About the DRAFT Readability Guideline (November 2006)

Please reconsider!

Some comments on the 'Draft guideline on the readability of the label and package leaflet of medicinal products for human use'.

Dr Karel van der Waarde

Summary

This paper provides some comments on the assumptions, contents and visual presentation of the *'Draft guideline on the readability of the label and package leaflet of medicinal products for human use'*. These comments are based on the practical use of the previous guideline (1998), substantial experience with user testing, and research findings.

Eight groups of comments

The Readability guideline aims to support applicants and Marketing Authorization holders to develop labelling and package leaflets. The following pages group the comments in the following categories:

1. The results and deliverables: what are the end results?
2. The description of criteria: how to measure success?
3. The description of people: who could evaluate the results?
4. The aims of providing information: why is it essential?
5. Writing guidance
6. Designing guidance
7. Testing guidance
8. Document development: is this the right approach?

Appendix 1 shows an example of an outline for a guideline. Appendix 2 provides a line by line comment of the Draft Readability guideline.

Conclusion

Following the advice in the Draft guideline should lead to information about medicines that 'enables users to act appropriately'. This Draft guideline is unlikely to achieve this. The terminology, criteria, aims, and activities are poorly described. The activities that must be undertaken to develop appropriate information about medicines - writing, designing, and testing - are not sufficiently supported.

For these reasons, please reconsider the implementation of this draft guideline.

In order to provide appropriate guidance, it is necessary to start from the activities that are necessary to develop optimal information, and support each step in this process. Four steps are required:

1. Restructure the contents of the guideline to follow the activities of intended users of this guidance.
2. Clarify the aims of each activity and clarify the relevant criteria.
3. Provide effective guidance, based on best practice and research.
4. Test the guidance before implementing it. Untested guidance might do more harm than good.

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Introduction

The Draft guideline promises 'to assist applicants and marketing authorisation holders when drawing up the labelling and package leaflet and preparing the specimens or 'mock-ups' of the sales presentations.'
Three additional objectives are mentioned:
1 - 'aid the production of high quality information',
2 - 'meet the legal requirements', and
3 - 'presented in a consistent way'.

In this comment, I'll check whether this Draft guideline fulfills these aims by asking the following questions:
1. What are the deliverables? What exactly needs to be produced?
2. What are the criteria to evaluate these deliverables?
3. Who are the people who can do this?
4. Does this guideline help to decrease some of the problematic issues related with information about medicines?

In the sections five, six and seven, I'll look at the different activities that an applicant or marketing authorisation holder must do in order to develop labelling and package leaflets: writing, designing and testing. In section 8, the general approach of this Draft guideline towards the development of information about medicines is discussed.

There are two appendices. Appendix 1 shows an outline of a Guideline that follows the comments in this paper. The second appendix provides a line-by-line comment of Chapter 1 and annex 1 of the Draft Readability guideline.

In previous papers, I addressed some of the issues related to the use of the template ('Enabling users or Readability?' May 2005), and comment on Chapter 3 of the guideline ('Some comments on the draft 'Guidance concerning "consultations with target patient groups" for the package leaflet'. September 2005). These papers can be downloaded by clicking on their titles.

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1. Artefacts: what exactly needs to be developed?

The Readability guideline provides advice for the development of the text and the visual design of labelling and package leaflet.

The following terms are used to describe the artefacts in the introduction and Chapter 1 of the Draft Readability guideline (in alphabetical order):
- blister foil
- blister pack presentation
- the carton
- content of labelling and package leaflet
- critical information
- a complete summary of product characteristics
- copy of the flat artwork design in full colour
- draft package leaflet
- element of a promotional nature
- face
- foil
- format resulting text
- formats appropriate for the blind and the partially-sighted
- formats suitable for the blind and partially sighted patients
- full colour mock of the package leaflet
- immediate packaging
- immediate packaging units
- immediate packaging information
- inner packaging
- inner packaging components
- information from the summary of product characteristics
- the information
- the information presented
- information on the label and package leaflet
- label text
- labelling
- labelling and packaging components
- labelling particulars
- labelling text
- leaflet
- the medicine
- medicinal products
- medicinal product package
- mock-ups
- mock-up of the outer and immediate packaging
- outer pack
- outer packaging
- outer packaging design
- outer packaging information

- outer or immediate packaging information (labelling)
- outer/inner labelling text
- the pack
- package leaflet
- packaging
- packaging information
- paper copy
- paper labels
- particulars
- presentation of the content of the labelling and package leaflet
- product
- product information
- replica of both the outer and immediate packaging
- relevant full colour mock up of the packaging
- the required information on labels
- sales presentations
- small containers
- small packs
- small pack sizes
- specimens
- statutory information
- a tear-off portion
- text
- three dimensional presentation.

The fundamental problem with all these descriptions is that it is not clear what exactly needs to be developed, and what needs to be submitted to the competent authorities.

The terminology is very confusing and often conflicting. Three examples:

Example 1: The word 'specimen' does not appear in the Directive anymore. It was deleted from article 8(j), article 15 and article 61. It is confusing to use 'specimen' in the Draft Readability guideline.

Example 2: The differences between 'text', 'information', 'particulars', 'statutory information', 'product information', 'labelling information', 'packaging information', and so on, is not clear. It is essential to make absolutely clear what is required.

Example 3: The Directive itself is not clear whether a 'package leaflet' (artilce 8.3(j)) or a 'draft package leaflet' (article 61(1)) needs to be submitted. A guideline must clarify this.

Concluding: It is essential to describe what exactly needs to be delivered. The guideline must provide answers to the following questions:

- What are the required results?
- How should these results be submitted to the competent authorities?

The terminology must be reconsidered. Adding more descriptors of 'things that might be required' is not helpful.

2. Criteria: What needs to be achieved?

The guideline provides the following criteria in section 1 and annex 1. This list is in alphabetical order. These are the criteria that - according to the guideline - could be applied to examine the quality of the information.

- Able to be understood
- Accessible
- Accessibility of the information
- Achieving readable text
- Active style
- Aid comprehension of information (graphic elements)
- Aid navigation (graphic elements)
- Appear consistently (headings)
- Avoid repetition of information
- Avoid abbreviations unless they are appropriate
- Being able to act on the information presented
- Clarify certain aspects (graphic element)
- Clarity of the text
- Clarity of the information
- Clear
- Clear demarcation between the languages used (leaflet only)
- Clear line space
- Clearly comprehensible
- Clearly distinguished (characters)
- Clearly legible
- Clearly recognisable (headings, leaflet only)
- Clearly worded (leaflet only)
- Comprehensibility
- Comprehensive
- Consistency in the explanations (technical terms)
- Context makes clear what the pronoun refers to.
- Difficult (reversed-out type, leaflet only)
- Difficult to read (thin paper, leaflet only)
- Doubt about the meaning (pictogram)
- Easily be turned over (leaflet dimensions)
- Easily distinguished (numbers/letters)
- Easily legible, legible
- Easy to use
- Easy to read / harder to read
- Easy to put back into the pack (paper dimensions, leaflet only)
- Enabling the users to act appropriately (leaflet only)
- Ensure consistency across a number of different medicines
- Facilitates navigation / help navigate (column)
- Facilitates access
- Few syllables
- Followed in a user-friendly way (paper dimensions, leaflet only)

- Give sufficient detail on how to recognise possible side effects
- Give sufficient detail to understand any action which may be necessary
- More difficult to understand
- Helpful to patients (landscape layout, leaflet only)
- Helpful as a navigational tool (leaflet only)
- Highlight (certain graphic elements)
- Inapproriate (pictogram)
- Inappropriate for the product (sequence of bulleted list)
- Indelible
- Language which patients can understand (technical terms)
- Legibility / impairs legibility
- Length of the leaflet
- Long paragraphs (leaflet only)
- Long leaflets (paper)
- Maximises the number of people who can use the information (leaflet only)
- Meaning is clear (pictogram)
- Meaning is generally understood (all symbols)
- Not be contrary to the standards of decency (Pictograms, symbols, graphics)
- Not be contrary to the standards of good taste (Pictograms, symbols, graphics)
- Not be confusing (Pictograms, symbols, graphics)
- Not be misleading (Pictograms, symbols, graphics)
- Not be promotional (Pictograms, symbols, graphics)
- Open approach
- Place verb at the beginning (style)
- Promotional nature
- Quality of the print
- Recognise word shapes (words, leaflet only)
- Short lists of bullet points
- Simple punctuation
- Simple words
- Size of the graphic
- Spell out meaning in full (abbreviations)
- Sufficient detail
- Transparant (paper weight, leaflet only)
- Twenty word sentence (leaflet only)
- Understandable
- Use the most appropriate term (Lay or medical) (technical terms).
- Useful (symbols and pictograms)
- Useful (reference to other pharmaceutical forms)
- Well designed (leaflet only)

The fundamental problem with these criteria is that only very few of these can be evaluated. The large majority of these criteria is subjective and is open for discussion. Most of the criteria cannot be quantified. It is not possible to establish or check if these criteria have been met.

These are simply the wrong kinds of criteria: they cannot be used in practice. Adding more unquantifiable criteria does not resolve this issue.

Furthermore, many of these criteria are in direct conflict with the requirement to test information. A usability test is the appropriate way to evaluate the quality of information. Many criteria, for example 'the twenty word sentence', might be overruled by the results of a usability test. This conflict between 'providing advice' and the 'obligation to test' needs to be addressed. It should be made clear in which situations the guideline prevails, and in which situations the results of the usability tests must be followed.

Quantifiable criteria

Fortunately, the EU-directives do mention unambiguous and quantifiable criteria. Directive 2001/83/EC states in point 40: 'The provisions governing the information supplied to users should provide a *high degree of consumer protection*, in order that medicinal products may be used correctly on the basis of *full and comprehensible* information.' This phrase provides criteria for all information about medicines.

For package leaflets, the criterion is even more specific. Directive 2004/27/EC, article 63(b)2 states 'The package leaflet must be written and designed to be clear and understandable, *enabling the users to act appropriately*, when necessary with the help of health professionals.' Directive 2004/27/EC therefore provides quantifiable criteria for the provision of information about medicines. Information must not only be 'comprehensible', but it must 'enable users to act appropriately'.

These phrases necessitate the involvement of people who handle medicines in the document development process. Only people who actually handle medicines (patients, nurses, pharmacists, doctors, ...) can judge if information 'protects', 'is comprehensible', is 'full', and is 'enabling to act appropriately'. Nobody else can do this.

Concluding

Criteria need to be clearly defined, unequivocal and measurable. Adding more criteria that cannot be used in practice does not help.

In view of the phrase 'enabling users to act appropriately' in Directive 2004/27/EC, it is necessary to make sure that information is usable. Section 8 outlines an approach that makes this possible.

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3. People: users, patients, consumers?

The Draft guidance and the EU-Directives about the provision of information about medicines do not clearly identify the recipient of this information. The draft guidance uses the following descriptors. In alphabetical order:

- adolescents
- blind
- by those who receive it
- different types of people (test participants)
- health professionals
- him
- hospital staff
- the least able
- literate adults
- new users (test participants)
- older children
- older readers
- older people (test participants)
- partially-sighted
- partially sighted patients
- participants
- patients
- patients' organisations
- patients with visual impairment
- people
- people with poor reading skills
- people who have poor health literacy
- people who can use the information
- people who have or have had the illness (test participants, rare illness)
- people who have previously taken or are currently taking the medicine
- people who do not normally use medicines (test participants)
- people who do not use written information in their working life (test participants)
- people who find written information difficult (test participants)
- population for whom the medicine is intended
- reader
- target patient groups
- those with poor literacy skills
- those with some degree of sight loss
- users
- visually impaired patients
- young people (test participants).

The use of different terms to indicate recipients of information about medicines has a longer history. Directives 92/27/EC, 2001/83/EC and 2004/27/EC also use several descriptors which are not clearly defined. Three examples are:

Example 1: The definition of a package leaflet (2001/83/EC, point 26) states: 'A leaflet containing information for the user which accompanies the medicinal

product.' In this article, the word 'user' can refer to patients, but equally well to nurses, pharmacists, hospital pharmacists or medical doctors. Directive 2001/83/EC, point 40 states: 'The provisions governing the information supplied to users should provide a high degree of consumer protection, in order that medicinal products may be used correctly on the basis of full and comprehensible information.' In this phrase, a 'user' is seen as a 'consumer'. This is an appropriate term for Over-the-counter medicines, where people can make a commercial decision themselves, but it is not suitable for Prescription-only-medicines. Furthermore, if healthcare providers are 'users' (point 26), than this article labels these professionals as 'consumers' too. That seems incorrect to me.

Example 2: Article 59(c) of Directive 2001/83/EC provides examples of users as 'children, pregnant or breast-feeding women, the elderly, persons with specific pathological conditions', while in article 67 of the same Directive the word user means health professional.

Example 3: Phrases like 'consultation with target patient groups ('user consultation')' indicate that 'patient' and 'user' are synonymous. For many medicinal products that might be the case, but for medicines administered by a healthcare professional, these two words have a clearly different meaning.

In order to develop guidance on the information about medicines, it is essential to make very clear for whom the information is intended. The different descriptions are confusing.

Concluding

The Draft guideline does not make it clear for whom information is intended. This confusion causes serious problems, because it makes it very difficult to develop appropriate guidelines, and it makes it very difficult to determine valid criteria to evaluate the effectiveness of the provision of information about medicines.

Together with the descriptions of the deliverables (section 1) and the criteria (section 2), it is unlikely that the description of the people who interpret information about medicines (section 3) will lead to guidelines that are helpful for applicants or marketing authorisation holders. It is not clear what needs to be developed, it is not clear for whom this needs te be developed, and it is not clear which criteria could be used to evaluate the quality.

4. Scope and aims: What are the fundamental problems?

The Draft guideline mentions three aims for the development of information about medicines. The guideline states that the first aim of the provision of information is to 'ensure that information is accessible and understood by those who receive it, so that they can use their medicines safely and appropriately'. This differs from the aim that is mentioned in the Directives. The Directive states: 'The provisions governing the information supplied to users should provide a high degree of consumer protection in order that medicinal products may be used correctly on the basis of full and comprehensible information' (EU Directive 2001/83/EC). There is a difference between 'safely and appropriately' and 'consumer protection and used correctly'. It is not clear why the 'high degree of consumer protection' is not mentioned in the Draft Guideline.

A second aim is the 'harmonisation of product information across all Member states'. Although this is not specifically highlighted, it is one of the main arguments to use standardised templates in different languages. This important argument deserves some more prominence.

A third aim is to minimise confusion and the number of errors. It is strange that this is only mentioned in the section about 'labelling' and therefore does not seem to apply to the information in the package leaflet.

The influence of information on the use of medicines is much wider than this guideline suggests. The provision of information about medicines has at least two other aims. These aims are:

- Consider cost-benefits and risk-benefits. It is likely that the costs of medicines in European countries will continue to increase. It is likely that information about medicines directly influences cost-benefit and risk-benefit decisions.
- Consider compliance (concordance). It is likely that information is directly related to the correct use of medicines. Substantial non-compliance rates could be reduced if appropriate information is provided.

There are therefore at least seven aims:

- 'avoid confusion'.
- 'enhance compliance and effective use'
- 'consumer protection'
- 'cost-benefits and risk-benefits considerations'
- 'error reduction'
- 'harmonisation of information across Europe'
- 'safe and appropriate use'

These aims can ony be considered in the longer term and include a number of factors that fall outside the area of labelling and package leaflets. However, not considering these issues is not an option: they are an integral part of the provision of information to people in Europe.

