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Pharmaceutical Committee	
A GUIDELINE ON THE READABILITY OF THE LABEL AND PACKAGE LEAFLET OF MEDICINAL PRODUCTS FOR HUMAN USE	
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Introduction

Legal framework

Article 4 of Council directive 92/27/EEC requires that the label text shall be easily legible, clearly comprehensible and indelible.

Article 8 of Council directive 92/27/EEC requires that the package leaflet must be written in clear and understandable terms for the patient and be clearly legible.

Article 12 of Council directive 92/27/EEC foresees guidelines being published, as necessary, by the Commission concerning, *inter alia*, the legibility of particulars on the labelling and package leaflet.

Although Article 12.2 provides that these guidelines should be adopted as a Commission Directive it seems more appropriate in this case, and in accordance with the principle of subsidiarity, to adopt the present text in the form of a guideline, as referred to in the Introduction to the Annex of Directive 75/318/EEC.

Purpose

This guideline is for use by applicants for a marketing authorisation (MA). It provides guidance on the factors which influence readability.

It outlines the format of the label and gives guidance on how each item on the label should be expressed.

It outlines the format of the package leaflet and provides an example of a model leaflet in Annex 1a together with further guidance on its content in Annex 1b. This example of a model leaflet and the guidance on its content should be followed in so far as the resulting leaflet complies with Directive 92/27/EEC and, upon testing (e.g. in accordance with Annex 2) by applicants for a MA, is shown to be readable to the patient/consumer.

Ensuring that the label and package leaflet are readable is the primary objective of this guideline.

It may not be necessary to test the readability of the package leaflet for each individual medicinal product if the required standard of readability can be assured by reference to a package leaflet (for another similar product) whose readability has been verified by testing.

In Annex 2, there is an example of a method, for use by applicants for a MA, to test readability before finalising a package leaflet.

When applicants for a marketing authorisation are preparing the specimens or 'mock-ups' of the sales presentation and the package leaflet they should use this guideline. As provided for in Article 4.9 of Directive 65/65/EEC, a mock-up of the sales presentation including the package leaflet must be submitted, to the competent authority, for approval, before commercialisation of the product. A mock-up of the sales presentation, including the package leaflet, is a flat artwork design in full colour, presented so that, (following cutting and folding, where necessary), it provides a replica, of both the outer and immediate packaging and of the leaflet, and clearly demonstrates the three dimensional presentation of the label text and of the leaflet text. This mock-up may be presented in paper form and not necessarily in the material of the sales presentation.

Section A - Readability of the Label and the Package Leaflet

1. Print size and type

The particulars appearing on the label of all medicinal products, should be printed in characters of at least 7 points Didot (or of a size where the lower case "x" is at least 1.4 mm in height), leaving a space between lines of at least 3 mm. The particulars appearing in the leaflet should be printed in characters of at least 8 points Didot, leaving a space between lines of at least 3 mm. Here are examples of different point sizes:

these characters are 5 point
these characters are 6 point
these characters are 7 point
these characters are 8 point
these characters are 9 point.

Words in full capitals/upper case should be avoided. The type of print chosen should be such as to ensure maximum legibility.

These recommendations may pose problems for the label on certain products. However, all possible steps should be taken to increase the available surface area of the label, without necessarily changing the size of the container or package. For example, the label may be lengthened and widened to increase its surface area, without changing the size of the container, or the information on the outer carton can in some instances be rotated 90° without changing the dimensions of the package. Where space on a label is necessarily very restricted prominence should be given to the information which is most crucial for the safe use of the product.

2. Print colour

Readability is not only determined by print size. Characters may be printed in one or several colours allowing them to be clearly distinguished from the background. A different type or colour is one way of making headings clearly recognisable.

3. Syntax

As far as possible, overlong sentences (i.e. more than 20 words) should be avoided. Moreover, it is recommended that lines of a length exceeding 70 characters are not used. Different fonts, upper and lower case, length of words, number of clauses per sentence and length of sentences can all influence readability. Run-on sentences and subordinate clauses should be avoided. Punctuation should be light, using commas, full stops, dashes and bullet points. A group of bullet points should be introduced with a colon and a single full stop should be placed at the end of the group. A list of bullet points should begin with the uncommon and specific case and end with the common or general case, unless this is inappropriate for the product. For example:

Tell your doctor if you are suffering from:

- pulmonary tuberculosis
- any allergies that affect your lungs
- any chronic lung condition.

A minimum number of words should be used in the bullet points and never more than one sentence. There should be no more than nine items where the bullet points are simple and no more than five when they are complex. Abbreviations should be avoided.

The pronoun (e.g. 'it') should be used in preference to repeating the name of the product, as long as the context makes clear what the pronoun refers to.

4. Braille

The use of Braille for the text of the label and package leaflet is encouraged.

5. 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.

