COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Policy document

Labelling of pharmaceutical products

MEB 6

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2 Abbreviations and definitions

2D	Two-dimensional
AV	General Sales
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures - Human
CMS	Concerned Member State *An EU member state which does not have the lead in terms of assessing a certain product.*
MEB	Medicines Evaluation Board
DCP	Decentralised Procedure
SUSP	Single Unit Suitable Packaging
SUP	Single Unit Packaging
EMA	European Medicines Agency
EU	European Union
IGJ	Health and Youth Care Inspectorate
MEB	Medicines Evaluation Board *English translation of 'College ter Beoordeling van Geneesmiddelen'*
MRP	Mutual Recognition Procedure *[Europese wederzijdse erkenningsprocedure]*
NR	Non-prescription *This is the combined AV+UAD+UA legal status of supply which applies to medicinal products which are available over the counter, otherwise known as self-care medicinal products or OTC medicinal products.*
NtA	Notice to Applicants
OTC	Over The Counter *Another name for medicinal products for which no prescription is required.*
QR	Quick Response
QRD	Quality Review of Documents
RMS	Reference Member State *An EU member state that is responsible for the assessment of a particular product.*

RVG number	Register Packaged Medicinal Products: Unique Dutch authorisation number for a medicinal product.
RVH number	Unique Dutch authorisation number for a homoeopathic medicinal product.
SmPC	Summary of Product Characteristics
UA	Pharmacy Only
UAD	Pharmacy and Drugstore Only
UR	Only on Prescription from doctor or specialist
URL	Uniform Resource Locator *The URL is an Internet address and indicates where certain information such as a file or image is located on the Internet.*

3 Introduction

The presentation of the primary and secondary packaging of a medicinal product are determining factors in the recognition of a product and make a significant contribution to the correct use of the product.

The information on the outer packaging and primary packaging is intended for the patient (as a user of the medicine), or the parent or carer and for the pharmacist.

The European legislation concerning the labelling is discussed in Directive 2001/83/EC. Implementation took place in the Netherlands in the Dutch Medicines Act and the Medicines Act Regulation. Chapter 7 of the Medicines Act and chapter 4.a of the Medicines Act Regulation deal with the labelling and the package leaflet.

This policy document (MEB 6) clarifies the policy on the labelling of pharmaceutical products in the Netherlands. This policy is based on the aforementioned European and Dutch legislation.

The practical implementation of this legislation has been given shape in Europe in the QRD template. An English template, which includes comments and a further explanation is available. There is also a Dutch translation of the sections and standard sentences. Information that can be found in the template will not be repeated in this policy document.

The MEB tests the entire packaging, not just the compulsory text information. Packaging therefore has to be submitted to the MEB in its definitive layout as well (as mock-up, electronically).

3.1 Other documents relevant to labelling

Via European Commission (Eudralex):

- Directive 2001/83/EC
- Volume 2c Notice to Applicants
- Guideline on the readability of the label and package leaflet
- Guidance concerning the Braille requirements for labelling and the package leaflet Article 56a of Directive 2001/83/EC as amended
- Guideline on the excipients in the label and the package leaflet of medicinal products for human use
- Blue box information for products authorised through the Central Procedure, see the Annex of the Guideline on the packaging information of medicinal products for human use authorised by the Union

- European Commission website on falsified medicines: with a reference to, among other things:
  - Commission Delegated Regulation (EU) 2016/161 (9 February 2016)
  - Questions and Answers document
  - Implementation of the rules on the safety features for medicinal products for human use
- Dutch translation Europese richtlijn vervalste geneesmiddelen 2011/62/EU): (with annexes 1 and 2; black and white list)
- List of details of national competent authority to contact for requests of translation exemption falling under Art. 63.3 of Directive 2001/83/EC and cases of shortages

Via EMA:

- Quality review of documents (QRD templates; both centrally and MRP/DCP [CMDh])
- Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products.
- Compilation of QRD decisions on stylistic matters in product information
- Recommendations for the implementation of the exemptions to the labelling and package leaflet obligations in the centralised procedure
- Quick Response (QR) codes in the labelling and package leaflet of centrally authorised medicinal products

Via CMDh

- Quality review of documents MRP/DCP (QRD templates)
- Questions &Answers (for example '*Product Information / Information on medicinal products*')
- Blue box requirements for products authorised via MRP/DCP (see 'Blue box' requirements on CMD(h) website: https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/procedural_guidance/Application_for_MA/CMDh_258_2012_Rev16_2019_07_clean_BlueBox_requirements.pdf
- Article 61(3) procedure
- https://www.hma.eu/90.html
  - Bullet point 12: CMDh position paper on the use of Mobile scanning and other technologies to be included in labelling and PL in order to provide information about the medicinal product

Via MEB

- MEB-08 Guideline on the excipients in the label and the package leaflet of medicinal products for human use (Dutch translation)
- MEB 13 Nomenclature of pharmaceutical products
- MEB 14 Parallel import: marketing authorisation and maintenance
- MEB 16 Duplex marketing authorisation
- MEB 21 Statements of 'abbreviated indications' packaging of OTC products
- Braille declaration form
- Declaration relating to the technical aspects of the readability of the package leaflet of pharmaceutical products for human use
- MEB 41 Policy on marketing authorisations without Dutch translations of the product information and/or mock-ups.
- QRD templates with reference to website for Central procedures and MRP/DCP procedures
- Toolkit for an understandable package leaflet

  Among other things, this contains the following:
  - List of patient-friendly terms

  - Sample sentences relating to ability to drive, forgetting to take the medicinal product, pregnancy and breastfeeding

  - General writing advice

Via Wetten.Overheid.nl

- Dutch Medicines Act (Gmw)
- Medicines Act Regulation (RGmw)

4 Legal framework

When applying for a marketing authorisation, a mock-up of the outer packaging and primary packaging must be submitted (Article 3.7 of the Medicines Act Regulation and Article 8(3)(j) of Directive 2001/83/EC).

Changes to the outer packaging and the primary packaging proposed by the marketing authorisation holder must be submitted to the MEB (Article 50, paragraph 2 of the Medicines Act).

If it becomes apparent after the granting of a marketing authorisation that the packaging text does not meet the requirements set out in, by virtue of or pursuant to Chapter 7 of the Medicines Act, marketing authorisation may be withdrawn, suspended or amended (Article 51, paragraph 1 of the Medicines Act).

The labelling (packaging texts) must be set out in accordance with the Summary of Product Characteristics (SmPC) (Article 4a.2, paragraph 1 of the Medicines Act Regulation and Article 54 of Directive 2001/83/EC). A consequence of this may be that new, amended packaging texts must be submitted simultaneously with any textual changes to the SmPC.
The text of the outer packaging and primary packaging must be worded in Dutch (Article 4a.3, paragraph 1 of the Medicines Act Regulation). Packaging texts in several languages are permitted, provided that a declaration is made that the information provided in all languages is the same, with the exception of the blue box requirements. In the case of packaging texts in several languages, the blue box requirements that only apply to the other countries do not have to be translated into Dutch.

Products accepted via mutual recognition procedure (MRP) and Decentralised Procedure (DCP) that will not be marketed in the Netherlands may be authorised without the Dutch product information. For more information, please refer to section 5.1.4 and to Policy Documents MEB 41 'Policy concerning marketing authorisations without Dutch translations of the product information and/or mock-ups' and MEB 5 'Package leaflet of pharmaceutical products'.
For products accepted via the Centralised Procedure, in some cases there is the option to submit a request to the MEB to market the product in question without the Dutch text on the packaging and/or the Dutch package leaflet. Please refer to the EMA website for further information about this and the procedure that should be followed.

Additional legal requirements apply for the labelling of homeopathic products and traditional herbal medicinal products: Article 4a.1, paragraph 1 of the Medicines Act Regulation and Articles 68 and 69 of Directive 2001/83/EC.

5 Readability and mock-ups

5.1 Readability and language

5.1.1 General

According to Article 4a.3, paragraph 1 of the Medicines Act Regulation the information on packaging must be clearly legible and non-erasable.

The MEB applies the standard set in the European Commission document 'Guideline on readability' concerning readability (including letter size, letter type, use of colour). Please refer to this Guideline for the current requirements.

It is permitted to present certain information (batch number, expiry date) in punched text rather than printed text on blister and strip packages (see also section 7.5 of this document).

5.1.2 Exemption Dutch language

An exemption from using the Dutch language will only be granted in very exceptional cases, in accordance with the stipulations set out in Article 4a.3, paragraphs 2 and 3, of the Medicines Act Regulation. In addition, the MEB permits marketing authorisation without a Dutch translation, see below in section 5.1.4.

Exemption of information in the Dutch language on the packaging of a product that is traded in the Netherlands can, in exceptional circumstances, be permitted for products which have to be administered exclusively by the professional groups in the event of

- a critical product that, due to a small number of users, would not be available on the Dutch market if a Dutch label text is required, or
- a manufacturing process for which it is impossible to pack a batch in various packages with labels in different languages, for example in the case of certain radiopharmaceuticals.

It should be noted that, in the event of an exemption from the use of the Dutch language, English is the only permitted alternative foreign language on the label. The dossier must include an approved English text when the request is submitted.
If the patient has to administer the product himself, the text on the marketed packaging must always be in Dutch.

The marketing authorisation holder sends the request for exemption, along with argumentation and documentation including a mock-up with English text, to NLtranslationexemptionCP@cbg-meb.nl. As regards the criteria of a critical product, reference is made to the EMA document entitled 'Criteria for classification of critical medicinal products'. In addition, the marketing authorisation holder must provide reasons as to why a multilingual packaging for numerous countries, for example together with Belgium, is impossible.
A product with English text may only be marketed after approval by the MEB.

It should be noted that the dossier must always contain a packaging label text in Dutch in accordance with the QRD template which has been submitted to the MEB.

Exemption from using the Dutch language on the packaging of orphan medicinal products is arranged via the EMA.

A request for a temporary exemption from using the Dutch language on packaging, for example in the case of shortages, is arranged via the Medicinal Products Shortages and Defects notification centre (www.medicineshortagesdefects.nl).

5.1.3 Packaging for more than one country

In principle it is possible to label packages in such a way that they are suitable for more than one country. This often concerns multilingual packaging. In all instances the data on the packaging must, both as regards content and layout and readability (including, for example, font size), comply with the requirements as laid down for the Netherlands. However, the information, except the administrative information such as marketing authorisation holder and registration numbers, must be the same in each language. The information must be stated per language on the packaging. For each language a clear indication must be given, by adding a country code ('NL'), of which country the information in this language is intended for, to avoid any possibility of confusion for the user. Blue box requirements which only apply to other countries do not need to be translated into Dutch.
If not all the above requirements can be fulfilled, the MEB will not accept the packaging for more than one country.

Multilingual packaging for countries outside the EEA is only acceptable if the SmPC is the same in all the countries involved and fulfils the requirements of Title V of Directive 2001/83/EC. The labelling and package leaflet must correspond entirely with the SmPC as determined in the EEA. Member states may require certain additional information to be included in the label text (the so-called blue box information). This information must be limited to administrative information.

5.1.4 Marketing authorisations without Dutch translations of the product information or mock-ups

As medicinal products are not always placed onto the Dutch market immediately after authorisation, the MEB has decided to allow exceptions concerning the submission of the Dutch translations of the product information.

There is the option of granting a marketing authorisation in the Netherlands for a product accepted via an MRP or DCP without having to submit Dutch translations of the product information and mock-ups. The MEB will then grant a marketing authorisation subject to certain conditions. During the authorisation, the English SmPC and package leaflet will be determined, for which sections 1 and 7-10 must be adapted and contain specific national information. In principle, the labelling does not need to be changed.

