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de formation permanente
des soignants

Independant organisation
continuing education
for health professionals

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Prescrire's contribution to the WHO consultation on List 110 of proposed INNs

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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 long 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).

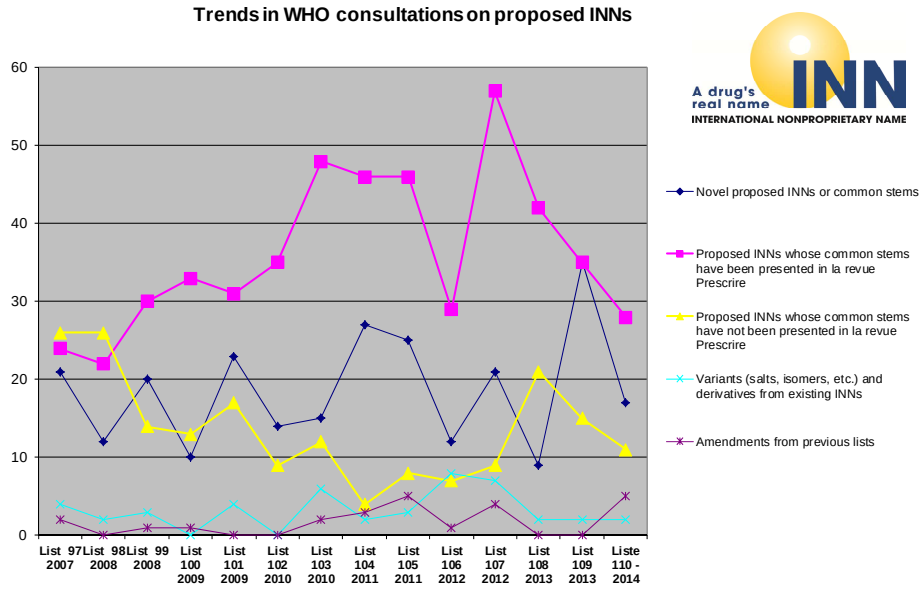
Making INNs safer. The principles underlying the creation of INNs are the same that apply to the prevention of medication errors: standardisation, differentiation, and facilitation of logic and redundancy checks (6).

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, as well as pharmacy academics and students through the initiative of a motivated professor, are participating in this phase of the consultation on List 110, which was published in January 2014 (**a**) (8).

Our critical analysis of the proposed INNs. Our analysis of the 59 proposed INNs and the 5 amendments to previous lists presented in List 110 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 (9-13).

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 27 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 27 contentious INNs whether a simple comment or a formal objection was more appropriate, and listed their arguments.

Less innovation. While the previous list contained 87 proposed INNs, List 110 is shorter and includes: 28 proposed INNs whose common stems have been presented in la revue *Prescrire* (44%); 11 proposed INNs whose common stems had not yet been presented at the start of our analysis of List 110 (17%); 18 novel proposed INNs or stems (28%); 2 variants, such as salts and isomers (3%); and 5 amendments to INNs proposed in previous lists (8%). 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 110 includes fewer novel proposed INNs or stems.



The examination of List 110 of proposed INNs provided an opportunity to identify some potential pre-stems proposed by the US drug nomenclature committee (USANC: United States Adopted Names Council): -manid for mycolic acid inhibitors, in *pretomanid*; -pertin for glycine transporter and reuptake inhibitors, in *tilapertin*; and -pirdine for inhibitors of the serotonin 5-HT6 receptor, in *idalopirdine*.

No formal objections

None of the risks of confusion or misunderstanding associated with the INNs proposed in List 110 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, particularly those that share similarity at the start of their names; some stems are easily confused with other stems; some INNs can

be confused with brand names; some common stems or INNs are difficult to interpret. Hence the following comments.

Confusion with other INNs. Some proposed INNs could be confused with existing INNs, in particular: *abametapir*, *deldeprevir* and *pexmetinib*.

The participants identified a risk of confusion between: *abametapir* and *abacavir*, which start and end with the same sequence of letters and share overall phonetic similarity; *deldeprevir* and *faldaprevir,* due to their phonetic and visual similarity; and *pexmetinib* and *pemetrexed* or *permethrin,* due to their visual resemblance. One way of preventing confusion between similar INNs would be to use different typographic styles to highlight their common stems, if they have one, or the dissimilar portions of their names.

The participants also identified a risk of confusion between: *apabetalone* and *labetalol* or *abiraterone*, which sound alike and contain a similar sequence of vowels; *bococizumab* and *bevacizumab*, especially in handwritten prescriptions; *lefamulin* and *lamivudine*; *mipsagargin* and *insulin glargine*, in which only a letter “l” differentiates the end of *mipsagargin* in French (*mipsagargine)* from the second term of *insulin glargine*; and *talazoparib* and *tinzaparin*.

Confusion between stems or proposed pre-stems. Some of the proposed INNs could generate errors due to similarity between their common stem and another stem or a planned pre-stem proposed by USANC.

