

World Health Organization
Raffaella Balocco
INN Programme Manager
Quality Assurance & Safety: Medicines
CH 1211 GENEVA 27
Switzerland

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Prescrire's contribution to the WHO consultation on List 111 of proposed INNs

Prescrire
83 boulevard Voltaire
75558 PARIS CEDEX 11
FRANCE

Tél. : (33) (0)1 49 23 72 80
Fax : (33) (0)1 47 00 33 20
contact@prescrire.org

Site internet
Web site
www.prescrire.org

Relations Abonnés :

Abonnements
Subscription Department
Tél. : (33) (0)1 49 23 72 86
Fax : (33) (0)1 49 23 76 48
relationsabonnes@prescrire.org
international@prescrire.org

Formations Prescrire
Tél. : (33) (0)1 49 23 72 90
Fax : (33) (0)1 49 23 76 48
formations@prescrire.org

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Since 1981, and also as an active member of the Medicines in Europe Forum, the International Society of Drug Bulletins (ISDB) and the International Medication Safety Network (IMSN), *Prescrire* has been advocating the routine use, by both healthcare professionals and patients, of international nonproprietary names (INNs), which are more informative, safer and clearer than brand names (1-5).

Making INNs safer. The principles underlying the creation of INNs are the same that apply to the prevention of medication errors: standardisation, differentiation, and facilitation of logic and redundancy checks (6).

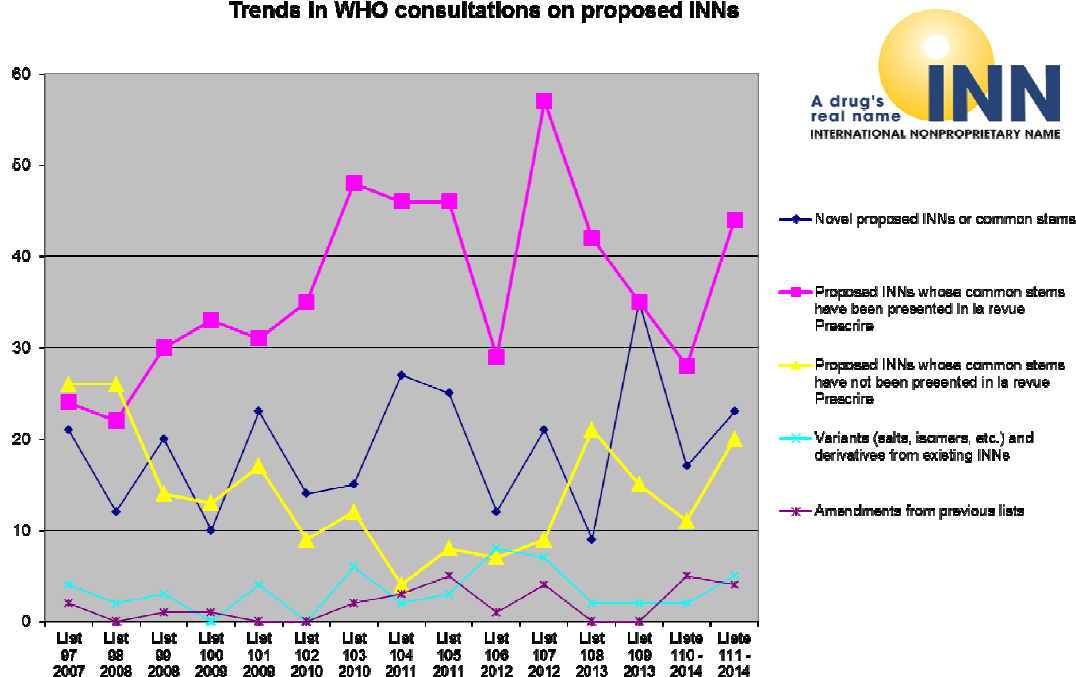
However, even with the INN system there is a residual risk of confusion, partly owing to the sheer number of INNs now in circulation. A report from the Council of Europe, which recommends the use of INNs, calls for active participation in the public consultations on proposed INNs organised by the World Health Organization (WHO), in order to identify any risk of confusion during their clinical use (7). The editorial staff of *Prescrire* and members of the not-for-profit organisation Association Mieux Prescrire, joined by some front-line healthcare professionals, are participating in this phase of the consultation on List 111, which was published in July 2014 (a) (8).

