**Instructions for producing the mock-up of medicinal product packaging**(Version 1.0, 16 March 2017)

These instructions are intended for applicants / marketing authorisation as a guide when producing a mock-up of medicinal product packaging, so as to best utilise the packaging surface area at their disposal for designating the stipulated mandatory information for the purpose of unambiguous identification of medicinal products and safe administering. The instructions explain the provisions of current laws that refer to the labelling of medicinal products and provides more detailed recommendations for producing high-quality and consistent presentation of information on the mock-ups of medicinal product packaging, which must be clear and legible in order to avoid confusing healthcare workers / users of medicinal products and the possibility of wrongly administering medicinal products.

1. **Regulatory procedures in which submitting mock-ups of medicinal product packaging is necessary**
   1. **Providing approval**

In the procedure for granting marketing authorisation, the applicant shall submit to HALMED one or more external and internal packaging mock-ups of the medicinal products in accordance with Article 26, Paragraph 3 Item o) Medicinal Products Act (Official Gazette, number 76/13 and 90/14, hereinafter: MPA) and Article 11 of the Ordinance Granting Marketing Authorisations for Medicinal Products (Official Gazette, number 83/13, hereinafter: Ordinance).

* 1. **Renewing marketing authorisation**

In the procedure for evaluating the application for renewal of marketing authorisation HALMED may seek the submission of a packaging mock-up if it assesses that it is necessary for the purpose of ensuring unambiguous identification and the safe administering of the medicinal product. In the event of renewed approval of a medicinal product with the manner of issuing being “without a prescription, the application / marketing authorisation holder shall submit to HALMED the external and internal packaging mock-up of the medicinal product.

* 1. **Changes to medicinal product documentation**

In the procedure for making changes to documentation on medicinal products according to Article 22 and 34 of the Ordinance, the applicant / marketing authorisation holder shall submit the external and internal packaging mock-up of the medicinal product.

In the procedure for changes in line with Article 36 of the Ordinance, the applicant / marketing authorisation holder shall submit the external and/or internal packaging mock-up of the medicinal product if the changes affect the textual content designating what is important for the safe administering of the medicinal product and/or changes to the design/graphical elements of the mock-up (with/without changes to the textual content) affecting the identification of a medicinal product and the legibility of mandatory information on the external and/or internal packaging of the medicinal product. The procedure for evaluating the application may include HALMED requesting the submission of the packaging mock-up if it deems it necessary for the purpose of ensuring unambiguous identification and safe administering of the medicinal product.

1. **Mock-ups of medicinal product packaging**

The mock-up is a flat display in colour and in the actual size of the devised cover of the external packaging box/sticker as well as the sticker/folio of the internal packaging container as will be printed on the packaging in distribution.

The mock-up includes:

* Label text in a font, letter size and arrangement as will be printed on the packaging,
* Design, and
* Layout of all graphical elements for print on the particular packaging surfaces.

The label text on the external and internal labelling of the medicinal product packaging must contain all the elements as stipulated in Articles 92, 93 and 94 of the MPA. Applicants / marketing authorisation holders when producing a draft of the medicinal product label text shall use the instructions on the content and manner of attaching draft textual information on medicinal products in the national procedure, i.e. the MRP/DCP procedure, whereas for herbal / traditional herbal medicines the template for medicinal product information for herbal / traditional herbal medicines.

HALMED evaluates in the product the submitted draft label text for the medicinal product (MS Word document) and approves the textual content of the label. The marketing authorisation holder is responsible for accurately printing the approved medicinal product label text on the packaging and compliance of the approved content of the packaging label text with the text on the final mock-up of external and internal medicinal product packaging prepared for printing on the medicinal product packaging material for distribution.

HALMED reviews the legibility of text on the mock-up in terms of the quality and consistency in presenting information with an emphasis on identification of the medicinal product and information important for proper and safe administering of the medicinal product as well as acceptability of the design and layout of graphical elements in terms of their impact on the legibility of information.

* 1. **Requirements for mock-ups of medicinal product packaging**

Producing the medicinal product packaging mock-up is to rely on these instructions as well as the [*"Guideline on the readability of the labelling and package leaflet of medicinal product for human use"*](http://ec.europa.eu/health/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf). The Ordinance (Article 11, Paragraph 3) stipulates:

“The external and internal medicinal product packaging mock-up

* May not lead to confusion with respect to doses and manner of administering the medicinal product,
* May not lead to confusion with respect to the medicinal product composition,
* May not lead to confusion with respect to safe administering and effective of the medicinal product,
* May not contain messages of the marketing character,
* May not lead to confusion on account of similarities in appearance with other medicinal products.”

