provided in the regulatory guidelines, in particular:

Guideline on Summary of Product Characteristics ("SmPC Guideline")⁴;

Guideline on the packaging information of medical products for human use authorised by the community ("Packaging Information Guideline")⁵;

Guideline on the readability of the labelling and package leaflet of medicinal products for human use ("Readability Guideline")⁶.

Further practical guidance can be found in the templates of the Quality Review of Documents group (QRD templates).⁷ The QRD templates provide the official wording to be used in the SmPC and PL in accordance with Directive 2001/83/EC. The aim of the QRD templates is to achieve consistency across different medicinal products and across all Member States. The templates define standard headings, standard statements and terms and the format and layout to be used.

When the marketing authorisation is issued by the competent authorities of the Member States, the Marketing Authorisation Holder shall be informed of the SmPC as approved by them⁸ and the national competent authority concerned shall, without delay, make publicly available the marketing authorisation together with the package leaflet and the summary of product characteristics.⁹ For decisions concerning centralised marketing authorisations, according to Article 10 of Regulation (EC) No 726/2004, the final Commission decision with the SmPC and the PL is addressed and notified to the Marketing Authorisation Holder.

After a marketing authorisation has been granted the content of the SmPC cannot be changed except with the approval of the competent authority that granted the marketing authorisation. The SmPC is the basis of information for healthcare professionals on how to use the medicinal product safely and effectively. It is not in the remit of the SmPC to give general advice on the treatment of particular medical conditions. On the other hand specific aspects of the treatment related to use of the medicinal product or its effects should be mentioned in the SmPC. Similarly, general advice on administration procedures should not be included but any advice specific to the concerned medicinal product should be included.¹⁰

The PL provides a set of comprehensible information enabling the use of the medicinal product safely and appropriately. The package leaflet is primarily intended for the patient/user. If the package leaflet is well designed and clearly worded, this maximises the number of people who can use the information, including older children and adolescents, elderly, those with poor literacy skills and those with some degree of sight loss.¹¹

⁴ http://ec.europa.eu/health/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf

⁵ http://ec.europa.eu/health/files/eudralex/vol-2/c/bluebox_06_2013_en.pdf

⁶ http://ec.europa.eu/health/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf

⁷ More information is available at the QRD website of the European Medicines Agency: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_00_0134.jsp

⁸ Article 21(2) of Directive 2001/83/EC.

⁹ Article 21(3) of Directive 2001/83/EC.

¹⁰ For more details see the Commission Guideline on the Summary of Product Characteristics.

¹¹ For more information see the Commission Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use.

3. ASSESSMENT

The Commission engaged external contractors to produce two studies in order to provide supporting information for this report. Details of these two studies are provided below.

3.1. **Study on the Package Leaflets and the Summaries of Product Characteristics of Medicinal Products for Human use ("PIL-S Study")¹²**

The study has been carried out by NIVEL (Netherlands Institute for Health Services Research) together with the University of Leeds.

The objective of this study was to provide the European Commission with:

an assessment of the readability and comprehensibility of the SmPC and the PL as sources of information on prescription and non-prescription medicines for patients and healthcare professionals;

an assessment of the causes and (potential) consequences of identified shortcomings, and

recommendations for improvement of the SmPC and the PL of prescription and non-prescription medicines based on this assessment.

The assessment included an extensive literature search, a European-wide stakeholder survey (including representatives of patients and consumers organisations, healthcare professionals, pharmaceutical industry and entities engaged in user testing) and an online discussion forum.

3.2. **Study on the feasibility and the value of a possible “key information section” in patient information leaflets and summaries of product characteristics of medicinal products for human use ("PILS-BOX Study")¹³**

Also this study has been carried out by NIVEL and the University of Leeds.

The objectives of the PILS-BOX study were:

to collect existing evidence on the potential impact of adding a key information section on the safety and efficacy of medicines' use;

to assess the feasibility of adding a key information section in the context of the EU legislation;

to assess the potential cost/efficacy of adding key information in the context of the EU legislation.

The assessment included an extensive literature search, a European-wide stakeholder consultation and an analysis of the Strengths, Weaknesses, Opportunities and Threats (SWOT analysis).

3.3. **Input from stakeholders and Member States**

As part of the two studies a European-wide stakeholder survey has been conducted in which the key stakeholders were asked to provide their views on existing strengths

¹² The study was produced and funded under the EU Health Programme (2008-2013) under the Framework Contract N°EAHC/2010/Health/01.

