Guideline for the naming of a medicinal product

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This guideline is intended for applicants/marketing authorisation holders (MAHs) as a guide for the creation of proposal of the name of a medicnal product in line with the current legislation for medicinal products in the Republic of Croatia. It applies to medicinal products authorised by the Agency for Medicinal Products and Medical Devices (HALMED) via either purely national procedure (NP) or mutual recognition (MRP) or decentralised procedure (DCP) for granting marketing authorisation.

In order to make it easier for European Union (EU) citizens travelling through the EU to identify a medicinal product of the same qualitative and quantitative composition authorised via different MS, it is recommended to the applicants/MAHs that medicinal products authorised via MRP/DCP have the same name in all pariticipating member states (MS) in the procedure. In cases where competent authority of the participating MSs cannot accept the name of the medicinal product proposed in the MRP/DCP due to non-compliance with any of the criteria for establishing an acceptable medicinal product's name, a differenet name may be approved in that MS, except in case of generics of the reference medicinal product authorised in EU via centralised procedure (CP), as specified in section 4 of this guideline.

For medicinal products authorised in the EU via CP, the acceptability of the CP proposed names are evaluated by the Name Review Group (NRG) within the European Medicines Agency (EMA) according to the *Guideline on the acceptability of names for human medicinal products processed throught the centralized procedure EMA/CHMP/287710*.

This guideline does not bring new requirements for the name of a medicinal product. It additionally explains provisions laid down in the current legislation for the medicinal products related to the naming of a medicinal product that applicants/MAHs should take into account when creating a proposal for the name of a medicinal product.

1. Criteria for the naming of a medicinal product

The criteria for the naming of a medicinal product is laid down in the national legislation as follows:

- Medicinal Products Act (Official Gazette, No. 76/13., 90/14. and 100/18., hereinafter: the Act) in Article 3 points (8) and (9) thereof,
- Ordinance on Granting Marketing Authorisations for Medicinal Products (Official Gazette, No. 83/13., 28/20. i 32/21., hereinafter: the Ordinance) in Article 10 paragraphs (3), (4) and (5) thereof.

The naming criteria are explained additionally in the following documents:

- *Guideline on the acceptability of names for human medicinal products processed throught the centralised procedure EMA/CHMP/287710*. In order to harmonise the approach to the naming of medicinal products, the critera set by this Guideline are applied also to the names of medicinal products approved via NP or MRP/DCP, as appropriate.
- World Health Organisation's documents:
  - the Resolution WHA46.19 *Nonproprietary names for pharmaceutical substances*,
  - *Guidance on INN* and other guidance/documents published on the WHO website *International Nonproprietary Names Programme and Classification of Medical Products*.

2. Name of a medicinal product

In accordance with Articles 3, 92, 93, 98 and 100 of the Act and the *Guideline on Summary of Product Characteristics* published by European Commission (EC), the name of a medicinal product shall be stated in a product information, in section 1 of the Summary of Product Characteristics (SmPC) and corresponding section of a package leaflet and labeling.

The full name of a medicinal product should be created using these three elements, the <name> given to a medicinal product followed by a strength and pharmaceutical form: <full name> = <name> + <strength> + <pharmaceutical form>. Therefore, two terms are distinguised in this guideline, the <full name> and the < name> of the medicinal product. The <full name> consists of all three mandatory elements (could be two or four elements also, depending on a specific group of medicinal products as explained below in this gudeline) and the <name> refers to an "invented name" given to a medicinal product or "common/scientific name" of a medicinal product.

For vaccines, in addition to the above listed elements of the <full name>, the title of a relevant monograph from the Croatian Pharmacopoeia, when published, or the relevant European Pharmacopoeia monograph should also be stated, in Croatian. Therefore, the <full name> of a vaccine may have four elements (name + strength + pharmaceutical form + title of a monograph) or three elements (name + pharmaceutical form + title of a monograph), depending on whether the strength is or not expressed in the <full name> of a vaccine. Details on creating the <full name> of a vaccine are published in the EMA guideline *Guideline on quality aspects included in the product information for vaccines for human use*.

For herbal/traditional herbal medicinal products, the rule how to create the <full name> usually cannot be applied in full, so the strength is usually not expressed in the <full name> of these products (two elements are usually applied when creating the <full name>, the <name> and <pharmaceutical form>). The strength of these medicinal products cannot be easily stated in the name due to complexity of composition (very complex description of herbal active substance/or herbal preparation, extract type, extraction solvent and relevant DER ratios). Full qualitative and quantitative composition of herbal/traditional herbal medicinal product should be described in section 2 of the SmPC according to the CMDh guideline *Addendum to the Quality Review of Documents templates for SmPC, Labelling and Patient Leaflet on Mutual-recognition and Decentralised procedures specific for (Traditional) Herbal Medicinal Products ((T)HMPs)* and the *Declaration of herbal substances and herbal preparations in herbal medicinal products/ traditional medicinal products-Scientific guideline* published by the EMA.

The <full name> of the medicinal product is important for accurate and unambiguously identification of the medicinal product in each step of treatment (prescribing, dispensing, preparation for use, administration/use or selection of a non-prescription product for self-medication) to prevent a medication error that may occur due to mixing-up of two different medicinal products with similar names.

The <full name> of the medicinal product and its graphic design on the packaging, as well as the whole design of the packaging, contribute to a clearer and accurate identification of the medicinal product, and are considered to be elements of routine risk minimisation measures. Therefore, the MAHs are recommended to use a high quality graphic design of the packaging to ensure that an approved <full name> of a medicinal product is more visible, clear, legible and understandable on the packaging. When designing the <full name> of the medicinal product on the packaging, the *Guideline for preparing a mock-up of the packaging of the medicinal product* published on HALMED's website should be used.

2.1. <Name> of a medicinal product

The <name> may be invented name or common/scientific name, and the <name> must meet the criteria stated below in the subsection 2.1.1 or 2.1.2 of this guideline.

