WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

INN Working Document 05.167/3
Distribution: General

International Nonproprietary Names Modified

Programme on International Nonproprietary Names (INN)
Quality Assurance & Safety: Medicines (QSM)
Medicines Policy and Standards (PSM)
World Health Organization
Geneva

International Nonproprietary Names Modified

Contents:

I. General

1. The INN Programme was established by World Health Organization (WHO) to facilitate communication among health professionals in relation to pharmaceutical products used for therapeutic and prophylactic purposes. To serve this purpose, International Nonproprietary Names (INNs) are selected as single designations for individual pharmaceutical substances. As substances used in medicine and pharmacy are of highly diverse nature, individual classes of such substances require specific rules of nomenclature for creation of pertinent INNs.

2. Special situations mentioned above comprise creation of names of individual members belonging to a group of closely related substances. When the INN Programme was initiated, it was decided that in such situations, in order to limit the number of published INNs, an INN should be selected for one member of such a group only. This approach, which concerns especially substance sets formed by salts or esters of the same active moiety was validated in the 20th report of the WHO Expert Committee on Nonproprietary Names for Pharmaceutical Substances (Technical Report Series No. 581). It has been left for the users of INNs (pharmacopoeia commissions, regulatory bodies, pharmaceutical manufacturers) to create the actual name of any individual substance that turns up in practical use, this to be done in conformity with the usual practice of naming chemical compounds. INNs created in this manner are referred to as INNMs (International Nonproprietary Names Modified).

3. Present review is addressed to those users of the INN system who have a need to create an INNM based on an existing INN. The review describes the approaches to be applied for the purpose and illustrates several frequent situations. When an INN is representing an acid, an INNM may sometimes be needed to designate a salt or an ester, when an INN has been selected for a base, an INNM may be necessary to designate a salt. In the case of an INN representing an alcohol, an INNM may be needed to designate an ester. Other situations when the INNM approach may be used include naming of quaternary salts differing in the anionic substituent. INNMs may be also needed for naming of combination products/complexes composed of substances for which an INN was selected. In presenting the INNM approach in the review, appropriate use was made of the "General principles for guidance in devising international nonproprietary names for pharmaceutical substances" (see Annex 2 to resolution EB 115//2005/REC/1), referred to in following as "General principles".

4. Names that are used to designate pharmaceutical substances should convey information about the properties of that substance. This is of value for health professionals involved in drug delivery, especially for medical practitioners who are prescribing medicinal products, as the lack of such information may, in some cases, lead to errors in prescribing or even in drug dispensation. The use of the INNM approach has an advantage of permitting to include in the name, in a logical way, some additional elements of information. However, the INNM approach is not without its inconvenience, as

names that are created have to be composed at least of two or, sometimes, of three distinct words.

5. The use of INNM approach requires sometimes utilization of chemical designations for radicals or groups of complex composition for which no trivial names exist in chemical nomenclature. To make substance names coined according to the INNM approach more user-friendly, the INN Programme has created a number of shortened designations for such radicals and groups. This avoids the use of specific features of systematic organic chemical nomenclature, like the use as locants of numerals or single letters, a feature that is highly inconvenient for prescribers. The INN Programme has also created such shortened designations to describe simultaneous substitution of a parent molecule by two different radicals. A complete list of such radicals and groups is published in a document WHO/EDM/QSM/2004.6 "Names for radicals & groups - comprehensive list (2004)". Some examples of such abbreviated designations are given in the following parts of the document, but are limited chiefly to designations describing a single substituent.

6. The rules described in the present document are intended primarily for creation of INNMs in Latin and in English. The examples selected to illustrate the INNM approach for naming different groups of pharmaceutical substances are therefore given in Latin and English only. When other linguistic versions of INNMs are to be created, the advice given in the document should be used together with the rules on transposition of INNs into the relevant language and taking also into account the usual practice of presenting chemical names in that language.

