



WORLD HEALTH ORGANIZATION

EXECUTIVE BOARD
115th Session
Provisional agenda item 4.7

EB115/11
9 December 2004

International Nonproprietary Names: revised procedure

Report by the Secretariat

1. The Executive Board at its 112th session took note of the proposed action plan for revising the procedure for the selection of International Nonproprietary Names (INN) for pharmaceutical substances.¹ The action plan envisaged further consultation on the proposed revision of the Procedure, as well as feasibility studies on means to speed up the INN selection process (including more meetings of the INN Expert Group, using modern technology, for example electronic voting and teleconferences) and the process of making newly selected INN known to the public before their official publication in *WHO Drug Information*.

PROGRESS SINCE THE 112TH SESSION OF THE EXECUTIVE BOARD

2. Comments received during preceding consultative phases and the public information meeting in November 2002 were taken into consideration in preparing a new draft of the revised procedure. As a result, the proposal to establish rules for the acceptance or rejection of objections to proposed INN was deleted.

3. The third consultative process envisaged in the action plan was started in 2003 with the sending of the new draft to the INN Expert Group, other members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations, national pharmacopoeia authorities and pharmacopoeia commissions, drug regulatory agencies and authorities, and the International Federation of Pharmaceutical Manufacturers Associations, with a request for further input from all parties that had expressed their interest to participate in this endeavour.

4. Comments received from various parties during this third consultation were evaluated, and a further revised draft was prepared. In addition to some corrections and clarifications to reflect the current state of affairs, the proposed modifications pertained mostly to establishing rules for a possible substitution of a previously recommended INN. These rules were inter alia designed to engage both the original applicant and the party making a request for substitution in the process.

¹ Documents EB112/3 and EB112/2003/REC/1, summary record of the first meeting, section 4.

5. In view of the comments received on this further revised draft, a fourth consultative process was started in 2004, with recirculation of the new version of the revised procedure to all parties mentioned in paragraph 3. The ensuing comments were evaluated and a further revised draft of the procedure was prepared. Opinions expressed during the third and the fourth consultative processes were in general favourable to establishing rules for substitution of a previously recommended INN. All comments received in the various rounds of consultations on the proposed revision of the procedure are available on the WHO web site,¹ as requested by the Board at its 112th session.

6. At the same time as the issue of the present report, the latest draft revision of the procedure was sent to all interested parties for information.

7. The current draft of the proposed revision to the procedure for the selection of recommended International Nonproprietary Names for pharmaceutical substances is attached as Annex 1 (with changes to the current procedure printed in **bold-face type**), including a new proposed working process for the INN Expert Group. Amended General principles for guidance in devising International Nonproprietary Names for pharmaceutical substances are attached as Annex 2.

8. The feasibility studies mentioned in paragraph 1 were undertaken. A report on these studies, with an executive summary, is attached as Annex 3.

ACTION BY THE EXECUTIVE BOARD

9. The Executive Board is invited to adopt the revised procedure for the selection of International Nonproprietary Names for pharmaceutical substances, including the proposed working process for the INN Expert Group.

10. When the Executive Board approved the General principles for guidance in devising International Nonproprietary Names for pharmaceutical substances in resolution EB37.R9, it authorized the Director-General “to make in the future such revisions of the General Principles as may seem desirable in the light of advances in science and of experience and as may be suggested by the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated to deal with the selection of nonproprietary names.” The Board may therefore wish to take note of the revised General Principles contained in Annex 2.

11. The Board is also invited to take note of the report on the feasibility studies.

¹ <http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/orginn.shtml>

ANNEX 1

**PROCEDURE FOR THE SELECTION OF RECOMMENDED
INTERNATIONAL NONPROPRIETARY NAMES
FOR PHARMACEUTICAL SUBSTANCES¹**

The following procedure shall be followed by the World Health Organization (hereinafter also referred to as “WHO”) in the selection of recommended international nonproprietary names for pharmaceutical substances, in accordance with resolution WHA3.11 of the World Health Assembly, **and in the substitution of such names.**

Article 1

Proposals for recommended international nonproprietary names and **proposals for substitution of such names** shall be submitted to WHO on the form provided therefor. **The consideration of such proposals shall be subject to the payment of an administrative fee designed only to cover the corresponding costs of the Secretariat of WHO (“the Secretariat”). The amount of this fee shall be determined by the Secretariat and may, from time to time, be adjusted.**

Article 2

Such proposals shall be submitted by the **Secretariat** to the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated for this purpose, **such designated members hereinafter referred to as “the INN Expert Group”**, for consideration in accordance with the “General principles for guidance in devising International Nonproprietary Names for Pharmaceutical Substances”, annexed to this procedure.² The name used by the person discovering or first developing and marketing a pharmaceutical substance shall be accepted, unless there are compelling reasons to the contrary.

Article 3

Subsequent to the examination provided for in article 2, the **Secretariat** shall give notice that a proposed international nonproprietary name is being considered.