The option of submitting an application for a marketing authorisation with additional conditions also exists for products already authorised with Dutch product information, which are not yet on the market in the Netherlands.

The obligation to keep the Dutch product information (including the label text) up-to-date remains for medicinal products for which the Dutch product information has already been approved and that have already been introduced on the market. In these instances, a commitment can be submitted for the mock-up. For further clarification see MEB 41 'MEB

policy concerning marketing authorisations without Dutch translations of the product information and/or mock-ups'.

There is the option of granting a marketing authorisation in the Netherlands for a product accepted via an MRP or DCP with a Dutch translation of the product information or accepted via a national recognition procedure without submitting mock-ups.
For further clarification see MEB 41 'MEB policy concerning marketing authorisations without Dutch translations of the product information and/or mock-ups'.

5.2 Mock-ups

5.2.1 Definition

A mock-up is a flat design of the packaging, in colour with the final font type and the final font size and graphic design, which gives a clear impression of the three-dimensional presentation of the packaging. A mock-up must be submitted for assessment before a medicinal product is brought onto the market.

5.2.2 Digital submission

The MEB will only accept digital submissions of mock-ups. Consequently, applicants are not meant to submit an actual (three-dimensional) cardboard box or a design on paper. However, a three-dimensional copy must be submitted for the so-called 'wallet packaging' (see section 7.1 of this document).

5.2.3 Different packaging forms, pharmaceutical forms and strengths

For the sake of recognised ability, to prevent mix-ups and to distinguish between various medicinal products, it is essential that the packaging of the various pharmaceutical forms and strengths can be clearly distinguished from one another. It is also important that products by the same marketing authorisation holder are sufficiently different from each other.

If there are different packaging forms (for example blister packaging and bottles) for different pharmaceutical forms and/or strengths, label texts and mock-ups must be submitted for all forms and strengths. This is necessary to allow an assessment of whether there are sufficient differences between the various packaging forms (see also section 6.3). It is possible to issue a commitment for packaging forms which are not available on the market (see section 5.1.4 and MEB 41). See section 5.2.6 for the various packaging sizes.

5.2.4 Sticky notes

For products that will not be marketed in the Netherlands, but for which a Dutch mock-up is submitted, the mock-up of another product from the same series may be used, provided that the differences are clearly marked. This can be done using sticky notes in PDFs of mock-ups. Differences in the presentation of the text or differences in colours compared to the final packaging cannot be indicated in this manner. Experience has shown that a mock-up

containing a lot of sticky notes and a lot of text in a small font size is difficult to assess. If a mock-up with sticky notes cannot be properly assessed, the MEB can still request the submission of a completely new mock-up (in other words without sticky notes).

5.2.5 House style

It is possible to have the MEB assess a marketing authorisation holder's house style. For this purpose, a national Article 61(3) notification must be submitted which must clearly state that it relates to an assessment of a house style. This notification should not be linked to a single specific product, but should be submitted with reference to 'new house style'. Such a notification must also be accompanied by mock-ups. The marketing authorisation holder can decide to submit a mock-up for all products involved. However, it is preferable to submit a number of mock-ups as an example and to submit the other mock-ups only after the house style has been approved. This is subject to the condition that the submitted mock-ups are representative of the other mock-ups, with sufficient clear differences between the various presentations (for example in terms of colour scheme) so that the mock-ups not yet submitted do not contain any new elements. Examples in this context include mock-ups for PO and NP products, for various pharmaceutical forms, strengths and/or for various dimensions of the packaging (including Unit Dose Packaging (EAV)).

An assessment of house styles must not only take account of the criteria referred to in this policy document, but also the *'Guideline on the readability of the label and package leaflet'* (see NtA volume 2c) and the QRD template.

An approved house style generally leads to less discussion about the layout of the packaging in the event of subsequent changes to product-specific mock-ups. However, the marketing authorisation holder must still comply with the existing conditions imposed on individual mock-ups. Policy changes may therefore mean it is essential to adapt the house style.

5.2.6 Different packaging sizes for a single medicinal product

If various packaging sizes are marketed for a medicinal product (with one registration number), the layout of these packages (colour scheme, font, mutual relationship between font sizes, etc.) must correspond as closely as possible. The order of the text may be adjusted accordingly for 'vertical' packages versus 'horizontal' packages. However, the layout will then also have to be maintained as closely as possible. For example, if the text on one package is printed in a blue banner, this will also have to be the case on the other package, with the proportions of the text and the banner corresponding as closely as possible.

If there are different packaging sizes for a medicinal product (under a single registration number), it is not always necessary to submit all packaging sizes. However, all mock-ups must be submitted of packaging sizes which fundamentally differ from each other (e.g. vertical versus and horizontal packaging), to allow an assessment of whether the mutual differences are acceptable (see also section 6.3). The EAV/EAG packages form an exception to a layout similar to the other packaging sizes (see also section 7.5).

It is emphatically not the intention that packages of one medicinal product (with a single registration number) with entirely different colour schemes exist together. This is in order to prevent confusion. The only exception is a transitional situation, in which a variation procedure is implemented for the packaging and the packaging with the 'old' layout is sold out.

5.2.7 Blank outer packaging with label sticker as secondary packaging

A blank outer package with a label sticker as secondary packaging is possible for both prescription and over-the-counter medicinal products. The criteria below must then be complied with. This will be assessed on a case-by-case basis.

- All compulsory information must be stated on the label that is affixed to the front of the packaging.
- The label sticker must meet all legal requirements as stated in this policy document (MEB 6). The label sticker must also meet the requirements for pre-printed label texts on secondary packaging (see bullets below) and the positioning of Braille text on the packaging must also be taken into consideration (on the label or on the blank outer packaging), unless an exemption has been granted as discussed elsewhere in this document (see also annex 1 point 16).
- Text on the labelling sticker must at all times conform to the Guideline on the readability of the labelling and package leaflet of medicinal products for human use. In addition to the font type, the font size and colour, the layout of the label text is essential in order to create a readable label text which is easy to read. In the case of a small secondary packaging, it may be that the legally required information does not all fit on a label sticker due to the available space. In such cases, this method of packaging is not acceptable. A mock-up of the sticker must be submitted for assessment.
- Text on the labelling sticker must be indelible.
- The packaging, including the affixing of labelling stickers, must occur under GMP. A labelling sticker must remain properly attached to the packaging for at least the entire period of the shelf life of the medicinal product, as stated on the packaging, under all the storage conditions that apply for the relevant medicinal product.

6 Formatting: image and text

6.1 Introduction

To clarify the information referred to in Article 54 and Article 59, paragraph 1 of Directive 2001/83/EC, provisions are included in Article 4a.1, paragraph 1 of the Medicines Act Regulation and Article 62 of Directive 2001/83/EC for the outer packaging and the package leaflet to include signs, images or pictograms, as well as other information which

corresponds to the SmPC and which contributes to the health information, with the exception of any information which could have a promotional/commercial character.

All the information on the packaging must therefore:

- be in accordance with the SmPC text that has been approved by the MEB;
- contribute to the health information and/or contribute to proper use of the medicinal product;
- not, in any way, have a sales promotional effect, or be open to interpretation as a promotion for using the product.

In addition to understandable text, images and all the formatting (including layout) can contribute to proper use if they help the user to use the medicinal product more effectively, safely and efficiently. This includes, for example, shading, colour differences, pictograms, images, signs and other graphical elements which:

- are clear and illustrative and help to make the text easier to understand for the user;
- do not contradict standards of good taste and decency;
- make the product recognisable so that the user can distinguish between different products.

An image on the packaging of OTC medicinal product can make it easier to choose from the range offered. Graphic elements can be important for users who have difficulty reading written texts, or do not have a good command of the Dutch language. The highlighting or emphasising of information by means of an image and other types of formatting may be a reason to engage in conversation with the care provider. A balanced choice must be made regarding what is, and is not, to be depicted (for example which user instructions and/or warning.

With regard to allowing the use of logos, illustrations, signs and pictograms the MEB recognises the value that such elements can have on the packaging in terms of clarifying the information and ensuring that the user reads the information properly. However, images may only be used on the packaging to clarify information and may not be used instead of the compulsory text, or as a repetition of the information.
Images such as pictograms can reinforce or clarify certain information/recommendations. The use of standardised pictograms will increase recognisability of this information.

That is why the MEB has compiled a Positive List of Pictograms, in which approved pictograms are included together with their meaning (see Annex 5 of this Policy document). These pictograms aim to warn patients or serve as a visual memory aid for information already displayed. This Positive List is a ‘living’ document to which newly approved standardised pictograms and texts can be added.

The pictograms are included together with their meaning to prevent the possibility of multiple possible interpretations.

Signs and images that portray information such as instructions (e.g. by telling a 'story') will not be included in the list. Also, assessment of this information will happen on an individual basis based on the statutory assessment criteria.

The MEB will maintain this policy based on definitions and admission criteria, which will be further set out in this chapter. A case-by-case assessment will take place on the basis of the mock-up to be submitted.

6.2 Definitions

Pictograms: The MEB defines these as standardised symbols and simple, styled images with a fixed meaning that have been included in the Positive List of Pictograms and communicate a prohibition, instruction or information in a simple manner.

Signs: Shapes based on agreements which portray a message in abbreviated form as simple styled images.

Logos: The MEB defines these as the identifying mark or distinguishing logo of a specific legal entity (for example, the marketing authorisation holder) with a set design.

Images: The MEB defines these as non-standardised graphic representations that are not logos or signs/pictograms. Images are not included in the Positive List of Pictograms and will be assessed by the MEB on a case-by-case basis in accordance with the assessment criteria below.

Information: Written text (based on the definition stipulated in Article 69 of the Medicines Act).

6.3 Assessment criteria

Image elements and layout may only be used for clarification purposes and not instead of the compulsory text. If the marketing authorisation holder wishes to use signs, pictograms, logos, images or other information in addition to the compulsory text information on the packaging of a medicinal product, these must – based on the Medicines Act – meet the following general criteria:

1. **Coherence between image and text**
   Images must always be assessed in conjunction with the written information. This is in accordance with Article 62 of Directive 2001/83/EC which describes that, in addition to compulsory text (Article 54 of Directive 2001/83/EC), the outer packaging 'may also include signs for pictograms for clarification purposes […]'.

Because signs and pictograms can often be interpreted in several ways, it is important that they are depicted together with (compulsory) text.

2. **Corresponds with the approved SmPC text and the text on the packaging of the medicinal product and is not misleading**
   The SmPC text and the accompanying package leaflet form the basis for all the information and communication about the medicinal product, so also for the information on the packaging. The way in which the information is presented on the obligatory packaging must be aimed at the user. For that reason, the information is usually not literally copied from the SmPC text, but must be a user-friendly derivation of the SmPC text. However, sometimes it is inevitable that the information on the packaging will contain elements that have not been derived directly from the SmPC text. This can involve both textual matters (for example batch number and expiry date) and images. If these characteristics are portrayed, the content must, of course, be correct.

   In order to avoid confusion about the set dosage, only one example of the pharmaceutical form may be shown. This image must correspond to the description of the characteristics in the SmPC.

   It is not permitted to use the packaging layout to suggest characteristics that the product does not contain, such as a broader indication area, or a higher efficacy of the medicinal product.

3. **In agreement with the 'guideline on readability of the label and package leaflet of medicinal products for human use'**
   The colour scheme and clarity of the images may not have a negative effect on the readability of the compulsory text on the packaging. The graphic elements may not be larger than 1/3 of the side of the packaging on which they are displayed. Colour scheme and clarity must be secondary to the minimum compulsory text and may not draw the user's attention away from the compulsory text.