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

Ensuring that the label and package leaflet are readable is the primary objective of this guideline. It may therefore be acceptable for a package leaflet, which achieves an acceptable level of performance in a readability test (e.g. as outlined in Annex 2), to deviate from the guidance in this section.

Section B - Label format

The following items shall appear on the label (outer packaging), as indicated in Article 2.1 of Council Directive 92/27/EEC.

1. Name of the medicinal product:

1.1 This may be one of the following:

- an invented name which shall not be liable to confusion with the common name (the INN or the usual common name)
- a common name [the international non-proprietary name (INN) should be used, otherwise the usual common name can be used], together with a trade mark or the name of the manufacturer;
- a scientific name, together with a trade mark or the name of the manufacturer.

1.2 Even when there is only one strength/pharmaceutical form it is recommended that the strength and the pharmaceutical form be included with the name. The information should be given in the following order: '(trade) name, strength, pharmaceutical form' followed by the common name of the active substance, as appropriate. For example:

- "Fareston 60 mg tablets
toremifene",
because the product contains 60 mg of toremifene;
- "Majeptil 10 mg tablets
thiopropazine (as dimesilate)",
because the product contains sufficient thiopropazine dimesilate to provide 10mg of thiopropazine.

This information may be presented on different lines of text or in different font sizes, provided that the appearance of the name is as an integrated item in the same field of vision, for example:-

(trade) name Z mg/ml
solution for injection

The European Pharmacopoeia (Ph. Eur.) List of Standard Terms¹ should be used for the pharmaceutical form. The list of Standard Terms contains short terms for some pharmaceutical forms, but these short terms should only be used if there is insufficient space on the label to print the full standard term in 7 points Didot.; e.g. on blisters and small labels.

1.3 In the case of a medicinal product containing one active substance, when the name of the medicinal product is an invented name it must be followed by the common name (INN or the usual common name), of the active substance. The INN/common name may be written on the line below the full expression of the name/strength/pharmaceutical form.

¹ published by the Council of Europe and regularly updated

2. Active substance

The active substance should be stated using the common name [the international non-proprietary name (INN) or the usual common name],

3. Quantitative declaration of the active substance

3.1 The quantity of the active substance should be expressed in one of the following ways:

- per dosage unit
- per unit of volume, if appropriate for the dose form
- per unit of weight, if appropriate for the dose form

3.2 A novel active substance present in the form of a compound or derivative (e.g. a salt or ester) should preferably be expressed in terms of the quantity of the active moiety/entity. For example, as for Fareston : "60 mg *Toremifene (as citrate)*".

All subsequently authorised products containing this active substance should express the quantity of the active substance as the quantity of the active moiety/entity, followed by the name (the INN or the usual common name), but not the quantity, of the form in which it is present (e.g. Toremifene citrate).

An active substance which forms a salt *in situ* should be expressed in terms of the quantity of the active moiety/entity plus '*in situ formation of...*(the salt).

3.3 Different strengths of the same product should be stated in the same way, for example tablets 250 mg, 500 mg, 750 mg (mg should be used from 1 mg to 999 mg). Micrograms should be always spelled out in full rather than abbreviated, for safety reasons. However, in certain instances where this poses a practical problem which cannot be solved by using a smaller point size (≤ 7 points Didot) then abbreviated forms may be used, if they are justified and there are no safety concerns. 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). For biological products I.U. should be used where relevant.

3.4 Parenterals:

For single dose parenterals the quantity of active substance(s) should be stated per ml and per total volume. For multi-dose and large volume parenterals the quantity of active substance(s) should be stated per ml, per 100ml, per 1000ml etc....as appropriate. For large volume parenterals containing inorganic salts, the quantity of these salts should also be indicated in millimoles.

3.4.1 Concentrates for parenteral use : When the active substance is presented in a concentrate (e.g. a concentrated solution) the label should state the total content of the active substance and the content of the active substance per ml. There should be a clear statement concerning dilution, such as: 'must be diluted before use - see leaflet'.

The label should state:-

- the total content of active substance in the concentrate
- the total content of the active substance per ml of the concentrate
- '*provides X mg per ml of active substance when diluted as recommended*', unless there are several means of diluting which result in different final concentrations.

3.4.2 Powder for reconstitution prior to parenteral administration : When the active substance is present as a powder for reconstitution the label should state:

- the total content of active substance in the container
- 'provides X mg per ml of active substance when reconstituted as recommended' unless there are several means of reconstituting which result in different final concentrations.

There should be a clear statement to consult the leaflet for information on reconstitution.

3.4.3 Diluents provided for either the reconstitution of a powder (as in 3.4.2 above) or the dilution of a concentrate (as in 3.4.1 above), should be labelled with the extractable volume.

3.5 Transdermal patches:

- the content of active substance(s) present in each patch,
- the mean dose delivered to the patient (that means the dose absorbed) per unit time (hour, day ...),
- the adherence surface .

Each of these numbers should be presented clearly and separately so that they can be distinguished from one another, otherwise they could cause confusion at dispensing level.