Concluding: The ultimate aim of the guideline is not considered sufficiently. It is likely that the scope of the guideline is too narrow to be effective. All effects of the provision of information about medicines must be considered.

5. Guidance: Writing

The Readability guideline provides some advice about the writing of information about medicines. It is remarkable that the guideline suggests to 'seek advice from specialists in information design' for the design, and to suggest that tests must be carried out by 'an experienced interviewer with good interview, observational and listening skills'. The guideline does not suggest to ask the advice from a 'medical writer' or 'technical writer' for the development of the text of information about medicines.

It would be very useful to have an explanation in the Readability guideline about the use of the EMEA-QRD templates. Especially the standard texts and phrases cause severe problems. An example is the sentence: 'If any of the side effects gets serious, ...'. This sentence is grammatically correct, but every English reader finds the word 'gets' after the plural 'side effects' an awkward construction. The Guideline should make it clear if 'standard statements' could be modified, or if they have to be used exactly as they appear in the template.

Some of the advice in the Draft guideline is in direct conflict with the EMEA-QRD templates. Three examples are:

Example 1: The example provided in section 6 'Style' states: 'take 1 tablet' instead of '1 tablet should be taken'. The second part of this example - '1 tablet should be taken' - is in conflict with EMEA guidance (Compilation of QRD decisions on stylistic matters in product information. Version 9, December 2005). In this guidance it states: 'it is advisable that the word "should" is avoided wherever possible in the English original itself.'

Example 2: The sentence 'If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist' consists of 26 words. It does contain new information, so this sentence must - according to the guidance in section 5 second bullet - be improved by using a couple of sentences. Unfortunately, the EMEA-QRD template prevents this: 'Standard statements must be used whenever they are applicable.'

Example 3: The guideline suggests to 'Give reasons when telling patients what actions to take. Instructions should come first, followed by the reasoning.' The EMEA/QRD template contains the following obligatory text: 'Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.' In these obligatory sentences, the instruction does not come first. Furthermore, the first sentence is not in the required 'active style by placing the verb at the beginning of the sentence'.

These three examples show that following the EMEA/QRD template unavoidably leads to the rejection of the advice of the Draft guideline.

Terminology

Apart from the terminology about the 'deliverables' (section 1), 'people' (section 2) and 'criteria' (section 3), there are many other terms that need to be clarified and defined. Three examples are:

- font, typeface, print, characters, text

- font size, type size, print size
- elements, particulars, items of information

Spelling

Several words are spelled in different ways in the guideline. Please use a consistent spelling for:

- ‘partially sighted’ or ‘partially-sighted’.
- ‘Package Leaflet’ or ‘package leaflet’.
- ‘word shape’ or ‘word-shape’.
- ‘side effects’ or ‘side-effects’.
- ‘mock up’, ‘mock-up’ or ‘mock’.

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6. Guidance: Designing

The Readability guideline provides some advice about the design of the labelling and package leaflet.

The main aim of the visual presentation of labelling information and the visual presentation of package leaflets is to support the main aim of the supply of information: 'to enable users to act appropriately'. Examples of activities are 'identification', 'locate a starting point', 'keep leaflets and packaging together', 'follow the instructions', 'check the leaflet', 'recognize a package', and so on. These visual actions are known or they can fairly easily be described.

Observing participants during a readability test provides valuable data about the ways in which people look at package leaflets. People rarely look at the detailed level of visual elements, and do not distinguish between 'typeface', 'typesize' or 'the use of columns'. Characteristic ways of looking at a package leaflet are a sequence of scanning, turning, rescanning, focussing on a detail, searching for another detail, and returning to the first detail to confirm the first interpretation. At this point, the participant focusses on a specific sequence of words and interprets these words.

Observing pharmacists while they select the medicines from a large cupboard shows how important visual design is for this activity. 'Visual memory' plays an important role here. It seems that searching for a specific package involves the matching of visual imput of colours and shapes within a limited area with a 'memory image' of a specific package.

The Draft guideline does not provide guidance to optimally support these different visual activities of people. The Draft guideline does not focus on the 'higher level' visual activities.

In stead, the Draft guideline focuses on the description of a limited number of visual elements, such as 'type', 'colour' and 'headings'. There are two fundamental objections to this 'single variable' approach. The first is that it directly conflicts with the obligation to test package leaflets. Three examples:

Example 1: The Draft guideline suggests to use a typesize for the main text of 12 points. A readability test might show that a package leaflet with a substantially smaller typesize passes the 'location and understanding' criteria. Either the results of a readability test are followed, and the textsize is smaller than 12 point, or the Draft guidance is followed, and the textsize is set at 12 points. However, it is likely that this larger typesize increases the dimensions of the package leaflet, which might have severe financial consequences.

Example 2: The Draft guideline suggests that 'a serif typeface is preferred, since the shape of the characters is easier to read'. If a package leaflet is set in a sans-serif typeface, and it passes a readability test, is it still necessary to follow the advice in the guideline?

Example 3: The Draft guideline suggest that 'reversed-out text is particularly difficult for older readers'. If a readability tests shows that this statement is incorrect, does this advice prevail, or should the guideline be ignored?

A second objection is that the Draft guideline suggests that it is possible to consider graphic variables independently. That is not the case. A graphic designer or information designer needs to consider all factors at the same time and choose the combination that best suits a specific situation. Focussing on a single graphic variable, or on a range of variables does not automatically lead to an appropriate design. Three examples:

Example 1: Headings in colour might interfere with the visual salience of warnings. They need to be considered at the same time to make sure that the contrast is as clear as possible, before a readability is conducted.

Example 2: The relation between 'emphasized texts' and headings need to be balanced in such a way that they do not lead to a confusion about their status.

Example 3: For the design of the information on the packaging, the guideline suggests to 'make best use of the space available'. This is not very helpful, because any design must follow this advice.

Furthermore, the design of the guideline seems to be in conflict with its own advice. Again three examples:

Example 1: It is not clear why section 1 and 2 use bullets and section 3 and 4 do not use bullets. The visual presentation indicates that the text in section 3 and 4 has a different status, or a different type of content than section 1 and 2.

Example 2: The guideline suggests to choose a typeface in which similar letters/numbers such as "i", "l" and "1" can be easily distinguished from eachother. The typeface of the guideline itself makes it impossible to distinguish the "1" and "l".

Example 3: The guideline states that 'same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) to aid the reader. The design of section heading B and section heading C differ in their space that follows the B and C, and the headings in Chapter 2 do not follow this advice.

Concluding

The Draft guideline seems to describe the visual design of information at the most detailed level only. It would be more beneficial to start from the visual activities of users at an overall level. The advice in the Draft guideline might be in conflict with the results of readability tests. The guideline does not provide any advice what to do if this situation occurs.

The Draft might actually prevent the developments of novel solutions. Furthermore, the Draft guideline treats graphic variables as separate elements. That is not a practical approach. Designers must consider the relations between the graphic variables.

7. Guidance: Testing

The Readability guideline provides testing advice in annex 1. Below are some comments related to the participants, criteria, method and validity.

Test participants: criteria for inclusion

The example method in Annex 1 suggests that it is necessary to select the test participants according to the following criteria.

- population for whom the medicine is intended.
- a range of different types of people who are able to imagine needing to use the medicine
- (rare illness only): people who actually have or have had the illness. It might be necessary to exclude people who have previously taken or are currently taking the medicine
- the least able
- new users
- people who do not normally use medicines
- people who do not use written documents in their working life
- people who find written information difficult
- literate adults

There is no motivation why these critiria need to be applied. There might be an expectation that these criteria have an influence on the results of a readability test, but this assumption is not supported by any evidence. The list leaves many questions open. Three examples:

Example 1: 'people who do not normally use medicines'. This implies that there are people who 'normally use medicines'. That is a very odd phrase because it makes 'people needing treatment' the standard, and it classifies 'healthy people who do not use medicines' as 'abnormal'.

Example 2: 'people who do not use written documents in their working life.' I'm not sure if there are any documents that are not 'written'. Is there any reason to assume that 'literate adults' must be subdivided into 'people who do not use written documents in their *working life*' (= manual labourer?), 'people *who do use* written documents in their working life' (= desk worker?), or 'people who do not use written documents *in any other life*' (= retired? housewife?). Every individual in our society has to deal with 'written documents'. Tax forms, bank statements, insurance letters and invoices are fairly common. The classification 'literate adults' varies between 'barely able to read' to 'fully competent'. I'm not sure why 'people who do not use written documents in their working life' need to be singled out in this guideline.

Example 3: 'people who find written information difficult.' This statement confuses cause and result. 'Finding information difficult' is not a classification of people, but an indication of the quality of information. I can easily read a Unix manual, but have severe problems with a tax form or a financial report.

If the guideline wants to suggest which participants should be approached, it needs to make this advice clear.

Test participants: illnesses and medicines.

The guideline states that for medicines for rare illnesses, it would be advised to approach people who have or have had this rare illness. However, in order to find out if a person has a rare disease, or has used certain medicines before, it is necessary ask this directly. 'Have you got Y?' and 'Have you ever used X before?'. Other ways to find the answers to these questions are not allowed due to privacy-legislation, and the strict codes of professional conduct of doctors and pharmacists. Asking these questions could be interpreted as a personal critique on the professional decision of a medical doctor. The following answers are possible:

1. 'yes'. The patients tells the interviewer that they have rare illness Y and that their doctor has prescribed medicine X. The implication is that this decision is questioned: 'That is an uncommon/strange decision of your doctor'.
2. 'no'. The patients tells the interviewer that they have rare illness Y and that their doctor has not prescribed medicine X. The implication is that this decision is questioned: 'That is an uncommon/strange decision of your doctor'.

Both answers are undesirable because they imply a judgement on the professional decision of a medical doctor.

The Draft guideline makes a difference between 'people with a rare illness' and 'people without a rare illness'. It is assumed that this difference will influence the test results of a readability test. I'm not sure if there is any evidence that people with a rare illness locate and interpret information in any other way if this group is compared to people without a rare illness.

The situation is likely to be different for 'experienced patients' and 'recently diagnosed patients'. The knowledge about a particular situation Y and medicines X of experienced patients certainly differs from 'novices'. However, it is not sure if experienced patients 'locate' and 'comprehend' information in a fundamentally different way, nor if this has any influence on the scores of a readability test.

Criteria: 90%?

The criteria of the Readability test need careful consideration. The following comments highlight some of the issues.

1. The Draft guideline suggests that it is possible to calculate 'quantitative results' from a 'qualitative test method'. The most useful results of the interviews are the remarks of participants, and not the number of correctly located answers or the number of correctly answered questions. The guideline should make clear that the verbal responses of participants are the main result of a Readability test. The calculated percentages are only a secondary result.
2. The aim of the readability test is not defined well. The first line in section 3 of the Annex states that 'the aim is to meet the success criteria in a total of 20 participants'. This is not correct. The main aim of the Readability test is to improve the text and design of the information in such a way that it optimally 'enables users to act appropriately'. With the rephrasing of the aim, the Draft guideline applies criteria that do not relate to a aim of the provision of information stated in the European Directive.

3. The success criterion relates percentages (90%) and the number of participants (20). Ninety per cent of 20 participants is 18 participants. Ninety per cent of 18 participants is 16.2 participants. This last number – 16.2 – makes it impossible to apply the 90% criteria to readability test results. Does this mean that a package leaflet fails the test if 16 people out of 20 can locate and understand the information?
4. Furthermore, it is not clear if this 90% level must be calculated per question, as it was mentioned in the previous version of the guideline. It might also be possible to achieve the 90% level calculated over all questions in a test (20 people times 15 questions = 300 questions. 90% =270 correctly located answers and 243 correctly understood)?
5. The '90% of 90%' makes different levels of understanding acceptable. If 100% of the participants can find the information, and 90% of this information is understood correctly, than 90% of the 'literate adults' might be 'enabled to use a medicine appropriately'. If 90% of the participants can find the information, and 90% of this information is understood correctly, than 81% of the 'literate adults' might be 'enabled to use a medicine appropriately'. The difference between 90% and 81% is very substantial. It means that between 1 out of 10 patients and 1 out of 5 patients is not able to understand information about medicines. That is a very low threshold if it is related to vital safety information. It seems necessary to vary the importance of questions according to their relevance and safety.

Method: context

A diagnostic test is a very useful tool to find out exactly where people encounter problems with a document. A diagnostic test is not meant to provide an overall score of the quality of a document. Other types of usability tests are likely to be more appropriate.

The diagnostic test, as it is described by David Sless and Rob Wiseman (1997), investigates the accessibility, comprehensibility or the capacity of the participants to act appropriately on the information (p 79) within an information design process. A diagnostic test does not measure 'readability', 'usefulness', 'legible', 'clear', 'easy to use' nor any of the other criteria mentioned in section 2. Diagnostic tests do not establish if people really act appropriately in practice. It only establishes if participants would be capable to act. In order to find out if people act appropriately, different types of experiments are needed. Before suitable test methods can be chosen, it is necessary to clarify users, criteria and acceptable performance level.

Example 1. Patients need to make a risk-benefit decision before they take prescribed medicines at home. A diagnostic test will not indicate if this decision is made at all, and whether this decision is made correctly.

Example 2. Patients also have to remember the effects (positive and negative) that they might experience after taking a medicine, such as 'feeling dizzy', or it's easier to breath'. A diagnostic test will not show if people will remember these effects when the situations occurs.

If the actions 'making (risk-)decisions' and 'remembering' are relevant to particular medicines, they need to be tested with suitable methods. A diagnostic test seems inappropriate to investigate the use of information for specific actions.

Other methods, such as contextual inquiries, observation studies, and

benchmark studies are more appropriate. The results of the tests in the analysis indicate which criteria are suitable, and which levels could be achieved. These provide a basis for the diagnostic test. Conducting diagnostic tests without those criteria and levels is futile. Diagnostic tests are only useful if they are used appropriately as an integrated part of a larger document development process.

The Guideline assumes that the testing technique proposed for the testing of Consumer medicines information in Australia is also suitable for Package leaflets in Europe. However, these are fundamentally different pieces of information. The source (industry or pharmacists), the delivery method (inside a box or at the local pharmacist), the required languages (multilingual or single language), the legal situation are ignored if the Australian model is copied. It is essential to make sure that this 'example method' is suitable for a European situation before it is implemented in a guideline.

Validity

The internal validity of a diagnostic test is not an issue. The tests clearly show that changes in the design and text of a document influence the test results. The ecological validity is however problematic. The question 'is there a relation between the results of a diagnostic test and the use of information about medicines in practice?' must still be asked and answered. Without some clear evidence, it is not possible to indicate if a test accurately detects information that could lead to dangerous situations or inappropriate use. Suggesting a testing method without any investigation into its ecological validity is very risky.

8. Approach to developing information about medicines.

There are four fundamental problems with this Draft guideline. These are related to:

1. The activities of people. If the aim of the provision of information is to 'enable users to act appropriately', than the starting point must be 'the action of users'. The draft guideline does not do this.
2. The Guideline does not make any reference to other information sources or other modes of communication that 'enable users to act appropriately'.
3. The Guideline does not use a suitable model for an 'information development process'. The division between writing, designing and testing is in practice hardly possible.
4. The judgement of the quality of the information is not integrated into a longer term process. The guideline suggests a 'standard', but does not leave enough room to improve on this.

Each of these problems is described below.