2.1.1. *Invented name*

The invented name of a medicinal product, in accordance with Article 10 paragraph (3) of the Ordinance, **SHOULD NOT**:

a) **lead to confusion arising from the similarity with a common name (international nonproprietary name (INN) or another common name) or a scientific name**, that is, the invented name:

- **should not include an INN stem** for its own or different INN, on the same position (as prefix-, -suffix or –infix–) as used by the WHO nomenclature**.**

  For evaluation of this similarity, the WHO lists of INN stems (*Stem Book* and *Stem Book Addendum*) published on the link https://www.who.int/teams/health-product-and-policy-standards/inn/stembook should be used.

- **should not be derived from its own or different INN,** or other common name or scientific name. When evaluating this similarity, a rule "50% or more" is used to identify cases of proposed invented names that contain a large number of shared letters from INNs or other common/scientific names. The shared letters lead to unacceptable similarity and the following criteria are teken into consideration to detect it:

  - **Is "50 % or more" of the invented name made up of parts/letters from INN or from other common/scientific name?**

    For example: GLUnAte (invented name) vs GLUkAgon (INN) → more than 50 % letters of the invented name are shared with the INN (4 shared letters of total 7 letters), the order and position of the shared letters are the same → unacceptable similarity.

  and/or

  - **Are "50 % or more" letters from an INN or other common/scientific name included in the invented name?**

    For example: GLUkAgon (INN) vs GLUnAte () → 50 % letters from the INN are included in the invented name (4 shared letters of total 8 letters), the order and position of the shared letters are the same → unacceptable similarity.

  The rule "50 % or more" is used to determine a degree of similarity of a proposed <name> with its own or different INN and to support a decision-making on this type of similarity. In addition to this rule, HALMED also takes into consideration other criteria relevant for the evaluation of this type of similarity, for example the order of shared letters (whether they are consecutive or nonconsecutive) and their position in the <name> (whether they are at the beginning, in the middle or at the end), phonetic similarity, pronounciation of particular syllables/letters in Croatian (e.g. "y" as "i"; "x" as "ks"; "th" as "t"; „ph" as „f"; „oe" or „ae"as „e"), risk of cognitive error and other, on a case-by-case basis.

  For evaluation of this type of similarity, the WHO on-line database "MedNet INN services" should be used. The MedNet database is publicly available and you should register for the School of International Nonproprietary Names at the link *https://extranet.who.int/soinn/*. Searching service the "Mednet Search Tool" is available at the link *https://extranet.who.int/soinn/mod/page/view.php?id=49* and allows to perform on-line queries of the WHO INN data and for Lists of Proposed and Recommended INNs.

When creating a proposal for an invented name, the applicants/MAHs are strongly advised to review INN similarity and/or INN stem inclusion before submitting the proposal in an application, applaying above given criteria under subsection 2.1.1. a) and using the relevant WHO data.

The similarity of the invented name with INN can:

- limit the WHO in assigning new INNs for new active substances from the same pharmacological group characterised by a common "stem", due to the "occupation of the position" in the INN nomenclature by the invented name. Any deviation from the established pinciples of the INN nomenclature, that the WHO would therefore be forced to make when assigning new INNs, can lead to confusion in the naming of active substances and threaten the INN system recognised globally as a public property and thus consequently rise a potential risk on patient safety,
- confuse healthcare profesionals and other users of INNs by leading them to the wrong conclusion that the proposed name is related to a new active substance and not to a new invented name.

As the similarity of proposed invented names with INNs is a common reason for non-acceptance of the proposed invented names, HALMED recommends applicants/MAHs to follow the WHO *Resolution*

WHA46.19 and propose the common names for generic medicinal products as recommended by the Resolution, in order to maintain the INN nomenclature system:

- *"(2) to encourage manufacturers to rely on their corporate name and the international nonproprietary names, rather than on trade marks, to promote and market multisource products introduced after the expiry of a patent."*

b) lead to confusion arising from the similarity with the approved name of another medicinal product (applies accordingly to the name of an approved medicinal product which has been withdrawn/revoked, expired or suspended, read for details in section 4 of these guideline) in:

- writing (handwriting and print), including Braille,
- speech.

In principle, the invented names of two different medicinal products should be distinguished by at least three letters in writing and speech (a difference of only two letters almost always results in an unacceptable name). However, the number of different letters is not always a sufficient criterion for an acceptable difference between two names, so when evaluating the similarity of proposed invented name with other approved names, the following criteria sholuld be taken into account:

- number of shared letters and their order (consecutive or not consecutive) and position in the name (at the beginning, in the midle or at the end),
- number of different letters,
- total number of letters in the proposed name,
- ratio of shared and different letters,
- phonetic similarity,
- cognitive error may be associated with the name. In some cases, even though two invented names do not share a large number of the same letters in the same order, the potential confusion may be related to the way the human brain perceives them, what can lead to a cognitive error.

When assessing the potential risk related to confusion due to similarity of thetwo invented names, the following aspects are additionally considered:

- strength,
- pharmaceutical form,
- indication(s),
- intended patient population,
- route of administration,
- posology,
- legal status (subject or not subject to medical prescription) and dispensing status (“in pharmacy” or “in pharmacy and specialised retail stores”),
- existence of additional controls/procedures in practice involved in the prescribing, dispensing, preparation or administration of the medicinal product which may reduce the risk of a medication error.

  Examples: prescribing on a “special” medical prescription (for narcotic or psychotropic substance) or a “restricted” medical prescription by a specialist (eg. for oncology medicinal product) or existence of other implementated measures from the RMP, specialised/personalised procedure for handling of medicinal products (e.g. radiopharmaceuticals) and others.

The proposed invented name of a medicinal product should not include the full invented name of another medicinal product.

c) convey misleading therapeutic connotations, that is, the invented name sholud not:

- narrow the indication in a way to contain or imply a single indication of the medicinal product where several indications are proposed/approved, supported by the dossier and listed in the SmPC,
- extend the indication in a way to contain or imply an indication that is not proposed and not supported/approved,
- carry or imply a message about other therapeutic or pharmacological effect or any other property of the medicinal product that is not supported/approved,

- contain indication in a foreign language (as a suffix, prefix or as a qualifier). It is not acceptable to include terms in English in the name, for example flu, cold, fever, cough, headache, pain, joints, stress, relief, etc.

d) be misleading with regard to the composition of the medicinal product, that is, the invented name sholud not:

- refer to or imply an ingredient not contained in the medicinal product (e.g. in case the product contains a strawberry flavour and not the substance/extract from the strawberry fruit itself, it sholud be stated <<Invented name> with strawberry flavour> instead of <<Invented name> strawberry>,
- refer to or imply only one of several active substances contained in the medicinal product,
- mislead about the nature of the medicinal product.