(a) Such notice shall be given by publication in *WHO Drug Information*³ and by letter to Member States and to national **and regional** pharmacopoeia commissions or other bodies designated by Member States.

(i) Notice **shall** also be sent to **the person who submitted the proposal (“the original applicant”)** and other persons known to be concerned with a name under consideration.

¹ See Annex 1 in WHO Technical Report Series, No. 581, 1975; proposed amendments are shown in bold-face type. The original text was adopted by the Executive Board in resolution EB15.R7 and amended in resolution EB43.R9.

² See Annex 2.

³ Before 1987, lists of international nonproprietary names were published in the *Chronicle of the World Health Organization*.

- (b) Such notice shall:
- (i) set forth the name under consideration;
 - (ii) identify the person who submitted **the** proposal for naming the substance, if so requested by such person;
 - (iii) identify the substance for which a name is being considered;
 - (iv) set forth the time within which comments and objections will be received and the person and place to whom they should be directed;
 - (v) state the authority under which WHO is acting and refer to these rules of procedure.
- (c) In forwarding the notice, the **Secretariat** shall request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the proposed name during the period it is under consideration by WHO.

Article 4

Comments on the proposed name may be forwarded by any person to WHO within four months of the date of publication, under article 3, of the name in ***WHO Drug Information***.

Article 5

A formal objection to a proposed name may be filed by any interested person within four months of the date of publication, under article 3, of the name in ***WHO Drug Information***.

Such objection shall:

- (i) identify the person objecting;
- (ii) state his **or her** interest in the name;
- (iii) set forth the reasons for his **or her** objection to the name proposed.

Article 6

Where there is a formal objection under article 5, WHO may either reconsider the proposed name or use its good offices to attempt to obtain withdrawal of the objection. Without prejudice to the consideration by WHO of a substitute name or names, a name shall not be selected by WHO as a recommended international nonproprietary name while there exists a formal objection thereto filed under article 5 which has not been withdrawn.

Article 7

Where no objection has been filed under article 5, or all objections previously filed have been withdrawn, the **Secretariat** shall give notice in accordance with subsection (a) of article 3 that the name has been selected by WHO as a recommended international nonproprietary name.

Article 8

In forwarding a recommended international nonproprietary name to Member States under article 7, the **Secretariat** shall:

- (a) request that it be recognized as the nonproprietary name for the substance; and
- (b) request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the name **and to prohibit** registration of the name as a trademark or trade name.

Article 9 [new]

(a) In the extraordinary circumstance that a previously recommended international nonproprietary name gives rise to errors in medication, prescription or distribution, or a demonstrable risk thereof, because of similarity with another name in pharmaceutical and/or prescription practices, and it appears that such errors or potential errors cannot readily be resolved through other interventions than a possible substitution of a previously recommended international nonproprietary name, or in the event that a previously recommended international nonproprietary name differs substantially from the nonproprietary name approved in a significant number of Member States, or in other such extraordinary circumstances that justify a substitution of a recommended international nonproprietary name, proposals to that effect may be filed by any interested person. Such proposals shall be submitted on the form provided therefor and shall:

- (i) identify the person making the proposal;**
- (ii) state his or her interest in the proposed substitution; and**
- (iii) set forth the reasons for the proposal; and**
- (iv) describe, and provide documentary evidence regarding, the other interventions undertaken in an effort to resolve the situation, and the reasons why these other interventions were inadequate.**

Such proposals may include a proposal for a new substitute international nonproprietary name, devised in accordance with the General principles, which takes into account the pharmaceutical substance for which the new substitute international nonproprietary name is being proposed.

The Secretariat shall forward a copy of the proposal, for consideration in accordance with the procedure described in subsection (b) below, to the INN Expert Group and the original applicant or its successor (if different from the person bringing the proposal for substitution and provided that the original applicant or its successor is known or can be found through diligent effort, including contacts with industry associations).

In addition, the Secretariat shall request comments on the proposal from:

- (i) Member States and national and regional pharmacopoeia commissions or other bodies designated by Member States (by including a notice to that effect in the letter referred to in article 3(a), and
- (ii) any other persons known to be concerned by the proposed substitution.

The request for comments shall:

- (i) state the recommended international nonproprietary name that is being proposed for substitution (and the proposed substitute name, if provided);
- (ii) identify the person who submitted the proposal for substitution (if so requested by such person);
- (iii) identify the substance to which the proposed substitution relates and reasons put forward for substitution;
- (iv) set forth the time within which comments will be received and the person and place to whom they should be directed; and
- (v) state the authority under which WHO is acting and refer to these rules of procedure.

Comments on the proposed substitution may be forwarded by any person to WHO within four months of the date of the request for comments.

(b) After the time period for comments referred to above has elapsed, the Secretariat shall forward any comments received to the INN Expert Group, the original applicant or its successor and the person bringing the proposal for substitution. If, after consideration of the proposal for substitution and the comments received, the INN Expert Group, the person bringing the proposal for substitution and the original applicant or its successor all agree that there is a need to substitute the previously recommended international nonproprietary name, the Secretariat shall submit the proposal for substitution to the INN Expert Group for further processing.

