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Guideline on the acceptability of names for human medicinal products processed through the centralised procedure

Draft

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Comments should be provided using this template. The completed comments form should be sent to NRG@ema.europa.eu

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Guideline on the acceptability of names for human medicinal products processed through the centralised procedure

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Executive summary

Based on the experience gathered by the Name Review Group (NRG) since the last revision of the guideline in May 2014, it became apparent that some areas of the guideline would benefit from further clarifications, in particular with regards to the requirements for acceptability of proposed (invented)[1] names of medicinal products processed through the centralised procedure.

This 7th update of the guideline further clarifies specific aspects of the criteria applied to address safety and public health concerns, international non-proprietary names issues and product-specific concerns in proposed (invented) names. This update also provides further information on the conditional acceptability of invented names and the process for bilateral negotiations, and proposes changes to the duration of the validity of an (invented) name and the review process of the NRG.

1. Introduction

A Community marketing authorisation (MA) is valid throughout the European Union and the (invented) name of the medicinal product is an integral part of the authorisation. In accordance with Article 6 of Regulation (EC) No 726/2004, *"each application for the authorisation of a medicinal product (…), otherwise than in exceptional cases relating to the application of the law on trade marks, shall include the use of a single name for the medicinal product."*

The centralised procedure therefore requires one single (invented) name for the medicinal product to be authorised. However, in exceptional cases, where the proposed trade mark has been cancelled, opposed or objected to under trade mark law in a Member State, the Commission may accept the existence of more than one name for a single product, in order not to disadvantage patients and their access to the concerned medicinal product in that Member State. To obtain such derogation, the marketing-authorisation holder (MAH) shall provide enough evidence of its failed efforts. Should derogation be granted, it will not affect the legal obligations throughout the Community and shall not be used to introduce any partitioning of the European market, i.e. to restrict or prevent the free movement of concerned medicinal product. It is reminded that the MAH/applicant must liaise directly with the European Commission to obtain derogation in writing.

Although it is not mandatory under European Union legislation, in practice, many companies submitting marketing authorisation applications (MAA) under the centralised procedure wish to use invented names for their medicinal products.

According to Article 1(20) of Directive 2001/83/EC, it should be noted that the name of the medicinal product *"may be either an invented name not liable to confusion with the common name, or a common name or scientific name accompanied by a trade mark or the name of the marketing authorisation holder"* (see section 4.3.6). It is also understood by legislation that a common name is, according to Article 1(21) of Directive 2001/83/EC, as amended*, "The international non-proprietary name (INN) recommended by the World Health Organization, or, if one does not exist, the usual common name."*

According to the Article 4 of Council Regulation (EC) No 207/2009 on the Community trade mark, a trade mark may consist *"of any signs capable of being represented graphically, particularly words, including personal names, designs, letters, numerals, the shape of goods or of their packaging,*

1 In certain sections of this document reference is made to the terms '(invented) name', with the term 'invented' presented in brackets preceding the term 'name'. This format aims to cover two possible scenarios in terms of proposed names: a purely 'invented name'; and a 'name' which can be the combination of the INN together with the name of the MAH/applicant company or its trademark.

provided that such signs are capable of distinguishing the goods or services of one undertaking from those of other undertakings."

The review of trademarks is outside the European Medicines Agency's (EMA) remit. The EMA will not take into consideration aspects of intellectual property rights/trademark registration within its review for the acceptability of a proposed (invented) name. The applicant/MAH is sole responsible for checking all legal requirements and criteria for trademark registration and ownership prior to submission to the NRG. The applicant/MAH will need to contact directly the appropriate authorities to apply for a trademark registration.

The checking of the proposed (invented) name is part of the EMA's role in evaluating the safety of medicinal products within the authorisation procedure, as the proposed (invented) name(s) could create a public-health concern or potential safety risk. This objective is captured in the Good practice guide on risk minimisation and prevention of medication errors which highlights that '*careful consideration should be given to the* ***name*** *and pharmaceutical design of a medicinal product (including its type of dosage form, appearance and other formulation characteristics, packaging and labelling) in order to minimise the risk of mix-ups between different products*'. The NRG performs this evaluation on the basis of best available evidence and research.

Although the review of names for medical devices and food supplements does not fall within the remit of the NRG, applicants are encouraged to give due consideration to possible confusion between medicinal products names and the names of such other products.

Proposals for invented names, as well as for names presented under the construction 'INN + company name/trademark', will be subject to EMA review. The latter case is not a default option in case no invented name for a specific product is accepted by the NRG. The 'INN + company name/trademark' option must also be submitted for review by the NRG (see section 6.4).

All information sent by applicants/MAHs in relation to (invented) names is considered confidential and all parties involved in the review of names within the centralised procedure are bound by the EMA's confidentiality policy and their own National or Authority rules of confidentiality.

2. Scope

The scope of this guideline is to provide information on the overall procedure for submitting and reviewing the acceptability of proposed (invented) names for human medicinal products processed through the centralised procedure, as well as detailed guidance on the criteria applied by the NRG when reviewing the acceptability of names.

The main aim is to promote patient safety as an essential principle.

3. Legal basis

This guideline has been developed in accordance with Article 6 of Regulation (EC) No 726/2004 and Article 1(20) of Directive 2001/83/EC, as amended, which require each authorisation application to include a single name not liable to confusion with the name of another medicinal product.

The EMA has established a review process performed by the NRG to ensure that the provisions set out in Article 6 of Regulation (EC) No 726/2004 and Article 1(20) of Directive 2001/83/EC are adhered to.

4. Criteria applied when reviewing the acceptability of proposed (invented) names

The following review criteria should be seen as general rules. The EMA may develop additional guidance on specific topics based on experience or newly identified safety concerns.

When reviewing the acceptability of proposed (invented) names, the NRG applies criteria based on public health concerns and in particular with regard to safety (see sections 4.1 and 6).

The applicant/MAH should ensure that the proposed (invented) name complies with the criteria outlined in this guideline before submitting a request to the EMA. To facilitate the review process, applicants/MAHs are advised to submit all available supporting documentation as outlined in section 6.1. and the NRG Application Form.