1. Start from the activities of people.

The main reason to provide information about medicines is to support people who handle medicines. The Directive states: 'enabling the user to act appropriately.' In order to comply with the legal requirement of Directive 2004/27/EC to 'enable the users to act appropriately', it is necessary to introduce a development process that leads to the realization of this requirement. Careful consideration must be given to determine which 'people' need to be taken into account, which 'actions' should be evaluated, and what 'appropriate use' exactly entails. These three factors cannot be considered without the involvement of people who have an interest in the provision of information about medicines. A careful analysis of the use of information within a specific context must be used as a starting point.

One specific situation can be used as an example:

> A patient has just arrived home from a visit to a dispensing pharmacist where she has acquired some Prescription only medicines. At her kitchen table, she unpacks a small plastic bag. A first step is that this patient needs to *identify* the products (what is it and what is it for?), to *locate a starting point* (which box and leafl et do I read first?, which information is most relevant for me?), and *keep leaflets, boxes and medicines together* (avoid confusion). As a second step, she needs to *make a decision* (Can I take this medicine?), *consider* if she wants to take it ('Do the benefits outweigh the risks?'), *remember the effects* ('I've got to drive later on today, but this makes me drowsy. I better take it later.') and *learn to understand* how her medicines work. The third step consists of taking the medicines. This consists of *following the instructions* ('Before dinner'), *noticing any effects* ('I feel drowsy'), *check the leaflets again* ('Where did it state that I could get drowsy?'), *react appropriately* ('Do I need to call a doctor?') and *store the medicines* in a safe place ('Roomtemperature?'). After taking the medicines, a patient has to make a *decision whether to stop or continue*, and *decide whether to consult a doctor* again. A final action is to *dispose of any remaining medicines*.

Each of these activities must be supported by relevant information in order to make it possible to use medicines correctly. Each of these activities can be tested when suitable criteria are chosen, and minimally acceptable standards can be discussed.

The description of the use of a medicine that is used in a hospital is very different. A hospital pharmacist approaches a label and package leaflet in a very different way and sequence. And even identical activities are influenced by the context in which they are executed. For example, the *identification* of an outer package by a pharmacist in a pharmacy differs from the *identification* of the same outer package by a patient in a medicine drawer in a kitchen at home. Not all activities are equally important, not all users are the same, and the context of use must be taken into account.

The guideline starts from the idea that all medicines must be accompanied by information that is structured in the same way ('harmonisation') . This is in direct conflict with the variety of available medicines and the variety of ways in which these are used in practice.

2. Make references to other information sources.

The guideline focuses on the labelling and package leaflet. The separation of the sections in the guideline seems to suggest that they are developed individually. That is not the case: all deliverables need to be considered simultaneously.

The main reason is that people will see the package leaflet, immediate packaging and outer packaging together. People (patients, doctors, nurses, pharmacists, ...) will always see the combination of these artefacts. People do not separate information according to 'labelling and package leaflet' but need answers to their immediate questions. For example 'is this inhaler for daily use, or for asthma attacks only?' At that moment, this information must be very prominent, and it does not matter if it is found on the labelling or in the package leaflet. Focussing on one artefact only - in stead of on the activity of the user - reduces the overall impact. The information must be considered as a whole concept, not as a collection of different details.

Furthermore, the information that must be mentioned on labelling and in package leaflets is not related to other external developments. The developments in digital resources (bar coding, world wide web, e-mail), telephone services (helplines, sms), and patient organisations are not integrated into this guideline.

The guideline starts from the idea that labelling and package leaflets can be developed separately and independently from other information sources. This is incorrect. People search and interpret all information that is available to achieve their goals. If the package leaflet or the packaging does not provide information quickly enough, they will be disregarded.

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3. Start from a suitable information development process: Writing, designing and testing cannot be separated.

The Readability guideline provides advice on the development of information about medicines on labelling and in package leaflets. The structure of the guideline suggests that it is possible to separate writing, designing and testing. The guideline mentions first some issues related to the visual design (Part A 1-4). That is followed by some advice about the style (Part A 5-6). The example of a testing method is mentioned in an annex. This division of activities is confusing.

In order to develop information about medicines is essential to describe and analyse the activities of people when they handle and use a specific medicine. These activities are known for each medicine. Every applicant or marketing authorisation holder knows exactly how their medicines are used in practice. The development process of information must start with an observation and an analysis of current practice. 'User experience mapping' and 'contextual enquiries' are examples of techniques to accurately determine the different actions. Observing and recording the current state of affairs needs to be done to find out what is going well, and which activities need additional or a different type of support. Both 'best practice' as well as 'worst cases' need to be recorded with supporting evidence of potentical causes. This observation will reveal the activities that are likely to be problemeatic in relation to safety, benefits, risks, compliance and errors. An added benefit of this description is that information can build upon the expectations and experience of people.

Based on this description of current practice, and the knowledge about a particular medicine, a 'concept for use' can be developed. This concept describes the actions that people need to do to handle a medicine appropriately and indicates which user actions require extra support. All deliverables (package leaflets, packaging, and later websites and telephone helplines) must be developed to support this concept.

From this point of view, it is hard to understand why only the package leaflet must be tested. It would be very helpful to test the labelling too. Many accidents happen due to confusing packaging: these can be avoided if simple tests are conducted.

These are the first steps in a normal 'information development process'. The guideline suggests that the choice of the printsize and type is the most important issue by placing it as the first element to be considered. This conflict between 'good practice' and 'suggested practice in the guideline' is very substantial.

The digital development of information requires a very strict version control of the different documents. This practical issue is not dealt with in the guideline.

The lack of a reference to the Product Information Management (PIM) system is a serious omission too. It would be beneficial if at least a reference to this system is included in the Draft guideline.

The guideline starts from the idea that there is only one type of development process in which writing, designing and testing are separated. The variations in writing, designing and testing are ignored.

4. Judging the quality of information is a continuous process.

The aim of the Readability guideline is to support applicants and marketing authorisation holders to produce 'high quality information' (section 'Purpose'). The judgement about the quality of the information is made by four groups of people:

1 - The applicant or marketing authorisation holder who checks if the information is conform the requirements. Different departments, such as legal, production, marketing, and medical, all have their influence.

2 - Participants in a Readability test, who check if information can be located and understood.

3 - The competent authorities, who check if the legal requirements have been met.

4 - People who handle a medicine after registration.

If 'high quality information' is the real aim, than the Readability guideline must provide a description of a process that relates to these four groups of people. Quality judgement is not a 'single point in time', but a continuous process. Ignoring this process has detrimental effects in a few years time. At the moment it is already very hard to follow the advice in the Draft guideline. In a few years time it is likely to be impossible.

The guideline does not provide guidance about the four different groups who judge the quality of the information about medicines. The guideline does not describe a process of quality improvements.

Concluding

There are four fundamental problems with the Draft guideline and the Directives is that they assume that the information about all medicines can be approached in an identical way. The provision of information about medicines is a lot more complex and requires a variety of approaches. The activities of people, integration with other information sources, information development processes and quality assurance processes are fundamental for a Readability guideline. The Draft guideline does not pay enough attention to these topics.

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Conclusions

The comments on the previous pages indicate that the Draft guideline is fundamentally flawed and should not be introduced in this format. The main arguments are:

1. It is not clear what exactly needs to be delivered.
The guideline does not tell what the end results must be. It is not clear what needs to be submitted to the authorities, nor what needs to be developed.

2. The criteria to evaluate and check the results are incorrect.
Adding more immeasurable criteria does not help. It is essential to use relevant and measurable criteria.

3. The people who are involved are inappropriately adressed.
A guideline must make clear who has to do what. The guideline lists many different potential groups, without suggesting how these groups have an influence on the texts in the EMEA-QRD template.

4. The scope of the guideline is too narrow to be effective.
Focussing on details of specific issues is not sufficient. The larger issues (costs, compliance and errors) must be taken into account.

5. The advice on the writing of information about medicines is based on incorrect assumptions.
Writing is not just related to syntax and style. Suggesting that it can reduced to a limited number of factors does not do justice to the writing professions (medical writers, technical writers, document developers, ...).

6. The advice on the designing of information about medicines is based on incorrect assumptions.
Designing is not about 'choosing the details', but to consider all factors simultaniousy to make a prototype of the most promising combination. Suggesting that it can be reduced to a limited number of factors does not do justice to the design professions (graphic designers, information designers, ...).

7. The advice on the testing of information about medicines is based on incorrect assumptions.
Testing is not a solitary activity at the end of the development process. It is an integral part of the process. Suggesting that it can be reduded to a limited number of factors does not do justice to the testing professions (usability professionals, marketing researchers, ...).

8. The approach to developing information about medicines is problematic. The provision of information about medicines is a lot more complex and requires a variety of approaches. The activities of people, integration with other information sources, information development processes and quality assurance processes are fundamental for a Readability guideline. The Draft guideline does not pay enough attention to these topics.

9. The editing, spelling and typography of the guideline itself needs attention. There are many spelling mistakes, poorly edited phrases and paragraphs, poor structuring and poor typography. If this guideline needs to be taken serious as an example of writing, designing and testing, it needs to stick to its own standards.

Based on these nine conclusions, I recommend in the strongest possible terms to reconsider this guideline.

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Contact details

Dr. Karel van der Waarde
Van der Waarde Graphic - Design Research

mail: Solariumlaan 15
1982 Elewijt
Belgium

tel.: +32 (0)15 610 932

e-mail: waarde@glo.be

About the author:
Dr Karel van der Waarde studied graphic design in the Netherlands (Eindhoven) and in the UK (Leicester, Reading). He received his doctorate in 1994 for: *'An investigation into the suitability of the graphic presentation of patient package inserts'*. In 1995, he started a design - research consultancy in Belgium specializing in the testing of information design. The company develops package leaflets, instructions, forms, protocols, and the information architecture for websites. Karel van der Waarde frequently publishes and lectures about visual information. He is moderator of the InfoDesign and InfoDesign-Café discussion lists and co-owner of the InformationDesign.org website.

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Appendix 1: Example guideline.

This appendix shows how a guideline could be presented. The guideline is aimed at applicants and marketing authorization holders to make it easier to develop information about medicines. A step by step guideline might be a more appropriate format.

Step 1. Develop a concept based on the activities of people who have to handle your medicine. The concept-document describes the actions, the users, and the acceptable level of achievement for each action. It is essential to investigate the actions and prioritise those that require most attention. After that, it is necessary to decide how each of the different deliverables could support these actions. This concept describes the approach that all information must follow. (*Link to an example of a concept document.)

Step 2. Download the EMEA/QRD templates from the website: www.emea.europa.eu Choose the relevant language(s) and the appropriate registration procedure. (*Link to an explanation of the different procedures.)

Step 3. Modify the template by inserting information about your product. Use the available guidance that can be downloaded from the same EMEA-website. (*Include a list of references and documents here.) Make sure all information of the SMPC is included and that all information conforms to the concept. (Practical issue: Who does the writing? Which software? Version management?) (*Include an example of a time planning here.)

Step 4. Design the leaflet. Start from the available dimensions of paper that are determined by the production facilities. The structure of the headings needs to be most prominent. (Practical issue: who does the design? External, internal, integrated in production? Consider all presentations: paper, sound, Braille, web, multilingual.) (*Include an example of a time planning here. *Include examples of approved leaflets here.)

Step 5. Make a list of the most important issues based on the preliminary research. These are the things that people must know when they handle this medicine. Write these issues in question format. Randomise their order. (*Include an example of a time planning here. *Include an example of a questionnaire.)

Step 6. Pilot test the leaflet. Interview three to five people to find out if the design, the text and the questionnaire do not contain major errors. Three participants are sufficient for a simple leaflet; five participants for a more complex leaflet. The participants of a pilot test do not have to be patients, but people who can imagine that they are in a particular situation. (*Include an example of a time planning here. *Include a list of the individual details of the test participants that must be submitted. *Include requirements in which the original data - comments and recordings - must be archived for future use.)

Description of a single interview:
- Recruitment: where to find people who can provide relevant feedback? (patients or healthy volunteers, How to deal with confidentiallity issues?)
- Location: what is a suitable venue?
- Interview: a step by step description of an interview. (It would be really useful if a video-recording would be made available on the web as an example to show how an interview is conducted.)
- Reporting: a step by step guide how to record, report, analyse and present responses. (*Include an example of a report.)

Step 7. Rewrite and redesign the leaflet and the questionnaire if the pilot test indicates that this is necessary. (*Provide a guide and examples on how to interpret the answers and motivate modifications.)

Step 8. Test 1 + report
Interview 10 people. (*Refer to the guide and examples on how to interpret the answers and motivate modifications. *Provide example of a test report.)

Step 9. Rewrite and redesign. Motivate all modifications. (*Provide examples of correct and incorrect motivations.)

Step 10. Test 2 + report.
Interview 10 people. (*Refer to the guide and examples on how to interpret the answers and motivate modifications. *Provide example of a test report.)

Step 11. Final conclusions + report + final text of the leaflet. (*Provide example of a test report. *Provide a checklist to control if all required files are available.)

Warning: It is absolutely vital to keep track of all versions. Version control of all required files is essential. It would be really useful if an example of all required files for a readability report would be made available on the web.

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Appendix 2: Line by line comment of the Draft Guideline.

Below are some comments on the actual text of the Draft Guideline. The texts in *italic* are the texts as they appear in the Draft Guideline.

Title: Draft Guideline on the Readability of the label and package leaflet of medicinal products for human use.

- Terminology: The word 'readability' indicates a criteria that indicates how well a text can be read. The aim of the labelling and package leaflet is not 'reading' but 'to enable people to act appropriately'. This is commonly refered to as 'usability'.
- Terminology: The first sentence in section B of the draft defines 'labelling' as 'both outer packaging and inner packaging'. The word 'label' is not further defined nor used in this guideline.

> Suggestion: Change the title to: 'Guideline on the usability of the labelling and package leaflet of medicinal products for human use'.

Introduction.
Legal Framework.

Paragraph 1.
All medicines are required by Community law to be accompanied by outer/inner labelling text and a Package Leaflet setting out comprehensive information which is accessible to and understandable by those who receive it, so that they can use their medicine safely and appropriately.

- Editing: The first sentence consists of 44 words. This is in conflict with the guidance provided in section A-5 second bullet. It would increase the confidence in the value of the advice in this guideline, if the guideline itself had followed its own advice.
- Editing: '… by outer/inner labelling text …'. The Directive (definition 25 in 2001/83/EC) and first paragraph of section B define 'labelling' as 'both outer packaging and inner packaging'. The words 'outer/inner' can be deleted in the guideline.
- Editing: Capitalization of 'Package Leaflet'. Please use lower-case to make it consistent with the rest of the document
- Terminology: 'Comprehensive information'. Does this mean the same as 'full' as it is mentioned in point 40 of the Directive?
- Criteria: The words 'accessible to' and 'understandable by' introduce new criteria that are not mentioned in the Directive. They are not the same as 'comprehensible' as stated in the Directive. If 'understandable' is the same as 'comprehensible', please use the same word. The Directive has as a main criterion: 'a high degree of consumer protection, in order that medicinal products may be used correctly'. The relation between 'used correctly' and 'can use their medicine safely and appropriately' needs to be outlined. Also the plural 'products' in the Directive and the singular in the guideline might cause problems.
- People: 'those who receive it'. This puts the people immediately in a passive position. A more active verb ('looking at it', 'interpreting it', 'applying it') might be more appropriate. 'They' also creates a difference between 'us' and 'them'. 'Us' is 'those who make the labelling and package leaflets, 'them' is everyone else. It suggests that those who make the labelling and package leaflets do not use medicines.
- Criteria: 'use their medicines safely and appropriately'. The main reason to use medicines is to improve health and/or improve the quality of life. The effectiveness of this improvement is the secondary aim. 'Safely' and 'appropriately' are tertiary aims related to the use of medicines.
- User action: 'users reading the labelling and packaging carefully and accurately'. 'Reading' might not be the right verb, because a lot of information is quickly scanned without consciously reading it. 'Interpreting', or 'using' is more appropriate.
- Terminology: In this sentence the phrase 'labelling and packaging' is unclear. Labelling is defined as inner and outer packaging. The package leaflet is not mentioned.
- Criteria: 'reading carefully' and 'reading accurately' differ from the main criteria listed in the Directive.