II. INNMs for salts of basic compounds

7. When an INN is given for a substance that is a base, the INNM of a salt is created by adding, as a second word, an appropriate designation of the acidic part of the molecule. For this part of the INNM, usual names of acids are used. Abbreviated designations for complicated anions included in the list indicated in para. 5. may also be used, if appropriate. Some examples of those shortened designations are given below:

INN abbreviation Latin	INN abbreviation English	structure
besilas	besilate	benzenesulfonate
edisilas	edisilate	ethane-1,2-disulfonate
embonas	embonate	4,4'-methylenebis(3-hydroxynaphthalene-2-carboxylate)
mesilas	mesilate	methanesulfonate

8. When creating an INNM for a salt of an inorganic acid, the usual rules of inorganic nomenclature are followed.

When creating an INNM for a salt of an organic acid the following approach is usually used:

In the Latin version, a modified INN of the base is followed by the name of the anion. The name of the base is given in the genitive case and the name of the acidic component (anion) in the nominative case (either second declension neuter or third declension masculine). To form the name of an anion derived of a carboxylic acid, the suffix *-oicum* (or *-icum*) in the acid name is replaced with *-oas* (or *-as*).

In the English version, the INN of the base remains unchanged and is followed by the name of the anion. To form the name of an anion derived of a carboxylic acid, the suffix *-oic* (or *-ic*) in the acid name is replaced with *-oate* (or *-ate*).

INN Latin	INN English	INNM Latin	INNM English
abanoquilum	abanoquil	abanoquili mesilas	abanoquil mesilate
amlodipinum	amlodipine	amlodipini besilas	amlodipine besilate
chlorphenaminum	chlorphen-amine	- chlorphenamini hydrogenomaleas - chlorphenamini maleas	- chlorphenamine hydrogenomaleate - chlorphenamine maleate
clindamycinum	clindamycin	- clindamycini hydrochloridum - clindamycini phosphas	- clindamycin hydrochloride - clindamycin phosphate
clomethiazolum	clomethiazole	clomethiazoli edisilas	clomethiazole edisilate
fenoterolum	fenoterol	fenoteroli hydrobromidum	fenoterol hydrobromide
mebeverinum	mebeverine	mebeverini embonas	mebeverine embonate
prednisolonum	prednisolone	prednisoloni natrii phosphas	prednisolone sodium phosphate
timololum	timolol	timololi maleas	timolol maleate

III. <u>INNMs for salts of acidic compounds</u>

9. The majority of organic compounds characterized as acids contain in their structure a carboxylic group (-COOH), a sulphonic group (-SO_3H) or a phosphonic group (-PO_3H_2). Also substances of other structure may show acid character and are classified as pseudo-acids. In all those cases, as indicated in para. 7., INNMs created for salts would consist of two words, one designating the acidic component, and another one indicating the basic component (the cation). The sequences in which these two words are placed and the form used for the acidic component depend on the mode used for presentation of INN for the acid as shown in paras 10 - 12. When the basic

part of a salt is a simple cation, its usual chemical name is used. For basic components of a complex structure shortened designations included in the list mentioned in para 5, may also be used, if appropriate. Some examples of relevant abbreviated designations are given below:

INN abbreviation Latin	INN abbreviation English	structure
erbuminum	erbumine	2-methylpropan-2-amine
olaminum	olamine	2-aminoethanol

10. In the INNM for a salt, in the case when INN for an acid is a two-word name containing the word "acid", an element describing acid component is formed from the name of the acid in the way described in para. 8. In the Latin version the suffix *-oicum* (or *-icum*) in the acid name is replaced with *-oas* (or *-as*). In the English version, the suffix *-oic* (or *-ic*) is replaced with *-oate* (or *-ate*).