Notwithstanding the foregoing, the original applicant or its successor shall not be entitled to withhold agreement to a proposal for substitution in the event the original applicant or its successor has no demonstrable continuing interest in the recommended international nonproprietary name proposed for substitution.

In the event that a proposal for substitution shall be submitted to the INN Expert Group for further processing, the INN Expert Group will select a new international nonproprietary name in accordance with the General principles referred to in article 2 and the procedure set forth in articles 3 to 8 inclusive. The notices to be given by the Secretariat under article 3 and article 7, respectively, including to the original applicant or its successor (if not the same as the person proposing the substitution, and provided that the original applicant or its successor is known or can be found through diligent effort, including contacts with industry associations), shall in such event indicate that the new

name is a substitute for a previously recommended international nonproprietary name and that Member States may wish to make transitional arrangements in order to accommodate existing products that use the previously recommended international nonproprietary name on their label in accordance with national legislation.

If, after consideration of the proposal for substitution and the comments received in accordance with the procedure described above, the INN Expert Group, the original applicant or its successor and the person bringing the proposal for substitution do not agree that there are compelling reasons for substitution of a previously recommended international nonproprietary name, this name shall be retained (provided always that the original applicant or its successor shall not be entitled to withhold agreement to a proposal for substitution in the event that the original applicant or its successor has no demonstrable continuing interest in the recommended international nonproprietary name proposed to be substituted). In such an event, the Secretariat shall advise the person having proposed the substitution, as well as the original applicant or its successor (if not the same as the person proposing the substitution, and provided that the original applicant or its successor is known or can be found through diligent effort, including contacts with industry associations), Member States, national and regional pharmacopoeia commissions, other bodies designated by Member States, and any other persons known to be concerned by the proposed substitution that, despite a proposal for substitution, it has been decided to retain the previously recommended international nonproprietary name (with a description of the reason(s) why the proposal for substitution was not considered sufficiently compelling).

Article 10 [new]

A working process, intended to serve as a guide for the INN Expert Group in the implementation of this procedure, is attached hereto as an appendix.

APPENDIX

WORKING PROCESS FOR THE INN EXPERT GROUP¹

1. This document serves as a guide for the INN Expert Group in the implementation of the procedure for the selection of recommended international nonproprietary names for pharmaceutical substances (“the procedure”).
2. The process of selecting an international nonproprietary name for a pharmaceutical substance is described in the procedure. The General principles for guidance in devising International Nonproprietary Names for pharmaceutical substances specify the criteria to be applied when selecting new INN.
3. The INN Expert Group is composed of specialists representing a broad range of expertise in the pharmaceutical, chemical, biochemical and pharmacological sciences pertinent to the selection of INN. The Group also aims to represent the widest possible geographical distribution. The INN Expert Group may invite co-opted experts in the field of pharmaceutical trademarks and linguists to advise it on issues within the sphere of their competence.
4. The decisions on the selection of new INN are taken as a result of consultations and ensuing correspondence, if necessary (see paragraph 11 below). The consultations take place at least twice a year during meetings of the INN Expert Group convened by the Secretariat. If and to the extent required, more frequent consultations may be held, through for instance tele- and video-conferences and other electronic means.
5. The members of the INN Expert Group may formulate their views in the following manner:
 - (a) unconditional acceptance of a suggested name;
 - (b) a negative opinion with a proposal to modify the suggested name;
 - (c) a conditional opinion (e.g. asking for further information from the originator of the request on the mode of action of the substance);
 - (d) abstention.
6. New INN requests and proposals for the resolution of outstanding, pending issues are regularly mailed by the Secretariat to the INN Expert Group. During the preliminary consultation phase, the Secretariat provides members of the Group with copies of each completed INN request form, together with the accompanying documentation submitted by the originator of each such request. The experts are usually also provided with an analysis in light of the General principles, previously recommended INN and trademarks (in use for medicines) from the Secretariat and related additional information.

¹ Designated members of the Expert Advisory Group on the International Pharmacopoeia and Pharmaceutical Preparations.

Experts are invited to provide comments in writing to the Secretariat before the forthcoming consultation, taking account of, in particular:

- correctness of classification and stem;
- similarity with other names in pharmaceutical and/or prescription practices;
- linguistic aspects.

The experts' comments are synthesized and analysed by the Secretariat for discussion during the consultation.

7. For the purpose of the INN consultations, the INN Expert Group selects a moderator from among its members. The moderator summarizes the opinions expressed during the preliminary consultation phase, after which the INN experts discuss the request for a new INN, and either select a proposed INN or defer the matter in accordance with the provisions set out in paragraphs 11 and 14.