- User action: The phrase ‘on users reading … and being able to understand’ differentiates between these two actions. Research indicates that it is not possible to distinguish between the two: ‘reading and understanding’ are inseparable.
- Criteria: ‘and act on the information presented’. This diverges from the text in the Directive which is more specific by stating that ‘information must enable users to act appropriately’. So, not only ‘act on the information’, but ‘to act appropriately’.

> Suggestion: Please rewrite this first sentence. Something like the following might be considered: ‘All medicines in the European Union must be accompanied by information. The aim of the provision of information is to enable people to act appropriately. This information must be presented on the outer packaging, the inner packaging and/or in a package leaflet.’

The safe and correct use of all medicines depends on users reading the labelling and packaging carefully and accurately and being able to understand and act on the information presented.
- Criteria: The first sentence mentioned: ‘can use their medicine safely and appropriately’. This differs from ‘safe and correct’, but the difference between ‘correct’ and ‘appropriately’ is not clear.
- People: The first sentence mentioned ‘use their medicines’. The second sentence describes ‘users reading the labelling and packaging.’ These might not be the same groups. ‘Their medicine’ refers to patients. ‘Users’ can refer to doctors, pharmacists, nurses and patients.

> Suggestion: Delete the second sentence.

Paragraph 2.
‘According to Article 54, Article 55 and Article 59 of Directive 2001/83/EC medicinal products must be accompanied by outer or immediate packaging information (labelling) and a package leaflet. Article 58 allows for the omission of a package leaflet where all the required information can be directly conveyed on the packaging.’
- Terminology: ‘outer or immediate packaging information (labelling) and a package leaflet’. This is in conflict with the phrase in the first paragraph that states that ‘users reading the labelling and packaging’ which suggests that there is a difference between ‘labelling’ and ‘packaging’. The phrase in the second paragraph states that labelling consists of ‘outer **or** immediate packaging information’. This is in conflict with definition 25 in the Directive.
- Package leaflet is not capitalized. It is capitalized in the first paragraph. Is there a difference?

Paragraph 3.
‘Article 56 of Directive 2001/83/EC requires that the label text shall be easily legible, clearly comprehensible and indelible.’
- Terminology: ‘Label text’ in article 56 does not only refer to the particulars that must appear on the ‘labelling’ but also the particulars in the package leaflet. Furthermore, the word ‘text’ seems to exclude the use of visual elements, such as illustrations, diagrams, pictograms and symbols.

Paragraph 4.
‘Article 56a of Directive 2001/83/EC requires the name of the medicinal product to be expressed in Braille format on the packaging, and the marketing authorisation holder to ensure that the package leaflet is made available on request from patients' organisations in formats appropriate for the blind and partially-sighted.’
- Typography: Patients’ organisations: please use apostrophy, not a ‘feet-mark’ (‘ not: ')

Paragraph 5.
‘Article 59(3) of Directive 2001/83/EC provides that the package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use.’
- Terminology: ‘consultations with target patient groups’. This is in conflict with the phrase in the first paragraph of this guideline: ‘to those who receive it’, because that includes ‘doctors, pharmacists, nurses’ as well. Either make clear who ‘those who receive it’ are, or use the phrase from the directive ‘target patients groups’.

- Criteria: The Directive mentions 'legible, clear and easy to use'. In article 56, the criteria re 'easily legible, clearly comprehensible and indelible'. The difference between 'legible' and 'easily legible', 'clear' and 'clearly comprehensible' is very confusing. The two criteria 'easy to use' and 'indelible' do not seem to be related.

Paragraph 6.
'Article 61(1) and 8(3)(j) of Directive 2001/83/EC specify that one or more mock-ups of the outer packaging and the immediate packaging of a medicinal product, together with the draft package leaflet, shall be submitted to the competent authority at the time of marketing authorisation application. The results of assessments carried out in cooperation with target patient groups shall also be provided.'
- Terminology: Article 8(j) states 'a mock-up of the outer packaging, … and of the immediate packaging …, together with a package leaflet.' Article 61 mentions '**draft** package leaflet' and 'mock-up'. Article 8 does not mention the word '**draft**'. Is this intentional?
- Terminology: 'assessments carried out in cooperation with target patient groups'. What is the difference between 'consultations' and 'assessments'?

Paragraph 7.
'Article 63(1) requires that the labelling and package leaflet shall be provided in the official language of the member state where the product is placed on the market. Additional languages can be included provided the information presented is the same in all languages and it does not impact adversely on the legibility, clarity and comprehensibility of the text.'
- Conflict: The use of more languages on labelling or in package leaflets will always have an impact on the way this information is handled by people. It is not possible to present several languages without an adverse impact. This statement cannot be followed in practice.
- Terminology: 'Labelling and package leaflet'. This is in conflict with the first paragraph in which 'labelling and packaging' are mentioned separately.
- Terminology: In the second sentence, the words 'information' and 'text' are used as synonyms.
- Criteria: 'legibility, clarity and comprehensibility of the text'. This adds three new criteria. It also focuses on 'text' and excludes the design of information. This is in conflict with article 63(2) which explicitly mentions 'design' of the package leaflet.

Paragraph 8.
'Article 63(2) of Directive 2001/83/EC requires that the package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals. The package leaflet must be clearly legible in the official language or languages of the member state(s) in which the medicinal product is placed on the market.'
- Criteria: 'package leaflet must be written and designed to be clear and understandable, enabling the users to act appropriately, when necessary with the help of health professionals'. ... 'clearly legible'. That is a lot of different criteria, but the main one is clear: '*enabling the users to act appropriately'*. Please note that in chapter 3 of the draft guideline, the plural of 'users' has been replaced by a singular 'user'. Another very important point is that the Directive puts equal emphasis on 'writing' and 'designing'.
- Terminology: difference between 'users' and 'health professionals'.

Paragraph 9.
'This guideline is published in accordance with Article 65 of Directive 2001/83/EC, which provides for the development of guidelines concerning, amongst other things, the legibility of particulars on the labelling and package leaflet.'
- Criteria: 'The legibility of particulars' introduces another criterion. The difference between 'legibility' and 'readability' is not clear. Discussions about these terms have a long tradition. See for example: Linda Reynolds (1984) 'The legibility of printed scientific and technical information.' pp 187-208 in: Harm Zwaga and Ronald Easterby (editors) 'Information design'. New York: John Wiley & sons.

Paragraph 10.
'The guideline is intended to apply to all marketing authorisation procedures and to all medicinal products, including those available without prescription.'
- Editing: 'is intended to apply' can be written more economically: 'applies'.

- Editing: ‘and to all medicinal products, including those available without prescription’. Medicinal products are defined in article 1 (2) of Directive 2004/27/EC. It is not clear why ‘those available without prescription’ need to be mentioned especially.

Purpose.

Paragraph 1.
‘The main purpose of this guideline is to ensure that the information on the label and package leaflet is accessible to and able to be understood by those who receive it, so that they can use their medicine safely and appropriately.’
- Editing: a guideline cannot ‘ensure’. Suggestion: ‘The main purpose of this guideline is to support the writing and designing of the particulars that must appear on the labelling and package leaflet.’
- Terminology: ‘label and package leaflet’. Conflict with earlier terminology: what is the difference between ‘label’ and ‘labelling’?
- Criteria: ‘accessible to and able to be understood by those who receive it’. This is incorrect. Information cannot be ‘able to understood’. People can understand information, but information on its own cannot do things. The phrase in the first paragraph of the legal framework is more correct.

Paragraph 2.
‘This guideline is written to assist applicants and marketing authorisation holders when drawing up the labelling and package leaflet and preparing the specimens or 'mock-ups' of the sales presentations.’
- Assumption: ‘The guideline is written to assist applicants…’. This claim suggests that it is not absolutely sure that the guideline assists applicants. It might be worthwhile to consider the testing of the guideline before it is introduced. ‘This guideline assists applicants …’
- Terminology: The word ‘specimen’ has disappeared from the Directive text (article 8(j), article 15, and article 61) . To re-introduce it in the Guideline is confusing. Please use ‘mock-up’ only and delete ‘specimens or’.
- Typography: Please use appropriate apostrophes: not ‘feet-marks’.

Paragraph 3.
‘The guidance sets out advice on the presentation of the content of the labelling and package leaflet (required in accordance with Title V of the Directive) and on the design and layout concepts which will aid the production of high quality information. It includes guidance on ‘consultations with target patient groups’ for the package leaflet, and provides references to guidance documents which can be used to ensure that the content of labelling and package leaflet meet the legal requirements and are presented in a consistent way. Taken together these will assist in the harmonisation of product information across all Member States.’
- Terminology: ‘the presentation of the content’ and ‘the design and layout concepts’ is not clearly differentiated. What is the difference? Furthermore, the Directive states that the guideline must deal with ‘the legibility of particulars’ (article 65 (c)).
- Terminology: ‘High quality information’ seems to suggest different levels of quality. The Directive asks for information that ‘enables people to act appropriately’. The quality does not really matter, as long as it enables people and protects consumers to a high degree.
- Unclear: ‘it provides references to guidance documents’. These references are not provided.
- Criteria of the guideline. The third paragraph is in conflict with the first. The third paragraph states that the guidance can be used to ensure that the contents meet the legal requirements. The guideline does not do this: references to relevant EMEA-guidelines are lacking.
- Criteria: This paragraph states that information must be presented in a consistent way. That is a new criterion for the presentation of the content: ‘consistent way’. I am not convinced that consistency across Europe benefits patients across Europe. Readability tests, or usability tests might indicate differences based on language or culture. Consistency is therefore in direct conflict with the differences between patients in Europe. Stating that ‘consistency’ is a requirement implies that all patients in Europe are treated as identical, regardless of their language, culture or healthcare system.
- The relation between ‘product information’ and ‘labelling and package leaflet’ is not clear.
- The assumption that ‘harmonisation of product information across all Member States’ is essential is the main reason for using templates. This means that the labelling and package leaflet must be designed in a similar way. This is in conflict with the ‘patient consultations’: not all Europeans might want the same information in the same way: it is likely to be in conflict with national and cultural traditions.

Paragraph 4.
'The guideline also includes information on how the requirements for Braille can be met, as well as how to make the package leaflet available in formats suitable for the blind and partially sighted patients.'
- Spelling: partially sighted is spelled with a hyphen in the fourth paragraph of the legal framework. The Directive (article 56a) also spells it with a hyphen.

Paragraph 5.
'Finally, the guideline includes advice on the preparation of specimens or 'mock-ups' of the sales presentation and the package leaflet. As provided for in Article 8.3(j) of Directive 2001/83/EC, a mock-up of the outer and immediate packaging together with the package leaflet must be submitted to the competent authority for approval, before commercialisation of the product. A mock-up is a copy of the flat artwork design in full colour, presented so that, provides a replica of both the outer and immediate packaging provides a three dimensional presentation of the labelling text. This mock-up is generally referred to as a paper copy and not necessarily in the material of the sales presentation.'
- Terminology: 'specimens or 'mock-ups' of the sales presentation and the package leaflet.' This is confusing. The Directive asks for a 'draft package leaflet', and this phrase seems to suggest that a 'specimen' or 'mock-up' is required. The word 'specimen' does not appear anymore in the Directive. Please do not use it in the Guideline. Furthermore, the difference between 'sales presentation' and 'labelling' is not clear.
- Article 8.3(j) is correctly quoted, but article 61(1) states that a *draft* package leaflet is required. This is a discrepancy in the European Directive. It is necessary to define both 'mock-up'and 'draft'.
- Typography: A mock-up. Please do not underline A.
- Terminology: This is not a clear definition of a 'mock-up': 'copy'?, 'flat artwork design', 'replica'.
- Grammar: This sentence is grammatically incorrect: … provides … provides … .

Chapter 1. Readability of the Label and the package leaflet.

- Terminology: 'label' or 'labelling'?
- Terminology: 'Readability'? The aim of labelling and package leaflet is to 'enable users to act appropriately' and to 'provide a high degree of consumer protection in order that medicinal products may be used correctly …'. The word 'readability' only covers one aspect of this aim by focusing on 'readability'. In order to 'act appropriately' and to 'use correctly' a lot more is required. This is commonly referred to as 'usability'.
- Terminology: Please add a definition of 'readability' in the guideline. It is now not clear what is exactly meant by this term.

Section A. The package leaflet.

'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, those with poor literacy skills and those with some degree of sight loss.'

- Criteria: The phrase 'well designed and clearly worded' adds two new quality criteria without specifiying how it is possible to determine if a package leaflet is 'well designed and clearly worded'.
- Aim: The phrase 'maximises the number of people who can use the information' adds another aim to the provision of information.
- People: The phrase 'including older children and adolescents, those with poor literacy skills and those with some degree of sight loss' extends the group of people that needs to read package leaflets.

'*Companies are encouraged to seek advice from specialists in information design when devising their house style for the package leaflet to ensure that the design facilitates navigation and access to information.'*

- Good point: get professional help from an information designer. It is however strange not to mention the profession of 'medical writers' or 'technical writers' here too. It is the combination of design and text that makes information usable.
- Assumption: It is assumed that there is a direct relation between 'house style' and 'navigation and access'. House style is a term to indicate the recognition of the brand or identity of a product or an organisation. It has little to do with 'navigation and access'.
- Assumption: It is assumed that 'the design facilitates navigation and access to information.' There is little hard evidence in support of this statement.

'A balance will need to be achieved between the length of the resulting leaflet and the accessibility of the information contained within it.'

- Conflict: This is in conflict with the Directive, that states that 'full information' must be provided. In combination with the requirement that information must be 'based on the SMPC', it is likely that the length of the text in package leaflets is hardly flexible. Furthermore, the structure of the leaflet is provided by the Directive, and by the EMEA/QRD templates. The combination makes the information in some package leaflets hard to access.

1. Print size and Type.

First bullet.

'Choose a font which is easy to read.'

- Incorrect assumption: This assumes that there are fonts that are 'easy to read' and other fonts that are 'less easy to read' and that this characteristic is inherent in the font itself. That is incorrect. Even the fonts that are supposed to be 'very easy to read' can be used in a way that makes it impossible to read them.

'For large quantities of text such as found in package leaflets a serif typeface is preferred since the shape of the characters is easier to read.'

- Incorrect assumption: This is not supported by any reliable research (See Ole Lund). It is a common myth. Furthermore, character shape is only one factor in the reading process (Microsoft research). This statement is also in conflict with the requirement of the directive to 'consult target patient groups', because it pre-supposes the reactions of people reading package inserts. This makes a test less valuable, and prevents the testing of alternatives with sans serif fonts that might be easier to read.

'Most books are set in a semi-bold serif typeface whereas bold sans serif fonts are more often used for signs.'

- Incorrect assumption: It is certainly not the case that most books are set in a semi-bold serif typeface. I guess that books imply 'novels' or 'fiction', but it is a gross simplification to group all books together. (manuals? dictionaries, encyclopedias, are not classified as 'books'?')
- Incorrect assumption: 'bold sans serif fonts are more often used for signs.' This is not correct (Please refer to the publications of Per Mollerup, Paul Mijksenaar, Gerard Unger about signage systems).