4.1 Addressing safety concerns and other public health concerns in proposed (invented) names

4.1.1 The (invented) name of a medicinal product should not be liable to cause confusion in print, handwriting or speech with the (invented) name of another medicinal product. Examples of attributes to take into consideration in determining the degree of similarity of the proposed name are provided in Appendix 1.

When assessing the potential for such confusion, at least the following aspects are considered:

- The indication(s);
- The intended patient population. Aspects which could influence the selection of the correct product such as training, literacy, comorbidities, vision, hearing, memory, disease state, mental clarity, etc should be considered;
- The intended Health Care Professionals (HCP);
- The pharmaceutical form(s);
- The route(s) of administration;
- The strength(s);
- Complexity of product handling (instructions for use) and environmental aspects which may impact the correct use, e.g. storage of the product, technologies used, previous medication errors, standard guidelines for HCPs etc;
- The setting for prescription, dispensing, preparation (if applicable) and use/administration;
- The existence of controls, i.e. procedures involved in the prescribing, dispensing, preparation or administration which may reduce the risk of a medication error. Examples of such procedures could be specialised prescriptions in the HIV/oncology setting, reconstitution steps for powder preparations, therapeutic patient education in chronic disease settings, highly specialised manufacturing and/or personalised processes for handling of advanced therapy medicinal products or radiopharmaceuticals.
- The legal status/classification for supply:
    - Medicinal product subject to medical (special and/or restricted) prescription;

- Medicinal product not subject to medical prescription;

- (Potential) New pharmaceutical forms, routes of administration and/or strengths for the medicinal product concerned, as appropriate.

- The degree of similarity *versus* the potential for harm to the patient in case of mix-up.

4.1.2. It should be noted that the NRG will consider potential for confusion of proposed (invented) names with the (invented) names of authorised, suspended and revoked/withdrawn medicinal products in the different Member States according to the relevant national legislation regardless of the route of authorisation.

When considering the potential for confusion with the name of a withdrawn/revoked medicinal product, a period of 5 years should have, in principle, elapsed after the official invalidity of the MA. This period could be reduced if it can reasonably be justified by the applicant/MAH, or extended in the case of withdrawal due to serious safety concerns, at the discretion of the NRG. In making these decisions the NRG may also take into account other aspects such as the existence of online information regarding the withdrawn medicinal product.

4.1.3. Additionally, the NRG will also consider proposed (invented) names which have been already accepted either by the NRG in the context of the centralised procedure or by a national competent authority (NCA) in any other procedure at national level.

If the risk of confusion is identified only with the invented name of a pending MAA (i.e. ongoing MA evaluation or MA in pre-submission stage), the proposed (invented) name will be conditionally accepted. Due to the fact that the objection is not endorsed with the name of an authorised medicinal product, and hence the risk of confusion cannot be confirmed, the applicant may use the proposed invented name for their MA application. However, only the application which is granted a MA first may retain the (invented) name. Once the first MA is granted, the second contending name will become rejected (see section 6.6).

4.1.4. The NRG also considers potential safety concerns and other public health concerns associated to the re-use of identical (invented) names. Specific assessment criteria applied by the NRG is described in section 6.9.

4.1.5. The (invented) name of a medicinal product should not include the full invented name of another medicinal product.

4.1.6. In some cases, even though two invented names do not share the same letters in the same order, the NRG may consider that the potential confusion is related to the way the human brain perceives them; this is considered as a *cognitive error* associated to at least a medium degree of similarity in print, speech and handwriting.

4.1.7. The (invented) name of a medicinal product should not convey misleading therapeutic connotations.

The NRG takes due consideration to the inclusion of elements related to the therapeutic indication and/or mechanism of action of the medicinal product in the invented name, with the aim of ensuring that it does not convey inaccurate claims in these regards (see section 4.1.8). Applicants should consider the future life-cycle of the medicinal product, and post-authorisation changes which may lead to discrepancies between the product profile and the invented name.

4.1.8 The (invented) name of a medicinal product should not convey a promotional message. An (invented) name is considered promotional if it is overly fanciful, so as to misleadingly imply

unsubstantiated unique effectiveness, composition or superiority claims, if it overstates the product efficacy, minimises the risk or broadens the product indications.

The (invented) name should not trivialise the use of the medicinal product.

Moreover, when names are composed by the INN or common name/scientific name followed by name of the MAH/applicant they should equally not be misleading or promotional in any of the EU/EEA languages. The trend to create MAH names variations with positive connotations should be avoided, and MAH name should not be ambiguous.

4.1.9 The (invented) name of a medicinal product should not be misleading with respect to the pharmaceutical connotations such as the qualitative or quantitative composition, or the pharmaceutical form.

The NRG gives due consideration to the inclusion of these aspects in the invented name. Applicants should consider the future life-cycle of the medicinal product, and post-authorisation changes which may lead to discrepancies between the product profile and the invented name.

4.1.10. The NRG may also object to invented names which are similar or allude to the name of pharmaceutical companies, if they are thought to be misleading in regards to the MAH of the product or cause confusion at the level of product information.

4.1.11 The inclusion of a common umbrella segment (e.g. part of the name of the sponsor) within the invented names of different medicinal products is not acceptable as it creates a link which may lead to confusion and medication errors. The use of an umbrella segment, unless the portion used is significant and evident when the name is considered as a whole, may however, be accepted the first time it is proposed for an invented name. The NRG will not accept the use of the same segment in a second instance.

4.1.12 Applicants should consider the phonetic characteristics of an invented name and the potential difficulties in pronunciation in the different EU official languages. The use of repeated vowels or consonants may create such difficulties, which, if considered sufficiently severe, may result in the rejection of the invented name on the grounds of potential confusion at the level of the correct identification of the medicinal product. Furthermore, the use of repeated vowels or consonants in the prefix of the invented name should in principle be avoided to ensure the correct identification of the product in electronic systems.