  It is not acceptable to propose invented name for a medicinal product same or similar (qualifier or suffix/prefix is not sufficient difference) to the name already given to a medical device, food supplement, cosmetic product or other consumer good in order to prevent confusion about the nature of the medicinal product, especially for a non-prescription medicinal product intended for use in self-medication

e) be misleading about safety of the medicinal product, that is, the invented name sholud not:

- contain or imply any safety concern related to safety use of the medicinal product,
- trivialise the use of the medicinal product implying a message that the product may be widely used,
- minimise the risk of the medicinal product implying that the product is completely safe, safer than other products or similar,
- extend the indication, as stated in subsection 2.1.1. c) of this guideline, implaying an “off-label” use what may increase a safety risk.

f) have any element of a promotional nature that is, the invented name sholud not:

- be overly fanciful or fantastic and implying a promotional claims related to unsubstantiated effectiveness, composition or superiority of the medicinal product,
- emphasize the product efficacy or any other property of the medicinal product, for example implying the medicinal product is more optimal, more effective, advanced or better/the best compared to other medicinal products,
- contain terms (not as qualifier neither as prefixes/suffixes) such as: *new, quick, instant, omni, total, optima, ultra, extra, strong, galaxy, guard, attack, advance, max(maxi), super, express, flash, clear, care, boost, active*, *comfort, flex, repair, effect, essential*, etc.

Also, when creating the invented name, in addition to the previously listed criteria in subsection 2.1.1., the following should be taken into account, that the invented name:

- Should be one word of at least four letters. Regulatory practice shows that the names with less than four letters are not appropriate for accurate/unambiguous identification of the medicinal product, as more than half or all letters from such very short names are usually contained in the names of the other already approved medicinal products, resulting with an unacceptable similarity.

  Duplicated letters (e.g. Axxonya) in the invented name are considered/counted as one letter when evaluating the acceptability of the name. The use of duplicated letters is not recommended, as it may create difficulties in writing/pronunciation/spelling/ as well as when selecting the invented name from the list in the electronic prescribing system, thus making it difficult for accurate/unambiguous identification of the medicinal product.

- Should be easy to pronounce in Croatian.
- Should not have any meaning in Croatian or an international well known meaning, it should be an abstract term.
- Should not have or imply an offensive/inappropriate meaning in Croatian or in a foreign language, when a meaning/connotation is well known in a foreign language.

- Should not be a personal Croatian name or an international well known personal name.
- Should not include or resemble the full or abbreviated name of the MAH.
- Should not be an acronym formed from initial letters/syllables of the MAH's name and the active substance name, or from the names of two active substances or be any other acronym that resembles a certain meaning (the invented name should be an abstract term, as previously stated).
- Should not contain a punctuation mark or symbol (such as dash "- ", slash"/", exclamation mark "!", &, @, etc.).
- Should not contain number(s), except for specific groups of the medicinal products (e.g. vaccines, radiopharmaceuticals, etc.), to avoid a confusion in reading/perception the strength that followed the <name>.
- Should not contain a combination of upper and lower case letters to highlight one part of the invented name, in accordance to the HALMED's *Guideline for preparing a mock-up of the packaging of the medicinal product*,
- Should not be entirely written in capital letters. Only the first letter of the invented name should be capitalised and other letters should be written in lowercase letters.

The invented name of a fixed dose combination medicinal product should be sufficiently different from the <names> of approved monocomponent medicinal products containing individual active substance from the combination, as well as from the <names> of other fixed dose combinations with the same composition of active substances.

For the final assessment of the acceptability of the invented name, HALMED takes into consideration all the criteria listed in this guideline important for evaluation of a safety risk of medication error that may occur due to "mixing-up" of different medicinal products with similar invented names.

When a registered trade mark is intended to be proposed as an invented name of the medicinal product, the applicant/MAH should take into account that the registration of the trade mark does not take precedence over the HALMED's assessment of the acceptability of the proposed name, i.e. the registration of the trade mark does not guarantee that such a name will be accepted. Therefore, the applicants/MAHs are advised to take into consideration all criteria according to this guideline relevant for the creation of an acceptable invented name before the registration of the trade mark which intend to be used as an invented name, to prevent registration of the trade mark unacceptable as the invented name.

The review of trade marks is outside the HALMED's remit. Therefore, HALMED will not take into consideration aspects of the registration/ownership of the trade mark within its evaluation of the acceptability of the proposed invented name. The applicant/MAH is solely responsible for checking all legal requirements for trade mark registration and ownership prior to submission to the HALMED.

2.1.2. Common/scientific name of a medicinal product

Common/scientific name is created using a common name or scientific name of the active substance, accompanied by a trade mark or a name of the MAH (according to Article 3, point (8) of the Act), followed by the strength and the pharmaceutical form.

The common name (according to Article 3, point (9) of the Act) is the international non-proprietary name (INN) recommended by the WHO, or other common or scientific name in case INN does not exist. The common/scientific name of the active substance in the medicinal product's name should be used in a full and in Croatian, without abbreviations or omissions of the parts of the common/scientific name. All linguistic versions of the common/scientific name of the same active substance shall be considered to be the same name in MRP/DCP procedures.

WHO assigns an INN only for the active part/active moiety of the molecule (it is usually base, acid or alcohol) to avoid multiple assignment of INNs for different molecules of active substances which have the same active moiety (a part of molecule of the active substance responsible for the physiological or pharmacological effect/action). In some cases, due to adaptation to formulation, bioavailability, absorption or other purposes, there are different molecules of the same active moiety, eg. different salts

or esters, that have the same active moiety. In this cases users of INNs (pharmaceutical manufacturers, pharmacopoeias, regulatory bodies and others) may create a modified INN (INNM) in line with the recommendations published in the WHO INN Working Document 05.167/3 *International Nonproprietary Names Modified*. Additional information on INNM concept is available in the *WHO Guidance on INN* in section „*Modified INN (INNM)*".