'Stylised fonts which are difficult to read should not be used.'
- Incorrect assumption: 'stylised fonts which are difficult to read should not be used.' Font classifications are notoriously hard to use, but none has a grouping called 'stylised'. All fonts are stylised to a certain extent. To group all of these together and give them the label 'difficult to read' is not correct.

'It is important to choose a typeface in which similar letters/numbers, such as "i", "l" and "1" can be easily distinguished from each other.'
- Internal conflict: It is important to choose a typeface in which similar letters/numbers, such as "i", "l", and "1" can be easily distinguished from each other'. The text of the guideline is set in a typeface that makes the "l" and "1" identical. Please use another typeface to show the importance of this guidance.
- Terminology: the words 'font' and 'typeface' are not identical. Font refers to the collection of all characters (glyphs) that are designed as a group. 'This font does not have an 'ampersand glyph'. 'Font' and visual characteristics have nothing to do with eachother. A typeface refers to the design of the characters. 'This ampersand glyph suits this typeface.' You can design a typeface (visual characteristics of characters/glyphs, but you can't design a font (collection of characters/glyphs).

Second bullet.
'Where practical your font size should generally be 12 point for the main body of the text and where practical a larger font size for headings is recommended e.g. 14 point.'
- Terminology: 'font size' or 'type size'?
- Problematic measure: point system. This is in conflict with the European guideline on the harmonization of measures to metric dimensions. Furthermore, the pointsize of a character is impossible to measure after a document has been printed. This unit of measurement cannot be used to 'control' afterwards if a typesize is correctly chosen. (The previous guideline mentioned the x-height. That is a very useful and measurable dimension of the vertical height of characters.)
- Problematic increase: the type size increased from 8 point Didot in the 1998 guideline to 12 points in this draft guideline. This increase of about 150% will mean that most leaflets need to be increased in size. This will create problems in the production and is most likely to lead to larger outer packaging-sizes.
- Incorrect assumption: It is assumed that larger typesize make leaflets easier to read. That is not the case. If the characters can be comfortably distinguished, it is not necessary to make them larger.
- Conflict: the suggestion of a typesize is in conflict with the necessity to 'consult target patient groups'. It assumes that people can read 12 point type easier than 8 point type. This is an untested assumption. Readability tests might indicate that a typesize smaller than 12 points is perfectly legible. This makes this specific advice in the guideline superfluous. If a test is obligatory, it is not necessary to specify a type size. Package leaflets with a typesize that is too small cannot pass a test.

'Consideration should be given to using larger fonts where it is known that patients with visual impairment are likely to be using the package leaflet, for example package leaflets supplied with eye drops.'
- Conflict: with the advice on 'recruiting participants' in annex 1. Only for rare diseases it is necessary to recruit patients with a particular illness. There is no mention of recruitment of patients with visual impairment.
- Terminology: Several different terms are used: 'patients with visual impairment' or 'partially sighted', or 'those with some degree of sight loss'.

'For visually impaired patients the preferred font size should be between 16 and 20.'
- Terminology: font size or type size? The unit of measurement 'point' is missing.
- Conflict: If visually impaired patients are likely to read the package leaflet, it is essential to include these patients in a readability test. If that is the requirement, it is not necessary anymore to suggest a type size: the test will be enough proof that the leaflet is readable.

Third bullet.
'The widespread use of capitals should be avoided.'
- This advice might be valid, but it seems to be in conflict with the use of capitals in the titles of the EMEA/QRD template. It might be necessary to modify the EMEA templates to conform to this draft guidance.

'The human eye recognises words in written documents by the word shape, so choose lower case text for large blocks of text. However, capitals may be useful for emphasis.'
- Terminology: There are several problems in this sentence. Only people can read. The word 'human' is superfluous. 'Words in written documents' indicates that there are also non-written documents. That is possible, but unlikely. Does 'lower case text' mean that 'no capitals' can be used? This advice is incorrect. Please define 'large block of text', because a characteristic of the package leaflet is that it does not contain large blocks of text.

    Suggestion: Delete this bullet completely. The readability test will indicate if the use of capitals is appropriate.

Fourth bullet.
'Do not use italic fonts and underlining as such devices make it more difficult for the reader to recognize the word-shape.'
- Terminology: 'italic font?' The term 'font' is used incorrectly here. Just 'italic' is sufficient. The word 'device' is uncommon in typographical terms. The guideline also uses 'factor', 'aspect' or 'tool' for similar visual variables.
- Spelling: word-shape is spelt in the previous bullet without a hyphen.
- Editing: 'for the reader' is superfluous. Who else?
- Assumption: Italic and underlining make it more difficult to recognize the word shape. Where is the proof for this?

The sequence of the four bullets in section 1 'Print size and type' indicates that the choice of a typeface and type size are the most important decisions when the readability of a package leaflet is concerned. This is not the case. All visual factors need to be considered together and related to the information that needs to be presented.

Section 2: Design and layout of the information.
- Editing: 'Design' and 'of the information' can be deleted. The four bullets are only about the layout of package leaflets.

Bullet 1.
'All text should be set horizontally ...'
- Unclear advice: patients are capable of turning a leaflet until they can read it. If it is difficult to read, because the text is set in different angles, it is unlikely to pass a readability test.

'and the use of "justified" text (that is text aligned to both left hand and right hand margins) should be avoided;'
- Unsupported assumption: There are many situations in which aligned text might be more appropriate.
- Terminology: the text is not aligned to the margins, but to the columnwidth.
- The avoidance of justified text leaves three options open: ranged left, ranged right, or centered. Although the guideline does not specify this, it should be made clear that 'ranged left' is the better option.

'however this may be acceptable where column format is used (see below).'
- Terminology: all western texts are set in 'column format'. It is not possible to set a text in 'non column format'.

    Suggestion: Delete this bullet. It is not really helpful. It suggests to use 'horizontal text' that is set 'not-justified'.

Bullet 2.
'Line spaces should be kept clear'.
- Terminology: the word 'line space' is unclear. This is a standard issue in typographical discussions, because it can mean two things. Line space can refer to the distance between baseline to baseline, or to the white space between lines. It is necessary to define 'line space' as the distance from baseline to baseline.
- Assumption: is it possible to fill line spaces or to have unclear line spaces?

'The space between lines is an important factor influencing the clarity of the text.'
- Unsupported assumption. It is a factor, and it is unclear if it influences the clarity of a text.
- Criteria: 'clarity of the text' adds another criteria to judge a quality of package leaflets. The relation with the other criteria is not clear.

'As a general rule the space between one line and the next should be at least 1.5 times the space between words on a line, where practical.'
- Internal conflict: The guideline itself uses justified texts in which the wordspaces vary substantially.
- Editing: 'on a line' can be deleted. 'the space between words' is sufficient.
- Assumption: it is possible to relate the linespace to the wordspace without considering other factors.
- Assumption: The measure 1.5 is not based on any available research. Please provide a reference.

Bullet 3.
'Contrast between the text and the background is important. Factors like paper weight, colour of the paper, size and weight of the type, colour of the type and the paper itself should be considered.'
- Incorrect assumption: these 'factors' are always considered when a package leaflet is designed. They are unavoidable. A guideline must give advice on how to consider them.
- The 'weight of the type' was not discussed in section 1, at least, the term does not appear in section 1.
- The 'colour of the paper' is mentioned twice in this sentence. Please delete once.

'Too little contrast between the text and the background adversely affects the accessibility of the information.'
- Incorrect assumption: This statement suggests that only the accessibility is affected by contrast. However, it is likely that a leaflet fails a readability test if the contrast is too little. If the readability test indicates that 20 people can find and understand the information in a package leaflet, it is not necessary anymore to mention 'contrast' in the guideline.

'Therefore, avoid background images behind the text which will interfere with the clarity of the information making it harder to read.'
- Incorrect assumption: it might be possible to use background images. A readability test will show if this affects the accessibility or the understanding of participants.

Fourth bullet.
'A column format for the text can help the reader navigate the information'.
- Assumption: All texts in western scripts use a column format. (It is very difficult to write a text without using column format: the dimensions of paper or screen are always limited. The exception is the circular text.)
- Assumption: A column format can help the reader navigate the information. True, but there is no alternative.
- Editing: 'for the text' can be deleted. Columns are always for texts.

'The margins between the columns should be large enough to adequately separate the text'.
- Assumption: This disregards the results of a readability test. The plural 'margins' is incorrect if two columns are used. 'The margins should be large enough.' And that is obvious.

'If space is limited a vertical line to separate the information should be used.'
- Terminology: In the previous sentence, the word 'text' is used. In this sentence, 'information' is used as a synonym. They are not the same.
- The advice here should be: 'use white space to indicate the relations between elements. Elements that belong together must be separated by less white space than groups that do not belong together'.

'Important information should be kept together so the text flows easily from one column to the next.'
- Unclear advice: I think that 'kept together in the same column' is meant here. The result is that the visual design indicates a connection in the information. If a text is divided over two columns, it might be an indication that the information is not related.
- Unclear advice: This phrase seems to imply that 'unimportant information can be separated.' That is incorrect. Information should be visually grouped in such a way that the relation between the elements becomes clear.

'Consideration should be given to using a landscape layout which can be helpful to patients.'
- Unsupported assumption: This advice surmises the results of a readability test.
- Unsupported assumption: it is not clear why a landscape layout might be more helpful than a portrait layout.
- Terminology: A layout cannot be 'landscape' or 'portrait'. These terms refer to the paper dimensions, not to the layout.

'Where a multi-lingual leaflet is proposed there should be a clear demarcation between the different languages used.'
- Correct. In a guideline, I expect a description how to do this. This is a very difficult problem in practice because some countries (Belgium, Finland, Switzerland) demand multi-lingual leaflets. The dimensions of the leaflet, or the number of pages in a booklet, make multi-lingual package leaflets very hard to handle. It is legal conflict: one part demands 'full and comprehensible', the other part demands 'include several languages'.

Section 3: Headings.
'Headings are an important aspect of written information and can help patients navigate the text if used well.'
-Terminology: Italic and underlining are called 'devices'. It is not clear why headings are called 'an aspect'.
- Editing: the word 'written' is superfluous. The text states: 'Headings can help patients to navigate through a text.'
- Editing: the words 'if used well' should not be used in a guideline. The guideline must explain exactly how headings must be used well.
- Incorrect assumption: headings not only help people navigate a text, but they also add to comprehension of the text. Ignoring the comprehension of headings, by making them only 'stand out' is not sufficient. The content of the headings must have a very direct relation with the content of the subsequent paragraph(s). [The EMEA-template causes some problems, because the headings are not easily to comprehend, or do not have a direct relation with the subsequent paragraph.]

'Therefore, bold text for the heading, underlining or a different colour, may help make this information stand out.'
- Terminology: 'Bold text' or 'bold typeface' of 'bold font'. Please be specific. There are fundamental differences between 'text', 'typeface' and 'font'.
- Internal conflict: The fourth bullet of section 2 clearly states: 'do not use italic fonts and underlining.' This advice is applicable to headings too.
- Assumption: if a heading stands out, it helps people to navigate a text. This advice pre-judges the results of a readability test.

'Same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) to aid the reader.'
- Assumption: consistency aids readers. This advice pre-judges the results of a readability test.
- Editing: the word 'bulleting' is not in the right section. Bulleted headings do not exist in the EMEA/QRD template. Nor are they 'good practice'. Please delete 'bulleting' from this sentence.

'The use of multiple levels of headings should be considered carefully, as more than two levels may make it difficult for patients to find their way around the leaflet.'
- Terminology: This paragraph switches from 'patient' to 'reader' and back to 'patient'. Those might not be the same people.
- Terminology: What is the difference between 'navigate the text' and 'find their way around the leaflet'? If the same action is implied, please use the same words.

- Editing: ‘multiple levels’ is ‘more than two’. The EMEA template uses two levels already. Does this mean that the guideline advises not to add another level of headings? If that is the case, please say so.
- Unsupported assumption: It is not clear why more than 2 levels make it difficult for patients. If that is the case, it will be shown in the readability test.

‘Using lines to separate the different sections within the text can also be helpful as a navigational tool.’
- Terminology: ‘Tool’, or ‘device’, or ‘aspect’ are all used to indicate the same type of things.
- Terminology: ‘line’ is an unclear indication, because it might mean two very different things. It might mean an ‘empty line’, as in ‘empty line space’, or it might mean a ‘rule’ (a printed element). Please clarify.
- Internal conflict: In the Draft guideline, white lines are frequently used to separate headings from the subsequent paragraph and to separate paragraphs. However, there are also several white lines within paragraphs. This might not be intentional, but it contradicts this advice.

Section 4. Print colour.
- Editing: The whole section is about package leaflets. The word ‘print’ in the title can be deleted.

‘Readability is not only determined by print size.’
- Terminology: ‘Readability’ is not the correct word: it is about the ‘accessibility, comprehension and applicability’ of information in package leaflets.
- Terminology: This is the third term: ‘print size’, ‘type size’, ‘font size’. Please clarify.

‘Characters may be printed in one or several colours allowing them to be clearly distinguished from the background.’
- Terminology: Characters cannot be printed in ‘several colours’.
- Terminology: ‘characters’ or ‘type’?
- Editing: The choice of the colour is strongly related to the ‘contrast’ in bullet 3 of section 2. It is not clear why the colour of the type is mentioned again.

‘A different type of colour is one way of making headings clearly recognisable.’
- Editing: This information is also mentioned in section ‘3. Headings’. It is not necessary to repeat it here.
- Editing: What is ‘a different type of colour’? Is this just ‘a different colour’?
- Criteria: it is suggested here that headings must be ‘clearly recognisable’. In the previous section, headings ‘help patients navigate a text’, ‘stand out’ and must appear ‘consistently’. The relation between ‘recognisable’ and these other three criteria is not clear.

‘Contrast is important, and the relationship between the colours used is as important as the colours themselves.’
- Editing: It is not clear which contrast is meant here. Contrast between different colours? Contrast between colour and background?
- Editing: In section 2, bullet 3, the contrast between the text and the background is classified as important. In this guidance, the relationship between colours is important and the colours themselves are important. That is not very useful guidance.

‘As a general rule dark text should be contrasted against a light background.’
- Terminology: ‘dark text should be contrasted’ is not an appropriate advice, if ‘printed on’ or ‘Use dark text on a light background’ is meant.

‘But there may be occasions when reverse type may be used to hightlight particular warnings.’
- Assumption: Can reversed type only be used to highlight particular warnings? It might be very suitable to make primary level headings more salient.
- Terminology: The term ‘reverse type’ is always confusing, because it might also mean ‘reading from right to left’. It might be clearer if an example is used. For example ‘white text on a black or coloured background’.

‘In such circumstances the quality of the print will need careful consideration and may require the use of a larger font or bold text.’
- Terminology: ‘larger font’? or ‘larger font size’? or ‘larger type size’?

- Editing: It is always necessary to consider the quality of print carefully, not only when reversed type is use.

'Reversed-out text is particularly difficult for older readers.'
- Unsupported assumption: please provide evidence for this statement. If this is the case, it will come out of a readability test. It should not be assumed in a guideline.
- Terminology: What exactly are 'older readers', and how do they differ from 'patients' or 'users'?
- Terminology: 'reversed-out text' or 'reverse type'? If the same thing is meant, please use the same words.

'A different colour is one way of making headings or important information clearly recognisable.'
- Editing: 'different colour'? Different from what? This is the third time that this advice about headings and colour is given.
- Editing: Colour can make 'important information' clearly recognisable. However, no advice is given how to establish what 'important information' is, and how this can be distinguished from 'not so important information'.