4. **Makes the text easier to understand**
   The purpose of the combination of text and images on the packaging is, among other things, to clarify the textual information on medicinal product packaging. This will enable users to understand the information better and help them find the information they need. If the user is unable to see the wood for the trees due to the multitude of text and images, the effect will be anything but clarifying. Pictograms which are, in themselves, clear and correct might, in certain cases, for example when combined, lead to confusion as well and this must be avoided.

   The product must always be recognisable as a medicinal product and the corresponding packaging and layout may not result in misconceptions about the

nature of the product (for example, the product being mistaken for a sweet or cosmetic).

5. **Is not contradictory to standards of good taste and decency**
   The text and images may not evoke any undesirable (insulting, racist, discriminatory, sexist, pornographic, blasphemous, etc.) associations among (some) users.

6. **Does not contain any recommendation of the product, nor an expression which may have a promotional effect**
   Any type of information about a product can contribute to the user preference for that product and can therefore – to a certain extent – be perceived as promotional in nature. The format/layout can also partly determine a product's attractiveness. However, the aim of the image on the packaging must be to provide visual information to clarify the compulsory text and, by doing so, help to ensure that the product is used properly. The MEB therefore has decided – as a general rule – not to permit photographs on the packaging (with the exception of the images of the pharmaceutical form).

   A package's attractiveness is not necessarily the same as an undesirable recommendation. Just as taste, shape and colour of the tablet, capsule or syrup, it can even promote acceptance by the user.

   Medicinal product packaging may not include direct or indirect references to (a recommendation by) scientists or healthcare professionals.

   In this context healthcare professionals include doctors, pharmacists, drugstore employees, midwives, nurses and dentists.

   The background to this provision is that the public have a special confidence in scientists and professionals, meaning that any recommendation would carry a disproportionately large weight. An indirect reference can consist of a reference or an illustration of matters closely associated with them (for example a doctor's or pharmacist's coat or the Rod of Aesculapius), a reference to the institution they work at (university, clinic, institute, laboratory, pharmacy, drugstore, etc.) or the type of work they perform (research, diagnoses), whether referred to jointly or otherwise (for example a pharmacy brand, drugstore brand, pharmacy emblem or pharmacy quality mark).

6.4 Specific points of attention for logos, pictograms, signs, images and information

This section describes the specific points that need to be taken into account with regard to image elements. These elements must comply with the policy referred to in this document and therefore also to the assessment criteria described in section 6.3.

6.4.1 Logos:

Only the logo of the marketing authorisation holder for the relevant product is permitted on the packaging. In the past, logos of the licensor, manufacturer and of the importer at the outer border of the EU were accepted. However, this is no longer permitted due to possible confusion and uncertainty about who is responsible for marketing of the product.

A logo must meet the same requirements and testing criteria as described above in section 6.3.

Examples

In the case of a merger of two companies, the company wants to maintain the logos of the individual companies for the relevant products.
As soon as the name of the merged company is stated on the packaging, only the accompanying logo may be used. It is not permitted to use two logos.

In addition to using the logo of the marketing authorisation holder, the company also wants to use the logo of the parent company.
This is possible under strict conditions (see example below), but it must be absolutely clear which company is responsible for marketing the product.

For example, the logo of company X (marketing authorisation holder) may be used on the packaging and the following information may also be included on the same side of the packaging as the logo of company X: *part of 'Company Y group' + {logo of Company Y}.*

In this case, it is permitted to place the logo of the parent company on the packaging because it is stated on the same side that this is the parent company and there can therefore be no confusion about who is the marketing authorisation holder.

It is therefore permitted to mention *'part of'* and/or *'company Y group'* and possibly the logo of the parent company Y *only* in combination with the logo of the marketing authorisation holder company X on the same side of the packaging.
NB: Mention of just the logo of the parent company Y in combination with the statement that '*company X is part of company Y'* is therefore not permitted without the logo of the marketing authorisation holder being stated because a mention of just the logo of the parent company Y can cause confusion about who is the marketing authorisation holder.

(Branding) sentences such as 'We care for your health', directly or indirectly linked to a logo

Such written text is not primarily intended to contribute to health education, or proper use of the product, but is regarded as promotional and will therefore be rejected (see also section 6.3.6).

A logo of an approved umbrella brand (see MEB 13, Nomenclature of pharmaceutical products) may be stated on the packaging.

6.4.2 Pictograms

Putting pictograms on medicine packaging can help to provide easily understandable information about the most important warnings relating to the use of medicines.

Currently, a number of standardised pictograms are available that companies can use on medicine packaging (see Annex 5: Positive List of Pictograms), provided the accompanying text is included. This set of pictograms brings vital warnings to the attention of the user.

The use of these pictograms on packaging is non-mandatory (so the marketing authorisation holder can choose to use them). The applicability of the pictogram will be assessed during the assessment of the packaging. There is no statutory obligation to include these pictograms on packaging unless such a pictogram is specified as a condition for the issue of the marketing authorisation (e.g. for products containing valproate). Pictograms that have been implemented in the past are not automatically included in the Positive List of Pictograms.

Design of established pictograms

Colour and design

As coloured pictograms are generally easier to understand, the MEB strongly favours the use of coloured pictograms. The standardised pictograms must be displayed in the specified colour in order to increase recognisability of these pictograms. However, in exceptional circumstances in which it is not possible or desirable to display coloured pictograms on specific packaging, they can also be displayed in black and white. The decision to display black and white pictograms must be justified. The MEB will assess this justification. The symbols displayed to the left of every pictogram (a round or triangular symbol indicating a prohibition or a warning respectively) helps to further increase understanding – particularly for the black and white versions of the pictograms – and can help users who have difficulty seeing and distinguishing colours.

Size

The pictograms must be large enough to be accurately interpreted.
For this specific set of pictograms the height must be a minimum of 0.7 cm.

Text

Use of the pictograms is only permitted in combination with the specified explanatory text as displayed alongside each pictogram in Annex 5. The font of the accompanying text must

comply with EU guidelines as specified in the 'Guideline on the readability of the labelling and package leaflet of medicinal products for human use'.

Standardised bottle bank and recycling pictograms

The generally standardised bottle bank and recycling pictograms are permitted. In order to avoid confusion and uncertainty, the bottle bank and recycling pictograms should not feature on the outside of the packaging. They may be placed on the sealing edge that only becomes visible after the package is opened. The bottle bank pictogram may also feature on the label on the primary packaging, or on the glass itself.

For pictograms which have not (yet) been standardised, please refer to the final point in section 6.4.3 Illustrations and signs.

6.4.3 Illustrations and signs

Abstract formatting elements:

No additional conditions apply to abstract (styled) formatting elements, such as stripes, arches, circles, background colours, etc., without further meaning.

Additional conditions which apply to specific types of illustrations:

The pharmaceutical form

The illustration of the pharmaceutical form must correspond exactly to the actual form and its appearance. It must therefore also match the description of the characteristics in the SmPC. For example, if there is a break mark, this must also feature in the illustration. A photo of the pharmaceutical form is permitted. Only one copy of the pharmaceutical form may be depicted. This is intended to prevent confusion with regard to dosage.

Administration devices

This is defined as a device that aids the dosage and/or use of the product. An illustration of this is permitted if the administration device is in the package and is essential for a proper and safe dosage and/or use.

The illustration must be subordinate to the compulsory elements on the packaging.

The target group

An image which portrays the target group is permitted, but there must not be any confusion about the target group. The illustration may not suggest any other age category than the one for which the product is intended. For example, in the case of a product for children, an illustration of the child's head alone is insufficient. An indication of the age category must also be included in or near the illustration. In the same way an illustration of, for example, a toy is not permitted because it does not provide a sufficient reference to the target group of children. It may lead to misunderstandings about the nature of the product and represent an undesirable recommendation for children.

Site of administration/treatment
It is permitted to portray an unambiguous, stylised representation of the site of administration and treatment, if the part of the body where the condition requiring treatment occurs is the same as the place where the medicinal product is to be administered. For example, an ear on a product to treat earache, a nose on a nasal decongestant or a foot on a product to treat athlete's foot. This is only permitted if the medicinal product may only be administered at a single site in accordance with the set indication.

The indication
Only one indication area can be portrayed per illustration. A stylised representation of the indication will then only be possible in a few cases and only if it concerns *all* authorised indications. The visual information will only be complete and confusion avoided if, for example, products have just one indication. It is therefore not permitted, for example, to depict only headache or only back pain on an analgesic that is also authorised for pain such as menstrual pain or pain after vaccinations. Neither is it permitted, in the case of the above-mentioned analgesic, to place circles around the head, abdomen, arms and legs to depict the multiple indication areas in a single image of the body.

In no way may the image create the impression that the medicinal product can also be used for indications that it has not been authorised for. This could be the case, for example, if an oesophagus is pictured along with a stomach on a product that is only authorised for stomach pain and not for acid reflux.

For OTC medicinal products, it is permitted to state an 'abbreviated indication' on the front of the packaging (see policy document MEB 21) in addition to the compulsory instructions for use (complete indication, Article 4a.1, paragraph 1 of the Medicines Act Regulation and Article 54, letter n, of Directive 2001/83/EC). However, the product name on the packaging continues to be the most important distinguishable point and it should therefore feature prominently on the packaging. All other information is subordinate to this. The aim of the abbreviated indication is to help identify possible application of the product. Image information could also support the textual description.
A condition for this is that the image must be in accordance with the abbreviated indication, but also be clear and meaningful on its own (for example, a coughing person may not be confused with a person who is vomiting).

If the image cannot provide any further detail of the indication (for example, a coughing person on a package of a medicinal product with abbreviated indication 'for expectorant cough due to viscid mucous'), one should firstly consider whether it is useful to place the image on the packaging. If a good well-founded reason can be found for its inclusion, the combination of the image and the abbreviated indication and/or product name must depict this indication unambiguously.

Pictograms or symbols which have not (yet) been standardised

The MEB defines pictograms as standardised symbols and simple, styled illustrations with a fixed meaning that have been included in the Positive List of Pictograms and communicate a prohibition, instruction or information in a simple manner. The MEB must assess a stylised representation of, for example, a warning or user instructions for which no standardised symbol is (yet) permitted on a case-by-case basis, even if similar standard pictograms have been approved in other EU countries. The general assessment criteria for images are applicable (see section 6.3).

All pictograms approved by the MEB are included – together with the approved accompanying text – in the MEB's Positive List of Pictograms in Annex 5.

6.4.4 Safety features

The coming into effect of the Falsified Medicines Directive [Europese richtlijn vervalste geneesmiddelen] (FMD) 2011/62/EU means it has been established that certain medicinal products for human use must be accompanied by safety features.

These safety features are:

- a *'unique identifier'* (incorporated into a 2D Data Matrix code)
- an ATD or '*anti-tampering device'* (for example a seal on the packaging that demonstrates that the packaging has not previously been opened).

These safety features must be applied to the packaging of prescription-only medicinal products and in a number of cases also to the packaging of non-prescription medicinal products (the latter are referred to in Annex II of Directive 2016/161, the so-called black list). In a number of cases these safety features do not need to be reported on the packaging of prescription-only medicinal products, these are referred to in Annex I of Directive 2016/161, the so-called white list. More information is available on the website of the European Commission. In addition to the implementation plan for centrally authorised products the *Questions & Answers document: 'Implementation of the rules on the safety features for medicinal products for human use* can also be found here which was drawn up by the European Commission in collaboration with the member states in order to facilitate the implementation of this directive.

Marketing authorisation holders are themselves responsible for ensuring that the safety features are included on the packaging and that the packaging continues to meet the readability guideline.