When the strength in the common name of the medicinal product is expressed on the INNM, then the INNM in full and in Croatian should be stated in the common name (e.g. methphorminchlorid, perindoprilarginine).

In case the medicinal product contains a combination of two or three active substances, the common names (INNs and/or INNMs) or scientific names of the individual active substances should be listed in the common name of a combination medicinal product according to hierarchy of the ATC classification for combination product (ATC classification is available on the WHO link https://www.whocc.no/atc_ddd_index/). For generic medicinal product which is a combination of active substances, the order of listing the names of individual active substances in the common name of generic should correspond to the reference medicinal product, even in the cases when the order of listing the active substances in the name of the reference medicinal product differs from that assigned by ATC classification to which the reference product belongs to. The first letter of the first active substance's name listed in the combination common name should be written in a capital letter, whereas the name(s) of other active substance(s) in lowercase letters (e.g. Ramipril/amlodipine instead of ~~Ramipril/Amlodipine~~) and the names of individual substances should be separated by a slash "/" without a speace.

In the case when the active substance comes from different sources, e.g. mixture of flavonoids containing 90 % diosmin (synthetic source) and 10 % flavonoids expressed as hesperidin (natural source), it is not acceptable to create the common name of the medicinal product in the way "Diosmin/hesperidin".

When the medicinal product contains more than three active substances, the creation of the medicinal product's name using the rule <common name/scientific name + name/trade mark of the MAH> is not acceptable, as the name would be too complex and difficult to remember, which could lead to confusion.

"The name of the MAH" within the common/scientific name of the medicinal product should correspond to all or part of the official name of the MAH, as registered and presented in the proof of establishment of the applicant/MAH. It is not necessary to include in "the name of the MAH" a description of area of the MAH's business (e.g. "MAH ~~Pharmaceuticals and cosmetics~~", MAH ~~Pharmaceuticals~~, MAH ~~Pharmaceutical industry~~, MAH ~~Health care~~ etc.) or a type of company (as d.d., d.o.o., GmbH, SpA, Ltd etc.), not in Croatian or in a foreign language. All linguistic versions of the MAH's name in MRP/DCP procedures are considered as the same MAH ("the same MAH" is defined according to *Commission Communication 98/C 229/03* and additionally explained in *The Notice to Applicants, 2A Chapter 1* in section 2.8.

"The name of the MAH" should not be an acronym or abbreviation, except when it is a registered trademark owned by the MAH and helps to identify the MAH more clearly. The MAH should confirm the ownership of this trademark.

"The name of the MAH" should not be ambiguous and misleading and/or have a promotional or any other positive connotations, which should be taken into account when creating/registering the name/trademark of the MAH.

Definition of the trade mark is set out in Article 6 of the Trade Mark Act (Official Gazette, No. 14/19.) and it is in line with Article 4 of the *Regulation (EU) 2017/1001 on the Community trade mark*). For understanding of this guideline, following part of the definition is important: *"A trade mark may consist of any signs capable of being represented graphically, particularly words, including personal names, designs, letters, numerals, colours,…"*

The trade mark of the MAH used in the common/scientific name may be a name, word or combination of letters.

However, although by definition it may be a part of the MAH's trademark, the following elements should not be used in the common name of the medicinal product:

- design, pictogram or symbol, because they convey a visual information and cannot be written as text, and, each element of the name of the medicinal product should be able to be written as text and be pronounceable. In addition, these elements may have a promotional nature and lead to confusion about the nature of the product (e.g. remind of a product that is not a medicinal product) and cause difficulties in recording/selecting names in the e-prescribing information system.
- number(s), because they can lead to confusion regarding reading or correct perception of the strength of the medicinal product followed the name.

The use of signs, such as dash "-", slash "/", plus "+", and “&” or similar, between the name of the active substance and “the name/trade mark of the MAH” is not acceptable.

The criteria listed in subsection 2.1.2 of this guideline for creation of the common name of a medicinal product apply accordingly for herbal and traditional herbal medicines, and each proposal will be considered by HALMED on a case-by-case basis.

Creating the <name> of a medicinal product using a combination of the rules specified under subsections 2.1.1 and 2.1.2 of this guideline is not acceptable. It is not acceptable to combine the invented name with elements of the common name (e.g. should not combine “the invented name and the name or a part ot the name/trademark of the MAH” or “the invented name and the common name of a substance” or similar).

2.2 Strength

Strength is a mandatory element of the <full name> of the medicinal product, it is a quantitative attribute for distinguishing the <full names> of different medicinal products having the same <name> and containing the same active substance(s). The strength is defined as the content (mass, volume or activity) of the active substance expressed quantitatively per dosage unit, per unit volume or mass, as appropriate for the pharmaceutical form. The strength in the <full name> should be expressed in accordance with a quantitative composition declared in section 2 of the SmPC. More details on the expression of strength should be read in the *Guideline on Summary of Product Characteristics*.

HALMED recommends that the strength in the <full name> is expressed according to the EMA's *QRD Recommendations on the expression of strength in the name of centrally authorised human medicinal products*.

Exceptionally, strength is not expressed in the <full name> of the medicinal product if it cannot be easily quantified due to the complex qualitative and quantitative composition of active substance(s) in specific groups of the medicinal products (e.g. vaccines, allergens or herbal/traditional herbal medicinal products; additional information is available in section 2 of this guideline). When the strength is not expressed in the <full name> due to justified reasons, a descriptive qualifier in line with this guideline may be used with the invented name to distinguish the strengths of different medicinal products having the same qualitative composition of active substance(s) and the same pharmaceutical form.

When expressing the strength in the <full name>, the following recommendations should also be taken into account:

- Different strengths of medicinal products of the same qualitative composition should be expressed with the same unit of measurement (e.g. 250 mg, 500 mg or 700 mg) allowing easier comparison between the products’ strengths and to avoid potential medication error due to misreading of the strengths caused by a possible wrong perception of units of measurement.
- Unit “µg” should be written in full term "microgram", not using symbol “µg" as it may lead to confusion with the “mg”.
- When appropriate, using of decimal numbers should be avoided (e.g. use of 250 micrograms instead of 0,25 mg).