Very short invented names composed of, for instance, a string of vowels or consonants may be inappropriate to identify medicinal products in certain Member States. In addition, applicants should give due consideration to any other element which may hamper readability and identification of the product.

Applicants are encouraged to provide evidence to support the ease of pronunciation of those invented names which may be particularly challenging from a reading/pronunciation stand-point in different groups of Member State languages.

4.1.13 The use of qualifiers/abbreviations by letters as part of the invented name should in principle be acceptable. Applicants should provide in all cases an explanation on the inclusion of the qualifier.

Applicants, however, should refrain from using symbols, dose designations, and medical abbreviations commonly used for prescription communication in their proposed invented name because their inclusion could inadvertently introduce a source of error.

The NRG recommends applicants/MAHs not to propose qualifiers consisting of a single letter or number(s) (Arabic and Roman), because they may be confused with the strength and/or posology of the medicinal product. However, the use of numbers may in certain cases be acceptable, e.g. vaccines (see section 4.3.1).

(Invented) names and qualifiers should always be separated by a space.

In reviewing the acceptability of a qualifier, the NRG will consider its potential added benefit *versus* the potential risk to public health, taking into account the following points:

- Whether the qualifier provides further information on characteristics of the medicinal product (e.g. duration of action, devices, route of administration, composition, patient population) without being misleading, or provides for a differentiation, which may help HCPs and/or patients to prescribe/select the appropriate medicinal product.
- The applicability and use of the qualifier across all European languages. Qualifiers should not require translation to provide further information in the respective EU Member States. In some justified circumstances, however, translation may be accepted to ensure the safe use of the medicinal product, e.g. qualifiers for COVID-19 vaccine variants.
- The potential risk resulting from more complex names, adversely affecting the ability to identify unambiguously a medicinal product.

4.1.14 When an (invented) name of a medicinal product is accompanied by a device name, the (invented) name should not be liable to cause confusion in print, speech or handwriting with the name of another medicinal product. The device name will not be considered as contributing to this differentiation except in exceptional circumstances.

In the context of post-authorisation activities, when a new device is introduced which needs to be differentiated from the existing one, it will not be considered as part of the invented name. In these cases the device name will be placed immediately after the strength of the product, thereby allowing for differentiation of the presentations without jeopardising the single name principle (see section 5).

4.1.15 The (invented) name of a medicinal product should not be offensive or have an inappropriate connotation in any of the official EU languages.

4.1.16 The invented name of a medicinal product should not be comprised wholly of initial letters (acronyms) or code numbers nor include punctuation marks.

4.1.17 The importance of other elements such as labelling and pack design should be taken into consideration as contributing factors for the safe use of a medicinal product.

The following are examples where labelling and pack design may play a role in the final decision of acceptability of (invented) names:

- The actual display of an invented name in the printed material may increase the level of similarity between two invented names or may convey a misleading connotation.
- The labelling and pack design may support the meaning of a qualifier which otherwise would have been rejected.
- When creating invented names the size limitations of the outer/immediate containers should be taken into consideration by the applicant prior to submission. The NRG may reject names if there are considered too long to be accommodated on very small containers.

- When the (invented) name is deemed similar to another (invented) name belonging to the same applicant or MAH.

These aspects will be further discussed at the time of the review of mock-ups, and may be referred back to the NRG during the MAA evaluation.

Applicants should take due consideration to aspects related to the naming and labelling in line with the Guideline on the readability of the labelling and package leaflet of medicinal products for human use.

4.1.18 Applicants should inform the NRG if the proposed (invented) name has been approved in another region for the same active substance, but with a different profile, as the potential for conflicting information about the product on the internet may lead to confusion and potential off label use. This information should be provided as part of the name application.

4.2 Addressing international non-proprietary names' concerns in proposed invented names

According to Article 1(20) of Directive 2001/83/EC, *"… an invented name shall not be liable to confusion with the common name…".* Furthermore, when proposing an invented name, applicant(s)/MAH(s) are advised to take into consideration World Health Organisation (WHO) resolution (WHA46.19), where appropriate, i.e. *"It would therefore be appreciated if invented names were not derived from international non-proprietary names (INNs) and if INN stems were not used in invented names".*

Two types of INN issues could be considered, i.e. a potential similarity with its own or different INN or the inclusion of an INN stem into the proposed invented name(s) (see Stem Book 2018).

When reviewing INN similarity, the NRG makes use of a 50% similarity rule to support its decision-making, with the aim of identifying cases where 50% or more of the proposed invented name is made up of INN parts, and/or 50% or more of the INN is included in the proposed invented name. The Group checks for shared letter-strings and their sequence, and whether the proposed invented name contains an INN stem for the same or different pharmacological/chemical trait. On the basis of these considerations the NRG discusses each proposal on a case by case basis.

When reviewing similarity to INN, phonetic similarities such as 'y' and 'i' may also play a role in the decision of the NRG, see Appendix 1 for further examples.

The applicant/MAH is strongly advised to review INN similarity (proposed, recommended or revised INNs) and/or INN stem inclusion before requesting that the proposed (invented) name(s) be considered for a medicinal product.

The NRG will review the above cases on the basis of WHO World Health Assembly resolution (WHA46.19) on protection of INNs/INN stems to prevent any potential risk of confusion between invented names and common names.

Where the applicant/MAH wishes to use the INN or common name/scientific name, together with the name of the MAH/applicant or a trademark, instead of the invented name, they should take into account the following rules:

- If an INN recommended by the WHO exists for the active moiety, it should be used within the name of the medicinal product exactly as published, without omissions or abbreviations. All the linguistic versions of the INN, including translations officially

recognised at the national level, shall be considered to be the same name. If one does not exist, the usual common name should be used.

