International Nonproprietary Names: Current Status and Future Challenges.

Dr R.G. Balocco Mattavelli, INN Programme Manager
"Some activities undertaken by WHO are largely invisible, quietly protecting the health of every person on this planet, every day. By assigning a single international name to drugs, WHO helps ensure that a prescription filled abroad is what doctor ordered back home."

Dr Margaret Chan, Director General - Working for Health: An introduction to the WHO
The WHO International Nonproprietary Name (INN) Programme

- Mandated by the Member States in 1953
- One of the oldest WHO programmes
- To devise a single name for a substance for use globally
- INNs are recognized in almost all Member States
- INNs can be used freely and cannot be registered as trade names
- Not concerned with formulations
The WHO International Nonproprietary Name (INN) Programme

- WHO has responsibility to develop, establish and promote international standards for pharmaceutical and biological products
- Need for universally available and accepted name for drug substance
- INN is a unique generic name that is recognized globally and is public property
- Intended for use in drug regulation, prescription, pharmacopoeias, labeling advertising, scientific literature
International Nonproprietary Name (INN) Programme
What's in a name?

- Safety
- Efficacy
- Quality
- Information
- Rational
- Regulation

INN: Current Status and Future Challenges, Dr R. G. Balocco Mattavelli
ICDRA preliminary meeting, Singapore 28-29 November 2010
INNs...

- unique name,
- distinctive in sound and spelling
- not liable to confusion with other names in common use
- formally placed by WHO in the public domain, (hence their designation as nonproprietary)
- can be used without any restriction to identify pharmaceutical substances
The INN System

- WHO Secretariat
- INN Expert Group
  - Can call on further experts if necessary
  - INN Advisory Group on Biologicals
- Publications
The Business Process Model

Broad consultation (experts, applicants, Nomenclature bodies, Pharmacopoeias, DRAs etc.)

Lot of correspondence

2 INN meetings/year

"Ad hoc" meetings

......
INN selection process

- Secretariat receives INN applications
- Consultation / INN Expert Group
- Secretariat informs applicants
- Validation of Information
- Published in a List of proposed INN
- 4-month period for objections and comments
- Published in a List of recommended INN
Publications

- Selection process of an INN
- Lists of proposed and recommended INN
- Cumulative List of INN
- Stem book  "The use of stems in the selection of INN for pharmaceutical substances"
- Radical book  "Names for radicals, groups & others, comprehensive list"
- Challenges
- Web pages
INN Lists

- New INNs are published in WHO Drug Information: 2 proposed and 2 recommended lists every year in English, French, Spanish and Latin.

- All INNs are published in a cumulative list with additionally INNs in Arabic, Chinese and Russian.

- About 8200 INNs have been published http://www.who.int/medicines/services/inn/publication/en/index.html.

- On-line INN information: Mednet - INN Extranet
In List 102 of proposed INN,

- 58 INNs (24% are biologicals)
- Range between 11 and 38 months.
- The average selection process was 15 months.
- 93% published after 1 or 2 rounds of discussion.
(-)-6(2amino-phenylacetamido)-3,3-demethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylic acid

ampicillin

[3B-L-lysine,29B-L-glutamic acid]insulin (human)

insulin glulisine
davalintidum # (101)
davalintide      amylin analogue
human islet amyloid polypeptide-(1-7)-peptidyl-[11-L-arginine(K>R),18-L-arginine(K>R)]salmon calcitonin-1 (Onchorhynchus keta)-(8-27)-peptidyl-human islet amyloid polypeptide-(33-37)-peptidamide
antidiabetic
davalintide      analogue de l'amyline
polypeptide amyloïde d'îlots pancréatiques humains-(1-7)-peptidyl-[11-L-arginine(K>R),18-L-arginine(K>R)]calcitonine-1 de saumon (Onchorhynchus keta)-(8-27)-peptidyl-polypeptide amyloïde d'îlots pancréatiques humains-(33-37)-peptidamide
antidiabétique
davalintida      análogo de la amilinapoli
péptido amiloide de los islotes pancreáticos humanos-(1-7)-peptidil-[11-L-arginina(K>R),18-L-arginina(K>R)]calcitonina-1 de salmón (Onchorhynchus keta)-(8-27)-peptidil-polipéptido amiloide de los islotes pancreáticos humanos -(33-37)-peptidamida
hipoglucemiante

C<sub>152</sub>H<sub>248</sub>N<sub>50</sub>O<sub>49</sub>S<sub>2</sub>  863919-85-1

H-Lys—Cys—Asn—Thr—Ala—Thr—Cys—Val—Leu—Gly—Arg—Leu—
Ser—Gln—Glu—Leu—His—Arg—Leu—Gln—Thr—Tyr—Pro—Arg—
Thr—Asn—Thr—Gly—Ser—Asn—Thr—Tyr—NH₂
INN Cumulative List 13

- Portable format
  - Information over 8200 published INN (names, structures, ...)