The stipulated conditions therefore imply that the packaging mock-up for various strengths and pharmaceutical forms of the same medicinal product or other medicinal products belonging from the same marketing authorisation holder must be clearly differentiated in order to avoid mistakenly substituting them.

To fulfil the stipulated conditions, the external and internal medicinal product packaging mock-up must be produced in accordance with the following requirements for:

1. **Manner of submitting the mock-up**

* Submitted in electronic form as a PDF document.
* Submitted in colour and actual size.

1. **A number of packaging sizes of the same medicinal product strength and pharmaceutical form**

* Submitted only for the smallest packaging size in the event that the label text is the same for all packaging sizes except for difference in the information on the packaging size / number of dose unit, whereas for other packaging sizes the same design and layout is retained (including the horizontal or vertical orientation) and the same font type and font size (letters may be the same or larger), whereas the box dimensions for other packaging sizes may be the same or larger.
* The recommendation is that mock-ups of various packaging sizes not differ significantly in terms of design / pallet of used colours, as it may lead to confusing when administering, except in the event if various packaging sizes relate to medicinal products that are issued in various manners, i.e. “with a prescription” or “without a prescription”, hence in such cases the design should differentiate the medicinal product with and without a prescription, in line with Item 3.1 of these instructions.
* If the application / marketing authorisation holder decides to differentiate the particular packaging sizes in the mock-up, the recommendation is that the design differentiate only the information on the packaging size (i.e. other colour, letter size or bolding the information, and the like).
* Submitted for other packaging sizes in the event that the mock-ups for various packaging sizes differ in the design (e.g. the use of other colours) or layout (the horizontal or vertical orientation is changed).
* In the event that a number of mock-ups are submitted for various packaging sizes of the same strength and same pharmaceutical form, it then becomes necessary to submit them in a single PDF document.

1. **Greater medicinal product strength of the same pharmaceutical form**

* Submitted for each strength as a separate PDF document.
* The strength of the medicinal product is differentiated in the design, use of various colours and/or graphical elements.
* The submitted mock-up of a previously approved medicinal product in the event that another strength of the same medicinal product has been authorised for the purpose of making comparisons (when expanding the authorisation).

1. **Various pharmaceutically forms of medicinal products**

* Submitted for each pharmaceutical form as a separate PDF document.
* Mock-ups of various pharmaceutical forms need to be differentiated in the design.
* Submitted mock-up of a previous approved medicinal product in the event that another pharmaceutical form of the same medicinal product has been approved for the purpose of making comparisons (when expanding the authorisation).

1. **Legibility of the label text**

* The mock-up packaging text should be printed using letters with a font size of at least 7 points and font type Times New Roman (or a size where the lowercase letters are at least 1.4 mm high), leaving a space between lines of at least 3 mm), whereas the mock-up should indicate which font type and font size are used. This applies to marketing authorisation application submitted after the publishing of these instructions and for marketing authorisation applications submitted earlier and which have as yet not been completed prior up to the publishing of these instructions. The change/renewal procedures in which it is necessary to submit a mock-up also requires that the marketing authorisation holder use the stated font size. In exceptional cases for very small packaging (e.g. 1ml ampule), smaller font sizes may be used where the legibility will be assessed by HALMED during the procedure.
* The recommendation by HALMED is that the mock-up use larger font sizes than the minimum required whenever the packaging surface area allows it due to better legibility of text.
* The legibility of text may not be degraded on account of the packaging design. The recommendation is not to use gloss and reflecting surfaces nor print text in colours with a metal effect, as it may negatively impact legibility. Background colours that negatively affect the legibility of text may not be used, whereas the colours that should be used are those that ensure good contrast between the text and the background in order to provide optimal legibility of information.
* The packaging design, besides text (selection of font type and font size) and colours, may also utilise other graphical elements (e.g. lines, pictograms, and the like), if the packaging surface allows it and there is no negative effect on the legibility of the mandatory label text and it does not redirect the user’s attention from the mandatory text. Pictograms / pictures / graphical elements that are not label txt may not take up more than 1/3 of the surface area of packaging on which it resides.