The QRD template was adapted in 2016 through the addition of sections 17 and 18. The submission and approval of label texts with changed sections 17 and 18 must take place before the medicinal product is launched onto the Dutch market with these safety features, or within 3 years after the coming into effect of the European Directive (in other words before February 2019). See Annex 1 to this document.

If the legal status changes from non-prescription to prescription (so from UA/UAD/AV to UR) the labelling must be adapted in accordance with QRD template sections 17 and 18: Implementation of 2D Data Matrix code and ATD.
Products with different legal statuses in member states must follow the QRD template whereby the relevant sections must be shaded grey in the submitted common text and then with a correct representation for the Dutch text.

Please refer to the implementation plan and the Q&A earlier in this section for regulations relating to the ATD.

6.4.5 Mobile scanning

2D barcode containing information about a medicine
It is permitted to display a 2D Data Matrix code on packaging and/or in the package leaflet, as long as this does not compromise the readability of the mandatory information. An example of a 2D Matrix code is a QR code which contains a link to information about the medicine in the packaging. The same approach applies for technologies that have the same function as the QR code.

Annex 3 at the end of this document describes the conditions that must be met for the use of the QR code on the packaging and/or in the package leaflet for products that have been/will be issued with a national marketing authorisation. This policy also applies to parallel-imported medicinal products and for marketing authorisations approved via replica authorisation procedures.

See also: https://www.hma.eu/90.html

- Bullet point 12: CMDh position paper on the use of Mobile scanning and other technologies to be included in labelling and PL in order to provide information about the medicinal product

2D barcode that does not contain information about a medicine
2D barcodes that are used exclusively for internal production processes or that form part of the mandatory safety features (the unique identifier) and do not contain information about the medicine do not fall under the scope of this policy. See also Chapter 6.4.4 of this document.

Combination of 2D barcodes
Multiple barcodes can be referred to on the packaging if they do not compromise the readability of the information required by law.

Given that the European Directive on Falsified medicinal products (see 6.4.4) states that a 2D Data Matrix code must be applied to the packaging of prescription medicinal products and, in a number of cases, also to the packaging of non-prescription medicinal products, it is recommended that the QR code be included, if possible, in the 2D Data Matrix code. As a

result, less visible codes will be shown on the packaging and there will be a smaller risk of confusion when scanning.

6.4.6 Other information

Packaging materials
References to the packaging materials on the packaging will be rejected if they contain superfluous information. However, it is permitted if the material is included in the name of the product.

Style and QRD
An overview of QRD agreements about style-related matters can be found in the EMA document Compilation of QRD decisions on stylistic matters in product information.

Pre-printing of information on pharmacy stickers
Information that is currently applied to the packaging in the form of stickers by the pharmacist (for example, a blue band containing the white text '*niet om in te nemen*' ('not for oral use')) may now be pre-printed on the packaging, provided that the general standard layout of the current stickers is used.

7 Special packaging

7.1 Wallets, cellophane sleeves as outer packaging, travel pharmacy cases

A wallet is a special type of packaging that is supplied as an integrated part of the product. It usually contains a tablet strip, with an extra cardboard foldaway flap attached to it, which contains information. The advantage of a wallet is that if the patient only has one strip on his/her person, he/she still has access to more information than if only a classic tablet strip had been taken along. The MEB notes that the complete patient information always consists of the sum of the package leaflet and the information as required on outer packaging. The MEB recognises that the patient often only carries one strip and not the entire package, particularly for certain products such as oral contraceptives or simple painkillers. Therefore, the MEB will allow the wallet under certain conditions. However, for the time being this will be assessed on a case-by-case basis.

The wallet forms part of the dossier and must be described in this document. In general, the wallet will not be given to the patient separately.
The wallet will be considered as outer packaging if the wallet is *not* wrapped in – for example – a cellophane sleeve. In principle the wallet must comply with all labelling requirements imposed on outer packaging.

However, sometimes the wallet will *indeed* be wrapped in a completely transparent cellophane sleeve, which holds several wallets and a package leaflet together. This

cellophane cover is considered to be outer packaging. The cellophane cover is part of the dossier and specifications must therefore be recorded in this document. The cellophane sleeve does not contain any labelling information of the manufacturer. One condition is that the packaging (wallet) under the cellophane sleeve states all the legally required labelling information for an outer package. The requirement that this information must be clearly legible through the cellophane also applies (of course). It has been decided at European level that it is not necessary for the information provided in Braille on the cardboard of the wallet to be tangible through the cellophane, as the cellophane will always be removed before use and the (blind or visually impaired) patient can then take note of the text in Braille after all.

Despite the fact that the manufacturer does not have to attach a label to the cellophane sleeve itself, a label will still be applied: namely the label from the pharmacy when the product is dispensed. The layout of the text on the packaging under the cellophane sleeve must therefore be set out in such a way that no information will be obscured if a pharmacy label is placed on the cellophane sleeve. A section of the packaging under the cellophane sleeve must be left blank intentionally, for the pharmacy label to be stuck on over the cellophane.

In the case of a non-resealable cellophane sleeve, it is preferable that this sleeve remains intact as far as possible after opening in order to prevent premature disposal of the sleeve and the pharmacy label.

For the time being, the MEB expects a specimen of the wallet to be submitted for the assessment of the packaging form 'wallet' and a (two-dimensional) mock-up alone is not sufficient. However, the medicinal product does not actually have to be present in the specimen.

An alternative option is that the extra packaging – in whatever form – is also made available separately when the medicinal product is dispensed from the pharmacy. The extra outer packaging then does not form part of the product and therefore does not need to be described in the dossier. The so-called travel pharmacy cases are known examples, in which several different products can be stored. The MEB will not object in the case of examples as described above.

7.2 Combination packages

The combination package has its own authorisation number, in addition to the RVG numbers of the individual products, if these products are authorised separately. The calendar packages with various products are a special case. Please refer to the policy in MEB 47 'Assessment criteria for combination packages'. It is particularly important that the text on the immediate packaging does not cause any confusion about use.

If one package contains several products, a clear distinction must be made between the various products in the combination package. If they are packaged separately, a label text must be submitted for the individual products. If the products are packaged separately, the label text for the individual products must only state the RVG number for the combination packaging (and not the RVG number of the individually authorised product), as the whole is authorised under the RVG number for the combination package. For more information see MEB 47.

7.3 Parallel import

The requirements concerning labelling in general apply to pharmaceutical products marketed via parallel import. The same applies to the requirement that the product name must also be stated in Braille. However, if the product name in the country of origin differs from the name in the Netherlands, the product name in the country of origin may still be written in Braille. The Dutch product name does not need to be added in Braille. It is important to ensure that the Braille remains legible when the labels of the parallel marketing authorisation holder are applied to the package. The Braille may be written through the printed text.

The following applies to the labelling of *primary* packaging of parallel import products: if the application of a Dutch label on the primary packaging causes problems that could be detrimental to the patient and the relevant information has been translated correctly in the package leaflet, the MEB will not maintain the requirement that a Dutch label must be placed on the primary packaging. However, the outer packaging must be labelled in Dutch.

Example: A tablet strip states the days of the week with abbreviations in a foreign language. However, applying an extra cover foil with Dutch text makes it much more difficult to release the tablets, which is detrimental to the patient. The foreign abbreviations are translated in the package leaflet and the outer packaging does contain a Dutch label. In this case, the MEB will not insist on the requirement for Dutch labelling on the primary packaging.

Example: An ampoule is placed in a so-called sterile 'inner blister', which is then packed in a cardboard outer package. The ampoule has not been labelled in Dutch. The information in the foreign language provided on the label of the ampoule is available in Dutch in the package leaflet. The blister would have to be opened in order to apply a Dutch label, which entails the risk of a loss of sterility. This is detrimental to the patient. In this case, the MEB will not insist on the requirement for Dutch labelling on the primary packaging.

For parallel products, it is *compulsory* to state the company (name + address) that accepts responsibility for the outer packaging on the label/the new outer packaging. It has to be clear who is responsible for the packaging. In practice this means that either the actual packager must be mentioned, in addition to the marketing authorisation holder, or the marketing authorisation holder alone must be mentioned as the 'marketing authorisation holder/packager'.

For OTC medicinal products the indications, contra-indications, dosage, method of use and method of administration must be worded in the same manner on the packaging of the parallel product as the information on the packaging of the Dutch reference product. Warnings on the packaging of the parallel product must be the same as the information on the packaging of the Dutch reference product.

If the indications, contra-indications and/or dosages from the country of origin are also stated on the package, they must be covered with a sticker if they differ from the approved specifications for the Dutch reference product. It is important to ensure that indications that have not been approved for the Dutch reference product cannot be read (in the foreign language) on the packaging. For further information, please refer to policy document MEB 14 'Parallel import: marketing authorisation and maintenance'.

7.4 Stock/bulk packaging

The MEB recognises that marketing authorisation holders sometimes wish to market (very) large packages. These packages (for which the specifications must be set out in the dossier) are apparently not intended for dispensing (by the pharmacy) to the individual patient, but are intended as stock from which the pharmacy can dispense the required quantity to several patients. However, the Medicines Act does not provide for separate (reduced) labelling requirements for such packages. The labelling of the (very large) packages will have to meet the normal requirements for (primary) packages. The MEB will grant exemption for stating the product name in Braille on products that are exclusively administered by a medical professional and not by the patients themselves. However, the criterion is then the nature of the medicinal product and not the packaging size. Administration by the professional refers to the doctor who will administer certain administration forms (for example, injections) to the patient where the patient is unable to do this himself/herself. This does not apply to the *dispensing* of the medicinal product by the pharmacist.

7.5 Blister packaging/strip packaging (including EAV/EAG packaging)

Blister packages or strip packages consist of two layers in which capsules or tablets are packaged. Please refer to the QRD template for the requirements that apply to the labelling of primary packaging (such as strip packaging and blister packaging).

According to the QRD template, the name of the packaging must be followed by the strength, the pharmaceutical form and (on the second line) the active substance. In accordance with the QRD template, the batch number and expiry date must also be stated, preceded by Lot/Batch and Exp/do not use after/shelf life respectively. This also applies to strip packaging and blister packaging. The MEB has included the above-mentioned recommendations in its national policy.

- It is permitted to present certain information (batch number, expiry date) in punched text rather than printed text on blister and strip packages. The location of this information must always be indicated on the mock-up as well.

- For strips and blisters of EAV/EAG (Unit Dispensing Packages / Unit Dispensing Suitable Packages), intended for hospitals and nursing homes, the above mentioned QRD requirements for primary packaging must be met on each individual packaging unit. If the EAV/EAG packaging deviates from the other packaging (for example number of items per package, material, type of packaging (e.g. strip or blister), text/text per dispensing unit, mock-ups) in any way, then they must be included separately in the dossier and also reported in SmPC section 6.5.

  It is permissible to mention EAV packaging in the national text of the packaging text, if SUP packaging contains the same packaging materials/size as the already approved packaging mentioned in the EU SmPC and package leaflet. An EAV/EAG package can be included in the SmPC during the national implementation of an application procedure for marketing authorisation or during a variation if the SmPC is involved in this variation and the materials/size are in accordance with the information about the strips/blisters mentioned in the SmPC. An MRP variation is not necessary for adding this information to the package leaflet/packaging text. A national Article 61 (3) procedure can be used.

- The strip packaging and blister packaging may also include extra information such as a barcode, instructions concerning the use or the order in which the tablets must be taken (calendar packaging), such on condition that this does not detract from the primary information. The MEB does not have a preference concerning a standard for the barcode.

- The name and address of the marketing authorisation holder must be stated on the strip or blister packaging. This name may be abbreviated, provided that the marketing authorisation holder's identity is sufficiently clear. If the (abbreviation of the) marketing authorisation holder's name is included in the trade name, it does not have to be stated separately.