- The applicant/MAH should inform the NRG of any revisions to already recommended INNs which may have an impact on the outcome of the NRG review.
- In the case of generics, when using an INN/common name + MAH/trademark structure, the order of the active substances should be aligned with that of the reference medicinal product.
- If a Modified INN (INNM) recommended by the WHO exists for the active moiety, it should be used within the name of the medicinal product exactly as published without omissions or abbreviations.
- In the case of established active substances where the strength has traditionally been expressed on the basis of an unpublished INNM instead of the WHO recommended INN, the unpublished INNM shall be used if the applicant/MAH can justify the extensive and well-known use of the INNM versus the recommended INN.
- The 'name of the MAH' within the name should correspond to all or part of the official name of the MAH as presented in the proof of establishment of the applicant/MAH.
- The 'name of the MAH' cannot be an acronym, unless it is a company trademark registered as such, which clearly refers to and helps identify the applicant/MAH. The applicant should be able to confirm ownership of this trademark (see section 1).
- The use of such acronyms should not convey promotional or inappropriate connotation with respect to the use of the active substance in the context of the proposed therapeutic indication (see section 4.1.8).
- For consistency reasons, ease in prescription by healthcare professionals and database entries, punctuation marks in between the INN and the name of the MAH/trademark are not acceptable (with the exception of fixed combinations, where multiple INNs should be clearly separated by a forward slash '/').
- The proposed (invented) name cannot be a mixture of legally available options: in accordance with Article 1(20) of Directive 2001/83/EC, the name of a medicinal product should either be an invented name or the common name accompanied by a trademark or the name of the MAH. Therefore, the use of combined structures such as acronyms or abbreviations together with part of the MAH name cannot be considered as part of the official name of the MAH.

'INN/common name + MAH/trademark' naming structures for fixed combination medicinal products carry the risk of incorrect selection in electronic prescribing and dispensing lists, if all the active substances of the product are displayed on screen. The correct identification and selection of the product may, therefore, not be possible. Applicants should take this into consideration when proposing generic names for fixed combination products (see section 4.1.17).

4.3 Addressing product specific concerns in proposed (invented) names

4.3.1 For vaccines composed of several serotypes, when adding a new serotype the original invented name may be kept, provided that the indication of the daughter vaccine covers the indications of the parent vaccine. It is recommended that the name is then followed by the number of

serotypes present in order to ensure differentiation between parent and daughter vaccines. The description of serotypes present is then listed in the qualitative and quantitative composition. An example of the format of the proposed invented name follows:

Invented name + X [number of serotypes]

The same applies when different types of antigens are added. This is of particular importance in situations where both vaccines are simultaneously available on the market in order to allow differentiation of the products.

Applicants are requested to submit a table comparing the proposed and the previous SmPC in order to highlight differences to ensure these will not compromise the safety of the product.

4.3.2 For radiopharmaceutical medicinal products, the inclusion of target organs in the (invented) name should be avoided in order to prevent misleading connotations should an extension of the indication include new target organs.

In principle, numbers should not be used in the name to avoid confusion with the strength. In cases where the numbers appear in the radionuclide, these should be displayed in superscript, i.e. $^{\text{mass number}}$Element + [(Invented) name]

Numbers included as part of commonly known abbreviations are assessed on a case by case basis.

4.3.3 A sponsor may apply for designation of a medicinal product as an orphan medicinal product for an already approved medicinal product provided the orphan designation concerns an unapproved therapeutic indication. In this case, in accordance with Article 7(3) of Regulation (EC) No 141/2000 of 16 December 1999 on Orphan medicinal products, and Commission Communication on the same Regulation (section C.2), at the time of application for a MA, the sponsor must apply for a separate MA (with a different [invented] name) which will cover only the orphan indication(s).

When reviewing the acceptability of (invented) names for orphan medicinal products, the NRG applies the same approach as for non-orphan medicinal products. It is of particular importance in these cases to provide detailed information on the specific setting in which the product is dispensed and used as well as on the target population.

4.3.4 For non-prescription medicinal products, due account should be given to the specific legal status of these medicinal products as defined in Articles 71 and 72 of Directive 2001/83/EC, as amended. The use of qualifiers/abbreviations within the invented name should aid selection/identification/differentiation of the product by the patient and should minimise the risk of inappropriate use.

In view of the above considerations, the specific criteria as described under sections 4.1.13 and 4.3.9 may not apply here.

In order to guarantee correct self-medication and compliance by patients/consumers, it is acceptable that invented names are informative without being promotional. The labelling and pack design could be considered as contributing factors to the informative aspect (see also section 4.1.17). The applicant should provide the NRG with an explanation in such cases.

In case of a switch from "prescription" to "non-prescription" status of an already authorised medicinal product, it is up to the applicant/MAH to choose whether to vary/extend the existing MA and consequently retain the same (invented) name or to submit a separate MAA under a different (invented) name (see section 5). In exceptional cases, depending on the therapeutic

context, the acceptability of the maintenance of the existing (invented) name may be further considered by the CHMP during the evaluation process.

4.3.5 For generic/hybrid/similar biological medicinal products the same criteria apply as for any other medicinal products in respect to the (invented) name.

Special consideration should be given to the proposed (invented) name of a hybrid medicinal product to allow for differentiation when the latter differs in pharmaceutical form, strength, expression of active substance and/or indication from the reference medicinal product or other generics in the market.

Furthermore, although Article 1(20) of Directive 2001/83/EC applies, applicants should take note of the WHO Guidelines on evaluation of similar biotherapeutic products which state that the name of biosimilar medicinal products should be clearly identifiable by a unique brand (i.e. invented) name.

4.3.6 Applications for a CHMP Scientific Opinion in the context of collaboration with the WHO pursuant to Article 58 of Regulation (EC) No 726/2004 do not require the submission of proposed names to the NRG as the medicinal product is not intended for use in the EU.

4.3.7 The invented name of a fixed combination medicinal product should be sufficiently different from those of the individual active substances and/or those of other fixed combinations with overlapping active substance(s).

Furthermore, it is not acceptable to insert the whole invented name of the individual active substance(s) in the proposed invented name for the fixed combination.

4.3.8 As multiple applications can have an independent life (e.g. may develop a different indication at a later stage), the proposed (invented) names of such applications should not lead to confusion (see section 6.1).