3.6 Multidose solid or semi-solid products² the quantity of active substance should be stated, where possible per unit dose, otherwise per gram or percentage.

3.7 Implants and intrauterine devices, (classified as medicinal products), the quantity of the active substance should be expressed in the following way:

- the content of active substance(s) present in each one
- the mean dose delivered to the patient (that means the dose released and absorbed) per unit time (hour, day ...),
- the total duration (hours, days ...) during which this mean dose is expected to be delivered.

4. **Pharmaceutical form and contents**

The European Pharmacopoeia (Ph. Eur.) List of Standard Terms should be used. The list of Standard Terms contains short terms for some pharmaceutical forms, but these short terms should only be used if there is insufficient space on the label to print the full standard term in 7 points Didot. e.g. on blisters and small packs. The contents should be specified by weight, volume, number of doses (number of doses of a solution, number of puffs of inhalers etc.), number of units of administration, pack size – as appropriate.

5. **Certain excipients**

See specific guidelines: *A guideline on the excipients in the label and package leaflet of medicinal products for human use* in The Rules governing Medicinal Products in the European Community Volume 3B: Guidelines. For parenteral products, topical products, ophthalmic products and products used for inhalation – all of the excipients should be stated on the label.

6. **The method of administration and, if necessary, the route of administration**

The Ph. Eur. List of Standard Terms, for the route of administration, should be used. Some information on the method of administration is particularly necessary if the product is available without a medical prescription.

7. **Keep out of the reach of children**

A warning to keep out of the reach and sight of children should appear on the label.

8. **Special warnings (if necessary)**

Specific guidelines on the formulation of certain specific warnings for certain categories of medicinal products may be elaborated in the future; as foreseen in Article 12.1 of Directive 92/27/EEC.

² For example: powders granules, creams and ointments

9. Expiry date

9.1 Expression of expiry date

Article 2.1h) of Directive 92/27/EEC specifies that the format for the expression of the expiry date should be in clear terms and should include month/year. The expiry date printed on medicinal products stating month and year should be taken to mean the last day of that month. Expiry dates should be expressed with the month given as 2 digits or at least 3 characters and the year as 4 digits, as illustrated in the following examples: February-2001, Feb-2001, 02-2001.

9.2 In-use shelf life

In the case of preparations with reduced stability following dilution, reconstitution or after the container has been opened, the maximum in-use shelf life should be stated. If however the maximum in-use shelf life for the reconstituted product varies, depending on how, or with what, it is reconstituted, then there should be a statement on the label, such as: 'read the leaflet for the shelf life of the reconstituted product'. Please refer to *Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution (CPMP/QWP/159/96)*

For certain products such as radiopharmaceuticals and some vaccines it may be necessary to state the expiry date and the shelf life following dilution, reconstitution or after the container has been opened, in detail: time, day, month and year.

10. Storage precautions

If the product is stable up to 30°C, no storage temperature is necessary. However, this does not preclude mentioning 30°C as the maximum storage temperature if a company wishes to do so. The storage precautions should be in accordance with the summary of product characteristics (SPC). Please refer to *Note for Guidance on Declaration of Storage Conditions for Medicinal Products in the Product Particular*" (CPMP/QWP/609/96). The following are the storage precautions which should be used:

- Do not store above 25°C/30°C
- Store at 2°C - 8°C (in a refrigerator)
- Store in a freezer
- Do not refrigerate/freeze
- Store in the original package
- Store in the original container
- Keep the container in the outer carton
- Keep the container tightly closed
- There are no special storage instructions

An additional short explanation of the storage statements, in consumer understandable language should be included when appropriate, e.g. 'in order to protect from light/moisture'. Where appropriate, there should be a warning about certain visible signs of deterioration.

11. Special precautions

For the disposal of materials, if relevant.

12. Name and address of the marketing authorisation holder

The marketing authorisation holder must be within the EU/EEA.

13. Marketing authorisation number

14. Manufacturer's batch number

The Commission will examine the possibility of harmonising the batch number. The manufacturer is as defined in Article 1.2 of Council Directive 92/27/EEC: the holder of the authorisation referred to in Article 16 of Directive 75/319/EEC, on behalf of whom the qualified person has performed the specific obligations laid down in Article 22 of that Directive; i.e. the manufacturer responsible for the release of each batch onto the EU/EEA market.

15. Instructions for use

If necessary and particularly if the product is for self medication.

Section C - Leaflet format

1. Content of the leaflet

The information contained in the leaflet must be in accordance with the Summary of Product Characteristics (SPC) but the text must be phrased so that it is readily understandable for the patient. Examples of such text are given in Annex 1a. Where a scientific or specialised term is used, an explanation should be given. The European Pharmacopoeia (Ph. Eur.) List of Standard Terms should be used. In addition, it may be necessary explain the standard terms used in consumer understandable language.

An example of a method for testing the readability, including the consumer-understandability, of the content of the leaflet is given in Annex 2.