¹³ Also this study was produced and funded under the EU Health Programme (2008-2013) under the Framework Contract N°EAHC/2010/Health/01.

and shortcomings of the SmPC and PL. The results of the survey have been taken into account in the conclusions of both studies and also in this report.

Once finalised the two external studies have been published on the Commission website¹⁴ and submitted for consultation to the Member States in the framework of the Pharmaceutical Committee. The Member States comments have been summarised in a document published on the Commission website¹⁵ and duly taken into account in this report.

The European Medicines Agency services collaborated closely with the Commission in the course of preparations of this report and provided valuable input related, for example, to the activities of the Working Group on Quality Review of Documents (QRD) and other areas of Agency's expertise.

4. OUTCOMES AND RECOMMENDATIONS

Based on the above mentioned assessment the following outcomes and recommendations have been identified.

It has been generally considered that the current EU legislation on medicinal products for human use allows for enhancement of the statutory medicines information to support the safe and effective use of medicinal products. The below recommendations should be, therefore, primarily taken forward by improvements of the existing regulatory guidelines, templates and other non-legislative means.

4.1. Room for improvement of PL rather than of SmPC

As far as the PL is concerned, patient's comprehension of the PL and its readability can be improved. The language used is often too complex and the design and lay-out are not always user-friendly. The elderly and those with low literate skills are particularly disadvantaged, but generally these problems hold for all patient groups.

On the other hand, less problems were identified with regard to the SmPC although improvements can still be made especially with regard to the readability of the SmPC. Representatives of healthcare professionals generally judge the quality of the SmPC as reasonable and value most of the current topics addressed in the SmPC as being important.

Recommendation: Generally, there should be more focus on improving the PL rather than the SmPC. However, for any potential improvement of the PL it should be also considered whether a corresponding or related change of the SmPC would be appropriate.

4.2. Amendments of Guidelines and QRD templates to enhance readability of PL

Content and layout-related issues have been identified in the PIL-S Study. It is considered that future work on guidelines relating to the PL, and possibly also the SmPC to some extent, has the potential to solve a number of these issues.

Guidelines should include more details on the principles of good information design in which content and layout are jointly considered. This would help to ensure compliance with the legal requirement that the PL shall be "clearly legible".

¹⁴ http://ec.europa.eu/health/files/committee/75meeting/pil_s.pdf and <http://ec.europa.eu/health/files/committee/75meeting/pilbx.pdf>

¹⁵ http://ec.europa.eu/health/files/committee/75meeting/pharm699_6a_pil_and_smpc_doc.pdf

Moreover improvements related to the language used would help to ensure that the information is "clear and understandable" as also required by the legislation.

These issues could be best addressed by improving the existing guidelines, in particular the Readability Guideline, the Packaging Information Guideline and, where appropriate, the SmPC Guideline. The relevance and importance of the QRD template is also acknowledged in this respect as it is the main tool to provide guidance to the industry in a harmonised way. The QRD template should rely on principles of good information design and pay attention also to the needs of some specific groups of patients, such as elderly, young people or people with mental illnesses.

Small font size, narrow line spacing and the length of the PL were identified as the main issues.

Guidelines and QRD templates are also considered too restrictive in some respects. They should allow for more flexibility to adapt the PL to the specificities of each product whilst respecting the limits provided by the legislation. Deletion of some information that is currently required by the QRD template but that is of limited relevance for patients may allow more space to improve the content and layout of package leaflets and should, therefore, be considered.

More attention should be also paid to the translation of the user-tested PL into other languages. It is considered important to keep the 'lay-ness' of the user-tested version when the leaflet is translated.

Recommendation: It should be considered to revise the existing guidelines, in particular the Readability Guideline, the Packaging Information Guideline and, where appropriate, the SmPC Guideline to include principles of good information design and consider allowing more flexibility in the information recommended in the QRD template, as long as the relevant legislation allows it. These revisions should also include introduction of guidance on translations that go beyond the principle of faithful translation. The aim should be to ensure that the lay language introduced through user testing in the original language version is not lost during translation.

4.3. Improving patient input in developing and testing of PLs

The assessment recognised the usefulness of patient involvement and the importance of user testing of the PL. It is equally important that methodology for such testing is well defined. The assessment further identified the need for strengthening the input from the patient perspective which could also help in getting more understanding on how to present risk-benefit information for a particular medicine.