- If the range of different strengths of the medicinal products of the same qualitative composition and the same pharmaceutical form can be expressed in different units (e.g. 250 micrograms and 5 mg), the strength should be expressed in the same unit for all strengths in range (e.g. 0,25 mg and 5 mg) in order to make them easier to compare.
- If the strength of the product is expressed in a “million” unit(s) (e.g. 5 000 000 IU), a number of million(s) should be written in a word (e.g. 5 millions IU) to assure a safe use of the medicinal product, because multiple use of zeros may reduce legibility of the strength.
- Strength should not be expressed in percentage (e.g. “0,2 %” cream is not accetptable) except in exceptional cases, e.g. for medicinal gases (e.g. 50 %/50 % V/V) or inhalation vapours of anesthetics (e.g. 100 % V/V) for which the strength is usually expressed as a percentage by volume.

In case the medicinal product contains a combination of several active substances (combination medicinal product), their individual strengths with corresponding units of measurement should be separated by a slash "/" without blank before and after (e.g. use 5 mg/80 mg instead of 5/80 mg).

For the combination medicinal product for which the individual strengths of each active substance are expressed by concentration (by volume or by mass), concentrations of individual active substances should be separated with the plus "+" instead of the slash “/”, so it should be written for example, <0,5 mg/ml + 50 mg/ml> instead of <0,5 mg/ml/50 mg/ml or 0,5 mg + 50 mg/ml (the slash is primarily used to express each concentration of individual active substance in the strength of the combination product so double use of the slash, for expressing individual concentration and between several concentrations, could lead to misreading the strength of the combination product).

The order of the strengths of each active substance in the <full name> of the combination medicinal product should be in line with the order of active substances in the ATC classification of corresponding combination medicinal product.

2.3. Pharmaceutical form

The pharmaceutical form is a mandatory element in the <full name> of the medicinal product, it is an attribute that enables to distinguish the <full names> of different medicinal products having the same <name> and containing the same active substance(s). The pharmaceutical form should be stated in Croatian in line with a valid standard term as published in the *Standard terms* database of the European Directorate for the Quality of Medicines and Health Care (EDQM).

The properties of the pharmaceutical form described by the standard term do not need to be additionally emphasized by a qualifier added in the <full name> of the medicinal product, for example:

- for prolonged-release tablets, modified-release tablets or similar forms, it is not acceptable to additionally highlight a pharmaceutical form in the <full name> using the qualifier such as *conti, prolong, long, retard, depo, extend*, *etc.*,
- for granules for oral solution, oral powder, orodispersible tablet or similar forms it is not acceptable to additionally use the qualifier in the <full name> such as *quick, instant* or similar,
- for a liquid pharmaceutical form (e.g. oral solution, oral emulsion or similar) it is not acceptable to additionally highlight the form using the qualifier in the <full name> such as *liquid, emulsion, syrup, elixir, hot drink, etc.*,
- route/method of administration should not be additionally stated using the qualifier in the <full name>, when the standard term for a pharmaceutical form already describes the route/method of adminstration (e.g. “Invented(Name) ~~Nasal~~ nasal spray, suspension”; qualifier “Nasal” in the <full name> is not acceptable).
- *“spray”* or “*gel”* as qualifiers should not be used in the <full name> in addition to a pharmaceutical form (e.g Invented(Name) ~~spray~~ 0.5 mg/ml nasal spray, solution or Invented(Name) ~~gel~~ 50 mg/g eye gel), because the pharmaceutical form is a mandatory element in the <full name> and should not be duplicated by a qualifier.

2.4. Combination pack

A combination pack is defined in the EDQM guidance Standard Terms - Introduction and Guidance for Use as:

"Single term to describe two or more medicinal products that are packaged together and marketed under a single licence, and which are intended to be administered independently, as separate pharmaceutical products."

The combination pack is further explained in the following documents:

- *CMD(h) Questions & answers Applications for marketing authorisation*, section "*Combination Packages"* in the Question/Answer No. 11,
- *Notice to Applicants (NtA)/Volume 2A/Chapter 1 Procedure for marketing authorisation,* subsection 5.5, as stated:

  „In very exceptional circumstances, which must be considered on a case by case basis, the marketing of distinct medicinal products in the same package may be indispensable for public health reasons. Such reasons cannot be related to convenience or commercial purposes."

HALMED follows the CMD(h) and NtA recommenndations for approval of combination packs and will only approve a combination pack in exceptional cases when such pack has a significant benefit for public health, which is evaluated on a case-by-case basis.

The <full name> of a combination pack consists of the usual elements: <name of a combination> + <strengths> + <pharmaceutical forms>.

The invented name of the combination pack may be the same as an invented name of the individual medicinal product forming the combination pack with the addition of a qualifier to distinguish the <name of a combination pack>, when it is necessary.

The strengths and pharmaceutical forms of each medicinal product/pharmaceutical product that make up the combination pack should be included in the <full name> of the combination pack, in a way that does not lead to confusion about individual medicinal products/pharmaceutical products included in the combination pack.

If pharmaceutical forms of the individual medicinal products/pharmaceutical products in the combination pack are different, each pharmaceutical form and corresponding strength should be included in the <full name> of the combination pack. However, in case pharmaceutical forms of individual medicinal products/pharmaceutical products that makes up the combination pack are the same, it is not necessary to repeat the pharmaceutical forms in the <full name> of the combination pack, and the strength for each medicinal product/pharmaceutical product should be clearly stated and separated.

The acceptable examples of the <full names> of the combination pack are following:

- Actonel Combi D 35 mg filmom obložene tablete + 1000 mg/880 IU šumeće granule (case when the strengths and paharmaceutical forms of individual medicinal products/pharmaceutical products are separated with the sign plus "+"),
- Orylmyte 100 IR i 300 IR sublingvalne tablete (in a case when pharmaceutical forms of the individual medicinal products/pharmaceutical products are the same, corresponding strengths are separated by the conjuction "and", used in Croatian "i"),
- Apremilast MAH 10 mg, 20 mg i 30 mg filmom obložene tablete (in a case when pharmaceutical forms are the same, but there are several strengths (more than two), corresponding strengths of individual medicinal products/pharmaceutical products are separated by the comma "," and the conjuction "and", used in Croatian "i").