The participants identified a number of potential problems with the pre-stem -manid, proposed by USANC for mycolic acid inhibitors and present in the proposed INN *pretomanid*. First, they did not feel that it was evocative of an antibacterial function. Secondly, it could be confused with the stem -**anide**, particularly since, in French, -anid and -**anide** are pronounced identically. Furthermore, slips involving inversion of the letters “n” and “m” could lead to confusion with one of the 25 INNs containing “namide”, again because “namid” and “namide” are pronounced identically in French. Finally, slips resulting in substitution of the letter “d” with a “b” could lead to confusion with INNs containing the stem -**anib**.

The participants identified a risk of confusion between the stem **-tercept**, adopted for transforming growth factor receptors and the stem **-nercept**, adopted for TNF receptors, and more particularly between *luspatercept* and *etanercept*.

The stem **-mulin**, adopted for antibacterials derived from *pleuromulin* and present in *lefamulin*, could be confused with the stem **-bulin** adopted for antineoplastics that inhibit mitosis.

Finally, the participants noted that the stem **-tide** in *aclerastide* is not sufficiently informative about the future use of this drug and that the succession of letters “as**tide”** at the end of the INN could be confused with the stem -**astine**, denoting an antihistaminic. The sequence “ast” evokes the common stem -ast provided as example in Annex 2 of the List 110 (antiasmatic, antiallergic substances not acting primarily as antihistaminics) (8). It is the same for *astodrimer*.

Confusion with brand names. Some of the proposed INNs, particularly *canoctakin, lefamulin* and *talazoparib*, resemble the brand names of drugs already marketed in France.

The participants identified a risk of confusion between *canoctakin* and the brand name Kanokad°, although the very specialised usage of this combination of coagulation factors reduces the likelihood of wrong-drug errors.

Lefamulin could be mistaken for an insulin of the Umuline° range.

Talazoparib and Salazopyrin° (*sulfasalazine*) both contain “alazop”, generating a risk of selection error in an alphabetical list (although the risk of selecting this antineoplastic drug instead of Salazopyrin° is attenuated by the fact that *talazoparib* would be lower down the list), as well as a risk of confusion in handwritten prescriptions if the “t” were mistaken for an “s”, or vice versa.

INNs that could be misinterpreted. Some participants found *ferric derisomaltose* a misleading name for an iron supplement due to the use of the adjective “ferric” in the proposed INN, which led them to assume that *derisomaltose* was the active ingredient.

In addition to the risks of confusion already mentioned for *lefamulin*, the “lefa” at the start of its name could be mistaken for the sub-stem -**lefa**-, used to denote lymphocyte function-associated antigen 3 receptors in -**lefacept**, which could generate misunderstanding over the drug’s properties.

In summary, our analysis of the INNs proposed in List 110 identified fewer problems with INN comprehensibility and potential confusion than for previous lists. As in the previous consultation, no formal objections appeared necessary, suggesting that the safety of the INNs proposed recently, as perceived by healthcare professionals in their everyday practice, has improved.

However, certain issues raised should be taken into account when educating healthcare professionals about INNs. Having identified these problems, we can anticipate some occasionally complex mechanisms through which errors could arise and consider how best to improve INN differentiation.

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
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References

1- Prescrire Rédaction “Prescrire et penser en DCI: une bonne pratique professionnelle” *Rev Prescrire* 2000; **20** (209): 606-623.

2- Prescrire Rédaction “DCI: la priorité” *Rev Prescrire* 2005; **25** (265): 641.

3- Prescrire Rédaction “Patients-soignants: priorité à la DCI” http://www.prescrire.org/cahiers/dossierDciAccueil.php

4- International Society of Drug Bulletins (ISDB) “Special issue on INNs” *ISDB Newsletter* November 2006; **20** (3): 27 pages.

5- Prescrire Rédaction "Ordonnance: la dénomination commune internationale (DCI) au quotidien" Rev Prescrire 2012; **32** (346): 586-591.

6- Prescrire Rédaction “Confusion entre noms commerciaux: entretenue par les agences du médicament” *Rev Prescrire* 2007; **27** (290): 941-945.

7- Council of Europe - Expert Group on Safe Medication Practices “Creation of a better medication safety culture in Europe: building up safe medication practices” 19 March 2007: 257 pages.

WHO “Proposed International Nonproprietary Names: List 110” *WHO Drug Information* 2013; **27** (4): 399-458.

9- WHO “The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances” WHO/EMP/RHT/TSN/2013.1: 192 pages.

10- WHO “International Nonproprietary Names (INN) for Pharmaceutical Substances” mednet.who.int.

11- WHO “Pre-stems: Suffixes used in the selection of INNs – October 2013” 28 October 2013: 5 pages.

12- WHO “International Nonproprietary Names (INN) for biological and biotechnological substances” Update 2012: 65 pages.

13- Thériaque database www.theriaque.org. Free access.