8. The Secretariat drafts a report of each meeting, in which all decisions are reflected.

9. Within approximately one month after the consultation, the Secretariat sends a draft of the report to all members of the INN Expert Group, inviting them to comment on whether the report accurately reflects the discussions and opinions expressed during the consultation, within a deadline of six weeks. In the absence of any written comments within the aforesaid six-week period, the report is assumed to accurately reflect the discussions and opinions expressed during the consultation.

10. Experts who are unable to participate in a consultation must express their opinion in writing. If no opinion is received, this will be considered as an abstention. No decision can be taken in the absence of a majority of the members of the INN Expert Group having expressed their opinion, either in person during a consultation or in writing before a consultation (quorum for decision). Decisions are taken by consensus of the INN Expert Group members expressing their opinion.

11. In the absence of a consensus, in accordance with the provision of paragraph 10 above, the matter will continue to be discussed by correspondence or at the next consultation, if necessary. If requested by the INN Expert Group, the Secretariat will provide additional information and/or alternative proposals to the INN Expert Group for such continued discussions. This process will continue until a decision on a proposed INN is confirmed in accordance with the provision of paragraph 10 above.

12. In the absence of any comments on the manner in which a decision is reflected in the draft report, the decision will be considered as finally adopted. In such an event, the Secretariat informs the originator of the new INN request about the name that has been selected as a proposed name. Simultaneously, the Secretariat proceeds to publish the selected name in the forthcoming proposed INN list (see article 2 of the procedure).

13. The rules set out above in regard to new INN equally apply in regard of:

- the selection of new common stems;

- a decision not to propose an INN (paragraph 14 below); and
- the consideration of substitution of previously recommended INN.

14. The INN Expert Group may decide not to propose an INN at all. Such a decision is usually taken when there is already a common name in general use for the pharmaceutical substance, and that name does not fit into the selection criteria for an INN or the selection of an INN may cause medication or prescription errors. INN are also not proposed when the General principles for selecting an INN are not met, for example in the case of a combination of two pharmaceutical substances.

Information available through the Internet

INN request form:

<http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/innform2000.pdf>

***Procedure for the selection of recommended International
Nonproprietary Names for pharmaceutical substances:***

<http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/innproc.html>

***General principles for guidance in devising International
Nonproprietary Names for pharmaceutical substances:***

<http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/inngen.html>

On-line access to published INN:

<http://mednet.who.int>

ANNEX 2

**GENERAL PRINCIPLES FOR GUIDANCE IN DEVISING INTERNATIONAL
NONPROPRIETARY NAMES FOR PHARMACEUTICAL SUBSTANCES¹**

1. International Nonproprietary Names (INN) should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names in common use.
2. The INN for a substance belonging to a group of pharmacologically related substances should, where appropriate, show this relationship. Names that are likely to convey to a patient an anatomical, physiological, pathological or therapeutic suggestion should be avoided.

These primary principles are to be implemented by using the following secondary principles:

3. In devising the INN of the first substance in a new pharmacological group, consideration should be given to the possibility of devising suitable INN for related substances, belonging to the new group.
4. In devising INN for acids, one-word names are preferred; their salts should be named without modifying the acid name, e.g. "oxacillin" and "oxacillin sodium", "ibufenac" and "ibufenac sodium".
5. INN for substances which are used as salts should in general apply to the active base or the active acid. Names for different salts or esters of the same active substance should differ only in respect of the name of the inactive acid or the inactive base.

For quaternary ammonium substances, the cation and anion should be named appropriately as separate components of a quaternary substance and not in the amine-salt style.

6. The use of an isolated letter or number should be avoided; hyphenated construction is also undesirable.
7. To facilitate the translation and pronunciation of INN, "f" should be used instead of "ph", "t" instead of "th", "e" instead of "ae" or "oe", and "i" instead of "y"; the use of the letters "h" and "k" should be avoided.
8. Provided that the names suggested are in accordance with these principles, names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or names already officially in use in any country, should receive preferential consideration.
9. Group relationship in INN (see General principle 2) should if possible be shown by using a common stem. The following list contains examples of stems for groups of substances, particularly for

¹ In its Twentieth report (WHO Technical Report Series, No. 581, 1975), the WHO Expert committee on Nonproprietary Names for Pharmaceutical Substances reviewed the general principles for devising, and the procedures for selecting, INN in the light of developments in pharmaceutical compounds in recent years. The most significant change has been the extension to the naming of synthetic chemical substances of the practice previously used for substances originating in or derived from natural products. This practice involves the use of a characteristic "stem" indicative of a common property of the members of a group. The reason for, and the implications of, the change are fully discussed.

The guiding principles were updated during the 13th consultation on nonproprietary names for pharmaceutical substances (Geneva, 27-29 April 1983) (PHARMS/NON 928 13 May 1983, revised 18 August 1983).

new groups. There are many other stems in active use.¹ Where a stem is shown without any hyphens it may be used anywhere in the name.