1. **Citing the medicinal product name and the active substances**

* The recommendation for the name of drug (one of the elements of the medicinal product name according to the instructions on the content and manner of attaching the proposed textual information on a medicinal product) is not to use a number of different letter colours, nor mix various font types or uppercase and lowercase letters to highlight one part of the medicinal product name, as it may lead to erroneous identification of a medicinal product due to possibly mistakenly reading the name.
* The recommendation for the full medicinal product name (full medicinal product name: name of drug + strength + pharmaceutical form, as stated in Item 1 of SmPC) is to cite it in the same cline if the surface area allows, and if that is not possible, then it is necessary to cite the full medicinal product name as one graphical entity which is not separated from other text or graphical elements.
* The recommendation is to cite the name of an active substance immediately under the full medicinal product name using a font size smaller than the full medicinal name.
* The full medicinal product name and active substance name on the mock-up are to be shown as a single graphical entity which is not separated from other text or the graphical element using a larger font on the front side of the packaging surface..
* The recommendation is to cite the medicinal product name and the active substance on at least three sides of the packaging that are not opposite one another (on the front side, at least on one adjacent side and upper (lid) side of the packaging), which is especially important for the pharmacist when issuing medicinal products for the exact identification of a medicinal product, as the information is visible regardless of who the packaging is placed on the shelve and/or in the drawer.
* The recommendation for medicinal products in a liquid pharmaceutical form in (small) bottles and for which packaging in kept in a vertical position, is that the full medicinal product name and active substance be cited on at least three sides (on the vertical sides (which may be the opposing sides) and the upper (lid) side so that the medicinal product can be identified when on a shelve (view of the front or rear side) or in a drawer (view of the top lid).
* The recommendation is that the full medicinal product name is cited on the sides of the packaging and include also the size of the medicinal product packaging if the surface area allow (size of packaging may be cited also on the other sides of the packaging).
* The mock-up of the external medicinal product packaging must be left as an empty surface on one side onto which the pharmacist designates the prescribed dose, in accordance with Article 92, Paragraph 1, Item e) of the MPA.

1. **Multilingual packaging**

* A multilingual packaging mock-up is acceptable only if the packaging surface allows it, under the condition that the label text in the other language has no negative effect on the legibility of the mandatory label text in the Croatian language, whereas the texts in the other languages must be clearly demarked. The content of information in another language must be identical to the content of information in the Croatian language (according to Article 94, Paragraph 3 of the MPA), and the market authorisation holder is responsible for the equivalency of the text in various languages on the mock-up.

1. **Trademark / logo**

* The medicinal product packaging mock-up may contain a trademark or registered logo (can be part of a registered trademark, but does not have to essentially be a trademark), under the condition that the registered trademark/logo due to its position (not positioned too close to the mandatory text so as to redirect one’s attention) or size (may not be dominant) so as not to negatively affect the legibility of the mandatory information on the packaging. The intention of presenting the registered trademark/logo is to be mentioned in the draft label text of the medicinal product according to the instructions on the content and manner of submitting the draft text with the information on the medicinal product in the national procedure, as described in the section “Labelling Medicinal Products” under item 11 INFORMATION THAT MUST BE FOUND ON THE <EXTERNAL PACKAGING> <AND> <INTERNAL PACKAGING.
* If the design or position of the registered trademark/log placed on the packaging is changed, HALMED need not be notified of it as a change referred to in Article 26 of the Ordinance if the change of position or size does not negatively affect the legibility of the mandatory information.
* The registered trademark/logo of the medicinal product manufacturer (importer or grantor of the licence) is not marked on the external and internal medicinal product packaging due to the possibility of causing confusing as to who is responsible for the medicinal product.

1. **Internal packaging of a medicinal product**

* The submitted stick mock-up used to mark the internal packaging or internal packaging folio on which all labelling elements are directly printed.
* The internal packing mock-up for blister/strip must show the number of schedule of dose units in the blister/strip and contain the mandatory label text in accordance with Paragraph 2, Article 93 of MPA (full medicinal product name, validity period, series number and name of authorisation holder → the abbreviated name as the registered trademark/logo may be cited).
* The mock-up of the perforated blister/strip containing a number of unit dose blisters, see definition in the EDQM database of standardised terms <https://standardterms.edqm.eu/>) which can easily be separated along the perforation into separate units, should be clear that it is a “unit dose perforated blister/strip”. The information stipulated in Paragraph 2, Article 93 of the MPA for labelling “normal” blisters/strips must be found in the mock-up on each unit of perforated blister/strip due to the traceability of information on the origin of dose units when a unit is separated from the perforated blister/strip. In the textual information on the medicinal product (in Item 6.5 SmPC, PL and package label text) it is necessary to clearly cite that it involves a unit dose blister/strip where the perforated unit dose blister is described in accordance with the EMA document “„Compilation of QRD decisions on stylistic matters in product information” in the section that refers to “Unit dose” packet sizes..
  1. **Pictograms/symbols**