2. Headings

Headings and sub-headings should be made conspicuous; if different colours are used for the print they should be reserved for headings. Repetition of information can sometimes be avoided by cross referring to information which is under another heading. Therefore the headings should be numbered, for ease of reference. More than two levels of headings may impair readability.

3. Style

3.1 An active and direct style should be used, by placing the verb at the beginning of the sentence, for example:-

- *'take 1 tablet'* instead of *'1 tablet should be taken',*

- *'you should...'* is better than *'it is recommended...'*

This principle should be adapted as;. for example, in the case of 'If ... then' instructions, such as: 'If you feel ill, tell your doctor'.

This guidance on style may not be appropriate in all languages.

3.2 Where possible reasons should be given for the recommended measures.

3.3 Pictograms may be used as an additional measure if they make the message clearer to the patient but excluding any element of a promotional nature.

3.4 Reserve red colour print for very important warnings only.

3.5 Avoid indiscriminate use of capitals because they detract from the readability. However capitals may be useful for emphasis.

3.6 Where explanations are given for instructions, the instructions should come first. For example: 'take care with X if you have asthma –it may bring on an attack'.

4. Order of items

The Commission has been made aware that placing the statements for excipients, marketing authorisation holder and manufacturer towards the end of the leaflet would make the leaflet more readable. Nevertheless, this guideline cannot be in conflict with the current legislation and therefore the order of the items will not change until the legislation is amended. The Commission will propose a modification of Directive 92/27/EEC to allow for this change.

5. Product ranges

There should, in principle, be a separate leaflet for each product of different quantitative strength and pharmaceutical form. In certain circumstances it may be useful to include information on the different strengths and pharmaceutical forms available; e.g. where achieving a recommended dose necessitates a combination of different strengths, or the dose varies from day to day depending on the clinical response. In such circumstances, other strengths and pharmaceutical forms with the same name can be included in the leaflet, provided that these other products have each of the following:-

- the same indication(s),
- the same posology,
- the same route of administration,
- the same contraindications, precautions, warnings and side-effects.

In the case of medicinal products available without prescription, it may also be useful to refer to other pharmaceutical forms; e.g. in the leaflet of a tablet, (which is unsuitable for children) to explain that there is an oral solution for children.

6. Products not for self-administration

6.1 For a product administered in hospital additional package leaflets may also be provided separately from the product package; e.g. a pad of tear-off leaflets supplied to the hospital for distribution to patients, as required. In this case the SPC (e.g. for the hospital staff) could be provided in the product package. When the package leaflet is provided separately, the MA holder should take appropriate measures to enable the hospital staff to provide the patient with the current version of the package leaflet.

6.2 For a product administered by a health professional, information from the SPC for the health professional (e.g. the instructions for use, inter alia) could be included at the end of the patient leaflet in a tear-off portion, to be removed prior to giving the leaflet to the patient.

7. Further information

Further information which is compatible with the SPC and useful for health education may be included provided it is not of a promotional nature.

8. Model leaflet in the annex

An example of a model leaflet is presented in Annex 1a, containing headings and text which should be used together with examples of text formulated in consumer understandable language. Further guidance on how to present the leaflet text in a readable way is given in Annex 1b. The model leaflet should be followed in so far as the resulting leaflet complies with Directive 92/27/EEC and upon evaluation, by applicants for a MA, is shown to be clearly understandable to the patient/consumer. For the purpose of presenting this model leaflet, the following tools are used:

- **bold type** for the headings;
- *italics* for text which is usually relevant and is not a heading
- 'text' with inverted commas for examples of text relevant in certain circumstances;
- normal type for the comments on the text and how it should be formulated.

All of the headings are numbered in this model however, for certain products, they may not all be relevant. In this case, the irrelevant headings should be dropped and the numbering of the remaining headings should be altered accordingly, while maintaining their sequence.

An example of a model leaflet

For medicinal products available only with a prescription:-

Read all of this leaflet carefully before you start taking/using this medicine.

- *Keep this leaflet. You may need to read it again.*
- *If you have further questions, please ask your doctor or your pharmacist.*
- *This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.*

For medicinal products available without a prescription:-

Read all of this leaflet carefully because it contains important information for you.

This medicine is available without prescription, for you to treat a mild illness without a doctor's help. Nevertheless, You still need to use X carefully to get the best results from it.

- *Keep this leaflet. You may need to read it again.*
- *Ask your pharmacist if you need more information or advice.*
- *You must see a doctor if your symptoms worsen or do not improve after ...days.*

In this leaflet:

1. *What X is and what it is used for*
2. *Before you take/use X*
3. *How to take/use X*
4. *Possible side effects*
5. *Storing X*

The (trade) name (referred to as X throughout this document) strength and pharmaceutical form of the medicinal product should be stated here.

- *The active substance is.....*
- *Other ingredients*

Marketing authorisation holder 'ABC Ltd. at address...'