Latin	English	
-acum	-ac	anti-inflammatory agents, ibufenac derivatives
-adolum	-adol }	analgesics
-adol-	-adol-}	
-astum	-ast	antiasthmatic, antiallergic substances not acting primarily as antihistaminics
-astinum	-astine	antihistaminics
-azepamum	-azepam	diazepam derivatives
bol	bol	steroids, anabolic
-cain-	-cain-	class I antiarrhythmics, procainamide and lidocaine derivatives
-cainum	-caine	local anaesthetics
cef-	cef-	antibiotics, cephalosporanic acid derivatives
-cillinum	-cillin	antibiotics, 6-aminopenicillanic acid derivatives
-conazolium	-conazole	systemic antifungal agents, miconazole derivatives
cort	cort	corticosteroids, except prednisolone derivatives
-coxibum	-coxib	selective cyclo-oxygenase inhibitors
-entanum	-entan	endothelin receptor antagonists
gab	gab	gabamimetic agents
gado-	gado-	diagnostic agents, gadolinium derivatives
-gatranum	-gatran	thrombin inhibitors, antithrombotic agents
gest	gest	steroids, progestogens

¹ A more extensive listing of stems is contained in the working document WHO/EDM/QSM/2004.5 which is regularly updated and can be requested from the INN Programme, WHO, Geneva.

gli	gli	antihyperglycaemics
io-	io-	iodine-containing contrast media
-metacinum	-metacin	anti-inflammatory, indometacin derivatives
-mycinum	-mycin	antibiotics, produced by <i>Streptomyces</i> strains
-nidazolium	-nidazole	antiprotozoal substances, metronidazole derivatives
-ololum	-olol	β -adrenoreceptor antagonists
-oxacinum	-oxacin	antibacterial agents, nalidixic acid derivatives
-platinum	-platin	antineoplastic agents, platinum derivatives
-poetinum	-poetin	erythropoietin type blood factors
-pril(at)um	-pril(at)	angiotensin-converting enzyme inhibitors
-profenum	-profen	anti-inflammatory substances, ibuprofen derivatives
prost	prost	prostaglandins
-relinum	-relin	pituitary hormone release-stimulating peptides
-sartanum	-sartan	angiotensin II receptor antagonists, antihypertensive (non-peptidic)
-vaptanum	-vaptan	vasopressin receptor antagonists
vin-	vin- }	vinca-type alkaloids
-vin-	-vin-}	

ANNEX 3

**FEASIBILITY OF SPEEDING UP THE INN SELECTION PROCESS AND
MAKING NEWLY SELECTED INN AVAILABLE TO THE PUBLIC BEFORE
THEIR OFFICIAL PUBLICATION IN *WHO DRUG INFORMATION*****EXECUTIVE SUMMARY**

This report describes the INN selection process and identifies the crucial elements that determine the time needed for completion of each of its phases. Emphasis is placed on the analysis of the steps that relate to public health concerns (assuring that new INN will not create confusion in prescribing and dispensing medicines), and those that are aimed at safeguarding existing trademarks.

To examine the performance of the process, data were collected for 443 recommended INN included in eight lists of recommended INN published between 2000 and 2004. This report describes the results of the analysis of these data and the conclusions drawn about the duration of the selection process. For example, only in 41% of the cases examined could the name originally proposed by the applicant be accepted; in all other cases modifications were required, thereby lengthening the process. The data also show that the publication phase of the lists of proposed INN and recommended INN takes up to 40% of total time of the selection process.

This report describes the progress made in recent years in upgrading the capabilities of the INN database and in improving the storage and retrieval of information on existing INN, by an extensive introduction of new electronic technology. A functional integrated information management system has been developed which permits a complete computerization of the INN selection process. The progress that has been made opens the way to further improvements that could be made to speed up the INN selection process; these would include an increase in the frequency of publication of INN lists and expanding the use of the INN web site for communication with national regulatory and trademark authorities. The question of allocation of resources that would be needed to make this change feasible is also addressed.

1. WHO's international proprietary names (INN) programme followed the adoption by the World Health Assembly in 1950 of resolution WHA3.11 which called for the selection and approval of nonproprietary names for pharmaceutical substances. Since then, it has provided unique names that globally serve to designate, in an unequivocal manner, the composition of medicinal products, and are also widely used as drug names for generic (multi-source) medicinal products. INN are extensively used in scientific and professional publications to designate individual pharmaceutical substances or medicines containing those substances. They also serve as a means of communication between health professionals and, in many cases, with patients.

2. The creation of pharmaceutical names, including INN, has to be governed by rules to ensure that their use in practice will not endanger the safety of patients. All newly created names have to be distinctive, that is, they have to differ from other names that are already in use for other substances or medicinal products. In addition, to better serve the needs of health professionals, names created under the INN programme should, in many cases, also indicate a specific therapeutic activity or a specific mode of action of the substance in question. This informative feature is achieved by including a distinctive syllable (called stem) in the INN.