3. Qualifiers

Qualifier is an attribute (a word that additionally describes/clarifies another word in more detail) added after the <name> of a medicinal product in order to distinguish the <full names> of two medicinal products, that provides additional **relevant/useful information** related to the other mandatory elements of the <full name>.

The qualifier **can be used only in justified cases** when:

- It has a meaning understandable in Croatian.
- Its meaning is supported by the dossier and reflected in the SmPC.
- It is used to distinguish the <full names> of different medicinal products when the strengths and pharmaceutical form(s), as mandatory elements of the <full names>, are not sufficient to distinguish their <full names>.
- Strength cannot be simply quantified in the <full name> for specific groups of medicinal products (vaccines, traditional/herbal medicines, etc.), also see section 2 of this guideline.
- It emphasizes a relevant property/information about the medicinal product important for healthcare professionals or patients and it should be highlighted in the <full name> for the purpose of safe use (e.g. formulation, population, etc.).
- It conveys clear and relevant information to the patients/users allowing easier identification and helps distinguishing different medicinal products, especially when selecting a non-prescription medicinal product (OTC) for self-medication.

The qualifier **should NOT**:

- be a term in a foreign language,
- have any element of a promotional nature,
- be used unjustified and contribute to unnecessarily difficult/complex name of the medicnal product ,
- lead to confusion regarding the quality, efficacy and safety of the medicnal product,
- have or imply a confusing, misleading or inappropriate meaning in Croatian or another language in which such a meaning is generally known,
- highlight only one of several indications that are supported by the clinical data in the dossier and listed in the SmPC,
- consist of one or two letters (e.g. BR, XL, etc.) except for specific groups of medicnal products (e.g. vaccines, radiopharmaceuticals),
- be an abbreviation (except HCT, see bellow in subsection 3.1.2 of this guideline) or an acronym,
- be a number, because this can lead to a cognitive error in reading and perceiving the strength of the medicinal product, which is a numerical value and follows the qualifier. A numerical qualifier, used after the product <name>, is acceptable only for specific groups of medicinal product when it indicates a component of the product composition (e.g. vaccines, plasma derived medicinal products, radiopharmaceuticals or vitamins, etc.).
- be a combination of a letter(s) and number(s), except for specific groups of medicinal products.

When a qualifier is used, it should be included after the invented name and before the strength (not after the strength or pharmaceutical form) and separated by a space. Using multiple qualifiers (two or more qualifiers) in the <full name> is not recommended.

When a qualifier is proposed in the <full name>, the applicant/MAH should provide an explanation in application (for granting marketing authorisation or variation) on the inclusion of the qualifier.

A qualifier sholud be used only with an invented name, but not for creating a common/scientific name of the medicinal product. A qualifier can only be used with the common name in exceptional cases, when justified, for safety reasons, and HALMED will evaluate each such case.

3.1. Examples of qualifiers

Some qualifiers in the <full names> of already approved medicinal products are the result of regulatory practice from the past, when the strength and pharmaceutical form were not mandatory part of the medicinal product's <full name>, so their use was reasonable at that time. However, this does not mean that all previously approved qualifiers are acceptable for the creation of <full names> today because they are not in line with valid regulatory practice according to this guideline. Harmonisation of such qualifiers/full names according to this guideline is not mandatory, but exceptionally HALMED may request change of some previously approved <full names>/qualifiers authorised before publication of this guideline to assure a safe use of the medicinal product and protection of public health.

HALMED evaluates the acceptability of each proposed qualifier on a case-by-case basis during the regulatory procedure, taking into accout additional benefit that the qualifier brings in comparison to the mandatory elements of the <full name>, in terms of more easier/accurate identification and safer use of the medicinal product, and possible confusion that may arise from more complex <full name> of the medicinal product when the qualifier is used.

The qualifiers listed below in this guideline do not represent a final list of qualifiers, but are listed as the most common examples.

3.1.1. Qualifiers to distinguish the strength

< forte or mini >

The use of these qualifiers in the <full name> of the medicinal product is acceptable only when the strength of the medicinal product cannot be simply quantified in<full name>, so a descriptive qualifier is necessary to distinguish the strenghts, as in the following cases:

- a medicinal product that contains a combination of more than one active substance (usually more than three) and therefore the strength cannot be expressed in a simple and understandable way,
- a herbal/traditional herbal medicinal product that contains one or more active substance(s) from a herbal source for which expression of the quantitative composition is too complex and could not be simply and clearly quantified as the strength in the <full name> (see details on the strength in section 2 of this guideline),
- an OTC medicinal product when additional clarification of strength is important to identify, differentiate and easily select the medicinal product for self-medication.

< max or maxi >

Use of this qualifier (also as a suffix or prefix) is not acceptable for description of the strength (in line with subsection 2.2 of this guideline, the strength should be expressed quantitatively or, in exceptional cases, by acceptable descriptive quantifier) or any other property/attribute of the medicinal product, as it conveys a promotional message that is especially important in case of the OTC products when advertising is permitted to the public (in most cases).

The qualifier <max or maxi> implies the meaning of <maximum activity or maximum value>, so patients/users can conclude that this qualifier refers to maximum/better/the best efficacy compared to other medicinal products without this qualifier in the <full name>.

3.1.2. Qualifiers used to distinguish a composition or formulation

Using of a qualifier to distinguish the <name> of the medicinal product containing a combination of active substances (the combination medicinal product) from the <name> of an already approved product, a mono-component medicinal product containing individual active substance from the combination or the <name> of an already approved same combination, is considered on a case-by-case basis.

In order to distinguish the <name> of a combination medicinal product, containing an additional active substance in comparison to composition of an existing medicinal product already authorised in the Republic of Croatia, in principle, it is acceptable to add the following qualifiers in the <name> of the approved medicinal product:

- < **Co**- > acceptable only for a “medicinal product subject to medical prescription” (Rx),
- <**kombi/ combi** >,
- < **plus** >,
- < **duo** > for a combination of two, or < **trio** > for a combination of three active substances,
- < **HCT** > in case that the additional active substance is hydrochlorothiazide.