Manufacturer: 'DEF Ltd. at address..'

1. What X is and what it is used for

The following should be stated here in consumer understandable language:

- The pharmaceutical form and contents and the pharmaco therapeutic group or type of activity;
- The contents by weight, volume, number of doses, pack size;
- The therapeutic indications (e.g. 'lowers temperature, 'eases pain' etc.); If appropriate, specify that the medicinal product is for diagnostic use only.

2. Before you take/use X

Do not take/use X ...

- ‘If you have a stomach ulcer (peptic ulcer) or used to have one.’

Contraindications should be stated here in consumer understandable language, including contraindications due to interactions with other medicines.

Take special care with X...

- ‘If you have asthma (or used to), because X can bring on an attack.’

Precautions, special warnings and interactions with other medicines, should be stated here in consumer understandable language.

- ‘If you are over 60/80....’
- ‘If X is given to children....’
- ‘X may make you feel sleepy’

‘Please consult your doctor, even if these statements were applicable to you at any time in the past’.

Taking/using X with food and drink

Pregnancy

Ask your doctor or pharmacist for advice before taking any medicine.

Breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

- ‘X may make you feel sleepy’
- ‘Do not drive because X could stop you driving safely’
- ‘Do not operate any tools or machines’

Important information about some of the ingredients of X

If appropriate, provide information on those excipients, knowledge of which is important for the safe and effective use of the medicinal product. Please refer to the *Guideline on Excipients in the Label and Package Leaflet of Medicinal Products for Human Use* (The rules governing medicinal products in the European Union, Volume 3B).

Taking/using other medicines

‘Please note that these statements may also apply to products used some time ago or at some time in the future’.

‘Please inform your doctor or pharmacist if you are taking, or have recently taken, any other medicine - even those not prescribed.’

3. How to take/use X

The instructions for proper use and the dosage should be stated here, together with the route and method of administration.

‘...one or two tablets (500 to 1000mg of Paracetamol) three times a day, this means a daily maximum of six tablets (3000mg of Paracetamol)’

‘...in the morning, at lunchtime, immediately before meals, with food, after food’..

‘Do not swallow’

‘Do not chew’

‘Shake well before use’

‘Dissolve the effervescent tablet in one glass of water. Then drink the whole contents of the glass’.

‘Take the tablets with a sufficient quantity of liquid (e.g. one glass of water)’.

‘Proceed as follows to obtain the solution you wish to take/use: Fill the bottle up to the mark (white line) with tap water. Shake the bottle until all of the dry powder is moist with water. Then the foam will settle. Refill the bottle up to the mark (white line) with tap water and shake it vigorously. You will obtain 100 ml of the ready-for-use solution’.

‘Take X once a day, every day, at about the same time each day’.

‘Taking your tablets at the same time each day will have the best effect on your blood pressure. It will also help you remember when to take the tablets.’

‘Follow these instructions unless your doctor gave you different advice’.

‘Remember to take your medicine’

‘Your doctor will tell you how long your treatment with X will last. Do not stop treatment early because ...’.

If you have the impression that the effect of X is too strong or too weak, talk to your doctor or pharmacist.

If you take/use more X than you should:

If you may have taken/used more X than you should, talk to a doctor or pharmacist immediately.

If you forget to take X:

Do not take a double dose to make up for forgotten individual doses.

Effects when treatment with X is stopped:

4. Possible side effects

Begin this section with:- *Like all medicines, X can have side effects.*

Here is an example of side effects grouped according to seriousness:

‘If any of the following happen, stop taking X and tell your doctor immediately or go to the casualty department at your nearest hospital’:

- ‘swelling of the hands, feet, ankles, face, lips, mouth, or throat which may cause difficulty in swallowing or breathing’,
- ‘hives’,
- ‘fainting’,
- ‘yellowing of the skin and eyes, also called jaundice’.

‘These are all very serious side effects. If you have them, you may have had a serious allergic reaction to X. You may need urgent medical attention or hospitalisation’.

‘All of these very serious side effects are very rare’.

‘Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following’:

- ‘chest pain’,
- ‘angina’,
- ‘changes in the way your heart beats, for example, if you notice it beating faster’,
- ‘difficulty breathing’,
- ‘signs of frequent infections such as fever or sore throat’,
- ‘less urine than is normal for you’,

‘These are all serious side effects. You may need urgent medical attention’.

‘Serious side effects are rare’.

‘Tell your doctor if you notice any of the following’:

- ‘nausea (feeling sick)’,
- ‘abdominal cramps or stomach pains’,
- ‘headache’,
- ‘dizziness’,
- ‘fatigue’,
- ‘light-headedness’,
- ‘dry cough’,
- ‘muscle cramps’,
- ‘flatulence or wind’,
- ‘diarrhoea’,
- ‘loss of appetite’.

‘These are all mild, side effects of X’.

If the consumer needs to seek help urgently, use the term ‘*immediately*’. For less urgent conditions use the phrase ‘*as soon as possible*’.