3. To be effective, the INN programme has been devised in a manner that permits the free and unrestricted use of INN by pharmaceutical manufacturers, by drug regulatory authorities and in the professional and scientific literature. In line herewith, measures need to be in place to prevent conflict between INN and trademarks. This approach, on the one hand, imposes constraints in the INN selection process (i.e. so as to avoid conflict with any existing trademarks) and, on the other hand, requires that trademark offices take measures to prevent the acquisition of proprietary rights in recommended INN.

4. The operation of the INN programme is governed by a procedure established in 1955 by the Executive Board in resolution EB15.R7, as amended in 1969 by resolution EB43.R9. The procedure provides that a request for the selection of an INN is submitted by the applicant to WHO. The Secretariat submits the request for review to a group of experts (the INN Expert Group), who are members of the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations. This group, which works by consensus, either approves the proposal or introduces corrections, if this is considered necessary. In the following step, WHO publishes the name (as submitted originally or as modified) as a proposed INN. This publication serves as a notice of the intention to select a recommended INN, and a four-month period is given for interested parties to raise any objection to the proposal. The main reason for an objection may be a conflict of the proposed name with any existing name, which is already in use to designate a pharmaceutical product, especially a name that has been registered formally as a trademark. If no objection has been raised in the four-month period, the name is published as a recommended INN.

5. For practical reasons, neither proposed INN nor recommended INN are published individually; they are grouped in lists, such lists being published twice a year. From 1987 onward the lists have been published in *WHO Drug Information*, which appears quarterly and has a worldwide circulation. In addition, the Secretariat separately notifies Member States about the intention to select the names that are included in the relevant list of proposed INN as new recommended INN. Subsequently, when the names reach the recommended INN stage, the Secretariat notifies Member States about the selection of the new recommended INN with a request to take such steps as are necessary to prevent the acquisition of proprietary rights in those names and to prohibit their registration as trademarks.

6. When WHO is informed about an application in any country to register a name identical to a recommended INN as a trademark, the Secretariat takes steps to safeguard the free availability of recommended INN. This is usually done by requesting the appropriate national authority to oppose formally the granting of such registration or, if the registration as a trademark has already occurred, to apply to reverse such a decision. In the vast majority of cases, these requests are successful.

7. In the course of the consultative process on the proposed revision of the INN procedure,¹ comments received by the Secretariat included the widespread perception that the process of selecting new INN is too protracted. The Executive Board at its 112th session agreed that, as proposed, the WHO Secretariat should study the feasibility of various means to speed up the selection process and the process of making newly selected INN known to the public.² Measures suggested included more meetings of the INN Expert Group, using modern technology, for example electronic voting and teleconferences, and preliminary publication of a reduced set of data on the web site.

¹ Document EB110/3.

² Document EB112/2003/REC/1, summary record of the first meeting, section 4.

8. The analysis of the INN selection process (with a view to examining possible ways to speed it up) included examination of its various phases and the review of the main operational improvements in the INN programme in the period 2001-2004 resulting from the introduction of electronic technology. The impact of these improvements on the selection process was considered, and the feasibility was examined of shortening the time needed for the completion of various phases of the selection process.

9. To assist in the analysis and to illustrate the present performance of the INN selection process, data were collected on the average duration of the process, from receipt of a request by the INN secretariat to publication of the recommended INN. The assessment was made on a sample of 443 recommended INN included in eight lists of recommended INN (Lists 44 to 51) that were published between June 2000 and June 2004.

10. Collected data were examined according to various criteria, including the question to what extent the name initially proposed by the originator could be accepted as an INN, or was found unacceptable and had to be modified in the course of the selection process. The assessment of the data showed that out of 443 recommended INN examined only 180 names (40.6%) could be accepted as initially proposed, while 263 names (59.4%) had to be modified in the process of selection. The average time taken by the process of selection for the 443 reviewed names was 26.4 months – 24.2 months for names that were accepted as originally proposed and 28.0 months for the group of names that had to be modified.

11. The process of INN selection comprises several phases and its duration is made up of the sum of time needed to complete each phase. The main phases of the selection process are: initial review of the proposed name by the INN secretariat followed by a review by the members of the INN Expert Group; discussions among the members of that group and with the INN secretariat on the suitability of the name as proposed by the applicant or on appropriate modifications; discussion of the name with the applicant in those cases where the initial proposal has to be modified; preliminary publication in *WHO Drug Information* of the name as a proposed INN, and final publication in *WHO Drug Information* of the name as a recommended INN.

12. The duration of each phase of the selection process depends on the individual nature of each request, but experience, supported by the data collected from the sample of 443 cases, has also shown that specific obstacles inherent to the selection of INN exist and need to be overcome in the course of the process. The constraints of each phase of the process are described below.

13. The first phase consists of the review of the proposed name, initially by the INN Secretariat and then individually by each member of the Expert Group, in order to ascertain whether the name proposed by the applicant can be accepted without any change or whether there are reasons to introduce modifications. This phase includes a separate examination of the elements of the new substance on the one hand and those related to the name itself on the other hand. In respect of the new substance, the existence of any relationship with other substances used as medicines is reviewed, and in respect of the proposed name, the absence of conflicts with existing names, undesirable medical connotations and other specific linguistic problems have to be examined.