A pictogram (Latin, *pictus*: pictured or painted) is a simplified illustrated picture or graphical sign used as visual communication element, and is read/understood as a symbol. The pictogram clearly and unambiguously visually presents meaning of a particular concept or information, and as a form of communication sometimes is superior over words. The standardised pictogram or prior agreed sign that has a generally accepted meaning for a certain concept or information is called a symbol.

The use of the pictogram/symbol on medicinal product package mock-ups is possible in accordance with Article 95 of the MPA and *Guideline on readability of the label and package leaflet of medicinal products for human use*, only if

* It additional explains the mandatory label text and does not replace the mandatory text,
* Has an unambiguous meaning and provides clear visual information,
* Is not contradictory in relation to the summary text describing the medicinal product’s properties, medicinal product instructions and labelling of the medicinal product,
* Does not lead to confusion on the effectiveness of the medicinal product (e.g. may not suggest a wider indication that what is approved or some other indications or emphasis an exaggerated effectiveness of a medicinal product,
* Does not lead to confusion as to the nature of the product (e.g. may not be associated with a foodstuff or cosmetic product),
* Not complicated or understandable for the average user,
* In regard to size and position it does not negatively affect legibility of the mandatory text.

What should be avoided is using combinations of multiple pictograms/symbols which on their own are clear and acceptable, but when used together may be unclear and lead to confusion.

Explanations for using pictograms/symbols should be stated textually beside them on the package or, in exceptionally, if the surface of the package does not permit, in the medicinal product instructions. Pictograms, together with the appropriate explanation, must be cited in the proposed label text on the medicinal product (if the explanation is cited in the medicinal product instructions, it should be stated in the proposed text of the instructions).

In the cases below, it is **permitted** to place a pictogram/picture on the medicinal product package mock-up under the condition that the pictogram/picture does not dominate with respect to the mandatory label information and along with the earlier stated requirements for the pictogram, the following additional requirements are met:

* displaying the pharmaceutical form:
* It must clearly and unambiguously show the pharmaceutical form of the medicinal product
* The details must conform to the specific pharmaceutical form (e.g. if the tablet has a grove, the grove must be shown)
* Showing a number of tablets/capsules is not permitted unless they comply with the recommended dose stated in section 4.2 of the description summery for the medicinal product properties, because multiple items may lead to confusion regarding unit doses of a medicinal product which are to be taken (e.g. displaying two or more tablets on the package may be associated with the need to take multiple tables at once, whereas it prescribes only taking one)
* It is desirable to place a real picture (photograph) of the pharmaceutical form (e.g. capsule/tablet) on the package mock-up, as it is a more authentic presentation than a pictogram.
* displaying the medicinal product:
* Only if a medicinal product is an integral part of the medicinal product package, as it is necessary for administering the medicinal product (e.g. spoon, syringe, and the like).
* displaying the target population:
* Only if serving the purpose of clearly identifying a target population and not leading to confusion with respect to the population for whom the medicinal product is intended (e.g. for medicinal products intended for administering to multiple population ages, adults, adolescents and children, displaying only once of these populations is not permitted as it may lead to confusion as for which population age the medicinal product is intended),
* Displaying a child/children must conform to the age subgroup of the paediatric population for which the medicinal product is intended and may not in any way suggest a different age subgroup that the one for which the medicinal product is intended (e.g. not to display a picture of a small child if the medicinal product is intended for children older than 12 years of age), and the information on the children’s age must be clearly textually cited along with the display.
* displaying the place of administering:
* Permitted only in the case of when the medicinal product may be administered only at one place,
* Only if the display of the body part shows unambiguously the place where the medicinal product is administered (e.g. shows ear on the package of a medicinal product intended for administering in the ear or nose for administering in the nose, and the like).
  + displaying the indication(s):
* Only the display of part(s) of the body suggests all approved indications of the medicinal product, e.g. it is not permitted to use a display for analgesics that suggests only one indication (e.g. headaches) if the medicinal product is approved for a number of indications (e.g. back pain, sore tooth and menstrual pains).
* displaying fruits or parts of the plant:
* Only if the herbal substance or preparation made from the displayed fruit or part of the plant is found in the composition of the medicinal property (e.g. if the medicinal product contains ivy leaf extract, a picture of an ivy leaf may be placed on the mock-up).
  1. **Other graphical elements** (e.g. lines, arches, circles)
* Only if the surface of the package allows that and has no negative impact on the legibility of the mandatory label text, and does not redirect the user’s attention from the mandatory text.
  1. **Pictures that are not permitted on package mock-up:**
* Picture of a (small) cup containing a drink which can be associated with a foodstuff, as it may lead to confusion on the nature of the product (e.g. a picture which is associated with a refreshing drink, tea or juice that is drunk when desired and as if there is no need to dose it is not acceptable),
* Picture of a toy as it may make the medicinal product package appear additionally appealing to children and create an wrong perception as to the nature of the product (e.g. a picture of a toy on a package of tablets may cause the child the associate it with lollies/bonbons, or associate an oral solution on a package with a fruit juice),
* Picture of exceedingly playful children on a package of a medicinal product that is approved for indication for which the recommendation is rest during treatment (e.g. for an antipyretic, a picture of children jumping or playing with a ball) may lead to confusion that children may play and do sport unconstrained instead of resting during treatment,
* A picture/pictogram of fruit may not be placed on the mock-up if the composition of the fruit is not contained in the medicinal product, but the picture/pictogram suggests a flavour/aroma (e.g. if the medicinal product contains a strawberry aroma, showing strawberries on the package is not permitted). The flavour/aroma may be identified/differentiated in the label text by citing (e.g. “strawberry flavoured) and/or using various colours in the package design for the medicinal product containing various flavours/aroma.