Close this section with:- *If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.*

5. Storing X

Keep X out of the reach and sight of children.

‘Do not store above 25°C/30°C’

‘Store at 2°C - 8°C (in a refrigerator)’

‘Store in a freezer’

‘Do not refrigerate/freeze’

‘Store in the original package’

‘Store in the original container’

‘Keep the container in the outer carton’

‘Keep the container tightly closed’

‘There are no special storage instructions’

An additional short explanation of the storage statements, in consumer understandable language should be included when appropriate, e.g. ‘in order to protect from light/moisture’.

Use by date *Do not use X after the expiry/use before date on the label/carton/bottle.*

Where appropriate, there should be a warning about certain visible signs of deterioration.

‘Do not use X if you notice.....’

This leaflet was approvedMonth and year when this leaflet was last approved.

Further Guidance on the content of a model leaflet

(i) The name of the product

At the beginning of the leaflet, the (trade) name of the medicinal product (referred to as X throughout this document) should be stated in bold, together with the strength and pharmaceutical form. This should be followed by the INN or common name of the active substance (as stated on the label), which may be written on the line below. The statements of the active substance and of the excipients should be identified as such. The full qualitative composition of all the excipients should be given here.

(ii) The marketing authorisation holder

The marketing authorisation holder must be established within the EU/EEA.

(iii) The manufacturer

The manufacturer is as defined in Article 1.2 of Council Directive 92/27/EEC: the holder of the authorisation referred to in Article 16 of Directive 75/319/EEC, on behalf of whom the qualified person has performed the specific obligations laid down in Article 22 of that Directive; i.e. the manufacturer responsible for the release of each batch onto the EU/EEA market.

1. What X is and what it is used for

The pharmaceutical form and contents and the pharmaco-therapeutic group, or type of activity, should be stated here, in accordance with the SPC. The pharmaceutical form should be stated according to the European Pharmacopoeia Standard Terms. In addition, it may be necessary to explain the pharmaceutical form in consumer understandable language.

The contents should be stated here as weight, volume, number of doses, pack size.

A physical description may be included e.g. shape, colour, texture, imprint.

The therapeutic indications should be stated here, using consumer understandable language.

2. Before you take/use X

This section should take into account the particular condition of certain categories of users, e.g. children, the elderly and special patient populations such as patients with renal or hepatic impairment. When specifying the age range; for children please refer to *CPMP Note for Guidance on Clinical Investigation of Medicinal Products in Children (CPMP/EWP/462/95)*.

Do not take/use X ...

The information here should be strictly limited to real contraindications, including those due to interaction with other medicines. Other precautions and special warnings should be given in next section. Duplication of information is to be avoided.

Care must be taken to ensure that complex details are not omitted. It is not acceptable to state only the common or major contraindications. Belief that a patient cannot understand a contraindication is not a reason for omitting it.

Contraindications due to excipients should be mentioned - see Annex to *A guideline on the excipients in the label and package leaflet of medicinal products for human use* (published in The Rules governing Medicinal Products in the European Community Volume 3B).

Include reference to chronic accompanying diseases (renal insufficiency, liver insufficiency, diabetes and other metabolic diseases).

Take special care with X...

Information on precautions, special warnings and interactions, including those due to interaction with other medicines, should be provided here. Care must be taken to ensure that complex details are not omitted and that they are expressed in a way that consumers can understand. It is not acceptable to state only the common or major precautions. Belief that a patient cannot understand a precaution is not a reason for omitting it.

Specific guidelines on the formulation of certain specific warnings for certain categories of medicinal products may be elaborated in the future; as foreseen in Article 12.1 of Directive 92/27/EEC.

A precaution should be presented as implying the action a patient should take, rather than as factual information which describes a medical condition.

The influence of the drug on the patient's behaviour should be described. A differentiation should be made between the influence on cognitive abilities, reactivity and judgement.

Also describe in what cases (if any) the consumer should only use X after consultation with a physician.

Include, (as appropriate and if not mentioned in the previous section), reference to chronic accompanying diseases (renal insufficiency, liver insufficiency diabetes and other metabolic diseases).

Give the information on necessary checks which may be carried out by the physician prior to, or during, the therapy, for example tests carried out in order to exclude contraindications.

Give information (if there is any) about important symptoms which may be masked by the product or if the product influences laboratory values. If relevant, reference should be made here to possibilities for intolerance to various materials (e.g. disposable plastic syringes) which must be used as part of this product.

Refer to the need for the avoidance of external influences, such as sunlight after the use of phytotoxic drugs. Other warnings concerning for example other diseases and the influence of the product on behaviour should be described. Statements should also include for example, reference to discolorations of underwear as a result of changes in the colour of urine and stool.

Taking/using X with food and drink

Interactions not related to medicinal products should be mentioned here. For example, patients should not consume milk in combination with tetracyclines and no alcohol should be consumed during treatment with benzodiazepines.