14. The examination of the relationship between the new substance and other substances used in medicines is necessary to find out whether other INN have already been selected for pharmacologically related substances and whether the new name should contain the syllable used to indicate the relationship between these substances (INN stem). At present, about 300 stems are used in the INN programme, indicating, as the case may be, the therapeutic group, mechanism of action, or

chemical or biochemical relationship. The applicability of one of the existing stems, which would indicate that the new substance is related to an existing group, or, conversely, the need to create a separate stem for the new substance, is a major point for discussion among the experts, and, as the case may be, with the applicant. The difficulty in arriving at a final judgment often relates to the fact that insufficient data were provided by the applicant. In many cases, this insufficiency is related to the fact that the application for a name is made in an early stage of drug development, usually before the clinical trials are concluded. However, the verification of the claims related to the mechanism of action of the new substance is difficult when all the required information is not yet available.

15. An absence of conflict between a new name and other names already used for pharmaceutical products has to be verified in respect of two areas: the absence of conflicts with existing INN, that is both recommended and proposed INN, and the absence of conflicts with established trademarks. Decisions in this area are facilitated by the availability of appropriate databases containing names that are already in existence. Such access is now comparatively easy for INN, because of the existence of a computerized database that is constantly updated by the INN Secretariat. Access to databases that contain registered trademarks and other names in use to designate pharmaceutical substances is more difficult, as no global databases of this type are publicly available. Although it is assumed that the name proposed by the applicant has been checked for the absence of this type of conflict, this position is, to the extent possible, further verified by the INN secretariat and by experts who have access to national databases. If a possibility of conflict is revealed during such searches, the significance of such a possible conflict is evaluated by the Expert Group. When a valid conflict is revealed, a modification of the name is necessary.

16. The experts also evaluate the absence of undesirable medical connotations with the proposed name and of other specific linguistic problems linked to that name. According to the General principles for devising INN, names that are likely to convey to a patient anatomical, physiological, pathological or therapeutic suggestions should be avoided. In this connection, it should be borne in mind that INN are finally recommended in all six official languages of WHO (Arabic, Chinese, French, English, Russian and Spanish) and used in even more languages. This fact is taken into account through the composition of the Expert Group, which includes native speakers of all official languages and of a few other languages, including Japanese. As INN are newly coined words, the review has to include all linguistic versions of the proposed name, and elicit not only the absence of undesirable medical connotations but also an absence of other undesirable meanings in any of these languages. If, in the opinion of the experts, such undesirable connotations or other specific linguistic problems exist, a modification of the proposed name becomes necessary.

17. The process of review of an application for an INN requires, as shown above, a discussion of several interrelated aspects of the proposal. As described in paragraph 10, only 41% of the names that were proposed by the applicants could be finally accepted as recommended INN. Even in this group, the analysis of the situation has shown that some requests (19 cases, 4% of the total) required a prolonged discussion among experts on the suitability of a proposed name, increasing the average time of processing their selection to 33 months.

18. In some 60% of the cases analysed, the name proposed by the applicant could not be accepted and a modification to the proposal was required. Such modifications can sometimes be substantial, thereby prolonging the process of review: several rounds of discussion become necessary in order to conciliate conflicting views among the experts; supplementary information has to be obtained from the originator of the request (for example, concerning the expected mode of action of the substance); and the modifications to the name need to be discussed with the applicant. Specific difficulties arise in respect of biological products, where both the composition of the substance and its mode of actions are

still not fully elucidated. In some of the cases, agreement on a modified name was reached without too long a delay, but in a substantial number several rounds of discussions were required. In fact, the analysis showed that several rounds of discussion were needed in 99 cases (22% of the total), increasing the average time of processing of these applications to 36.4 months.

19. As described above, the selection of a new INN is discussed extensively by the members of the INN Expert Group. Such discussions are carried out initially by correspondence, every expert indicating his or her views on each request for the selection of a name. These opinions are exchanged among all experts and further discussed and finally agreed upon by consensus during the INN consultations, held twice a year in Geneva. If the views of the experts are divergent, or when a modified name is discussed but no agreement on the modification can be reached with the applicant, a further round of discussions is needed, initially by correspondence, followed by a further exchange of views during the next INN expert meeting. The INN experts are expected to review the documentation for new INN (100-120 a year) and for modified proposals (40-60 a year), express their opinion on each name by correspondence, and participate twice a year in a discussion meeting in Geneva. The burden imposed on INN experts is thus considerable. Moreover, they are requested to produce their opinions within a specific time, without regard for the fact that this is done on a voluntary basis, outside the scope of their habitual work.