In case of a herbal/traditional herbal medicinal product, , it is acceptable in addition to the invented name to use as a qualifier the name of the plant (not a part of the plant) in Croatian which is the sorce of herbal active substance(s) according to the declared in the composition of the medicinal product in section 2 of the SmPC.

In case of herbal/traditional herbal medicinal products these qualifiers are not acceptable e.g. *eliksir/elixir, natural/naturals* and similar.

Non-conventional formulations

Non-conventional medicinal product formulations (formulations such as “liposomal”, “pegylated liposomal” and “lipid complex”, that contain the same active substance but have different distribution/release profiles/dosage) must be distinguished from each other and from conventional medicinal product formulations. It is recommended to use qualifiers in the <full name> of the non-conventional formulation, in Croatian or English (an english term is understandable, usually acceptable for multilingual packaging), such as <liposomalni> or <liposomal>, <pegilirani liposomalni> or <pegylated liposomal>, <lipidni kompleks> or <lipid complex> or similar. This distinction between different medicinal product formulations is important in order to avoid potentially serious medication errors due to mixing-up different formulations.

For the non-conventional medicinal product formulations administered topically or by non-parenteral routes, the above listed qualifiers should be added in the <full name> only if a clear risk to patient safety has been identified.

The qualifiers **not acceptable** to distinguish a composition of different medicinal products are:

< original >

- This qualifier has a promotional nature, it emphasizes “originality” that may be associated with better/original quality or any other better/original property of the medicinal product, consequently implying that medicinal products that have a similar composition of active substance(s) and don’t have this qualifier in the <full name> are copies or may be considered more poor/inferior to an “original” having this qualifier in the <full name>.

< pro >

- This qualifier has a promotional nature, it reminds of the meaning of the word <proactive> and consequently implies < proactive action, making things happen, taking activities/actions in order to achieve results or take control>, and thus emphasizes the medicinal product with this qualifier in the <full name> as better/more favourable in comparison to other medicinal products that have a similar composition of active substance(s) and don’t have this qualifier in the <full name>
- In case when a medicinal product contains an active substance derived from a previously approved “*parent”* active substance contained in an approved medicinal product or is a pro-drug of an approved medicinal product, which is significantly different from the approved active substance and is considered to be a new active substance, a new product name different from an existing already approved product name should be proposed. Adding “pro” as a qualifier or a prefix/suffix to the existing approved invented name is not considered as an acceptable difference.

Acceptability of using any other qualifier to differentiate a composition of different medicinal products, HALMED will consider on a case-by-case basis.

3.1.3. Qualifiers releated to therapeutic effect/action

< rapid >

The qualifier <rapid> is **acceptable** in the <full name> only if it is justified, when:

- It refers to a faster onset of therapeutic effect/action of the medicinal product compared to another medicinal product that contains the same active substance/active moiety (can be different salts or esters), and the faster action is relevant for a treatment.
- The faster action should be supported by a dossier (studies providing a clinical/therapeutic relevance have to be submitted) and reflected in the SmPC acordingly.

Following qualifiers are **NOT ACCEPTABLE** in the <full name> of a medicinal product, because they have elements of a **promotional nature**:

< effect/efekt > and **< aktiv/active >**

- The qualifier < effect/efekt > reminds of the meaning < activity or effectiveness > or < achieving an effective outcome or a result of an action>. The qualifier < aktiv/active > reminds of a similar meaning such as < activity or action >.
  Therefore, both qualifiers are not acceptable when used in the <full name> because additionally emphasize the "action/effect/effectiveness" of the medicinal product. "Efficacy/effectiveness/action" is an essential/core propertiy of the medicinal product on which its approval is based and should not be additionally emphasized using these or similar qualifiers in the <full name>. Therefore, these qualifiers are considered to be a promotional nature.
- Additionally, the qualifier < effect/efekt > can mean a way in which something works, e.g. <a more effective/efficient or faster way of achieving an intended result/outcome>, consequently implying that the medicinal product with this qualifier in the <full name> is more effective in comparison to the medicinal products that have the same composition of active substance(s) and don't have this qualifier in the <full name>. Therefore, this qualifier conveys a promotional message.

< essential >

- This qualifier in not in Croatian language but it has a generally known meaning <something what is absolutely necessary, extremely important or fundamental>.
- If used the qualifier would imply that a medicinal product with this qualifier in the <full name> is more important/more necessary in comparison with medicinal products without this qualifier in the <full name>, consequently conveying a promotional message.

< control/kontrol >

- This qualifier is related to the verb <to control> which means < very well regulate something> or < to control something precisely/accurately > and it emphasizes the "control". The "control" of a disease or condition of the body is one of the essential attribute of the medicinal product on which its approval is based, and should not be additionally emphasized using this qualifier in the <full name>.
- In addition, use of <control> as a qualifier in the <full name> of the medicinal product has a promotional nature, as it implies that the medicinal product with this qualifier in the <full name> better controls a disease/or a condition in comparison with other medicinal products that have the same composition of active substance(s) and don't have this qualifier in the <full name>.

< protect/protekt >

- This qualifier is related to the meaning of the noun < protection > or verb < to protect>, which means < to provide a guard or shield > or < keep safe from damage or injury > or < to ensure someone or something to be safe/protected >.
- The mentioned meanings have a promotional nature, and use of this qualifier implies that the medicinal product with this qualifier in the <full name> better protects against diseases in comparison to other medicinal products that have the same composition of active substance(s) and don't have this qualifier in the <full name>.

< relief >

- This qualifier is in not in Croatian, therefore is not understandable to the ordinary patient/user. Undarstanding of all elements of the <full name> is important for accurate identification and selection of the medicinal product for treatment, especially for an OTC medicinal product when selecting it for self-medication.
- The meaning of the qualifier in English, if it is understandable, is < something that relieve or remove a pain, discomfort or distress > and is considered to have a promotional character, as it may implay that the medicinal product with this qualifier in the <full name> better relieves/removes the pain/disease in comparison to other medicinal products that have the same composition of active substance(s) and don't have this qualifier in the <full name>.