Our critical analysis of the proposed INNs. Our analysis of the 92 proposed INNs and the 4 amendments to previous lists presented in List 111 was based on the 2013 list of common stems, on the INN database, on a database of drugs marketed in France, which enables searches on both brand names and INNs, and on *Prescrire's* own data search (9-14).

Prescrire used a two-step Delphi method. First, the participants compiled a list of potentially contentious INNs, along with the reasons for their doubts. For each of the 34 proposed INNs selected for further scrutiny in this first step, the participants assessed the risk of confusion and/or misunderstanding, along with the potential clinical consequences of such errors. Finally they decided for each of these 34 contentious INNs whether a simple comment or a formal objection was more appropriate, and listed their arguments.

More INNs than the previous list. While List 110 contained 59 proposed INNs and 5 amendments, List 111 is longer and includes: 23 novel proposed INNs or common stems (24%); 44 proposed INNs whose common stems have been presented in la revue *Prescrire* (46%); 20 proposed INNs whose common stems have not yet been presented in la revue *Prescrire* (21%); 5 variants (such as salts and isomers) and INNs that have undergone specific modifications (5%); and 4 amendments to INNs proposed in previous lists (4%). The graph plotted to monitor *Prescrire's* contributions to the WHO's public consultations on proposed INNs shows that, in comparison with the previous consultation, List 111 includes a few more novel proposed INNs or stems.

Trends In WHO consultations on proposed INNs



Our examination of List 111 of proposed INNs also identified the reuse of the planned pre-stem -urad, proposed by the United States Adopted Names Council (USANC) for urate transporter inhibitors, in *verinurad*. It was previously identified in List 105, in *lesinurad* (15).

No formal objections. None of the risks of confusion or misunderstanding associated with the INNs proposed in List 111 were of sufficient concern to warrant a formal objection.

Comments

Some proposed INNs generate a risk of medication errors, for a variety of reasons: some could be confused with other INNs; some stems are easily confused with other stems; some INNs can be confused with brand names; certain stems or infixes are difficult to interpret because they are insufficiently obvious; and some INNs are incomprehensible because they lack a common stem. Many participants also pointed out that some INNs are too complex, making them difficult to memorise, especially when certain rules governing their construction have not been explained. Hence the following comments.

Confusion with other INNs. Some proposed INNs could be confused with existing INNs, in particular: *albenatide*, *dalazatide*, *emactuzumab*, *evofosfamide*, *idasanutlin*, *irbinitinib*, *peficitinib*, *pegargiminase* and *ribociclib*.

The participants identified a risk of confusion between *albenatide* and *albiglutide*, a GLP-1 (glucagon-like peptide 1) receptor agonist that was recently authorised in Europe in injectable form. The likelihood of confusing these drugs is high because: their INNs start with the same three letters (*albenatide* would be the ninth INN to start with “alb”) and share overall phonetic similarity; they belong to related therapeutic classes; their route of administration is probably identical; and healthcare professionals generally have limited knowledge about these new drug classes.

A risk of confusion was identified between *emactuzumab* and *epratuzumab*, since 9 of their 11 letters are identical. The participants pointed out that there are now so many INNs ending in **-tuzumab** that they have become difficult to memorise, differentiate, pronounce and transcribe. Our search identified 52 INNs containing the stem **-tuzumab**.

Idasanutlin could be confused with *idarubicin* because they start and end with the same sequence of letters and share overall visual similarity; there is also potential for confusion with INNs that start with “dasa”, such as *dasatafil*, *dasatinib* and *dasabuvir*.

In addition to sharing the same stem **-tinib** and visual resemblance, the risk of confusing *irbinitinib* with *ibrutinib* is further enhanced because *irbinitinib* is hard to pronounce (5 syllables, all containing the vowel “i”) and could easily be mispronounced as “ibritinib”, which is very close to *ibrutinib*.

The participants felt that *peficitinib* could be confused with *gefitinib*, particularly when transcribed by hand, due to the risk of interpreting the “p” as a “g”.

The participants also identified the potential for confusion between *evofosfamide* and *ifosfamide*, due to their phonetic and orthographic similarity; between *dalazatide* and *daclatasvir*, and between *pegargiminase* and certain enzymes such as *pegaspargase*, the complexity of which was considered conducive to error.

Confusion between stems. Some of the proposed INNs could generate errors due to similarity between their common stem and another stem, particularly INNs containing the common stem **-ciclib**.