5. Regulatory aspects related to the acceptability of proposed (invented) names

(Invented) names for variation/extension applications should be the same as those of the existing medicinal product. The addition of a qualifier to an invented name which is already in use, constitutes a different invented name, which would require submission as new MAA.

In case the applicant wants to submit a separate MAA for instance a new indication, a different (invented) name shall be used.

In the case of line extensions to introduce a prodrug formulation, which is thereby considered not to be significantly different from parent active substance, the medicinal product will maintain the same (invented) name. If the prodrug, however, is significantly different from the parent substance, then a new MA should apply.

6. EMA procedure for checking proposed (invented) names

The EMA operates a procedure to ensure that objections raised by national competent authorities against the (invented) name of a medicinal product due to potential safety risks or other criteria as defined in section 4 of this document are identified.

An important aspect of the procedure is the assessment of phonetic and orthographic similarity with other invented names. In order to ensure rational, objective and consistent decision-making process, the NRG makes use of an assessment checklist to support the review of these similarity-based objections (see Appendix 2). With the aim of improving overall quality of submissions to the NRG, applicants are strongly advised to consult this checklist to verify this aspect while researching name candidates or drafting their justification for the retention of names previously rejected.

The practical experience of the EMA to date has shown that early intervention and checking of the (invented) name(s) have permitted MAs to be granted without delays related to (invented) name issues. To best support this activity, applicants are strongly encouraged to adequately research their naming proposals before making a submission to the NRG. The Public data from Article 57 database which holds the following information: product name, active substance, route of administration, country of authorisation and name of the MAH, is a valuable resource which applicants can readily make use of for this purpose (see section 6.3).

6.1 Submission of the (invented) name request by the applicant/MAH

Provided that the medicinal product was deemed eligible by CHMP for evaluation under the Centralised Procedure, the applicant should inform the EMA of the proposed (invented) name(s) for their medicinal product (i.e. at the earliest 18 months prior to planned submission date of the MAA). In case the applicant submits the name review request in parallel to the eligibility request, the actual review would only take place provided that positive eligibility is granted prior to the NRG meeting. The NRG may, however, consider some exceptions on a case-by-case basis and on duly justified grounds.

To allow for review of proposed (invented) names, the applicant(s)/MAH(s) are requested to send to the EMA (NRG@ema.europa.eu) their proposed (invented) name(s) and the draft summary of product characteristics (SmPC) or product profile. Other relevant information may be submitted, such as justifications for deviation from the guideline, justifications for inclusion of a qualifier, results of research in connection to similarity with other invented names, patient information form distributed during clinical trials, justifications for multiple applications, description of a medical device etc. The 'Proposed (Invented) Name Request form' and further details of timing and content of an (invented) name application are available on the EMA website.[2]

Up to two proposed (invented) names per MAA can be accepted, either fully or conditionally, by the NRG. A maximum of two (invented) names per name review request can be proposed for consideration at each NRG meeting.

In principle, where two proposed (invented) names have been accepted by the NRG for a MAA, new requests for the review of additional proposed (invented) names under the same application will not be allowed. The NRG may, on duly justified grounds (i.e. identification of safety issue/health concern after acceptance of (invented) names, conditional acceptability of previously reviewed (invented) names, constraints achieving a global (invented) name, issues relating to the application of the law on trademarks, etc.), allow the assessment of further proposed names in which case the applicant/MAH is required to indicate which two fully accepted (invented) names should finally be maintained for a given MAA provided that they have been accepted. If an applicant wishes to retain a conditionally accepted name together with a fully accepted name, no further submissions will be accepted. In those cases where additional names are submitted based on constraints achieving a global name, applicants are required to submit documentary evidence from the relevant regulatory authority.

2 See the 'Pre-authorisation guidance' section of the Agency's website.

Furthermore, when the limit of two accepted (invented) names is reached within a meeting, the NRG will refer to the submitted order of preference for retention of names, and will stop the review of any subsequent proposals. Applicants are strongly recommended to take due notice of this practice and submit accordingly the order of preference in advance of the NRG meeting. The order of preference should include justification applications as applicable, which will always be reviewed in a first instance.

The applicant/MAH should clearly indicate at the time of submission whether the proposed (invented) names are intended to be used in the context of multiple MAAs. This is to allow the NRG to review whether the proposed (invented) names are not potentially confusing with each other. As an exception to the general rule, up to two proposed (invented) names per duplicate can be accepted by the NRG in the context of multiple applications.

6.2 Consultation with the Member States

The proposed (invented) name(s) and all the background information provided by the applicant(s)/MAH(s) are shared with the NRG contact points nominated by national competent authorities (NCAs) of EU Member States. The information is also shared with experts in medication safety as part of the consultation.

The NCAs are requested to inform the EMA of any objections/comments to the proposed (invented) name(s) on grounds of safety concerns or other concerns as described above within 30 days of receipt of such notification.

Representatives from the European Commission (EC), the WHO, patient/consumer organisations, HCP organisations and relevant experts selected from the European experts list may participate in the group's activities and are consulted on a case by case basis regarding naming issues.

6.3 NRG/CHMP discussion/adoption

In order to make best use of the NRG meeting discussion time, applicants are required to perform the adequate due diligence of the name before coming forward with a submission. To this end, Applicants are reminded that information on authorised medicinal products is publicly available via the Public data from Article 57 database. In case an unacceptably high number of objections are raised to a given proposed invented name, which would indicate that this proposed name has been poorly researched prior to submission, the NRG reserves the right to limit the number of similarity-based objections reviewed once it is ascertained that the name will be rejected. The remaining objections will be communicated to the applicant. Before submitting a justification to address the rejected names, applicants are advised to review all remaining objections raised during the meeting.

During the NRG meeting, the objection(s) and/or comment(s) to the proposed (invented) name(s) received from the different Member States are reviewed. The group evaluates these objections/comments based on the criteria described above in section 4.

If an objection is raised on the basis of similarity between the proposed (invented) name and another (invented) name, leading to a risk of confusion in print, speech and/or handwriting, the objection will always be evaluated taking into account other distinguishing factors as listed in section 4.