Qualifiers such as *extra, strong, super, boost, ultima, optima, fast, quick, express, instant, elixir, intense/intensive, attack, advance, comfort, repair, care, clear, acting, double/or triple action, fantasy, one or once daily/weekly*, and similar listed in subsections 2.1.1. c) and f) of this guideline, are not acceptable as they convey promotional messages and can lead to trivialitisation of the medicinal product's use (e.g. by association on very wide use of the medicine or on a food supplement or cosmetics).

3.1.4. Qualifier indicating a patient population

It is unnecessary to add the qualifier < for adults > in the <full names> of medicinal products not intended to use in children. Inclusion of the qualifier < for children > in the <full name> is acceptable only when children is a target population and another medicinal product intended to use in the adult age group is/will be approved under the same name, so it is necessary to distinguish two medicinal products intended for different age groups.

When used, it should be stated in Croatian after the <name> and before the strength (or before the pharmaceutical form, when the strength is not expressed), e.g. "Name < za djecu >" instead of in English "Name ~~< for kids >~~ or < ~~for children~~ >".

The qualifier "lady" is not acceptable for new proposals, it remains only in the <full names> of medicinal products approved before publishing of this guideline.

3.1.5. Qualifiers indicating a flavour/aroma

Inclusion of a qualifier indicating a flavour/aroma in the <full name> is acceptable in case when medicinal products differ only in the flavour or aroma. When used, it should be stated in Croatian after the <name> and before the strength or pharmaceutical form (when strength is not expressed), e.g. if the product contains strawberry flavor, it should be stated "Name < s okusom jagode > instead of "Name < ~~jagoda~~ >".

Qualifiers such as *Fruit, Hot, Hot Lemon, Mint, Cool, Cool Mint/Coolmint, Fresh, Fresh Mint/Freshmint, Polar Ice/ PolarIce, Arctic, Naturals/Natural* and similar are not acceptable.

3.1.6. Qualifiers for the administration devices

It is acceptable to include as a qualifier the brand name of the medical device used for administration in the <full name> of the medicinal product (e.g: Novolizer, Breezhaler, FlexPen and others). It should be included after the name.

3.1.7. Other qualifier

It is not acceptable to use "negative claims" as qualifiers in the <full names> as „*free" forms*, e.g., < alcohol-free >, < colour-free >, < latex-free > or similar, because they are considered as promotional.

The inclusion of the „*free" forms* in the <full name> may be considered in an exceptional case, when it is important to distinguish between different formulations of the medicinal product for safe use and patient education, e.g. <preservative free> or <sugar free>.

4. Regulatory aspect

The proposed <full name> of the medicinal product is assessed during the marketing authorisation or variation procedure. In case of a line extension (line extensions of marketing authorisation are complex variations listed in Annex I to the current Commission Regulation (EC) No1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products), for which an application for granting marketing authorisation should be submitted based on the same legal basis as the initial authorisation to which it relates, it is necessary to propose the same <name> of the medicinal product as initially authorised medicinal product. Use of a qualifier in the proposed <full name> in line extension procedure, in addition to the mandatory elements (the strength and the pharmaceutical form), will be assessed by HALMED on a case-by-case basis.

In case when applicant/MAH intends to submit a new application for granting a marketing authorisation for a medicinal product with a new or additional indication in comparison to an already approved medicinal product with the same active substance, a new name different from the name of already approved product should be proposed.

If more than one application for marketing authorisation (duplicates) has been submitted based on the same dossier, the names of duplicates from different authorisation procedures must be different.

For medicinal products containing the same active substance(s) for which marketing authorisation procedures are submitted under different legal basis, different names should be proposed taking into consideration that the difference only in the qualifier is not considered sufficient.

The <name> of the generic medicinal product in the MRP/DCP should be the same in all Member States included in the procedure if its reference medicinal product has been authorised via CP. Further details for creating the name of generics are available in the CMDh document *Questions & Answers - Generics*, in section "*Naming of generics*".

If marketing authorisation for a medicinal product has became invalid (withdrawn, revoked or expired) after the medicinal product had been placed on the market in the Republic of Croatia, its invented name may be re-used for another medicinal product after five years of the date of official invalidity of the marketing authorisation has elapsed. In case the medicinal product has not been placed on the market in the Republic of Croatia after the approval, HALMED may consider re-using this name before the expiration of the specified period.

If applicant/MAH applys for change of a classification from a "medicinal product subject to medical prescription/Rx" into a "medicinal product not subject to medical prescription/OTC" for an already approved medicinal product, in case when some strength(s) and/or pharmaceutical form(s) and/or package size(s) still remain approved in the "prescription"/Rx status, a new <name> should be proposed in the procedure for granting OTC status (Rx to OTC switch), different from the existing <name> already approved for the Rx medical product.

5. Assessment of the proposed medicinal product's name

HALMED evaluates the <full name> of medicinal product in line with the criteria laid down in this guideline. The evaluation of the proposed <full name> is part of the assessment of the dossier. When assessing the similarity of the proposed<full name>, HALMED takes into consideration all names of approved medicinal products in the Republic of Croatia (approved via NP, MRP/DCP and CP), as well as the proposed medicinal product names in ongoing procedures.

When submitting an application (for granting marketing authorisation or variation), a maximum up to three proposednames may be submitted initially. The same applies in case of additional name proposals submitted as amendments during the procedure.

HALMED does not evaluate the acceptability of the medicinal product's name in advance, outside the procedure (marketing authorisation or variation application). In case the application has not been submitted yet, the evaluation of the name in advance may not cover or predict all names that will be proposed/approved for other medicinal products by the time of the submission of the application for which the evaluation of the name is asked in advance.

The <full names> of the medicinal products for which a marketing authorisation have been granted in the Republic of Croatia prior to the publication of this guideline do not necessarily need to be harmonised with this guideline. For reasons of public health protection, HALMED may request a change/harmonisation of the name of the medicinal product approved before the publication of this guideline to assure safe use of the medicinal product.

The MAH is responsible for the risks, actual or potential, associated with the medicinal product's name that may arise after the medicinal product has been placed on the market. The MAH is required to inform HALMED of any risks associated with the medicinal product's name that he becomes aware of after placing the medicinal product on the market, in order to take appropriate measures to protect public health.