INN Latin	INN English	INNM Latin	INNM English
acidum clavulanicum	clavulanic acid	kalii clavulanas	potassium clavulanate
acidum piridronicum	piridronic acid	natrii piridronas	sodium piridronate
acidum tiludronicum	tiludronic acid	- natrii tiludronas - dinatrii tiludronas	- sodium tiludronate - disodium tiludronate
acidum valproicum	valproic acid	- magnesii valproas - natrii valproas	- magnesium valproate - sodium valproate

11. In the case of complexes formed of a basic component and an acidic one, when the INN for the acid element is a two-word name containing the word "acid" but an INN exists also for the basic component, the procedure to create an INNM is as follows: for the name of the acidic component the approach described in para. 10. is used, while the name of the base remains unchanged (see also para. 24).

INN Latin	INN English	INNM Latin	INNM English
acidum gadopenteticum	gadopentetic acid	gadopentas megluminum	gadopentate meglumine
acidum iodoxamicum	iodoxamic acid	iodoxamas megluminum	iodoxamate meglumine

12. When, in accordance with item 4 of the "General principles", the INN for an acid is formed as a one-word name, the name of the acid remains unchanged when creating an INNM for a salt, both in the Latin and the English versions.

INN Latin	INN English	INNM Latin	INNM English
acamprosatum	acamprosate	acamprosatum calcium	acamprosate calcium
ciclopiroxum	ciclopirox	ciclopiroxum olaminum	ciclopirox olamine
dinoprostum	dinoprost	dinoprostum trometamolum	dinoprost trometamol
fostriecinum	fostriecin	fostriecinum natrium	fostriecin sodium
ibuprofenum	ibuprofen	ibuprofenum natrium	ibuprofen sodium
perindoprilum	perindopril	perindoprilum erbuminum	perindopril erbumine
zofenoprilum	zofenopril	zofenoprilum calcium	zofenopril calcium

13. When creating an INNM for a salt of a compound that is not a true acid (a pseudo-acid), a two-word approach is also used. In the Latin version the INN of the acid remains in the nominative case (i.e. unchanged), treating it as a neuter substantive. The complementary component (the cation) is given in an adjectival form in agreement with the substantive. Consequently, "natricus" as the adjectival form of "natrium" has to be turned to "natricum". In the English version both the name of the acid and the name of the cation remain unchanged.

INN Latin	INN English	INNM Latin	INNM English
acesulfamum	acesulfam	acesulfamum kalicum	acesulfam potassium
amobarbitalum	amobarbital	amobarbitalum natricum	amobarbital natrium
carmellosum	carmellose	carmellosum natricum	carmellose sodium
cefalotinum	cefalotin	cefalotinum natricum	cefalotin sodium
flucloxacillinum	flucloxacillin	flucloxacillinum natricum	flucloxacillin sodium
liothyroninum	liothyronine	liothyroninum natricum	liothyronine sodium
mupirocinum	mupirocin	mupirocinum calcicum	mupirocin calcium

IV. INNMs for hydrates and other solvates

14. The occurrence of water in the composition of the substance is indicated by attaching the word hydrate to an INN, sometimes with a Latin or Greek prefix to indicate the number of molecules present. A shortened designation for a combination of the acid element and the degree of hydratation/solvatation included in the list indicated in para 5. may also be used, when appropriate.

INN abbreviation Latin	INN abbreviation English	composition
hyclas	hyclate	EtOH - HCl - H_2O (0.5/1/0.5)

15. When creating an INNM for a hydrate, the INN remains unchanged.

INN Latin	INN English	INNM Latin	INNM English
estradiolum	estradiol	estradiolum hemihydricum	estradiol hemihydrate
niclosamidum	niclosamide	niclosamidum monohydricum	niclosamide monohydrate
oxytetracyclinum	oxytetracycline	oxytetracyclinum dihydricum	oxytetracycline dihydrate

16. When creating an INNM for a compound which is a hydrate of a salt, the word *hydrate* follows the designation of the salt, unless an abbreviated designation is used.

INN Latin	INN English	INNM Latin	INNM English
doxycyclinum	doxycycline	doxycyclini hyclas	doxycycline hyclate
ethacridinum	ethacridine	ethacridini lactas monohydricus	ethacridine lactate monohydrate