After evaluation of all relevant factors, the NRG will decide if the proposed (invented) name of a medicinal product may be accepted or if further clarifications are to be submitted by the company. Its conclusions/recommendations are presented to the CHMP for adoption.

Once an invented name has been accepted, any changes to key aspects of the product profile such as indication, route of administration, strength or pharmaceutical form, which may have an impact on the

outcome of the review, should be notified to the NRG in order to ensure that the invented name remains acceptable. Such changes should be notified at the time of the initial MAA or during the evaluation procedure, as applicable.

The NRG considers the acceptability of invented names for a period of 2 years from the time of CHMP adoption; this period can be extended once for a further 2 years upon request from the applicant (see section 6.9.2).

The (invented) name review is valid, at a certain point in time, which does not prohibit the possibility of objections being raised at any time prior or after the granting of the MA.

6.4 Applicant/MAH communication and follow-up

After adoption by CHMP, the applicant/MAH will be informed by the NRG Chair of the outcome of the discussion of the proposed (invented) name(s) for their medicinal product(s) together with the reasons and source for the objection(s) raised.

In case of objections to the proposed (invented) name(s), the applicant may justify the retention of the proposed (invented) name (see section 6.5).

During the NRG meeting the maintenance or withdrawal of the previous objections to the proposed (invented) name(s), as well as any comment(s) received from the different Member States and the applicant's justification are reviewed.

If the proposed (invented) name cannot be accepted prior to submission, the MAA can be submitted either under any of the proposed invented names or the common name/scientific name accompanied by a trademark or the name of the MAH.

At the latest one month prior to the adoption of the CHMP opinion on the concerned MAA, the applicant will have to inform the EMA (via the Product Lead) and the NRG secretariat about their choice of the accepted (invented) name.

If no suitable invented name has been identified at that stage, the opinion will be adopted according to the common name or scientific name accompanied by the name of the MAH. However, such name also needs the NRG endorsement prior to adoption of the opinion; therefore, sufficient time should be allowed for the NRG review to be performed at a regular meeting (see section 1). An accelerated review of proposed (invented) names may be performed in very exceptional cases and when adequately justified.

6.5 Rejection by NRG/CHMP of a proposed (invented) name

In the case of rejection of proposed (invented) names, the applicant/MAH can submit a new request to the NRG for the review of new proposed (invented) names, provided that the number of finally accepted (invented) names (either fully or conditionally) does not exceed two (e.g. if one of the initially proposed two (invented) names has been rejected, then the applicant/MAH can submit up to 2 more names for review. If with a new review there is a possibility of exceeding the limit of accepted names, an order of preference must be submitted (see section 6.1).

It is emphasised that although objections due to conflicting names with existing medicinal products may have only been raised by the Member State(s) indicated in the outcome document, this does not exclude the possibility that the medicinal products referred to may exist in other Member States.

In those cases where a proposed (invented) name is rejected the applicant/MAH has the following possibilities:

- To submit proposals for new (invented) names, which are checked through the same procedure as described above.

- To justify retaining the (invented) name addressing specifically all the objections raised. The applicant/MAH should note that where objection(s) identified in the outcome letter were raised for conflicting names nationally authorised by the particular Member State(s), this does not exclude the possibility that the medicinal products referred to may exist in other Member States. The applicant/MAH should verify whether this is the case. The justification will also need to include an assessment of potential for harm to the patient in case of a mix-up. This guideline should be taken into consideration, as appropriate, to address points for the original objection(s).

  Where new information not previously brought to the attention of the NRG becomes available to the applicant, the submission of additional/subsequent justifications to the NRG are considered acceptable.

  Applicants/MAHs should submit their request using the Justification form option of the Proposed (Invented) Name Request form which is available on the EMA website[3].

  Such justification will thereafter be shared with all Member States for consideration, and comments received discussed at the subsequent NRG meeting. The Member States which raised objections are requested to assess the justification and reconsider their objection.

- If no invented name is accepted before adoption of the CHMP opinion, the opinion will be adopted under the common name or scientific name together with the name of the MAH (section 6.4).

  In such a case, as soon as the Commission Decision is granted, the concerned MAH has the possibility to submit a variation (section 6.7.1) if they wish to use an invented name, on the condition that such name has been considered acceptable by the NRG in accordance with the procedure described under section 6.

- Exceptionally, provided all means have been exhausted, the applicant/MAH may request the matter to be presented to the CHMP within the context of the evaluation of the medicinal product.

6.6 Conditional acceptability and bilateral negotiations

Similarity-based objections are endorsed against approved invented names with a MA in place, an ongoing MAA, or which are in the MA pre-submission phase. When a MA is not in place, the application is referred to as a 'pending submission'.

Proposed names which only have similarity-based objections with the name(s) of a pending submission, but not of authorised products, are considered to be 'conditionally' accepted.

The NRG secretariat is responsible for informing concerned applicants of any changes to the conditional acceptability of their invented name (i.e. when the invented name becomes rejected or fully accepted). Should an applicant intend to use a conditionally accepted name for a MAA, they are required to liaise with the NRG secretariat to confirm the suitability of the name at the latest one month prior to CHMP opinion. A MA may be granted with the conditionally accepted name, if a MA for the contending name has not yet been granted.

An applicant may request to enter into a *bilateral negotiation* with the applicant of the conflicting name with a view to resolving the situation between them. This process requires that both parties provide

3 See the 'Pre-authorisation guidance' section of the Agency's website.

consent for the NRG secretariat to disclose applicant identities and invented names, thereby triggering a negotiation process between the affected parties.

Before a negotiation process has been established, the EMA cannot disclose any information regarding the contending name; this is considered commercially confidential information whose disclosure might prejudice the commercial interests of the other applicant to an unreasonable degree.

When an applicant confirms their wish to initiate a bilateral negotiation, the NRG secretariat informs the contending applicant, and requests confirmation of their interest to participate in the process. If both companies are in agreement they will be requested to provide consent for EMA to disclose the relevant commercially confidential information (i.e. the invented name, applicant/MAH name and contact person for the negotiation process). This consent should be provided in the form of a signed agreement by the relevant/authorised signatory. In those cases where the contending name is that of a national pending MAA, the communication with the relevant applicant at national level is made by the corresponding NCA.