'Red colour print should be reserved for very important warnings only'
- Terminology: 'print', or 'characters', or 'text', or 'type'? Please use terminology consistently.
- Assumption: This statement assumes that there are 'very important warnings', 'important warnings' and 'warnings'. The guideline should give advice on how to distinguish between these three levels, so that the 'very important warnings' can be treated in a different way.
- Typography: Please add a full stop at the end of the sentence.

Section 5. Syntax.

'Some people may have poor reading skills, and some may have poor health literacy'.
- Assumption: This certainly is true, but the Directive states 'full and comprehensible information'. Poor reading skills and poor health literacy certainly need attention, but it is not clear how this statement relates to the first paragraph in section A, where 'older children and adolescents, those with poor literacy skills and those with some degree of sight loss' are mentioned. Is there a difference between 'poor literacy skills' and 'poor reading skills' or 'poor health literacy'? If there is, please clarify. If there isn't please use the same terms. The fundamental problem is touched on here: how can we provide people with relevant information about medicines? Simple solutions like: 'Aim to use simple words of few syllables'do not even scratch the surface of this issue.
- Assumption: 'Simple words of a few syllables' assumes that they are easier to understand, but how can we distinguish between 'simple words' and 'other words'? Again, the readability test will provide a very clear indication if words are understood.

'Punctuation should be simple.'
- Terminology: punctuation is always simple because there is a very limited number of symbols available. What is meant here is that long sentences should be avoided. The guidance is: 'Avoid long sentences by dividing them into shorter ones.'

'Sentences should be no more than about 20 words. It is better to use a couple of sentences rather than one longer sentence, especially for new information.'
- Assumption: It is assumed that sentences longer than 20 words are harder to read than sentences shorter than 20 words. The figure 20 is questionable (why not 18 or 21?) as well as its applicability in different languages (is this figure the same for all European languages?). Again, this statement pre-judges the test results of a readability test.
- Assumption: The phrase 'especially for new information' is confusing. This guidance suggests that new information can only be introduced in sentences shorter than 20 words.

'Long paragraphs can confuse readers, particularly where lists of side effects are included.'
- Unclear terminology: A paragraph is a textual unit that is visualised by typographic means. A paragraph cannot include 'lists'. Those lists would separate the paragraph. What might be meant here is that a single paragraph describes several side effects.
- Assumption: 'long paragraphs can confuse readers'. This is unsubstantiated and assumes the reactions of test-participants. Furthermore, it is not clear what a 'long' paragraph exactly is. Please define.

'The use of bullet points for such lists give a more open approach.'
- Criteria: 'open approach'. It is not clear why this 'open approach' would be beneficial, and what an 'open approach' exactly entails.
- Unclear advice. There is a suggestion that only lists of side effects must be bulleted. That is not the case. The use of bulleted items in a list format must be considered for all lists.

'No more than five or six bullet points in a list are recommended.'
- Unsubstantiated assumption. Please provide a reference for this statement. It pre-judges the results of readability tests. If a readability test shows that lists with more than 5 or 6 bullet points are acceptable, there is a conflict.

Fourth bullet.
- Typography: the first sentence needs to be indented further. (The space between the bullet and the capital A is smaller than in the previous bullet.)

'A list of bullet points should be short and should be introduced with a colon, with a single full stop at the end of the list.'
- Editing: this sentence is grammatically incorrect. Suggestion: 'A list of bullet points should be short. It should be introduced with a colon. The individual list items should not have punctuation at the end of the item. The list should end with a single full stop at the end of the last item.'
- Editing: 'a list of bullet points should be short'. In the third bullet, the suggested length of a list is limited to a maximum of 5 or 6 bullet items. This replication of advice must be avoided.
- Editing: 'single full stop'? In which situations are 'multiple full stops' used? Please delete 'single'.

'The list should begin with the uncommon and specific case, and end with the common or general case, unless this is inappropriate for the product.
- Advice conflicts with research findings. Steehouder & Janssen found that it is beneficial for readers to start with the most common situations. See: Michael F. Steehouder and Carel J.M. Jansen (1996): The Sequential Order of Instructions: Impact on Text Quality in: Theory and research.

- 'Inappropriate for the product' is not the right phrase. The aim of the readability guideline is to make information for readers of package leaflets. The aim is not to modify the sequence of list items to suit specific products.

'For example:
Tell your doctor if you are suffering from:
• pulmonary tuberculosis
• any allergies that affect your lungs
• any chronic lung condition.'
- The example shows white lines between each item. In the limited space of package leaflets, there is rarely possible. If these white lines are not intentional, please delete them and put the four lines of text without extra white space on four subsequent lines.
- Terminology: the words pulmonary (= lung related), affect (= related to), condition (= problem) are difficult. It is also not clear why 'allergies' can be mentioned here without the word 'hypersensitive' in brackets, while this is obligatory in the EMEA/QRD template.
- Practical: How can a patient know if it is an 'allergy that affects their lungs'? Patients are unlikely to know if an allergy causes their lung problems. Their lung problems might be caused by something else (virus, bacteria, smoking). And does this exclude all other reasons that affect their lungs? Do patients have to mention that they smoke?) It also raises complex questions: Is asthma an allergy? Does this phrase actually mean 'hay fever', or 'penicillin allergy'?
- Suggested alternative:
  'Tell your doctor if you have lung problems, including
  • allergic problems (for example asthma, wheezing)
  • tuberculosis (also called TB or pulmonary tuberculosis)
  • other long-term lung conditions.'

Section 6. Style.
'When writing, use an active style by placing the verb at the beginning of the sentence, for example:-'
- Good point: use an active style.

- Languages: I'm not convinced that this is correct in all EU-languages. It is certainly applicable to some, but not all.
- Editing. The style of the presentation of the 'for example' differs from the presentation in section 5. The sentence should be: '… of the sentence. For example:' The hyphen after the colon can be deleted.

'- 'take 1 tablet' instead of '1 tablet should be taken',''
'- 'you must….' is better than 'it is necessary …''
- Typography. Please use single quotation marks, and not 'feet-marks'. Please use the ellipsis accurately and consistently: first a space, than 3 full stops.
- Editing: The EMEA guidelines state that the word 'should' must be avoided. It can therefore not appear in a guideline, because this example is in direct conflict with the EMEA-guidelines.

'Give reasons when telling patients what action to take.'
- Assumption: Every action needs to be supported by a motivation. This is not appropriate in all situations. For example 'Take 1 tablet'. In this example, it is not necessary to 'give reasons when telling patients what action to take'. It is necessary to modify this advice.

'Instructions should come first, followed by the reasoning, for example: 'take care with X if you have asthma –it may bring on an attack'.
- Assumption: instruction should come first. Michael Wogalter showed that that is not very beneficial for warnings. Warnings must start with a clear 'attention-grabbing' device, before the instruction can be given.
- Editing. The style of the sentence differs from the style in section 5. '… reasoning. For example: 'take …'.
- Internal conflict. The action in this example is 'to take care'. However, this is not very helpful for patients. Just 'taking care' is not a suitable advice, because it does not tell patients what to do. What does a patient exactly have to do to avoid an attack?
- Typography: please insert a space between the hyphen and 'it'.

"It" should be used rather than repeating the name of the product, as long as the context makes clear what the pronoun refers to.'
- Typography: Please replace the double quotation marks by single ones: 'it'.
- Conflict with testing: 'as long as the context makes clear'. That is up for the participants in the readability test to decide. It cannot be assumed beforehand.

Avoid repetition of information by cross-referencing to information which is under another heading where this is appropriate.
- Editing: Please delete 'where this is appropriate'. It is unclear. It might mean that some information must be mentioned under another 'appropriate' heading and that a cross reference must be used. This implies that some information can appear in different locations in the leaflet. This will certainly confuse readers. It might also mean 'Cross-reference to information, where this is appropriate.'
- Assumption: Cross referencing is more effective than repetition. Repetition is in some situations required. It cannot be assumed that patients read the whole leaflet, or that they can be bothered to follow a cross-reference.
- Conflict with EMEA-template. In section 2, there is a standard phrase: <If you are allergic (hypersensitive) to {active substance(s)} or any of the other ingredients of X.> The list of other ingredients appears in section 6. In this case it would be 'appropriate' to include a cross-reference. The EMEA-template does not conform on this point with the Draft readability guideline.

'Avoid abbreviations unless they are appropriate.'
- Guideline: I expect that a guideline would tell me when an 'abbreviation is appropriate', or at least provide me with practical advice on how to establish this.
- Assumption: 'appropriate' for whom? This pre-judges the results of consultations with target patient groups. Only readability test participants can determine if an abbreviation is appropriate or not.

'When first used in the text, the meaning should be spelled out in full.'
- Terminology: it is not clear if this applies to all abbreviations, or only to the appropriate abbreviations. For example, the strength must be mentioned in the second line of the package leaflet.

The abbreviation ‘mg’ or ‘IE/ml’ is appropriate here. This guidance states that these abbreviations should be spelled out in full. This is further complicated by brandnames which include the strength.

‘All technical terms should be translated into language which patients can understand.’
- Good point: but how? Especially if patients also includes ‘those with poor literacy skills or poor health literacy.’

‘*Consistency should be assured in how translations are explained by giving the lay term with a description first and the detailed medical term immediately after.’*
- Good point: The EMEA-template gives an example: ‘… if you are allergic (hypersensitive) to …’

‘On a case by case basis the most appropriate term (lay or medical) may then be used thereafter throughout the package leaflet in order to achieve a readable text.’
- Editing: delete ‘the package leaflet in order to achieve a readable text’ This is confusing, because it is not only the text that determines readability.

‘Make sure that the language used alerts patients to all the information relevant to him, and gives sufficient detail on how to recognise possible side effects and understand any action which may be necessary.’
- Poor guidance: How can we make sure? This suggests that the ‘language’ alerts patients. In many situation, the design must emphasise this alert.
- Editing: the words ‘patients’ (plural) and ‘him’ do not match.
- Terminology: ‘sufficient detail’. This is not enough. The directive clearly states: ‘full and comprehensible’. This is not the same as ‘sufficient’.
- Unclear: The word ‘possible’ in the phrase ‘possible side effects’ can be deleted. Patients must be able to recognise all side effects.
- Unclear: Patients must take actions. Just understanding the action is not sufficient.

Suggestion: delete this paragraph.

‘All main section headings will be included within the leaflet but sub-headings and associated text within the leaflet should only be included if these are relevant for the particular medicine.’
- Editing. The sequence of information of the whole guideline turns out to be problematic. This advice refers to ‘all main section headings’. Unfortunately, these ‘main section headings’ have not been mentioned yet. It is likely that this phrase refers to the main section headings in the EMEA/QRD template, but this reference is lacking. The reference is described in section 10.
- Terminology: ‘sub-headings and associated text’ = ‘items’ in the EMEA-template.
- Internal inconsistency: ‘relevant for the particular medicine.’ This is incorrect. All information of the SMPC must be included. The information cannot be relevant ‘for the particular medicine’. Information can only be relevant to ‘people’.

‘For example if there is no information in relation to excipients of known effect this section may be omitted from the package leaflet.’
- This is very strange advice. If there is no information, it will not be included in the SMPC. It can therefore not be included into the package leaflet.
- Terminology: It is not clear which section is exactly refered to here. It might be ‘Important information about some of the ingredients of X’, or it could be in the section ‘What X contains’ the phrase ‘The other ingredient(s) is (are) …’
- Editing. The phrase ‘excipients of known effect’ is not very clear.

Section 7. Paper.

‘For long leaflets, paper size of A4/A5 is preferable because paper of these dimensions can most easily be turned over and followed in a user-friendly way and is also easier for the patient to put back into the pack.’
- Assumption: It is not possible to get the text of the EMEA-template in 12 points onto an A5 sheet of paper. There is simply too much text in the template to use an A5 size.
- Assumption: There is no research that indicates that A-size leaflets are easier to turned over than leaflets of non-A-size dimensions.
- Assumption: There is no research that indicates that A-size leaflets are easier to follow in a user-friendly way.

- Assumption: There is no research that indicates that A-size leaflets are easier to put back into the pack.

All four assumptions pre-judge the results of readability test. Other dimensions might just be as good.

Suggestion: Delete this advice. It is inaccurate and inappropriate.

'Paper weight should be no less than 40g/m2. Thinner paper may be too transparant and thus difficult to read.'

- Assumption: The threshold is 40 g/m^2. There is no reason to assume that 40 g/m^2 is the minimum weight. Only readability testing can indicate this.
- Terminology: This is the first time that the abbreviation 'g/m^2' is used. According to the guideline, the meaning needs to be spelled out in full.
- Typography: Please use a superscript 2 in m^2.
- Typography: The EMEA suggests separating the number and the unit by a non-breaking space. Please follow the EMEA-suggestion in this guideline.
- Editing: the paper is not difficult to read. The text on the paper might be difficult to read.

'Glossy paper reflects light making the information difficult to read, so choose uncoated paper.'

- Editing: All paper reflects light.

Section 8. Use of symbols and pictograms.

The legal provisions within Article 62 of Directive 2001/83/EC permit the use of images, pictograms and other graphics to aid comprehension of the information, but these exclude any element of a promotional nature.

- Terminology: 'The words 'images' and 'other graphics' do not appear in the Directive. The directive states: 'The outer packaging and the package leaflet may include symbols or pictograms designed to clarify certain information … which is useful for the patient, to the exclusion of any element of a promotional nature.' There are some fundamental differences between 'symbols', 'pictograms', 'images' and 'other graphics'. A guideline should not add to the confusion about the terminology.
- Terminology: There is a fundamental difference between 'to clarify certain information … which is useful for the patient' and 'to aid comprehension'. These two things are not the same. Please make the guideline in line with the Directive texts.

'Symbols and pictograms can be useful provided the meaning of the symbol is clear and the size of the graphic makes it easily legible.'

- Editing: What happens to the pictograms in the second part of the sentence? Delete: 'of the symbol'.
- Assumption: 'provided the symbol is clear'. This assumes that 'symbols and pictograms' have an inherent quality that makes them 'clear' or 'less clear'. This is not the case. Only people can interpret symbols and pictograms.
- Assumption: 'There is a direct relation between the size of the graphic and 'easily legible'.' This is unlikely to be true in all situations.
- Terminology: The terms 'Symbols', 'pictograms', and 'graphics' are not used consistently. They are different types of visual elements and need to be treated as such.
- Criteria: The criteria for the visual elements are 'a clear meaning' and 'easily legible'. These two criteria do not do justice to the use of visual objects. There are many more appropriate criteria, such as, for example the speed of recognition.

'They should only be used to aid navigation, clarify or highlight certain aspects of the text and should not replace the actual text.'

- This advice is in conflict with the text in the Directive. The directive states that symbols and pictograms 'clarify certain information, which is useful for the patient'. The above phrase interprets 'information' as 'text'. This is a severe limitation, because some information cannot be given in text-only formats. Visual instructions for inhalers are an example.

'Consultation of patients of all symbols will be useful to ensure the meaning is generally understood.'

- Terminology: Why only 'symbols'? What happened to the other visual elements, such as graphics, pictograms and images?
- Criteria: 'the meaning is generally understood.' This is another criteria related to visual elements only? How does this relate to the 90% of 90%. Is that the same as 'generally understood'?
- Editing: It might be clearer to state: 'It is necessary to include the visual elements in the user test.'