Important information about some of the ingredients of X

Information on intolerances to excipients - see Annex to *A guideline on the excipients in the label and package leaflet of medicinal products for human use* (published in The Rules governing Medicinal Products in the European Community Volume 3B).

Taking/using other medicines

Describe the effects of other products on the product in question and vice versa. Reference should be made to the intensification/weakening and the extension/shortening of effects.

3. How to take/use X

The instructions for proper use and the intended dosage ranges (individual and daily doses separately), as well as the maximum daily dose, the frequency, method, route of administration and the duration of treatment, should be stated if relevant.

The route of administration should be stated according to the European Pharmacopoeia Standard Terms. In addition, it may be necessary to explain the route of administration in consumer understandable language.

For products containing one active substance the number of dosage units should be stated first, followed directly by the quantity of the active constituent in brackets; e.g.

'one or two tablets (50 mg to 100mg of 'active'-the name of the active ingredient should be given) twice daily, this means a daily maximum of four tablets (200 mg of 'active')'.

In addition, the times for administration should be stated (frequency of administration).

The text should be structured according to indication, age and sex, taking into account organic disorders.

Reference should also be made here to a dosage reduction in case of renal insufficiency and/or liver insufficiency.

Instructions should:

- be used to tell people what to do. They should not be used to justify or explain an action.
- be described in a practical way.
- tell consumers how to use a product properly.
- be positive rather than negative, whenever possible. Negative instructions should only be used when the consumer should avoid specific actions.
- be given as separate instructions when the consumer is to carry out two separate actions. Separate actions should not be compressed into a single sentence.
- be numbered and put into the exact order which the consumer should follow.
- usually be understandable without explanations, so as not to overburden consumers with information.

Explanations should be used to expand on the reasons for instructions and not to give further information. Instructions may be presented in bold type with explanations in plain type, so as to give consumers a guide as to the importance of the information.

Explanations should be placed immediately after the instructions when:

- an instruction is contrary to expected behaviour,
- the reasons for an instruction are not self-evident,
- an instruction can be made more memorable by using an explanation.

An instruction and its related explanation should be kept on the same side of the leaflet. Also, related groups of instructions and explanations should be on the same side of the leaflet.

When applicable, there should be descriptions (if useful with illustrations) of opening techniques for child-resistant containers and other containers to be opened in an unusual way.

Specific instructions for administration may be important, for example: *Take the tablets with a sufficient quantity of liquid - one glass of water.*

If appropriate, precise statements should be included on:

- the usual duration of the therapy;
- the maximum duration of the therapy;
- the intervals with no treatment;
- the cases in which the duration of treatment should be limited.

In particular and if at all possible, for products available without prescription, precise statements should be included on the usual duration of the therapy, the maximum duration of the therapy and intervals with no treatment, together with clear guidance on when to consult a doctor. For medicinal products available only with a prescription a statement such as the following should be included:

'your doctor will tell you how long your treatment with X will last. Do not stop treatment early because ...'.

If you take/use more X than you should:

Describe how to recognise if someone has taken an overdose and what to do.

If you forget to take X:

Make clear to consumers what they should/should not do if one or more doses have been missed.

Effects when treatment with X is stopped:

These should be described.

4. Possible side effects

The information given on undesirable/side effects should be in accordance with the SPC.

Side effects should be subdivided according to seriousness and frequency, or according to symptom type. Wherever possible, for all undesirable effects the frequency with which they occur is to be mentioned in the package leaflet to allow patients to know the risk. If exact data are available, numbers can be given in per cent. Within the different groups of frequency, undesirable effects should be listed in a decreasing order of seriousness if possible. Irrespective of their frequency, very serious, typical, undesirable effects of the product should be mentioned first or specially emphasised. This applies in particular to undesirable effects where there is an urgent need to take action.

The estimated frequency is currently subdivided:

- very common 10%+, (more than 1 per 10);
- common > 1% and < 10%, (less than 1 per 10 but more than 1 per 100);
- uncommon 0.1% to 1%, (less than 1 per 100 but more than 1 per 1000);
- rare 0.01% to 0.1%, (less than 1 per 1000);
- very rare up to 0.01%, (less than 1 per 10,000).

A structure based on organic systems is also possible.

Should there be undesirable effects that occur mostly at the beginning of the treatment and then subside or that only occur after prolonged treatment, these are to be mentioned here.

The measures to be taken to remedy or at least alleviate the undesirable effects should be mentioned here, if relevant. If the consumer needs to seek help urgently, use the term 'immediately'. For less urgent conditions use the phrase 'as soon as possible'. The consumer should be expressly invited to communicate any undesirable effect, especially if it is not mentioned in the leaflet, to a doctor or pharmacist.

5. Storing X

Please refer to *Note for Guidance on Declaration of Storage Conditions for Medicinal Products in the Product Particulars (CPMP/QWP/609/96)*.