The EMA is the sole responsible for the initial communication between both parties. The EMA, and NCAs (in the case of national pending MAAs) are not involved in the negotiation *per se*; therefore, once the agreement for a bilateral negotiation is in place and relevant details have been disclosed, the NRG Secretariat withdraws from process. Both applicants are expected to inform the NRG Secretariat of the outcome of the negotiation.

6.7 Post-authorisation issues related to (invented) names

Applicants should consider the future life-cycle of the medicinal product and post-authorisation changes which may lead to discrepancies between the product profile and the invented name. Changes to key aspects of the product profile which may have an impact on the acceptability of a name should be communicated by the MAH to the NRG.

6.7.1 Change of the (invented) name

The (invented) name can be changed at the post-authorisation stage through a variation procedure, e.g. in case the (invented) name has not been accepted prior to the adoption of the opinion(s) by the CHMP or if the MAH wishes to change the name.

Post-authorisation procedural advice with regards to the change of (invented) name can be found at the EMA website[4].

6.7.2 Other post-authorisation activities

6.7.2.1 Report of prescription errors/medication errors due to the (invented) names of medicinal products:

If prescription errors/medication errors due to the (invented) names of medicinal products (e.g. mix-up with another medicinal product) result in an adverse reaction, such adverse, such adverse reactions should be reported within the pharmacovigilance systems established at the side of the MAHs, within Member States and at EU level (for pharmacovigilance obligations see Regulation (EC) No 726/2004, Directive 2001/83/EC and Good Pharmacovigilance Practices), i.e. expedited or periodic reporting of adverse reactions in accordance with the legislation.

4 See the 'Post-marketing authorisation section of the Agency's website.

Regardless of the association with adverse reaction(s), medication errors related to the (invented) name of a medicinal product (e.g. product name confusion) should be notified by marketing authorisation holders or applicants to the NRG via the dedicated mailbox (NRG@ema.europa.eu) for centrally authorised products.

It is acknowledged that there is underreporting of potential medication errors related to names of medicinal products, therefore, if applicants become aware of information (for instance through a HCP) or relevant literature related to near-misses, they are requested to inform the NRG accordingly.

Further it should be recognised that, where names convey misleading therapeutic connotations, there may be a risk for misuse or abuse of the product. Where such misuse or abuse leads to an adverse reaction, reporting within the pharmacovigilance system applies.

NRG will take measures within its area of responsibility to prevent possible medication errors by close collaboration with the Quality Review of Documents (QRD) Group and the Pharmacovigilance Risk Assessment Committee (PRAC).

6.8 Maintenance of (invented) names

6.8.1 Withdrawal of an accepted (invented) name

The withdrawal notification should be made to the NRG secretariat by email (NRG@ema.europa.eu). No further document or justification is required.

The withdrawal of a MAA, whether it is in the pre-authorisation phase, or during the evaluation procedure automatically entails the withdrawal of the accepted (invented) name(s) (see section 6.8.2).

6.8.2 Expiry of an accepted (invented) name

Once a MAA is submitted the accepted (invented) name is considered to be 'in use' and will not expire during the MA procedure, even if the expiry date is reached. However, when an ongoing MAA is withdrawn during the procedure, the (invented) name is automatically considered withdrawn (see section 6.8.1).

6.9 Re-use and reconfirmation of (invented) names

The general principles applied by the NRG when reviewing requests for re-use or reconfirmation are presented below. These criteria do not apply to (invented) names which have expired, in which case a full new name review process will be undertaken (see section 6.1).

In case the applicant for a re-use or reconfirmation application of a given approved (invented) name is different from the initial one, proof of agreement between the two parties should be provided.

Applications for re-use and reconfirmation should be submitted to the EMA using the 'Proposed (Invented) Name Request form'.

6.9.1 Re-use

The re-use of an (invented) name is the use of the same name for a product with the same or a different product profile to that originally applied for. Applicants may choose to re-use names that have been used in MAAs (granted or not, marketed or not) or that have not been used in MAAs. The re-use

of an (invented) name may lead to the potential risk of confusion with different medicines depending on the specific case, and calls for decisions to be taken on a case by case basis by the NRG.

The NRG conclusion on any proposed (invented) name is strictly related to the product profile presented by the applicant (see section 4.1). When reviewing the re-use of (invented) names already used in a marketing authorisation application, the NRG will take into consideration aspects related to product awareness (e.g. safety issues, industry communications, public documents released by health authorities, healthcare professionals, patient organisations, etc.) as well as the potential risk for mix-up. The applicant may provide supportive documentation in order to alleviate such concerns.

According to the current name review process, up to two proposed (invented) names per marketing authorisation application can be accepted by the NRG, out of which only one single (invented) name is to be used as part of the centralised marketing authorisation. The accumulation of a high number of accepted invented names which are not used by applicants creates difficulties in finding future acceptable invented names. Therefore, applicants are encouraged to re-use approved invented names taking into consideration the general principles above.

6.9.2 Reconfirmation

The reconfirmation on an approved (invented) name is the extension of the expiry date by a further two-year period. Requests for reconfirmation are applicable to approved (invented) names with the same product profile only, and can be granted only once, before the expiry of the (invented) name.

It is the responsibility of the applicant to monitor the lapse of the acceptance period. Requests for reconfirmation should be submitted sufficiently in advance to ensure a review by the NRG prior to the expiry of the (invented) name.

7. Addressing transparency

Periodically, the EMA publishes statistical information on the outcome of the NRG review on (invented) names.

8. General contact details

General (invented) names queries can be submitted to NRG@ema.europa.eu.