- It is permitted to add a blister holder to the packaging. The blister holder is a type of cover intended to carry one blister/strip instead of several as packaged in a box. The same information must be stated on the blister holder as described in the QRD template for the outer packaging. The following details form an exception to this:
  - batch number and expiry date (the blister holder can be used again, including for different batches)
  - packaging size (the blister holder is intended for one blister/strip)
  Braille must be stated on the blister holder, in order to make the blister holder recognisable to blind and visually impaired individuals.

- **Strip/blister packaging with calendar indication and strip/blister packaging with various types of tablets in a single product**
  These packages, including mock-up, may not cause any confusion about the use and the identity of the tablet, if there are different types of tablets.

7.6 Small primary packaging (ampoule, cartridge and other small packages)

For small primary packages (and possibly also for larger packages), it is not always necessary to include all the details if a sound argument for dispensation is submitted. Please refer to the QRD template, the English annotated version of the QRD template and the 'Guideline on readability'.

7.7 Intermediate packaging

The rules in accordance with the QRD template apply to the outer packaging and the label of the primary packaging. Sometimes there is another type of packaging between the outer packaging and the primary packaging, which is referred to as the intermediate packaging. The requirements concerning the inclusion of information that apply to the outer packaging also apply to the intermediate packaging. A proposal must also be submitted for the intermediate packaging concerning the text on the packaging and a mock-up must be submitted. If these requirements are not met, a reason must be provided as to why there is a deviation from the requirements set for the outer packaging.

7.8 Claims related to opening the packaging

The MEB is of the opinion that completely childproof packaging does not exist. The MEB therefore considers claims concerning child safety as misleading.
However, the packaging can ensure that it takes longer before a child can open the packaging. For that reason, the MEB accepts the following claim on the packaging with regard to childproof packaging, provided it is sufficiently substantiated in the dossier: '*Difficult for children to open*'.

If, during an MRP/DCP procedure, a claim concerning child safety on the packaging is established, the MEB will only accept the claim '*Difficult for children to open*' [Moeilijk te openen door kinderen] on Dutch packaging as a translation, irrespective of the term in the European adopted text (*child resistant, child safe* etc.).

Claims concerning '*senior-citizen-friendly packaging'* [seniorvriendelijke verpakking] are not permitted. The term 'senior' is subjective and does not provide a proper description of the target group.

8 Labelling of specific product groups

It must be taken into consideration that the European Pharmacopoeia and the Dutch Medicines Act requires additional requirements for labelling for a number of pharmaceutical forms:

8.1 Radiopharmaceutical products

The primary packaging of a radiopharmaceutical product must state:

- the name or the code of the medicinal product, including the name or chemical symbol of the radionuclide,
- the identification of the batch,
- the expiry date of the batch,
- the international symbol for radioactivity,
- the manufacturer's name,
- the amount of radioactivity, as indicated in Article 2, see below.

The outer packaging must meet the requirements set out in Article 4a.1 of the Medicines Act Regulation and Article 54 of Directive 2001/83. Article 66, paragraphs 1 and 2, of Directive 2001/83/EC also applies to these products. These provisions set out further rules for the information that has to be provided on the different types of packaging for this product. The label of a product that contains radionuclides must also provide a complete explanation of the codes that are used on the primary packaging. If necessary, the amount of radioactivity per dosage unit or per package must be stated for a certain time or date, as well as the number of dosage units or – for liquids – the millilitres contained in the object in which a radiopharmaceutical is dispensed.

8.2 Sera and vaccines

Additional requirements apply to sera and vaccines, as defined in the relevant monographs in the European Pharmacopoeia, please refer to that document.

8.3 Blood products

A number of additional labelling requirements have been formulated for blood products in the European Pharmacopoeia, please refer to that document.

8.4 Homeopathic pharmaceutical products

All homeopathic medicinal products must state on the outer packaging – or if this is missing, on the primary packaging – that this is a homeopathic medicinal product (Article 4a.1, paragraph 1 of the Medicines Act Regulation and Article 69 (1) of Directive 2001/83/EC).

Pursuant to Article 4a.1, paragraph 1 of the Medicines Act Regulation and Article 68 of Directive 2001/83, the labelling of a homeopathic medicinal product must also comply with the provisions of Part V of Directive 2001/83/EC and Article 69 of Directive 2001/83/EC.

The following amended labelling requirements apply to homeopathic medicinal products for which no therapeutic indication is stated on the packaging and in the package leaflet, medicinal products that are intended for oral or external use and for medicinal products for which the degree of dilution meets certain requirements to guarantee that they are harmless (Article 14, paragraph 1 of Directive 2001/83/EC):

- the scientific name or other name of the homeopathic stock or stocks, followed by the degree of dilution, making use of the symbols of the pharmacopoeia used in accordance with article 1(5),
- the name and address of the authorisation holder and, where appropriate, of the manufacturer,
- the method of use and, if necessary, administration,
- the expiry date, in clear terms (month, year),
- the pharmaceutical form
- the contents of the sales presentation,
- the special storage precautions, if any,
- a special warning if necessary,
- the batch number,
- the authorisation number,
- 'homeopathic medicinal product without approved therapeutic indications',
- a warning advising the user to consult a doctor if the symptoms persist during the use of the medicinal product.
- (Article 4a.1 of the Medicines Act Regulation and Article 69(1) of Directive 2001/83/EC)

The normal labelling requirements apply to homeopathic products that do not fall into these categories.

8.5 Traditional herbal medicinal products

For traditional herbal medicinal products, the normal labelling requirements apply pursuant to Article 4a.1 of the Medicines Act Regulation plus the requirements as set out in Articles 54, 55 and 62 of Directive 2001/83/EC.

The outer packaging – or, if this is missing, the primary packaging – of so-called traditional herbal medicinal products must state that this is a traditional herbal medicinal product. This packaging must also state that the user must consult a doctor or another suitably qualified professional (for example a dentist or midwife) in individual healthcare if the symptoms persist whilst using the traditional herbal medicinal product.

Annex 1: Clarification of sections in the QRD template

The information below is intended as a supplement to the English annotated QRD template. The QRD templates can be found on the EMA website. Information that can be found there will not be repeated here.

Clarification is provided per section in the English annotated template. The Dutch template only contains translations of section titles, standard sentences and examples (and not the clarification).

The Dutch QRD template follows below and deals with the remaining points that are not (sufficiently) discussed in the above-mentioned documents.

A diagrammatic overview of the de QRD sections discussed below feature in the 'Checklist' in Annex 2 to this document.

1. Name of the medicinal product

According to the QRD template, the name, strength and pharmaceutical form must be stated on the first line of the label text. The name, strength and pharmaceutical must form a whole. This should be expressed on the mock-up of the packaging. The active substance(s) must be stated below this, on the second line.
The name is one of the most important distinguishing features of the packaging. The name of the medicinal product must therefore be stated prominently on the packaging and it must form a whole.

The term 'must form a whole' means that the name on the product must be identical to the name as approved in Section 1 of the SmPC. This means that the different parts of the name must be displayed in the correct order (as specified in Section 1 of the SmPC) and placed together on the packaging. This does not exclude the possibility that various parts of the name can be placed on multiple lines beneath one another if this is necessary to fit the format of the packaging, as long as the name still constitutes a whole. In this way, the name remains recognisable and is displayed on the packaging without interruption. The details which must be placed on the main side can be found in, for example, Annex 2.

See the policy document MEB 13 'Nomenclature of Pharmaceutical Products' for naming details.

Name for special age group

If a pharmaceutical product is exclusively intended for use by a certain age group, the indication of this age group must be stated *additionally* on the packaging (see Article 54a of Directive 2001/83/EC). However, the information no longer needs to be included in the name. See also MEB 13 'Nomenclature of Pharmaceutical Products'.

The reference to the medicinal product's name on the packaging must take account of the following points:

- **Avoiding double entries**

- **General or scientific name of the active substance**
  If the name of the product is built up of the *general* or scientific name and the name of the marketing authorisation holder (or a [umbrella] brand), then it is *not* compulsory to state this general or scientific name of the active substance *again immediately after (below or next to)* the name on the packaging. In this case, the second line can be omitted in order to prevent repetition.
  Example: For the name 'Paracetamol Company X 500 mg tablet', the word 'paracetamol' does not have to be repeated immediately after the name on the packaging. If the name is an *invented name*, for example 'Panadol', then it must be included.

  The above requirement is separate from the requirement to mention the qualitative and quantitative composition of the active substances per dosage unit separately on the package ('one tablet contains 500 mg paracetamol'). This dosage unit must be stated on the most important side of the packaging (see section 2 below for more information).

  If an active substance is present in the medicinal product as a salt or an ester form, it may be necessary to state the active substance in the immediate vicinity of the name (on the 'second line') of the packaging, in order to give a correct representation of the nature of the incorporated substance (see section 2 below for more information). This is clarified in the examples in Annex 4 of this document.

- **Pharmaceutical form**
  If the pharmaceutical form is included in the name, it does not need to be stated again immediately following the name on the packaging. However, the pharmaceutical form must always be stated separately on the packaging (see also section 4 below). The product name must always be stated as a single whole on the packaging.

  On small primary blister packaging it may be permitted, in connection with the space, to state a shortened pharmaceutical form in accordance with the patient-friendly terms of the EDQM which are generally shorter and which have been approved and authorised by the national authorities, as long as the pharmaceutical form is stated in full on the outer packaging.

- **Strength**
  If the strength (number AND strength unit) is included in the name, it does not need to be stated again after the name on the packaging. However, salts and esters, as stated under 'Name, active substance and strength', must be taken into account. The

composition *per dosage unit* will still have to be stated separately ('one tablet contains x mg of y').

The MEB does not object to the addition of the symbol ® or ™ to the product name when stating this product name on the *packaging* (the use of these symbols is not permitted when stating the product name in the Summary of Product Characteristics, please refer to the English annotated QRD template).

2. Statement of active substance(s)

The details of the composition must also be viewed in combination with the name, strength and pharmaceutical form.
If the active substance in the product is present as a salt or an ester form, this must be clearly indicated. This is clarified in the examples in Annex 4 of this document.

Other points concerning references to the composition of active substances:

- For pharmaceutical products with a maximum of two active substances, the details of the composition and the quantity ('one tablet contains x mg of y') must be stated immediately with the name (and the subsequent information on the strength and pharmaceutical form) and therefore feature on the main side of the packaging. If the name of the product is stated on various sides of the packaging, the reference to the composition ('one tablet contains x mg of y') only has to be stated on the most important side of the packaging.

- In the case of products with an invented name and a single active substance, the active substance must also be referred to on each side that the product name is stated. The MEB also prefers this qualitative and quantitative composition always to be included (so also with several active substances) on the same side of the packaging as the name.

- The composition must be referred to in the nomenclature recommended by the World Health Organisation (INN name Dutch). If there is no INN name, a common standard name such as a Pharmacopoeia name, USAN or BAN may be included.

- For new active substances, the strength indication must refer to the active part of the molecule.

- If a substance also occurs as a hydrate, it must be stated whether this is the hydrate or the anhydrous substance, even if this information does not form part of the name of the substance in a pharmacopoeia.

- The concentration should not be expressed in percentages. It is permitted to show a concentration in percentages in the *name* for those products where the

concentration determines the effect more than the total amount and where reporting the strength in percentages has been common practice for some time, for example Sodium Chloride 0.9 %.