The common stem **-ciclib**, adopted for cyclin-dependent kinase inhibitors, and present in *ribociclib*, was felt to be too similar to the common stem **-cycline**. This risk of confusion was noticed by all of the participants, and will have to be taken into account, especially since tetracycline antibiotics are so numerous and commonly used.

Confusion with brand names. Some of the proposed INNs resemble the brand names of drugs already marketed in France, in particular: *dalazatide*, *odasvir* and *velpatasvir*.

The similarity at the start of the names *dalazatide* and Dalacine^o creates a risk of error through selection of the wrong drug in a pull-down menu containing both INNs and brand names. This risk is not limited to France, because *clindamycin* is marketed under the brand name Dalacin^o in many countries and in various pharmaceutical forms. The participants also identified a risk of confusion, albeit smaller, between Dalacine^o and *odasvir*.

Similarly, when selecting drugs from an on-screen menu containing both INNs and brand names, there would be a risk of confusion between *velpatasvir* and Velcade^o, a brand name under which *bortezomib* is very widely marketed.

Incomprehensible INNs. *Asvasiran*, *basmisanil*, *tenofovir alafenamide* and *revusiran* were considered difficult to decipher because they lacked a common stem or their stem was insufficiently obvious.

For *asvasiran* and *revusiran*, the participants were unaware whether INNs containing the pre-stem **-siran**, denoting small interfering RNA (siRNA), convey information about their claimed uses, which in this case appear very different. They wondered whether the presence of the letter “v” indicates their potential use as antivirals, and if so whether a single letter would be sufficiently obvious.

The participants were puzzled by the proposed INN *basmisanil*, presented as a GABA_A receptor negative allosteric modulator, because it lacks an obvious stem. They felt a stem conveying the notion of negative modulation would have been helpful, along the lines of the stem **gab**, for GABA agonist properties.

As regards *tenofovir alafenamide*, some participants noted that the term *alafenamide* is not included in the current list of “Names for radicals, groups and others” (13). They were concerned about the dose equivalence of *tenofovir* and *tenofovir alafenamide* and the clinical consequences of confusing these INNs, which would depend on the relative potency of the units used to express their dose strength.

The proposed INN *enadenotucirev* provided an opportunity to discover the nomenclature for the new therapeutic class of oncolytic viruses, based on a single word instead of the two-word scheme adopted for the INNs of gene therapy products. In the absence of any explanations about the syntax of this INN, the participants found it too complex.

Amendments. The participants identified no problems with the amendments to previous lists of proposed INNs. We note that *saridegib* has been replaced with *patidegib*, eliminating the risk of confusion with *sonidegib* that led us to lodge a formal objection in the public consultation on List 107 of proposed INNs (16,17).

In summary, our analysis of the INNs proposed in List 111 identified fewer problems with INN comprehensibility and potential confusion than for previous lists. As in the last 3 consultations, no formal objections appeared necessary, suggesting that the safety of the INNs proposed recently, from the point of view of healthcare professionals in their everyday practice, has improved.

However, certain issues raised should be taken into account when educating healthcare professionals about INNs, such as the increasing complexity of INNs noted by many of the participants, and the depletion of distinct names of manageable length for monoclonal antibodies and tyrosine kinase inhibitors.

Having identified these problems, we can anticipate some occasionally complex mechanisms through which errors could arise and adapt the information given about INNs so as to avert these errors.

Healthcare professionals and patients can only think and act successfully in terms of INNs when these names are devised and taught in a rigorous, coherent and effective way; and when they are presented to them as legibly as possible.



Bruno Toussaint
Publishing Director

**Review produced collectively
by the Prescrire Editorial Staff
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a- This response was prepared using the resources of the entire Prescrire team. Head of team analysis and preparation: *Éric Bel*. Prescrire editorial team members involved in this particular project: *Christian Bouret (GP)*; *Éric Cerqueira (pharmacist)*; *Sophie Chalons (pharmacist)*; *Helen Genevier (translator)*; *Sophie Ginolhac (pharmacist)*; *Christine Guilbaud (pharmacist)*; *Marie-France Gonzalvez (pharmacist)*; *Mélanie Hardy (pharmacist)*; *Olivier Huyghe (pharmacist)*; *Laurence Le Quang Trieu (pharmacist)*; *Étienne Schmitt (pharmacist)*. Other participants: *Pascale Cancouët (GP)*; *Jacques Cogitore (GP)*; *Thérèse Foucher (nurse)*.

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