List of acronyms

ADR	Adverse reaction
CHMP	Committee for Medicinal Products for Human Use
EC	European Commission
EMA	European Medicines Agency
EU	European Union
HCP	Healthcare professional
INN	International non-proprietary name
INNM	Modified international non-proprietary name
MA	Marketing authorisation
MAA	Marketing authorisation application
MAH	Marketing-authorisation holder
NCA	National competent authority
NRG	Name Review Group
PRAC	Pharmacovigilance Risk Assessment Committee
RoA	Route of administration
SmPC	Summary of product characteristics
WHO	World Health Organization

Appendix 1 – Additional attributes to assist in determining the degree of similarity

Below, are additional examples of attributes to take into consideration in determining the degree of similarity of the proposed invented name (see section 6). This should not be considered as an exhaustive list. Applicants should take into consideration the multilingual aspects of the single name principle:

- Identical prefix
- Identical infix
- Identical suffix
- Similar length of the name
- Similar spelling
- Upstrokes (capital and lower case e.g. 'P', 'd') in similar locations
- Downstrokes (e.g. 'q', 'y') in similar locations
- Cross-strokes (e.g. 'x', 't') in similar locations
- Dotted letters (e.g. 'i') in similar locations
- Ambiguity introduced when scripting letters (e.g., 'P' may appear as 'B', 'D', or 'R'; lower case 'r' may appear as 'e', 'v' or 'I'; lower case 'a' may appear as any vowel; lower case 'x' may appear as lower case 't', 'f' or 'y' etc.)
- Similar number of words/groups of characters in a name (A "word" is considered as any group of characters separated by a space)
- Similar number of syllables
- Similar stresses (e.g., Trycel and Triafil have similar stresses: TRY-cel and TRIA-fil; try-CEL and tria-FIL)
- Placement of vowel sounds is similar (e.g., 'e' may sound like 'a' or 'i'; 'i' may sound like 'a' or 'e'; 'a' may sound like 'e' or 'i' etc.)
- Placement of consonant sounds is similar (e.g., 'n' may sound like 'm', 'dn', 'gn', 'kn', 'mn', 'pn'; 't' may sound like 'd', 'b' or 'pt' etc.)
- First letter and/or sound (but made with the same letter) is identical
- Last letter is identical
- Same letters but in different order (e.g., Termix and Trevisc - the "er" and "re" can be interpreted as the same and do not provide protection from name confusion)
- Some letters are written but not pronounced (silent letters)

Appendix 2 – NRG checklist for assessment of objections on the basis of name similarities

				High	Medium	Low							
1	**Degree of orthographic and phonetic similarity**	**Print**											
		Speech											
		Handwriting											
		Cognitive error											
							Yes	**No**	**n/a**	**Unclear**	**Are any medicine management process controls in place**	**Yes**	**No**
2	**Setting of use**	Possible risk identified at **PRESCRIPTION** level?											
		e.g. - Same therapeutic area/indication - Same prescriber - Close on electronic prescribing lists - Handwritten prescriptions - Emergency situations											
		Possible risk identified at **DISPENSING** level?					**Yes**	**No**	**n/a**	**Unclear**			
		e.g. - Same storage conditions and proximity (e.g. shelf, fridge, controlled drugs locked cupboard, etc.) - Close on electronic dispensing lists. - Same dispensing facility (hospital pharmacy, community pharmacy, aseptic department, directly from ward stock, directly shipped by manufacturer on patient named basis, etc.) -Emergency situations											
		Possible risk identified at **PREPARATION** level?					**Yes**	**No**	**n/a**	**Unclear**			
		e.g. - Both to be mixed together prior to administration (e.g. error of dosing)? - Can they both be put in a Monitored Dosage System (MDS)/Individualised dosing system?											
		Possible risk identified at **ADMINISTRATION** level?					**Yes**	**No**	**n/a**	**Unclear**			
		e.g. - Self-administration in same patient population? (patient may confuse both products at home) - Emergency situations - Administered by HCP											
				Same	**Similar**	**Different**	**n/a**						
3	**Elements that may**	**Strengths**											

	increase/reduce the risk of confusion	**Pharmaceutical forms**										
		Route of administration										
		Legal status										
		Proposed labeling										
4	**Potential for harm in case of accidental mix-up**	**High**			e.g. death or major injury.							
		Medium			e.g. minor injury.							
		Low			e.g. no injury.							
		n/a			e.g. no risk of confusion identified.							
		Unknown			e.g. when the actual potential for harm is unknown.							

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References and useful websites

1 Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

2 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

3. Council Regulation (EC) No 207/2009 of 26 February 2009 on the Community trade mark.

http://www.emea.europa.eu/docs/en_GB/document_library/Other/2011/07/WC500109576.pdf

4 Notice to Applicants (NTA) VOLUME 2A Procedures for marketing authorisation CHAPTER 1 MARKETING AUTHORISATION.

5 Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

6 Communication from the Commission on Regulation (EC) No 141/2000 on orphan medicinal products.

7 Good pharmacovigilance practices:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c

8 Good practice guide on risk minimisation and prevention of medication errors (EMA/606103/2014).

9 Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products.

10 EMA pre-authorisation guidance document:

https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/pre-authorisation-guidance

11 EMA post-authorisation guidance document:

https://www.ema.europa.eu/en/human-regulatory/post-authorisation

4. EMA website: https://www.ema.europa.eu/en

5. Eur-Lex website: https://eur-lex.europa.eu/homepage.html

12 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000090.jsp&mid=WC0b01ac0580023398Guideline on the readability of the labelling and package leaflet of medicinal products for human use (Revision 1, 12 January 2009).

13 WHO website: http://www.who.int/en/

14 WHO Guidelines on evaluation of similar biotherapeutic products (SBPs).

6. Information on INNs http://apps.who.int/medicinedocs/en/d/Jh1806e/5.html

15 _WHO paper on International Nonproprietary Names Modified.

16 INN Stem Book 2018.

17 Public data from Article 57 database:

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/public-data-article-57-database

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/data-medicines-iso-idmp-standards/public-data-article-57-database

18 (Invented) Name Review Group attendees and contact points

https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/invented-name-review-group

https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/invented-name-review-group

19 NRG Application form for new (invented) names and justifications:
https://www.ema.europa.eu/en/documents/template-form/name-review-group-form_en.pdf