- If a substance is declared in micrograms, this strength unit must be written out in full in the declaration for safety reasons (mix-ups with milligrams). Only when this results in practical problems that cannot be solved with a smaller font size (<7 Didot points) may the abbreviation 'mcg' be used in the declaration. Under no circumstances may the abbreviation 'µg' be used in the declaration, as the Greek 'mu' for microgram poses too great a risk of being confused with the 'm' for mg. The MEB wants the above-mentioned requirement concerning mcg to apply both to the outer packaging and the primary packaging, including blister packaging. See also the document of the European Commission entitled *Guideline on readability*.

Liquid pharmaceutical forms

- For liquid pharmaceutical forms, it must be clear in which concentration the active substance is present:

  Oral forms
  The strength is indicated in mg/ml and also – in the case of a specific dosage unit (for example a 5 ml measuring spoon) – per dosage unit, for example 400 mg/5 ml or 400 mg = 5 ml.

  Parenteral forms (single use)
  The concentration of the active substance is expressed in mg(IE)/ml or in mg(IE)/l for volumes greater than 500 ml and also in relation to the final volume of the product. So not only 40 mg/ml, but also 80 mg/ 2 ml or 80 mg = 2 ml. The same applies for 1 ml flacons/vials, etc. So, for example, not only 40 mg/ml, but also 40 mg/ 1 ml or 40 mg = 1 ml.

  Parenteral forms (multiple use)
  The labels of pharmaceutical products for multiple use deserve special attention. The concentration is stated both in mg/ml and as the total quantity calculated according to the final volume. A statement must also be included at all times as to whether the pharmaceutical product is intended for multiple administrations.

  Parenteral forms as concentrates
  The total quantity in the concentrate and the quantity per ml are stated for the active substance, as well as the quantity per ml after dilution.

  Parenteral forms as powders
  The total quantity in the primary packaging and the quantity per ml after reconstitution are stated for the active substance.

Solutions for dilution or for reconstitution
The volume that is actually used, for example the quantity extracted from the vial, must be stated.

Administration forms for transdermal use

- The total quantity per administration form (for example per plaster) is stated for the active substance, as well as the quantity released per unit of time. The surface area per form must also be reported (for example, the surface area of the plaster).

Implants and intra-uterine devices

- The total quantity per administration form is stated for the active substance, as well as the quantity released per unit of time.

3. List of excipients

- *All* excipients must be listed qualitatively in the case of pharmaceutical products destined for parenteral administration and for local administration (including the ear and the eye). This obligation applies to both the outer packaging and the primary packaging. If the space available on the label is not sufficient, as may be the case with regard to small ampoules, this obligation will no longer apply to the primary packaging.

- For pharmaceutical forms other than the ones described above, the European Commission has published a list of excipients that must always be stated (see the '[Guideline on the excipients in the label and package leaflet of medicinal products for human use]').

  Of course the complete composition may always be stated on the label of any pharmaceutical product.

- The basic principle is that only excipients that are present must be stated. Therefore, it is not permitted, for example, to state the description '*alcohol-free*' or *sodium-free* on the packaging. Several descriptions can be included in the **product name**. See also policy document MEB 13 'Nomenclature of pharmaceutical products'.

- According to the guideline 'Excipients in the label and package leaflet of medicinal products for human use', the label must include a reference to the package leaflet in the case of an excipient that is listed in the guideline, for example 'see package leaflet for more information'. This means that, in some cases, the label must contain two references to the package leaflet, namely in section 3 of the QRD template for the excipients and in section 5 of the QRD template. The reference may be included twice on the mock-up, but this is not essential.

4. Pharmaceutical form and contents

The description of the pharmaceutical form must be in agreement with the recommendations in the Standard Terms, as set out by the European Pharmacopoeia. The Standard Terms apply to label texts for new authorisations. These terms must be taken into consideration during the revision or repeat registration of products already on the market. A Dutch translation has been included in the above-mentioned list of Standard Terms.

Small packaging, strips

The preference is very much for the entire pharmaceutical form to be shown. If this is **truly** impossible, an abbreviation of the Standard Term will be accepted. What is acceptable will have to be assessed on a case-by-case basis.

Contents: Everything in the packaging (with the exception of the package leaflet) must be mentioned.

This includes enclosed devices (and their number) such as needles, disinfectant wipes (so-called 'swabs'), etc. if applicable. The same information must be shown as referred to in section 6.5 of the SmPC.

This includes the following case (example as an illustration):
There are two different packaging forms for the product Cernevit, powder for solution for injection. In addition to a standard aluminium capped vial, a vial with an alternative cap has been authorised that allows for direct connection to an infusion bag (called BIO-SET). A syringe with needle is required for the first packaging form. This is not necessary for the BIO-SET, as this can be connected directly to the infusion bag. The solvent is transferred to the vial by squeezing the bag. The dissolved product is then returned to the infusion bag.

As it is important for professionals to know which packaging form they are dealing with, the MEB has a strong preference for the relevant information to be included on both the outer packaging and the label. In this example, this has been performed correctly by including the following text:
'1 injection vial with BIO-SET'

It should be noted that such additional information about the packaging form may of course not be promotional in nature, as this would contravene the Medicines Act.

5. Method and route(s) of administration

The standard sentence as referred to in the QRD template must *always* be included here.

- In general, it is essential to mention the route of administration if this cannot be deduced from the pharmaceutical form.

Technical instructions for the correct use of the medicinal product also fall under this category.

Examples:
For use under the tongue
For vaginal use
For rectal use
Swallow whole
Shake before use

It is very important that it is expressed clearly whether a product must be used as is, or only after dilution, dissolving, heating or similar.

In the case of over-the-counter products, it is even more important that people understand the information on the packaging properly. This must be taken into account in the information relating to the route of administration. In other words, the details on the packaging and therefore also the details relating to the route of administration must be made easy to understand for a broad group of patients. For example, it is better to use the expression 'in the ear' than the term 'auricular'. The same applies to, for example, oral/parenteral. For more information about making packaging easy to understand, see the toolkit for understandable package leaflets on the MEB website, which includes a patient-friendly terminology list, among other information.

The following instructions must always be included if applicable:

* *Concentrate for solution for infusion*
  Only administer after dilution with an infusion liquid.
  Name and quantity of any added preservatives.

* *Concentrate for solution for injection*
  Dilute with x mL of y (recommended solvent) before administration.
  Name and quantity of any added preservatives.

* *Powder for solution for injection*
  Name and quantity of any added preservatives.
  Method of preparing the solution for injection.

Preparations in which a relatively large quantity of solid substance need to be dissolved result in volume expansion, meaning that the final concentration cannot be calculated as such. This final concentration must be determined and the result must be reported. For example in the following manner: 'Addition of … ml of solvent results in … ml of solution at a concentration of … mg/ml'.

- The method of administration is listed on ampoules and cartridges. Use the terms in the List of Standard Terms for this purpose.

Examples:
intravenous

intradiscal

epidural

The method of administration must also be listed in this manner on other packages of products for parenteral use.

- The abbreviations I.V. (intravenous) and I.M. (intramuscular) are permitted if the primary packaging does not offer enough space to list the full name of the route of administration.

6. A special warning that the medicinal product must be kept out of the sight and reach of children

The standard sentence from the QRD template must be included. This sentence must also be stated on products that are used in hospital.

7. Other special warning(s), if necessary

If the relevant product has a quality requirement that it must be sterile and/or pyrogen-free, then it is permitted to list this on the label. The QRD template makes no mention of this, but the MEB has no objection to listing this.

Special warnings on the packaging can be deemed necessary by the MEB in special cases which are not specified in any greater detail. However, the MEB will be cautious in doing so.

8. Expiry date

There must be an understandable reference to the expiry date by which the product is deemed suitable for use. The month must be stated in two digits or at least three letters and the year in four digits. Example: February-2018, Feb_2018, 02_2018.

In principle terms such as 'do not use after', 'shelf life', 'exp' may also be stated on the packaging, supplementary to the details from Annex IV of the QRD template. These obligatory particulars must be followed by the final expiry date.

For some products (radiopharmaceuticals, vaccines), it may be necessary to specify the information for use even further.

In-use shelf life

If the in-use shelf-life of the primary packaging is not shorter than the expiry date for resealable packaging/packaging for multiple use, this does not explicitly have to be stated, such in accordance with the 'Note for Guidance on in-use stability testing of human medicinal products'.

In contrast to European policy, however, the MEB is of the opinion that this information is important for the patient in the case of OTS medicinal products. Since September 2016 the MEB has applied the national policy referred to below with regard to the in-use shelf life of OTC medicinal products with a resealable packaging for:

- Non-prescription medicinal products (AV, UAD, UA legal status of supply) with resealable packaging, authorised via the national or MR/DC procedure and regardless of authorisation date, with the exception of medical gases.
- Traditional herbal medicinal products;
- Homeopathic medicinal products.

The following standard sentences can be used:

If the in-use shelf life is at least **as long as** the entire shelf life, the expiry date must be followed by the following text:

This date also applies after opening of the <packaging><vial><tube><…>.

If the in-use shelf life is **shorter** than the entire shelf life of the unopened product, the following text should be included after the expiry date:

After opening of the <packaging><vial><tube><…> this product will expire in <XX days/weeks/months>.

The in-use shelf life must be stated on both the primary and outer packaging. What is more, this information must be included in the Summary of Product Characteristics and the package leaflet.

If necessary, the blue box can be used for products which have been/are authorised via MRP/DCP in order to include in-use shelf life information.

Substantiation of the in-use shelf life

Directive 2001/83/EC states that details of the shelf life must be submitted along with the application for authorisation of a medicinal product. The 'Note for Guidance on in-use stability testing of human medicinal products' states how applicants of a medicinal product for multiple use must investigate the in-use shelf life of the packaging, all how they can clarify why such an investigation is not necessary.

An exception to this applies to homoeopathic products which have been authorised in accordance with Article 14 of Directive 2001/83/EC provided they:

- have a liquid pharmaceutical form with an ethanol content of > 30% V/V, or
- do not contain water.

No additional substantiation is necessary for these products if the proposed in-use shelf life corresponds with table 22.15 of Practical Pharmaceutics (see preference point 3 below).

The package leaflet of parallel-authorised OTC medicinal products mentions the storage conditions of the foreign product, including the in-use shelf life. If the foreign package leaflet does not state any in-use shelf life, the package leaflet of the Dutch reference product can be used. NB: this is only possible if it can be demonstrated that the Dutch reference product is equivalent to the parallel product. For more information on the assessment, please refer to the Policy Document 'Parallel import: authorisation and maintenance' (MEB 14).

For products which have been authorised before 2001 it was not yet obligatory, at the time of authorisation, to carry out an in-use stability study. For the in-use shelf life for these products, the applicant should *preferably* have obtained in-use stability data based on a study with the product itself. If there is no in-use stability data available for the product itself, the applicant can substantiate the information by providing (in declining order of preference):

1. In-use stability data of other, comparable products, whereby the applicant substantiates why this data is applicable to the product or why the applicant has deviated from it.
2. Literature which is as specific as possible for your product, with substantiation of the way in which the applicant applies this literature to the product (the literature referred to must be sent as well).
3. Practical Pharmaceutics: An International Guideline for the Preparation, Care and Use of Medicinal Products; Yvonne Bouwman, V'Iain Fenton-May, Paul Le Brun; Springer, 24 Aug. 2015. P.457 Table 22.15: assigned usage periods for dosage forms. When using this table the applicant must substantiate why the shelf life mentioned in this table is applicable to the product or why the applicant has deviated from it.
   If additional storage conditions have been included in the table, the applicant must include these (in QRD terminology) in the product information.

Existing marketing authorisations

If a product is marketed in resealable packaging and no in-use shelf life has yet been stated on this medicinal product, the applicant will be asked to submit an Article 61(3) notification or a variation well before the product is marketed with the changed packaging.