'Pictograms, symbols and graphics should not be misleading, confusing, or contrary to the standards of good taste and decency, and should not be promotional.'
- Editing: this is the general aim of the provision of information to patients. It is not specifically applicable to symbols and pictograms.

'If there is any doubt about the meaning of a particular pictogram it may be considered inappropriate.'
- Assumption: It is possible to make pictograms that cannot cause any doubt. The ISO-tests of pictograms indicate that the maximum score is well below the 100% level. This guidance makes it impossible to use pictograms of any kind.

'Particular care will be needed when symbols are transferred or used in other language versions of the leaflet and further user testing of these may be necessary.'
- Practical problem: If a user test in a particular situation indicates that a symbol is less well understood, can it still be included in package leaflets where it is well understood? Does this not create a difference between countries and makes the harmonization less likely (equal access to information for patients).

Section 9: Additional information.
Section 9.1. Product ranges.
- Please modify the design of the list according to the guidance in section 5 by deleting the hyphen after the colon and deleting the three commas at the end of the first three bullets.
- Spelling: please spell side-effects without a hyphen.
- Please replace the URL of the EMEA with the new one: http://www.emea.europa.eu
- Editing: It is not clear why section 9 is subdivided into sections 9.1 and 9.2, while the subheadings in all other sections do not get a secondary numbering.

9.2. Products administered by a healthcare professional.
- Terminology: The title mentions 'healthcare professional', the first line mentions 'health professional'. Are these the same?
- Typography: Second paragraph, second line. Delete space after the first (.

Section 10. Templates for the package leaflet.
- Typography. Third paragraph: remove double quotation marks.
- Terminology: 'full colour mock up of the package leaflet.'? The Directive makes a difference here: it requires a draft.
- Spelling: mock up is spelled earlier with a hyphen.
- Editing: please use 'mock up' in the final sentence, and not 'mock'.

Section B. Recommendations for the Labelling.

Paragraph 1

Labelling covers both outer packaging and inner packaging which may include a lesser set of particulars. Nevertheless, many of the principles of good practice in relation to outer packaging will apply equally to the labelling applied to small containers and other inner packaging components.

- Editing: 'which may include a lesser set of particulars' can be deleted. The word 'may' is confusing. The Directives describe exactly what needs to be mentioned on the labelling.
- Terminology: 'Many of the principles of good practice' is not very specific. Does this mean that the Draft guidance describes these principles? Or are they mentioned elsewhere?
- Terminology: Is there a difference between 'inner packaging' in line 1 and 'inner packaging components' in line 4?

Paragraph 2

'Labelling ensures that the critical information necessary for the safe use of the medicine is legible, easily accessible and that users of medicines are assisted in assimilating this information so that confusion and error are minimised.'

- Criteria: 'legible', 'easily accessible' and 'users of medicines are assisted in assimilating this information' are all three new criteria. The Directive mentions: 'easily legible, clearly comprehensible' and indelible'. These are not the same as 'legible', 'easily accessible' and 'users of medicines are assisted in assimilating this information'.
- Two new aims: 'confusion is minimised' and 'errors are minimised'.
- People: 'users of medicines' is another way to describe a specific group of people.

'In preparing this guidance, it is acknowledged that different users of medicines require and use information differently. Those involved in the design of labelling and packaging components should ensure that the following sections are taken into account prior to submission to the competent authority as any deviations from this guidance may need to be justified.'

- Terminology: 'Users of medicines' is a confusing term. It could mean 'patients', but it might just as well refer to 'healthcare professionals'.
- Terminology: The phrase 'labelling and packaging components' is not clear. According to the first line of Section B does labelling cover both outer packaging and inner packaging. What are the packaging components?

'The recommendations on print size and type, layout and colour given in relation to the package leaflet (section A) are equally applicable to labelling and should be borne in mind in designing and laying out the required information on labels.'

- Editing: The reference to section A is not very clear. 'Print size and Type' is the title of a section. 'Layout' is only part of the title of a section 'Design and layout of the Information'. 'Colour' is part of the section 'Print colour'. What happened to the sections 'Headings', 'Syntax', 'Style' and so on? Are these parts of section A not applicable to the labelling?
- Terminology: 'required information on labels' is confusing. Is 'labels' the same as 'labelling'?

'In particular the information presented on small packs will need careful consideration so that the text is presented in as large a font as possible to reduce the likelihood of medication error.'

- Advice: 'will need careful consideration' implies that other information does not need to be considered as carefully.
- Editing: The word 'particular' means something different from the word 'particular' in the Directive. It is not necessary here. This phrase can be deleted. The information repeats the previous sentences.
- Terminology: 'as large a font' is incorrect. A font cannot change its size. Type size might be more appropriate here.
- Assumption: This phrase makes a direct link between the type size and the likelihood of medication error. Although it is very likely that such a relation exists, it is not proven to be the case.
- Editing: This phrase confuses 'information' (= content) and 'visual design' (presented in as large a font as possible). Both the contents and the design need to be considered together in such a way that it 'enables the user to act appropriately'.

General considerations

Labelling must contain all elements required by Article 54 of Directive 2001/83/EC or a lesser set of particulars where the provisions of Article 55 apply. Nevertheless, out of a total of 15 information items, certain items of information are deemed critical for the safe use of the medicine.

- Terminology: Is there a difference between 'elements', 'items of information' and 'particulars'?

These items are:
• name of the medicine and its strength
• total content (where relevant)
• route of administration
Where possible these should be brought together using a sufficiently large font on the pack and on immediate packaging in the same field of view to aid users.
- Terminology: 'sufficiently large font' is incorrect. A font cannot change its size. It is not clear what 'sufficiently large' is. That should be tested.
- Terminology: The phrase 'on the pack and on the immediate packaging' can be deleted. This is covered by the main heading of section B in the term 'labelling'.
- Assumption: Placing the three particulars in the same field aids user. I'm not sure that that is the case. In some situations, it might be beneficial to describe the pharmaceutical form, or the method of administration.
- Typography: Please add a full stop after the third item of this bulleted list. The guideline should follow its own advice.

1. Name of the Medicinal Product
Article 54(a) of Directive 2001/83/EC sets out what is required in relation to the name of the medicinal product: The full name of the medicinal product, with its strength and its pharmaceutical form, and, if appropriate, whether it is intended for babies should appear on the outer packaging (the carton) and on the immediate packaging to aid accurate identification of the medicinal product. Where the medicinal product contains up to three active ingredients, the common name(s) of these active ingredient(s) should immediately follow the invented name of the medicinal product on the outer packaging and the immediate packaging, unless the common name(s) is part of the name. For requirements concerning Braille, see chapter 2.
- Editing: This paragraph seems to quote from article 54(a) of Directive 2001/83/EC. This text does not appear there: it is amended by Directive 2004/27/EC. Please note that the text in the Draft Guideline is not a copy of the text in the Directive. The Directive states: '(a) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults; where the products contains up to three active substances, the international non-proprietary name (INN) shall be included, or, if one does not exist, the common namen;' Can this difference be explained?
- Typography: A substantial part of this paragraph is a quote from the Directive. This is not visually made clear.

2. Strength and total content
- Editing: Please note that the titles of the sections 1, 2 and 3 do not exactly follow the descriptions of the items in the list of bullets in the General considerations. Is there a difference between 'medicine' and 'medicinal product'? Why is 'strength' linked to the 'name of the medicine' in the bulleted list, and linked to 'total content' in section 2?

In some cases the packaging may need to contain information on the quantity per unit volume and also on the total quantity per total volume. The total quantity per total volume can be particularly important for safety reasons for injectable products and other medicines available in solution or suspension.
- Editing: 'Some cases' is not clearly explained. Is it possible to be more specific?

Different strengths of the same medicinal product should be expressed in the same manner: for example 250mg, 500mg, 750mg, 1000mg and NOT 1g.
- Typography: The EMEA suggests to use a non-breaking space between the number and the unit.

Trailing zeros should not appear (2.5mg and NOT 2.50mg). The use of decimal points should be avoided where these can be easily removed (i.e. 250 mg is acceptable whereas 0.25 g is not).
- Editing: It is always 'easy' to remove decimal points. Please delete 'easily'.
- Typography: In the last two instances, there is a space between the number and the unit.

The decimal point need not be centred, provided that if a full stop is used it is clearly visible.
- Editing: 'Clearly visible' is a criterion. For whom?

For safety reasons it is important that micrograms is spelt out in full and not abbreviated. However, in

certain instances where this poses a practical problem which cannot be solved by using a smaller point size then abbreviated forms may be used, if justified and there are no safety concerns.
- Terminology: It is not possible to use a smaller point size. 'Type size' or 'character size' is more correct here. (Point size is a unit of measurement.)
- Editing: Which 'abbreviated forms' of 'microgram' are acceptable?

3. Route of administration
This should be as registered in the summary of product characteristics only according to the standard terms. Positive messages should be used; for example "For intravenous use only" and only standard abbreviations may be acceptable (i.v., i.m., s.c.,).
- Internal conflict: Section 6 'Style' in Chapter 1 advises to avoid abbreviations unless they are appropriate and states that the meaning should be spelled out in full.

Non-standard routes of administration should be spelt out in full to avoid confusion. Some routes of administration will be unfamiliar to patients and may need careful explanation. This is particularly important when medicinal products are made available for self-medication.
- Spelling: Chapter 1, section 6 uses 'spelled'. Here 'spelt' is used.
- Critirion: 'To avoid confusion' is a new criterion. Is it the 'unfamiliarity' that causes 'confusion'? Unfamiliarity might cause several other things too.
- Editing: 'need careful explanation' might be replaced by 'need to be explained.' I'm not sure how I could 'carefully explain things'. All explanations must be 'careful'.
- Editing: The last sentence can be deleted. It is in conflict with the provision of a license to 'self-medication medicines'. Self-medication medicines can only be registered when they are 'relatively safe'. If their route of administration is unfamiliar to patients (consumers?), and causes confusion, it should not have been registered as 'self-medication'.

4. Design and layout
Applicants/marketing authorisation holders must make best use of the space available to ensure that the critical / important information is clearly mentioned on prime spaces on the outer and immediate packaging, printed in a sufficiently large font.
- Typography: Please use the spaces around the slash consistently.
- Criterion: 'clearly mentioned'. Please delete 'clearly' or provide guidance on how to establish if information is 'clearly mentioned'.
- Editing: What is the difference between 'critical information' and 'important information'?
- Editing: What are 'prime spaces'?
- Terminology: 'sufficiently large font': please use 'type size'. How can 'sufficient' be measured?
- Terminology: Some information is not 'printed' in the traditional sense of the word. 'Presented' might be clearer.
- Editing: Please delete 'on the outer and immediate packaging'. Chapter 2 is about 'Labelling'.

Consequently, company logos and pictograms (if accepted) may be presented where space permits in a discreet manner on the outer packaging and on immediate packaging units, provided it does not interfere with the legibility of the legislative text.
- Criterion: How can I find out what 'a discreet manner' is? Can this Guideline guide me?
- Terminology: 'outer packaging and on immediate packaging units'. What is the difference with 'labelling'?
- Assumption: Visual elements (logos, pictograms) always interfere with the legibility of the legislative text. A visual element will always attract attention earlier because it is visually more salient. This phrase prevents the use of any visual elements on labelling.

Use of a large font will be appropriate, although other factors may also be important in making the information legible.
- Terminology: 'Large font' is incorrect: large type size.
- Editing: 'although other factors may': The whole guideline is about the legibility of information. It is fairly clear that other factors 'are important'.
- Editing: The need to make texts on labelling as large as possible is mentioned in paragraph 2 of chapter 2. It is not necessary to repeat it here.

Consideration should be given to the line-spacing and use of white space to enhance the legibility of the information provided.

- This is a correct statement, but a guideline should provide advice on how to do consider these factors.

For some small pack sizes it may not be possible to present all the critical information on one face.
- Terminology: Is 'one face' the same thing as 'field of view' as it is mentioned in 'General recommendations'?
- Editing: 'small packs' or 'small pack sizes'?

Colours should be chosen carefully to ensure a good contrast between the text and the background to assure maximum legibility and accessibility of the information.
- Advice: How can colours be chosen carefully? Please delete 'carefully'.
- Assumption: There is a direct relation between the accessibility of the information and colours. This is unlikely to be the case. People cannot separate colours from the other graphic variables.

Highly glossy, metallic or reflective packaging should be avoided, as this affects the readability of the information.
- Terminology: Here 'readability' is used, while the previous sentence states 'legibility'. What is the difference?

Different colours in the (invented) name of the product should be avoided, whereas use of different colours to distinguish different strengths is strongly recommended.
- Unclear: Why is it essential to avoid different colours in the name of the product?

Similarity in packaging which contributes to medication error can be reduced by the judicious use of colour by marketing authorisation holders.
- Terminology: Please add 'applicants'.
- Advice: Please provide advice on how to develop a 'judicious use of colour'. How can I establish if I have achieved that?
- Assumption: The only people who can judge if there is a similarity in packaging are those who use it. Pharmacists, nurses and patients can provide very valuable reactions if they are involved in the development of packaging. A reduction of medication errors can only be achieved if the marketing authorisation holder integrates the contacts with 'people who handle their products' into their information development process.

The number of colours used on packs will need careful consideration as too many colours could be detrimental to patient safety.
- Assumption: the number of colours is directly related to patient safety. I'm not sure that this is correct. Four colours are safe, five are unsafe?
- Editing: Please delete 'careful': all details need to be considered.

The use of innovative outer packaging design is regarded to be of particular importance where space is at a premium. Any colour used on the outer pack should be carried onto small containers to aid identification of the medicine.
- Editing: Space on outer packaging is always at a premium. This sentence is placed oddly between two sentences about the use of colour.

5. Templates for labelling

The templates provided in all EEA languages on the EMEA Website http://www.emea.europa.eu/index/indexh1.htm (Human Medicines - Application Procedures – Product Information Templates) reflect the items which must appear on the labelling and package leaflet of medicinal products according to Directive 2001/83/EC.
- Terminology: 'Items' or 'particulars'?

They will help to ensure that the statutory information appears as intended by the Directive, and to ensure consistency in the information provided across a number of different medicines.
- There is one discrepancy between the EMEA template and the Directive. The sequence of the particulars in article 59 (f) is not followed in the sequence of the template. The name and address of the manufacturer (item vii in the Directive) is mentioned before the names of the appointed representatives in the Member states (item v in the Directive).

The use of these templates applies to Mutual Recognition, Decentralised and Centralised applications. For national applications, national templates may apply.

For applications in the Centralised Procedure, product information is to be presented in the mandatory format and lay-out (see "QRD convention" on the EMEA Website) using the electronic product information templates
- Editing: Please add a full stop after templates.

Section C Immediate Packaging
The guidance provided in section B above will apply (where relevant) to immediate packaging.
- Editing: Please delete 'above'.
- Terminology: Section B starts with 'inner packaging'. This section is called 'immediate packaging'. Is there a difference?

1. Blister Pack Presentation
For blister pack presentations it is important that the particulars remain available to the user up to the point at which the last dose is removed. Often it will not be possible to apply all the information over each blister pocket, consequently where a random display of the information is proposed it should frequently appear across the pack. In all cases it will be acceptable to apply the batch number and expiry date to the end of the blister strip. As it is technically possible applying this information to both ends of each strip should be considered. Where a unit-dose blister presentation is proposed all the information required for blister packs must appear on each unit dose presentation. In addition, blister foils should be printed to ensure maximum legibility of the statutory information using a sufficiently large font.
- Terminology: Printing does not ensure maximum legibility. Only people can judge if information on blister foils can be read.
- Terminology: 'sufficiently large font' is not possible. Type size is required.