Recommendation: The input from patients during the process and the related methodology should be further improved, for example, by considering the requirement to make the user testing process more iterative and to ensure that a sufficiently mature version of the PL is user-tested. This iterative user-testing would be coordinated by regulatory authorities in parallel to the assessment in a way that does not disrupt the whole marketing authorisation process. The iterative testing should focus on the content of the PL, rather than the format and layout, to ensure that information is clear and written in a way which is easily understood by patients. Potential amendments of the Readability Guideline could be considered in this respect taking also into account the use of structured benefit-risk approaches and visual representations to communicate benefits and risks to different stakeholders in different situations, including those approaches developed by the European

Medicines Agency in the context of the Benefit-Risk Methodology project¹⁶ and by the Innovative Medicines Initiative (IMI) Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT) project.¹⁷

4.4. Promotion and exchanges of best practice

The assessment concluded that good, user-tested examples of the PL and to some extent also the SmPC as well as their development process could be promoted more by regulators to facilitate and improve the development of these documents.

Recommendation: Best practice examples of aspects of the PL (and the SmPC) design could be made available for pharmaceutical companies on a platform that would be suitable for that purpose and that could be regularly updated. These examples should include not only the end products, but also information on the process of development, where possible. The selection of these examples should be evidence-based.

4.5. Electronic SmPC/PL formats

Electronic formats bring new opportunities for SmPC and PL. As more Europeans gain access to information technologies, the assessment identified potential benefits in developing key principles as to how electronic formats can be used to provide the information to individual EU-citizens in accordance with the existing legislation (e.g. in terms of presentation, format or use of multiple languages). In any event the electronic PL formats should be complementary to paper PLs that are required by the legislation and should not replace them at this stage in order to ensure availability of the information for all patients.

Recommendation: It is recommended to explore the use of electronic media to provide the information included in the SmPC and PL in the future. It should be further explored what opportunities new technologies offer to optimize the presentation and design of SmPC and PL. In this context the opportunities for the information included in the SmPC and the PL to be more easily used as an integrated part of the care process should be explored. For example, developing mechanisms through electronic tools to inform patients and healthcare professionals on changes in the SmPC and PL should be considered. The exploratory work in this area should be based on and further develop the existing work done by the European Medicines Agency in this area and should follow a multi-stakeholder approach involving also the pharmaceutical industry, patients, consumers, healthcare professionals, the Member States and the Commission. The aim will be to develop the key principles for the use of electronic SmPC and PL formats. The results of this exploratory work should be submitted to the Commission for any follow-up action as appropriate.

4.6. Potential key information section in the SmPC and PL

The potential introduction of the “key information” section in the SmPC and PL with the objective to allow patients and healthcare professionals to rapidly identify key safety messages, balanced with information on the benefits of medicines, has been also subject to the assessment. The key information section is not specifically envisaged in the existing EU legislation on medicinal products for human use. The outcome of the assessment is that more experience and evidence needs to be gathered

¹⁶ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2012/03/WC500123819.pdf

¹⁷ <http://www.imi-protect.eu>

and that currently testing can be considered as a means to further determine the potential usefulness of the inclusion of a key information section in the SmPC or PL.

Recommendation: More evidence would need to be gathered before considering introduction of a key information section in the Product Information. It is suggested to continue further exploratory work on the use of such key information in the PL as well as the possibility to use Quick Response (QR) codes¹⁸ as another way to make available information to patients. Appropriate testing (e.g. user testing) could be a way to demonstrate the clear evidence of the usefulness and added value to patients to introduce a key information section in the PL. In this respect, the work currently being undertaken by EMA as part of its strategy to improve information on benefit-risk to patients and healthcare professionals could be taken into account. In particular, the planned testing of adding a ‘key information section’ to the ‘EPAR¹⁹ summary’ for each centrally authorised medicinal product could be used for this purpose. This may help to decide on the type of information that should be provided in the PL and the category or type of medicines where such a key information section could be useful and appropriate.

5. CONCLUSIONS

The Commission and the European Medicines Agency will work towards implementation of the above mentioned recommendations in order to improve certain aspects of the SmPC and PL and to better meet the needs of patients and healthcare professionals. The work will be taken forward in close collaboration with the Member States. It will be ensured that the key stakeholders, in particular representatives of patient organisations, healthcare professionals, industry representatives, national regulators and other relevant parties will be duly consulted and involved as appropriate with regards to the respective proposed possible actions.

¹⁸ QR code is a machine-readable optical label (bar code) that contains information about the item to which it is attached. A QR code may link to a website, web page (e.g. standalone PDF document) and/or smartphone applications specifically created for that purpose.

¹⁹ European Public Assessment Report.