Notifications are only possible if the SmPC already includes information about the in-use shelf life. When changes to module 3 and/or adjustments to the SmPC are made, variations must be submitted. In this case a Type IB variation category B.II.f.1.z is applicable.

For products authorised via the MRP/DCP procedure, the notifications/variations must be submitted in the RMS and CMSes.

9. Special storage conditions

The standard sentences from Annex III in the QRD template must be adhered to.

The MEB has no objection to stating on the label that there are no special storage conditions (in accordance with the Package Leaflet). This option is not stated in the annex to the QRD template.

10. Special precautions for disposal of unused medicinal products or waste materials derived from such medicinal products, if applicable

No additions to the text of the QRD template are required for this section.

11. Name and address of the marketing authorisation holder

According to the Medicines Act, the party that is responsible for marketing the product must submit the application for authorisation. This means that the person or legal entity listed on the packaging is the marketing authorisation holder. Examples of contact options are: correspondence address, telephone number, fax number, e-mail address.

Address details

The following applies to the address (including the correspondence address): a PO Box (plus city) is not acceptable. This cannot be considered an address from a legal perspective. The stated address should therefore consist of a street + street number (plus city). The country name 'The Netherlands' does not have to be added here, provided that the city is located in the Netherlands. The MEB is aware that this deviates from the QRD template, because this template does require the country to be mentioned. However, in order to save space and due to the fact that it may be assumed that patients in the Netherlands will not be impeded if they wish to visit the address of a city in the Netherlands, this exception is permitted. For the record: if the marketing authorisation holder is located in a foreign city, then the country will have to be added. If the latter case (listing of country name, because city located in foreign country) results in a lack of space on the outer packaging, then it is acceptable by exception to omit the street + street number and only mention the place of business (city) and the country. Thus: 'Marketing authorisation holder X, Munich, Germany'. Of course this only applies in the case of a lack of space, because such limited information is generally not desirable. The fact that the label text has to be drawn up in Dutch means that the Dutch notation of city and country names must be used, in other words 'Praag, Boekarest' etc.

Contact details

The telephone number listed on the packaging must be the general telephone number for the marketing authorisation holder, which can be used by anyone wishing to get in touch. Special telephone numbers that redirect the caller from the marketing authorisation holder to special 'patient information programmes' or 'patient support programmes' are not permitted.

For the sake of completeness, it should be noted that it is permitted to provide an alternative address for correspondence and information (and the accompanying representative), in *addition* to that of the marketing authorisation holder. This applies not only to the package leaflet but also to the packaging. Whether the marketing authorisation holder is located in the Netherlands or abroad is not relevant. This additional information to the information on the marketing authorisation holder may make it easier to correspond and provide information, particularly if the marketing authorisation holder is not based in the Netherlands. The way this is presented on the packaging must be aimed at users. For that reason the term 'local representative' is not acceptable. The preference is for '*For correspondence and information:*'.

The name of the distributor may not be explicitly listed in the capacity of 'distributor', because the distributor must be viewed as wholesale supplier and therefore carries no responsibility whatsoever for the marketing of the product. Any mention of the term 'distributor' could create confusion about who is responsible for marketing the product. An exception applies if the marketing authorisation holder, whose contact details are listed as 'alternative address for correspondence and information', coincidentally fulfils the role of distributor *as well*. This representative may then of course be mentioned by name, however only in his role as 'representative for correspondence and information'. The role of the representative for correspondence and information must therefore be stated clearly, preceded by the name of this representative (see above).

(Trade) marks

In line with the policy about adding the symbol ® or ™ to the product name (see Annex 1, section 1 above) additions such as *'Trademark of <xxx>'* or 'Trademarks owned by, or licensed to, <xxx>' are accepted in the package leaflet and on the packaging, but not in the SmPC (here the term licence means the licence holder of the trademark or copyright).

It is not permitted to list chemists or a licence holder (of the marketing authorisation) on the trade packaging, as the Medicines Act does not offer scope for this. The Medicines Act does provide the opportunity to use a name for a medicinal product in which a brand has been included (that is not the marketing authorisation holder). This brand could be the name of a chain of chemists or a licence holder, assuming that they are the marketing authorisation holder for that brand.

Copyright statement

Copyright statements and copyright declarations may not be included on the packaging.

12. Marketing authorisation number(s)

The marketing authorisation number consists of the designation RVG or RVH (capital letters, no full stops between the letters) followed by a number. However, for products authorised via the Centralised Procedure, the letters 'RVG' or 'RVH' are not included in the number of the marketing authorisation. In that case, the number starts with the designation EU/1/… for human medicinal products and with the designation EU/2/… for veterinary medicinal products.

If a product has a combined number, for example RVG 08916//104217 or RVG 55595=03869, the entire number must be listed on the packaging.

13. Batch number

- The batch number must be a characteristic combination of numbers and/or letters that specifically identify a batch in accordance with the European GMP guide. Moreover, the information must be clearly readable, easy to understand and indelible (article 56 of Directive 2001/83/EC).

- Supplementary to the requirements in Annex IV of the QRD template, the batch number must be preceded on the packaging by set terms such as 'Batch', 'Lot', 'consignment'.

- For products marketed via parallel import that are repackaged, the consignment number listed on the original packaging must be included on the new packaging.

14. General classification for supply

Although stated differently in the QRD template, the following classification applies to the Netherlands:
UR, UA, UAD, AV (Article 4a, paragraph 1 of the Medicines Act Regulation).

The dispensing status of a product is determined by the MEB based on the Medicines Act Regulation. A choice must be made from one of the following designations on the packaging:

UR: for a medicinal product that may only be dispensed on prescription.
UA: for a medicinal product that may only be dispensed in a pharmacy.
UAD: for a medicinal product that may only be dispensed in a pharmacy or drugstore.
AV: for a medicinal product that may be sold in general sale.

15. Instructions on use

The instructions for use must be listed on the packaging for non-PO medicinal product. Instructions for use include at least: indications and contra-indications. Dosage may be added. The use of the 'abbreviated indication' is permitted on the main side of the packaging, provided that the full indication is listed elsewhere on the packaging. Please also refer to the corresponding MEB 21 policy document.

It is not essential to list the use on the packaging of PO medicinal products. However, in some cases where the dosage differs from the usual dosage, for example *'once a week'*, it can be advisable to list the dosage on the packaging.

For the sake of completeness, it should be noted that the standard sentence as referred to in section 5 of the QRD template must always be stated (see above in section 5).

16. Information in Braille

The name of the medicinal product must be expressed in Braille format on the packaging (Article 56a of Directive 2001/83/EC).

Chapter 2 of the 'Guideline on readability' provides an explanation of the information that must be listed on the packaging/label in Braille.

In the Netherlands, the information in Braille is assessed by means of a template that must be completed by the applicant/marketing authorisation holder, the so-called Braille declaration. This template can be found on the MEB website. It is not necessary to submit a box/label with Braille text.

The product name must be shown in Braille on the outer packaging. This will usually be the outer packaging. However, if the product only has a primary packaging, the product name must be included in Braille on this primary packaging. It is not necessary to create a special space for the Braille text and it may extend across the original packaging text.

This obligation does not apply to products that are only administered by a medical professional and not by the patient himself/herself. If the Braille text is omitted, a reason for this must be submitted to the MEB for evaluation. Consequently, a Braille statement must always be submitted showing the Braille text, or a reason for not complying with the obligation.

If the Braille text is too large for the relevant packaging, information from the name may be omitted: the salt (if this forms part of the name), the company name (if this forms part of the product name), and for NP medicinal products: information about indication, taste, etc. The point of departure is that the product must be recognisable.

For parallel products, the original foreign Braille text is sufficient. If the packaging is going to be repackaged, the parallel importer/distributor must ensure that the Braille text is presented in the correct language and that the original Braille text cannot result in confusion in the country of importation.

Technical information:

Braille is not a language, but a way of reading and writing a language. A single basic character is called a Braille cell. As there are no differences in Braille (per country), the Braille font (size of the Braille Cell) must be standardised. The use of the *Marburg Medium* is strongly recommended. Otherwise, the name should be written in uncontracted (Grade 1) Braille. This means that one letter occupies one Braille cell. Contracted Braille (the contraction of characters in one Braille cell) is not permitted, also not for packaging smaller than 10 mL, as this script is not well known in the Netherlands.

17. Unique identifier – 2D Data Matrix code

Safety features must be displayed on outer packaging and, if there is no outer packaging, on the primary packaging.

The text options shown below between angle brackets <...> can be used literally in the label text which is submitted to the MEB. The real 2D Data Matrix code will be stated on the actual packaging if applicable. The location of this code must always be indicated on the mock-up as well.

<2D Data Matrix code with the unique identifier.>

For products for which the unique identifier is not required in accordance with Article 54a(1) or Article 54a(5) of Directive 2001/83/EC, the following must be stated in grey shading in this section:
<Not applicable.>

In general, it implies that the 2D Data Matrix code is obligatory for prescription medicinal products and not applicable to OTC medicinal products. For more information and exceptions (Annex I and Annex II of Commission delegated regulation 2016/161, also referred to as the whitelist and blacklist (Annex I includes the PO medicinal products which do not have to display safety characteristics and Annex II OTC medicinal products which do have to display safety characteristics))) see the information on the website of the European Commission (Commission delegated regulation 2016/161).

18. Unique identifier - data legible for people

The text options shown below between angle brackets <...> can be used literally in the label text which is submitted to the MEB. The actual numbers and codes are to be stated on the actual packaging. See also comment under section 17 about the location of these characteristics.

<PC: {number} [product code]
SN: {number} [serial number]
NN: {number} [national reimbursement or national identification number]> (on the basis of national obligation [see below])

For products for which the unique identifier is not required in accordance with Article 54a(1) or Article 54a(5) of Directive 2001/83/EC, the following must be stated in grey shading in this section:
<Not applicable.>

In general, it implies that the PC and SN codes are obligatory for prescription medicinal products and not applicable to OTC medicinal products. For more information and exceptions (whitelist and blacklist) see the information on the website of the European Commission (Commission delegated regulation 2016/161).

The NN code is part of the QRD template, but is not used in the Netherlands. That is why the label text must be stated in the grey shaded area. The NN code does not feature on the packaging.

19. Other information essential for correct use and administration

- This relates to a special option, introduced by the QRD working group and adopted by the MEB, to include certain information on the blister packaging that is essential for correct use and administration. Example: calendar indications.
- A very reticent approach is adopted concerning the temporary placement of stickers on the packaging, for example, if the appearance or an excipient in the product is changed. The company must submit argumentation for this after which the MEB will assess on a case-by-case basis, together with the Health and Youth Care Inspectorate (IGJ).

20. Blue box information

For products authorised via MR/DC procedure or via the Centralised procedure, additional information may be required nationally in the package leaflet or on the packaging.

For further information:

- products authorised via MR/DC procedures: see website CMD(h) 'Blue-box' requirement

- products authorised via the Centralised Procedure: see Notice to Applicants volume 2c Guideline on the packaging information of medicinal products for human use authorised by the Community.

These documents describe the blue box information per country.