20. Newly agreed INN are compiled by the INN secretariat into lists of proposed INN which are published twice a year in *WHO Drug Information*. Technical preparation of the publication is time consuming, owing to the complexity of the organic chemical nomenclature and also the need to draw appropriate structural formulae, requiring the assistance of outside specialists. The publication of proposed INN serves as a formal notification on the part of WHO of its intention to select the published names as recommended INN. Each list of proposed INN therefore contains a closing date (four months after its publication), before which interested parties may submit to WHO formal objections to the name.

21. As usually only a few objections are lodged against proposed INN in each list, and sometimes none at all, most of the new INN that were published in a list of proposed INN (with the exception of those that were subjected to a formal objection) are published once more (after the formal period of four months allowed for raising objections) in *WHO Drug Information* in a list of recommended INNs. Because of the publication schedules of *WHO Drug Information*, the publication phase of the procedure takes in practice some 10-12 months, that is about 40% of the average time (26.4 months) needed for the selection of a recommended INN.

22. Since 2001, the INN Secretariat has taken several steps to extend and upgrade the INN database capabilities and to improve the storage and retrieval of information on existing INN, by the introduction of new electronic technology. A functional, integrated, management information system has been developed so that the whole selection process is computerized, from acknowledgment of a request to the applicant through the selection process to the publication of the lists of proposed and recommended INN.

23. The INN selection process has been greatly facilitated by the inclusion in the computerized information system of records, for each INN name, of the individual opinions of experts and the discussions during expert meetings. Access to this information has made the decision-taking process considerably easier. Since 2004, the computerized information system has also permitted the circulation of INN documents to the experts in electronic format.

24. The introduction of the possibility to generate electronic files has also accelerated technical operations and made them more reliable, including the reproduction of complex chemical designations and structural formulae, needed for the publication of INN lists in *WHO Drug Information* (especially the drawing and subsequent validation of structural formulae of all INN in electronic format). Based on these developments, an automated publication process integrated with the INN database has been operational since 2003, allowing rapid generation of the lists of proposed and recommended INN. In 2002, 68% of names were published (in List 85 of proposed INN) after only one or two rounds of discussions between experts and with the applicants, while in 2004, this percentage has been increased (in List 91 of proposed INN) to 84%: a notable speeding up of the selection process.

25. The extension and upgrading of the INN database have also facilitated access to information on existing INN for their worldwide users through a WHO electronic information service called Mednet.¹ Although intended primarily for use by drug regulatory authorities, pharmaceutical industry and other interested parties that need access to updated information on existing INN, this service also supports the INN selection process by enabling experts to access relevant information in the course of the review of new names.

26. The analysis described in paragraphs 11-21 indicates two areas where improvements could accelerate the INN selection process: further use of new electronic technology and a change in the publication pattern of the INN programme.

27. The possibility of speeding up the process through further use of the electronic technology introduced by the INN programme in 2001, as described in paragraphs 22-25, was discussed by the INN experts during the thirty-seventh INN consultation (Geneva, 4 and 5 November 2003). The experts assessed positively this approach, welcomed the progress on the INN database and information retrieval systems, and considered that continued improvements could further speed up the selection process.

28. A much greater saving in time would result from changing the publication pattern of the INN programme. Increasing the number of lists of proposed INN to 3-4 per year, and similarly the lists of recommended INN, would considerably shorten the average time needed to complete the INN selection process. Obviously, if more publications were distributed over the year, number of names per list will become smaller. The increase in the number of publications of proposed INN and recommended INN would need to be reflected in the Working process for the INN Expert Group.²

29. Such an increase in the frequency of publication of INN lists would make the system more flexible enabling more rapid processing of those applications that are uncomplicated or for which the final opinion of experts can be obtained promptly. As an accompanying step, consideration could be given to combining the required formal notification to Member States and other interested parties with electronic communication. Based on the existence of an automated publication process (see paragraph 24), allowing rapid generation of lists of proposed and recommended INN, formal notifications to Member States and other interested parties could be limited to an official letter about the establishment of an INN list, with an indication that the list is available electronically.

¹ <http://mednet.who.int>

² See Annex 2.

30. Among the possible ways to speed up the process of INN selection, a change in the INN experts' modus operandi could have a positive impact. In 2003, when assessing possible approaches during the thirty-seventh INN consultation, the INN experts agreed that some of the proposals in the action plan noted by the Board at its 112th session, like electronic voting for names on which unanimous agreement has been reached, are feasible. They expressed doubts, however, about the feasibility of increasing the number of INN meetings, because of the present financial constraints of the INN programme and the consequent increase in the work demand by the INN programme (over and above the extent described in paragraph 19), which was generally viewed by the experts as highly burdensome.

31. The introduction of an electronic service that provides worldwide users with access to all newly selected proposed and recommended INN also promotes their more rapid communication to the public. This might also include the preliminary publication of reduced sets of data on the WHO web site. Such actions would not, however, shorten the INN selection process. The requirement of a four-month period for objections after publication of a list of proposed INN, and the need for formal notification of Member States and other interested parties on the selection of proposed INN and recommended INN will have to be maintained, regardless of whether more frequent publication schedules are introduced.

= = =