Colour for the text and the font style, should be chosen carefully as the legibility of the text on the foil is already impaired due to the nature of the material.
- Terminology: 'Font style'? Is this the same as typeface?
- Editing: Please delete 'carefully'. All design factors need to be considered.
- Editing: 'The nature of the material impairs the legibility' is incorrect. It is not the material, but the way in which we can look at foils that makes information on foils difficult to read.

Where possible, nonreflective material or coloured foils should be considered to enhance the readability of the information presented and the correct identification of the medicine.
- Terminology: In the previous sentence, the nature of the material impaired the 'legibility'. In this sentence, nonreflective materials enhance the 'readability'. Why are both terms used?
- Assumption: the identification of the medicine is related to 'nonreflective materials'.

2. Small Containers
Where the labelling particulars set out in article 54 of Directive 2001/83/EC cannot be applied in full to the labelling of small containers, as a minimum the particulars set out in Article 55(3) of the directive should be applied.
- Editing: incorrect sentence structure.

Other information required in Article 54 can be added where space permits. The criteria for small container status would normally apply to containers of nominal capacity of 10ml or less.
- Typography: please add a non-breaking space between 10 and ml.

However, other factors may need to be taken into account such as the amount of information which has to be included and the font size necessary to ensure the legibility of the information.
- Terminology: Please replace 'font size' by 'type size'.

Innovative pack design will be of particular importance where space is at a premium (e.g. the use of wrap-around or concertina labels).
- Editing: Space is always at a premium when information on small containers need to be developed. The advice is: 'Consider other forms of pack design that enables people to act appropiately.'

Paper labels are recommended to increase the legibility of the information applied to for example ampoules.
- Assumption: paper labels increase the legibility.

Annex 1.
Illustration – One Way of Undertaking a Test of a Package Leaflet
This information is included for illustrative purposes only and is an example of a method that could be used for consultation with target patient groups.

The method described covers one-to-one, face-to-face, structured sets of interviews, involving at least 20 participants reflecting the population for whom the medicine is intended[1]. As indicated above, other performance-based methods are equally valid, and competent authorities will judge applications on a case by case basis.
- Test participants: 'reflecting the population for whom the medicine is intended'. That is not very clear: does this mean 'real patients', or 'healthy volunteers'?
- Typography: Delete the superscript 1 after intended.

1. Performing the test
- *Testing of Package Leaflets may be done by the MA holder or a suitably qualified company on its behalf.*
- Assumption: It is not clear how a company can be 'suitably qualified' and how to distinguish this from companies who are not.
- Typography: Package Leaflet should be spelled in lowercase characters.

- *It should be carried out by an experienced interviewer with good interview, observational and listening skills.*
- *Ideally the writer of the Package Leaflet will carry out the interviews, or occasionally accompany the interviewer during testing, to enable direct transfer of learning.*
- Assumption: there is a single writer who can be present at the interviews. A characteristic of the writing of package leaflets is that many people are involved in the development of the texts.
- Furthermore, it is not only the 'writer', but also the 'designer' who needs to be involved.

2. ***Recruiting Participants***
- Typography: Please make the number 2 bold.

- *Ensure a range of different types of people who are able to imagine needing to use the medicine.*
- Participants: 'a range of different types of people' 'who are able to imaginge needing to use the medicine'. I'm not sure if I can distinguish 'types of people'. I can distinguish between the characteristics of individual people.
- Participants: 'imagine needing to use the medicine'. This seems to be in conflict with the first line of this section: 'reflecting the population for whom the medicine is intended'. This difference can be fundamental.

- *If the medicine is intended for a rare illness, then where possible test the leaflet among people who actually have or have had the illness. You may need to exclude people who have previously taken or are currently taking the medicine.*
- Participants: There are four categories now: 'people who can imagine needing to use the medicine', 'people who reflect the population for whom the medicine is intended', 'people who actually have or have had a rare illness' and 'people who actually have or have had a rare illness and use or have used the medicine'. Not clear if these differences really affect the results of a readability test.
- Ethical issue: It is in some situations difficult to ask for previous use of medicines and it is not possible to ask for current use of medicines.

• *Remember that information which can be used by the least able will be beneficial for all users.*
- Assumption: Not sure that this is the case. Different levels might be more appropriate.
- Terminology: 'the least able' is another description of people who read package leaflets.

Try and include:
• *particular age groups such as young people and older people – especially if the medicine is particularly relevant to their age group*
- Are 'young people' and 'older people' examples of 'different types of people'?

• *new users or people who do not normally use medicines, particularly for information provided with new medicines likely to be used by a wide range of people (e.g. analgesics or antihistamines)*
- Terminology: 'new users' … 'particularly for new medicines'? I'm not sure how to approach 'new users'. For prescription only medicines, this requires that the medicine must be available on the market. It also depends on the co-operation of a prescriber who brings the interviewer into contact

with this patient. For medicines that are not registered yet, 'new users' are an impossible demand: there cannot be any 'new users'. For OTC medicines, people must be approached at the point of sale with the question: 'Is this the first time that you have bought this medicine?' That might be possible. For medicines used in hospitals, this is an impossible guideline. 'Have you used this anesthetic before?' These patients must have received a medicine for the first time. That can only be true for medicines that are already available on the market. I'm not sure what the effect on the readability test results would be.

• *people who do not use written documents in their working life*
- Assumption: The success criteria mention 'literate adults'. Is there any reason to assume that 'literate adults' must be subdivided into 'people who do not use written documents in their working life' (= manual labourer?), 'people who do use written information in their working life' (= desk worker?), or 'people who do not use written information in any other life' (= retired? housewife?). Unfortunately, every individual in our society has to deal with 'written documents'. Tax forms, bank statements, insurance letters and invoices are fairly common. The classification 'literate adults' varies between 'barely able to read' to 'fully competent'. I'm not sure why 'people who do not use written documents in their working life' need to be singled out in this guideline.

• *people who find written information difficult.*
- Assumption: who doesn't? 'Written information' is a very broad classification. the problem is not in the 'written information'. The problem is in 'reading skills' and 'health literacy' of individual people. I can quite easily interpret IKEA instructions and UNIX software manuals. I personally struggle to interpret a financial annual report or a salary-slip.
- Terminology: is there a difference between 'written information' and 'written documents'?

• *Recruit participants from wherever is most relevant and practical.*
- This is in direct conflict with the advice to recruit people who have or have had a rare illness. Those patients are notoriously hard to find.

For example you could use:
o older people's lunch clubs
o self-help groups
o patient support groups
o community centres
o parent and toddler groups.

3. ***Sample Size and Use***
- Editing: I am not sure what the words 'and Use' refer to in this title.

• *Only small numbers of participants are needed. The aim is to meet the success criteria in a total of 20 participants. The important thing is not to re-test participants whom you have already tested.*
- Unclear advice: 20 participants is an arbitrary figure.

You can achieve this by undertaking:
• *A pilot of around 3-6 participants to test that the questions will work in practice. As you gain experience, you may be able to use just two or three participants in the pilot test.*
- Assumption: It is not about 'gaining experience'. Pilot tests are absolutely essential.

• *Next, at least two rounds of 10 people each, reviewing the results after the first round and making any necessary amendments to the Package Leaflet*
- Unclear advice: How? This is an absolutely crucial stage in the improvement of package leaflets. The guidance must explain how the 'test results' should be interpreted and lead to modifications of the text, the visual design or both.
- Unclear advice: at least 2 rounds of 10 people. Arbitrary figure. It might be more appropriate to use groups of 6 participants.

• *Repeat tests until you have satisfactory data from a group of 10 participants.*

• *A final test of a further 10 to see if the success criteria are also met in this further 10 (i.e. in 20 participants in total).*
- Unclear advice: The minimum number of tests is unclear. The text suggests now to do first 20 interviews, and than a final test. That is 30 interviews in total.

4. ***Success Criteria***

A satisfactory test outcome for the method outlined above is when 90% of literate adults are able to find the information requested within the Package Leaflet, of whom 90% can show that they understand it.

- Participants: now it is 'literate adults'. All other groups seem to be forgotten.
- Unclear guidance. The first line states that 'the aim is to meet the success criteria in a total of 20 participants'. This criteria is now mentioned in percentages. 90% of 20 participants is 18 participants. 90% of 18 participants is 16.2 participants. This last number – 16.2 – makes it impossible to apply the 90% criteria to readability test results. This guidance states that a package leaflet fails the test if 16 people out of 20 can locate and understand the information?

  Furthermore, it is not clear if this 90% level must be calculated per question, as it was mentioned in the previous version of the guideline? Or is it necessary to achieve that level calculated over all questions in a test (20 people times 15 questions = 300 questions. 90% =270 correctly located answers?/243 correctly understood)?
- Criteria: The '90% of 90%' makes different levels of understanding acceptable. (If 100% of the participants can find the information, and 90% of this information is understood correctly, than 90% of the 'literate adults' might be 'enabled to use a medicine appropriately'. If 90% of the participants can find the information, and 90% of this information is understood correctly, than 81% of the 'literate adults' might be 'enabled to use a medicine appropriately'. The difference between 90% and 81% is very substantial. It means that between 1 out of 10 patients and 1 out of 5 patients is not able to understand information about medicines. That is a very low criteria if it is related to vital safety information. It seems necessary to vary the importance of questions according to their relevance and safety.
- Criteria: There is a fundamental issue here by asking 'quantitative results' from a 'quantitative test method'. Those are not compatitable. The main results of the interviews are the remarks of participants, not the correctly located answers or correctly answered questions.

If you use a different method of testing, different success criteria may be appropriate. Competent authorities will consider these on a case-by-case basis.

- Spelling: in the first paragraph 'case by case' is spelled without hyphens.
- Editing: 'method of testing' or 'performance-based method'. Please use consistent terminology.

5. ***Test Protocol***

• You are advised to:

• Draw up a new protocol for each product

- Advice: How? This is not a guideline. It does not explain HOW this protocol must be drawn up. It needs examples or instructions.

• Include questions that address all the important and difficult issues, and use rigorous assessment criteria

- Advice: The sequence of this guidance is strange. This is one of the first things to do. It should not be described at the end of the guidance under 'protocol', but under a heading: 'Preparing for the test'.

• Include a set of expected correct answers

- Advice: The sequence of this guidance is strange. This is one of the first things to do. It should not be described at the end of the guidance under 'protocol', but under a heading: 'Preparing for the test'.

• Design the test to last no more than 45 minutes, to avoid tiring participants

- Advice: How? This is not useful guidance. The pilot test will indicate if a test is long enough or too long.

• Ensure that the questions reflect any specific issues for safe and effective use and compliance issues related to the medicine being tested.

- Assumption: compliance issues? How do you know beforehand if there are compliance issues? The guideline must provide an approach to figure out if there might be compliance issues.
- Terminology: Are the 'specific issues for safe and effective use' the same as the 'important and difficult issues' mentioned earlier? If so, please use same terminology.

Testing is most beneficial when the questions relate to areas where patients' fears are greatest, such as side effects. Avoiding serious safety issues with a medicine during user testing of the Package Leaflet would invalidate the test.
- Advice: How? I expected that the guideline would give advice on how to select the 'serious safety issues' from the 'less serious safety issues.'.
- Terminology: Are the 'areas where patients' fears are greatest' the same as the 'specific issues for safe and effective use' and/or 'important and difficult issues' mentioned earlier? Are 'serious safety issues' the same as 'specific issues for safe and effective use'? How can this be determined?

The interviewer should:
• *Use a written set of questions for reference*
• *Ask the questions orally*
• *Adopt a conversational manner, allowing ample opportunity for interaction with the participant*
- Advice: Ok, but that is not related to the success criteria of the test. What is the aim of 'interaction' if only correctly located scores and correctly answered questions are measured? The main aim of the readability test is to improve the text and design of the leaflet.

• *Ask participants, once they have located the required information, not to repeat it parrot-fashion but to put it into their own words where appropriate.*
- Advice: And record these words verbatim. Participants frequently rephrase medical terminology into perfect common language.
- Terminology: 'parrot-fashion' is a paternalistic term and does not show much respect for test participants. Suggestion: 'If the participant finds the answer and reads the text aloud, it is necessary to ask the participants to rephrase the answer in their own words. A question like: 'What does that mean?', or 'What would you exactly do?' stimulate participants to rethink and rephrase the answer.'

• *As well as recording the answers to the questions, observe how each participant handles the leaflet and searches for information, noting, for example, whether people become lost or confused. This will yield valuable information about how to improve the structure of the Package Leaflet.*
- Advice: Unfortunately, this advice cannot be followed in practice, because the structure of the package leaflet is determined by the Directive and the EMEA template.

• *The questions should:*
- Typography: the design of this bulleted list does not follow the advice of the guideline itself.

• *Adequately cover any critical safety issues with the medicine.*
- Editing: This issue has been dealt with before: double information.
- Terminology: Is there a difference between 'critical safety issues', 'serious safety issues' and 'specific issues for safe and effective use'?

• *Be kept to a minimum; usually 12 -15 will be enough, though more may be required in special cases, e.g. if there are significant safety issues to be investigated*
- Conflicting advice: why should the minimum number of questions be asked? Each interview will provide valuable information about the interpretation of information about medicines. It is therefore essential to optimise each interview, and obtain the maximum amount of feedback. In order to make this advice more appropriate, please delete 'Be kept to a minimum;'
- Terminology: Is there a difference between 'significant safety issues', 'critical safety issues', 'serious safety issues' and 'specific issues for safe and effective use'?

• *Cover a balance of general and specific issues. A general issue might be what to do if a dose is missed, while a specific issue might relate to a side effect that occurs particularly with that medicine.*
- Assumption: Is there any motivation why this balance need to be covered? Some medicines might have many 'significant safety issues' and need to focus the whole interview on these issues.
- Incorrect example: It might be better to use 'disposal' as an example of a general issue.

• *Be phrased differently from the text of the leaflet to avoid "copy-cat" answers, based merely on identifying groups of words.*
- Terminology: It's funny to use both 'copy-cat' as well as 'parrot-fashion'. I would prefer not to address test-participants as animals. Suggestion: 'Be phrased differently from the text of the leaflet. If a participant can find the answer, it is an indication that the issue is understood. After locating the correct answer, a participant still needs to be asked to rephrase their answer in their own words to

check whether the information in the leaflet is understood.'
- The advice is not always appropriate. For example if you need to ask for a particular side effect. 'What should you do if you get a severe stomach ache after you have taken these tablets?' It is very likely that the list of side effects mentions 'stomach ache'. It would not be appropriate to phrase 'stomach ache' in any other way, nor to ask the participant to rephrase this in their own words. The correct answer would be: 'if it gets serious, I need to contact my doctor or pharmacist'.

• *Appear in a random order (i.e. not in the order the information appears in the leaflet).*
- Advice: Correct.

Copies of the protocol(s) including the questions asked, the responses offered, the interviewer's written observations and the different versions of the Package Leaflet tested must be submitted to the competent authority for review.
- Advice: This repeats section 6 of Chapter 3. It violates the guidelines own advice to make cross-reference to other sections.
- Typography: Why is Package Leaflet suddenly spelled with capitals again?
- Clarity: 'The responses offered' might be interpreted as 'all responses'. In a readability test, it is likely that more than 90% of the responses are correct. Adding these correct responses to the readability report does not improve the quality of the package leaflet. It is necessary to include all responses that are related to the ways in which participants found or onderstood information. The report must explain how these responses are considered. These consideration might lead to a modification of the text or the design of the package leaflet, or they might not lead to a modification. It is this argument that is fundamental to the readability test.