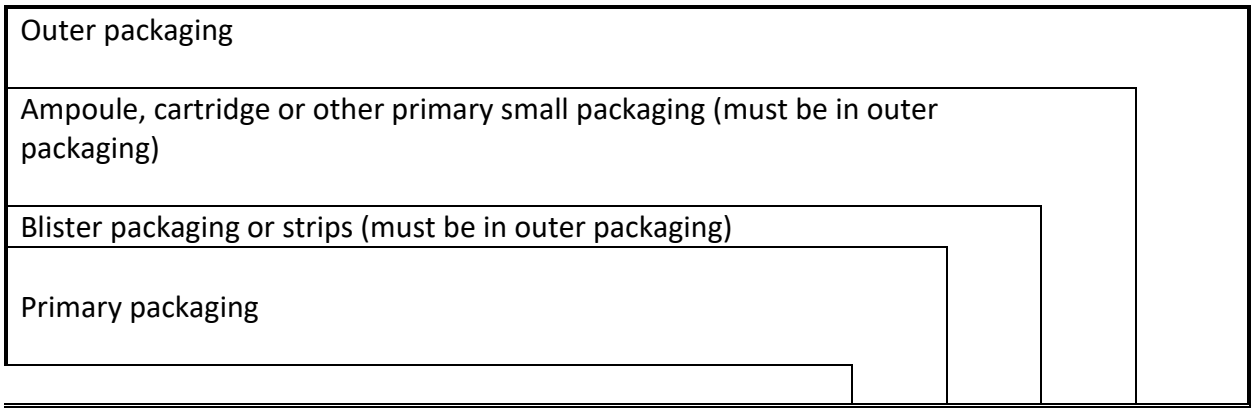
Annex 2: Overview of the items that must be listed on the various packaging forms

For a more detailed clarification see Annex 1 above.

(the Checklist)

Outer packaging				
Ampoule, cartridge or other primary small packaging (must be in outer packaging)				
Blister packaging or strips (must be in outer packaging)				
Primary packaging				
a. **Name,** followed by **strength**, **pharmaceutical form** and then **active substance*** (for which the active substance referred to must correspond to the above-mentioned strength). All these details must be depicted on the <u>main</u> side of the packaging (usually the front).	x	x	x	x
* Mention of active substance(s): compulsory in accordance with a. if the medicinal product contains no more than three active substances. For more than three active substances, these do not have to be mentioned in accordance with a. The active substances do have to be mentioned in accordance with b. (see below) on the primary packaging (with the exception of blisters and small packaging) and on the outer packaging. In practice the exemption relating to more than three active substances only applies to blisters and small packages, and not to other primary packages and outer packaging.				
b. Qualitative AND quantitative composition of active substances *('one tablet contains x mg of y').*	x			x
c. Pharmaceutical form *(do not mention again separately, but include under a, see above)*	x	x	x	x
d. Contents of the trade packaging in units of mass or volume, in I.U. or in number	x		x	x
e. Excipients	x[1]			x[1]
f. The method of use and method of administration	x		x	x

	Outer packaging	Ampoule, cartridge or other primary small packaging (must be in outer packaging)	Blister packaging or strips (must be in outer packaging)	Primary packaging
g. Reference to package leaflet	x			x
h. A warning that the pharmaceutical product must be stored outside the reach and sight of children.	x			x
i. Special warnings [if necessary]	x			x
j. Exp/do not use after/shelf life + expiry date (month/year), in understandable wording	x	x	x	x
k. Indications concerning storage [if necessary]	x			x
l. Indications for the disposal of unused products or waste products [if necessary].	x			x
m. The name and address of the marketing authorisation holder	x	x[2]		x
n. Authorisation number (marketing authorisation number)	x			x
o. Lot/Batch + batch number of the manufacturer	x	x	x	x
p. Legal status of supply (UR, UA, UAD, or AV)	x			x
q. Instructions for use, including what the MEB considers indications, contra-indications, (in-use) shelf life and dosage, if necessary. This applies to a non-PO medicinal product.	x			x
r. Name of the medicinal product in Braille				x[3]
s. Certain other information essential for correct use and administration		x		



[1] Only if the pharmaceutical product is intended for parenteral administration, for local application and for the eye is it obligatory to include all excipients on the packaging; for the primary packaging if space permits. See also the 'Guideline on the excipients in the label and package leaflet of medicinal products for human use'. For all products it applies that excipients referred to in this guideline must always be mentioned on the packaging.

[2] The name of the marketing authorisation holder alone is sufficient. As part of the product name, containing the name of the marketing authorisation holder in abbreviated form (although the MEB does not prefer the latter).

[3] The Braille obligation does not apply to medicinal products which can only be administered by medical staff in a hospital. However, a Braille declaration must always be submitted which states that the obligation does not apply.

Annex 3: URL via two-dimensional matrix of blocks (for example QR code)

Introduction

The QR code presents a URL for a website with a two-dimensional matrix of blocks. The URL is encoded and printed on the outer packaging of, for example, a medicinal product and/or in the package leaflet. A special reader of such codes (application) on, for example, a smartphone, is used to scan the code. The application translates this scan to the URL and the device's browser opens the relevant website. This provides access to (digital) information about a certain medicinal product. An example of a two-dimensional matrix of blocks is the QR (quick response) code.

The policy for the QR code in the Netherlands that is described below applies to all medicinal products that will be or have been awarded a national marketing authorisation. This policy concurs with the policy as set out in the CMDh for products in the MRP and DCP. The policy also applies to parallel-imported medicinal products and to marketing authorisations awarded via derived authorisation procedures.

This policy only relates to the use of QR codes that refer to web pages, URL links and videos containing information about the relevant medicinal product. 2D barcodes that are used exclusively for internal production processes and do not contain information about the medicinal product do not fall under the scope of this policy, see Chapter 6.4.4 of this document. The same approach applies for techniques that have the same function as the QR code.

See also https://www.hma.eu/90.html

- Bullet point 12: CMDh position paper on the use of Mobile scanning and other technologies to be included in labelling and PL in order to provide information about the medicinal product

Conditions for use of a QR code

In order to place a QR code on the packaging and/or in the package leaflet, the conditions listed in Article 69 of the Medicines Act Regulation, the policy document 'Labelling of pharmaceutical products' (MEB 6) and/or the policy document 'Package leaflet for pharmaceutical products' (MEB 5) must be met. This includes that the QR code and the underlying information must not contradict the approved Summary of Product Characteristics, must be useful for the patient and must not promote the medicinal product. The content may not include public advertisements.

The following information can be stated below the QR code (called '*positive list for QR codes*'):

- mandatory product information, such as the information in the SmPC, package leaflet and labelling
- information in relation to pharmacovigilance, such as educational material

The format in which the information is provided can be determined freely, provided that the requirements for the information underlying the QR code have been met.

The information from this positive list for QR codes is made available via the QR code by the marketing authorisation holder. The marketing authorisation holder ensures that this information is kept up to date on the relevant website.

A QR code can be included on the packaging and in the package leaflet, on condition that this is secondary in prominence and position to the mandatory information that must be stated on the packaging. In the case of small packages, the QR code can also be positioned on the inside of the packaging. Several barcodes can be stated on the packaging, provided this does not compromise the legibility of the mandatory information.

In order to draw patients' attention to the potential differences between the last approved product information and the printed package leaflet, the following sentences must be stated in the package leaflet:
'Detailed and up-to-date information for this medicinal product can be obtained through the QR code by scanning the QR code with a QR reader, an application (app) for smartphone or a tablet. The same up-to-date information about the medicinal product is also available via the following URL: <…> and on the website of the Medicines Evaluation Board (www.geneesmiddeleninformatiebank.nl)'.

These sentences must be included at the end of the package leaflet (as the last sentences).

The entire URL to which the QR code refers is to be listed with the QR code so that the information can also be accessed by patients who are not able to scan the QR code.

The listing of the QR code is not dependent on the legal status of supply and can be used both for medicinal products that are only available with a prescription and for medicinal products that are available without a prescription.

Procedure for inclusion of a QR code

When applying for a marketing authorisation, the applicant must submit a declaration stating that the QR code meets and will continue to meet all the set requirements. In the case of a DCP or MRP, the declaration must be submitted no later than Day 106. In the case of a national procedure, the applicant must submit the declaration in the second round at the

latest. After that, a declaration will no longer be accepted during the procedure of an application for a marketing authorisation.

By submitting this declaration, the applicant confirms that the content of the QR code is and will continue to be compliant with the relevant regulations. If a marketing authorisation has been awarded for a medicinal product already, an Article 61(3) notification can be submitted for the addition of a QR code. Furthermore, the addition of a QR code can also be submitted in combination with another change in the product information in a type IB or type II variation of the C category or during a reauthorisation.

In the case of parallel-imported medicinal products, the QR code of the original applicant for the medicinal product must be covered with tape.

Documentation for submission

The following documentation must be submitted when applying for a QR code on the packaging and/or in the package leaflet:

1. 1. Completed declaration for the QR code:
    - For MRPs/DCPs: Annex 2 - Applicant's declaration template, see http://www.hma.eu/90.html
    - For national procedures: See Application to include a QR code in national procedures under the heading 'documentation to be submitted

2. Full-size mock-ups of the packaging and/or the package leaflet (depending on where the QR code is displayed)
.

3. Package leaflet: Please take into consideration that the following text must be included: 'Detailed and up-to-date information for this medicinal product can be obtained by scanning the QR code with a QR reader, an application (app) for smartphone or a tablet. The same up-to-date information about the medicinal product is also available via the following URL: <…> and on the website of the Medicines Evaluation Board (www.geneesmiddeleninformatiebank.nl)'.

Annex 4: Examples of active substance declarations on packaging

This annex provides several examples concerning labelling and including information on the composition:
For more information about these different particulars please refer to policy document MEB 13 'Nomenclature of pharmaceutical products'.

Example 1:

Depiction of section 1 according to QRD template:

(invented) name 60 mg capsules toremifene

The product contains a quantity of toremifene citrate, which converts to 60 mg toremifene (base). Toremifene (base) is the active substance.

Depiction of section 2 according to QRD template:

Each capsule contains toremifene citrate, corresponding to 60 mg toremifene

The MEB prefers this method of description. If this method of description is not possible, the following is acceptable:
'Each capsule contains 60 mg toremifene (as citrate)'

Example 2:

Depiction of section 1 according to QRD template:

Amlodipine (as malate) X 5 mg tablets amlodipine

The above-mentioned situation applies if the marketing authorisation holder has authorised various types of compounds (salts/esters). The use of the term '(as malate)' in the name (the first line) is essential in this case, because confusion may otherwise occur with the other forms of the compound with this active ingredient that have been authorised by this marketing authorisation holder (mesilate, besilate). The MEB has been approached by professionals in the field who stated that the name should immediately clarify which type of compound is involved. There may be allergies to one type of compound and not to another type of compound. The MEB shares this opinion and has adjusted its policy accordingly.

Note that the word 'amlodipine' on the second line may not be omitted here. The inclusion on the second line actually provides certainty about the question whether the product contains 5 mg amlodipine base or 5 mg amlodipine malate (it contains 5 mg base).

Depiction of section 2 according to QRD template:

The following must still always be stated on the main side of the outer packaging:

Each tablet contains amlodipine malate corresponding to 5 mg amlodipine

Annex 5: Positive List of Pictograms

When displaying the established pictograms below on packaging, the colour codes specified below must be used.

Colour numbers

CMYK values of the colours:
Coloured areas of pictograms:
Red: 0 / 30 / 40 / 0
Yellow: 0 / 10 / 50 / 0
Green: 20 / 0 / 40 / 0

Pregnancy	
	Please note! Do not use if you are pregnant.
	If you are pregnant, or are trying to get pregnant, ask your <doctor> <or> <pharmacist> for advice.

Breastfeeding	
	Please note! Do not breastfeed if you are taking this medication.
	If you breastfeed, ask your <doctor> <or> <pharmacist> for advice.

Operating motor vehicles	
	Please note! Do not operate motor vehicles or machinery if you are taking this medication.
	Do not operate motor vehicles or machinery if you are experiencing side effects.

Alcohol	
	Please note! Do not drink alcohol.
	You should avoid drinking alcohol. Ask your <doctor> <or> <pharmacist> for advice.