In the case of products with reduced stability following reconstitution, or after the container has been opened, the maximum in-use shelf life should be stated together with the storage conditions. Please refer to *Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution* (CPMP/QWP/159/96).

Where appropriate, there should be a warning about certain visible signs of deterioration.

An example of a Method for Testing the Readability of the Leaflet

Ensuring that the label and package leaflet are readable is the primary objective of this guideline. It may therefore be acceptable for a package leaflet, which achieves an acceptable level of performance in a readability test (e.g. as outlined here in Annex 2), to deviate from the rest of the guideline.

Confirmation by a MA applicant that a package leaflet achieves an acceptable level of performance when tested as described here in Annex 2, should be sufficient to meet competent authorities' requirements with regard to readability of package leaflets.

This testing method is based on the approach taken in Australia's requirements for consumer medicine information³.

Objectives:

- To find out what is wrong with the leaflet, not simply to confirm what works well.
- To have at least 16 out of 20 consumers able to answer each question correctly. However, it is not necessary for the same 16 people to answer each question correctly. It may be necessary to retest several times in order to achieve this level of performance.

What type of test?

Diagnostic testing is the most useful and consists of:

- asking users to carry out the tasks they would normally carry out when using the leaflet
- observing and recording what they do
- noting how they describe what they do
- probing to find out whether they can use the information they read appropriately
- noting what they say about the leaflet.

Diagnostic testing is widely used where readability is a critical concern. It is cheaper than more traditional methods such as surveys and focus groups, and the quality of the resulting data is good.

Who should do the testing?

The person who wrote the leaflet is best. The writer will learn from the experience of testing and can then directly transfer this to subsequent work.

Who should be tested?

The people tested should be from population(s) at risk – those who are likely to have problems using the medicinal product. For example, in many instances it is appropriate to recruit older consumers because they are known to have problems with medication.

³ "Writing about medicines for people – Usability guidelines for Consumer Medicine Information – David Sless and Rob Wiseman – Communication Institute of Australia.

It may not be necessary to test people who suffer from the illness which the medicinal product treats. Often it is sufficient if the participant is reasonably able to imagine that they might need to use the medicine in the future. This is especially so for the more common illnesses. However, if the medicine is for a rarer illness, or if it is for some longer term condition which might entail a degree of patient knowledge, then it may be better to test the leaflet on actual sufferers.

Recruiting from a population of convenience, such as fellow workers, should be avoided. However, such people can be used to pilot test questions, to check that these questions can elicit the sort of answers expected.

What to test?

The leaflet should be in the layout and on the same paper as it will be presented to consumers once the medicinal product is marketed.

There are two questions:

- Can consumers find information quickly and easily in the leaflet,
- Having found the information, can they understand and act on it appropriately?

The testing procedure is as follows:

1. There is a core of tasks associated with the leaflet for each medicinal product, which are critical for its appropriate use. This will vary from one product to the next.

The critical areas of a leaflet are usually:

- What is it used for?
- How to use it?
- Undesirable effects.

The number of tasks selected (in the form of questions) for the consumers to perform, using the leaflet, should not normally exceed fifteen. It is not practical, or necessary, to test every task since many are very simple or of minor significance.

2. The questions should be compiled in a single document.

3. Ten consumers should be recruited, preferably people who are likely to have problems with this particular product; for example, older consumers.

4. One consumer should be tested at a time and at least a half an hour allowed for each person. More than one leaflet could be tested on each participant. For example, two short and relatively simple leaflets. However, testing that lasts more than 45 minutes may not be useful because the participants will begin to tire.

5. The order in which the questions are asked should be randomised and two questions which refer to adjacent information should not be asked in sequence. When asking each question, observe how the consumers handle the leaflet - how do they search for information? To test the structure, it is necessary to notice when people get lost or confused and how they try to deal with the problem.

6. When consumers find the information which has been asked of them, they will probably just read out the information. They should be asked to put it into their own words and explain what it means. This will reveal whether or not they understand what is written. If the question involves them in describing a procedure, such as using an inhaler, they should be given a placebo of the inhaler and asked to go through the procedure using the leaflet. An

alternative is to ask them to describe the procedure themselves. Remember one of the main objectives is to try to find out what they misunderstand not just what they understand.

Sometimes, when consumers have difficulty understanding something, they will ask what it means. Avoid giving an answer and turn it around by asking them ‘What do you think it means?’ or ‘What would you normally do if you read that?’

7. After these ten consumers have been tested, the data should be reviewed. If there is a major fault with the leaflet, some patterns may emerge after this number of tests. Then there may be sufficient data to rewrite some parts of the leaflet, before testing further.

8. Once satisfactory data have been obtained from testing ten consumers, then a further ten should be tested. The objective is to have at least sixteen out of twenty consumers able to answer each question correctly. However, it is not necessary for the same 16 people to answer each question correctly. It may be necessary to modify the leaflet and then retest several times in order to achieve this level of performance.