When using a pictogram/symbol/picture on the package mock-up, it is important to assess whether it contributes to a better understanding of the mandatory textual information, as the addition of the pictogram/symbol/picture that does not provide additional information to the user/patient in terms of better understanding the information about the medicinal product might not only unnecessarily take up the package surface which is otherwise necessary for the clear and legible denoting of mandatory textual information which is crucial for safely administering the medicinal product.

The acceptability of the pictogram/symbol/picture on a package mock-up of a medicinal product along with the appropriate textual explanation will be assessed by HALMED in the regulatory procedure.

1. **Additional requirements for package mock-ups of medicinal product issued without a prescription**

When producing the package mock-up for a “non-prescription” medicinal product, the applicant / market authorisation holder must, along with the requirements for the package mock-up for the medicinal product stated under Item 2 of these instructions, additionally meet the following requirements:

1. The design of a package mock-up for a “non-prescription” medicinal product must be adequately differentiated from the design of a package mock-up for a “prescription” medicinal product, such that the users clearly visually recognises a prescription and non-prescription medicinal product without any possibility of confusion.
2. The text indicated under Item “15. INSTRUCTIONS FOR USE”, in the section on labelling the medicinal product “INFORMATION THAT MUST BE FOUND ON THE <EXTERNAL PACKAGE> <AND> <INTERNAL PACKAGE>” instructions on the content and manner of submitting the draft text with the information on the medicinal product in the national procedure which, among the other mandatory information, must be cited on the package of non-prescription medicinal products, should be presented on the mock-up in a high-quality manner.

The text referred to in item “15. INSTRUCTIONS FOR USE” on the package is important for the proper and safe administering of a non-prescription medicinal product during self-medication and should be cited:

* As one graphical entity which is not separated from the other text or graphical element(s),
* On one of the main sides (largest surface) of the external package, or on the rear main side of the external package. On the side containing the text referred to in Item 15 , it is not necessary to cite the entire textual unit “full medicinal product name + active substance”, but if the “full medicinal product name + active substance” is cited, it should be done so using a smaller size font with respect to the font size used on the front main side, in order to better utilise the area of the rear main side for a better quality presentation of the mandatory text referred to in Item 15,
* In a larger font that ensures good legibility of text, the recommendation is not to use the smallest recommended font size as stated in Item 2.1 of these instructions, if the area of the side allows the use of larger font,
* Using a better-quality presentation of the text referred to in Item 15 should be given preference before placing pictogram/picture/graphical elements on the package mock-up which does not have added value for users. The area of the side used for the texts should be utilised mostly for that actual text with respect to the placement of other design elements on that side.

HALMED will assess each particular case, while taking into account key information necessary for the safe administering and limitation of the package surfaces.