- Published every two years

- Searchable database
  - All or part of name (e.g. -profen)
  - In the six UN official languages
  - CAS RN
  - Alternate names
  - ATC (Anatomic Therapeutic Chemical) codes
  - Etc...
Cumulative List N°13

INTERNATIONAL NONPROPRIETARY NAMES (INN) FOR PHARMACEUTICAL SUBSTANCES
Lists 1-101 of Proposed INN and Lists 1-62 of Recommended INN
Cumulative List N°13

DENOMINATIONS COMMUNES INTERNATIONALES (DCI) POUR LES SUBSTANCES PHARMACEUTIQUES
Listes 1-101 de DCI proposées et Listes 1-62 de DCI recommandées
Liste récapitulative N°13
Use of stems

Names of "pharmacologically-related" substances have a common stem

- To indicate chemical and/or pharmacological group relationship
- Published for 'established series of related compounds'
- WHO publication 'The use of stems in the selection of INN' rev.2009
- INNs and stems have protection within trade mark arena

Stem book
INN Stem: Marketing exercise?

- Latin  |  English

- *acum*  |  *ac*  anti-inflammatory agents, ibufenac derivatives

- *coxibum*  |  *coxib*  selective cyclo-oxygenase inhibitors

- Suffixes as well have implications….

- *pristone* → *prisnil*?
Recent Developments in biological nomenclature

- 2002 Consultation to review policies and anticipate developments in biological field

- 2005 Gene therapy products

- 2006
  - WHO meeting with Drug Regulatory Authorities and biological experts for clarification of approaches to biosimilars
  - WHO meeting with pharmaceutical industry associations (research based industry and generic) to present views on biosimilars

- 2007
  - WHO meeting to develop regulatory guidelines
  - WHO Meeting to review INN policies for biologicals
  - 44th INN Consultation (22-24 May 2007)

- 2010 Definition of epoetins; Fusion proteins; Interferon nomenclature; Cell therapy?
Current INN position for biological products:

- 20 biological groups with stems
- 5 groups with an INN nomenclature scheme
- Generals policies developed for 10 groups of biological products
- 'INN for biological and biotechnological substances a review' [http://www.who.int/medicines/services/inn/INN_Biorev11-06.pdf]
Healthcare biologicals and biotechnologicals

Medicines on the market

New medicines in development

Source: European Commission (2005)
Biosimilars

Europe  
USA and Japan  
Canada  

Biosimilars  
Follow-on protein products,  
Subsequent-entry biologics.
Biosimilars – considerations

- The concept of biosimilar is a regulatory one.
- Generic substitution and reimbursement are health policy matters.
- Decision on interchangeability is not done by WHO.
- INNs are part of the pharmacovigilance system.
- There is no specific INN policy for biosimilars.
- Glycosylated proteins from different sources expected to differ in their glycosylation profile so are given distinct names; the same approach is valid for all the other post-translational modifications.
Protection

WHA46.19 requests Member States:

1) to enact rules and regulations, as necessary to ensure that INNs ... used in the labelling and advertising of pharmaceutical products are displayed prominently;

2) to encourage manufacturers to rely on their corporate name and the INNs, rather than on trade marks, to promote and market multisource products introduced after patent expiration;

3) to develop policy guidelines on the use and protection of INNs, and discourage the use of names derived from INNs, and particularly names including established INN stem as trade-marks.
INNs have to be distinctive in sound and spelling, and should not be liable to confusion with other names in common use....they are formally placed by WHO in the public domain.

INN Leaflet for TM departments.
Promotion

- **INN campaign**: “La DCI, le vrai nom du médicament”
  
  La Revue Prescrire
  Mutualité Française

- **ISDB (International Society of Drug Bulletins) Newsletter November 2006**
  "INN: an essential tool"
  International Society Drug Bulletins
Recent progress

- Improved system
- Defined and documented business process
- Improved tools for WHO's scientific screening process
- Web-based request status
- Web-based on-line queries
- Cross link between INN and ATC/DDD databases
INN Integrated Data Management Information System

- Access from internet
- Worldwide multiusers
- Multiplatform application
- All the user tasks have been "integrated" within the process
- Standard and open source technologies
- Secure and protected environment: confidentiality of data and process steps
- Electronic documentation at each step
- Track of each process step
Digital Certificates
INN On Line Application

Automatic Data Entry
Data Validation
Confidential Communication
Electronic format for structures

Hand made Data Entry
• Missing data validation
• Increasing Annex files dimension
• Missing electronic format for structures
INN On-line Application Architecture

INN OLAS

INN IDMIS

Staff User

Submit

Download
Data Bases Network

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INN

WIPO

FDA

IMGT

JSP

DRAs

VIDAL

AFSAPS

SIB-University of Geneva

BPh

harmacopoeia
INN Challenge: collaborative network...
INN Challenge: collaborative network...
...for a global data hub

Software Company

Pharmaceutical Industry

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Challenges

- Protection of INNs: need to improve collaboration with DRAs (WHA46.19) and INN users.

- Userfriendlyness of INNs: need to avoid unpronounceable INNs that discourage use of generic names.
Challenges

- The complexity of substances
- The number-induced difficulty
- The emerging of new types of substances (new policies?)

mAbs: 211 INNs published + 19 INNs planned to be published in PL

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Thank you

- http://www.who.int/medicines/services/inn/
- On-line INN information: Mednet - INN Extranet