Application of INN to biological products

Professor Derek Calam

Disclaimer

The viewpoints and opinions stated in this presentation are personal and are not to be taken as attributable to any body with which I am associated.

International Non-proprietary Names (INNs)

- **WHO has responsibility to develop, establish and promote international standards for pharmaceutical and biological products**
- **Need for unique, universally available and accepted name for a drug substance**
- **INN is a unique generic name that is recognised globally and is public property**
- **Intended for use in drug regulation, prescription, pharmacopoeias, labelling, advertising, scientific literature**

The 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 recognised and used in almost all member States**
- **INNs can be used freely and cannot be registered as trade names**
- **Not concerned with formulations**

The INN system

- **WHO Secretariat**
- **INN Expert Group**
  - **Can call on further experts if necessary**
  - **INN Advisory group for Biologicals**
- **Cumulative list of INNs**
- **Proposed lists twice a year and recommended lists once a year in WHO Drug Information**
- **Procedure and General principles in each pINN list**

www.who.int/medicines/services/inn/en

The INN process

- **Application is voluntary**
- **Application from company or national body normally not before clinical phase II stage**
- **Information generally thin and preliminary**
- **Application checked by Secretariat, circulated to Expert Group and reviewed at meeting**
- **Selected name agreed with applicant**
- **Publication as proposed INN then as recommended INN**
- **INN are rarely changed or withdrawn**

Use of stems

- **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 INNs’ revision 2006**
- **INNs and stems have protection within trade mark arena**

Current position for biological products

- **20 biological groups with stems**
- **5 groups with an INN nomenclature scheme**
- **General policies developed for 10 groups of biological products**
- **‘INN for biological and biotechnological substances (a review)’**
  - **WHO INN Working Document 05.179 (28.10.2006)**

General policies

- **Non-glycosylated proteins**
- **Glycosylated proteins**
- **Fusion proteins**
- **Transgenic products**
- **Immunoglobulins** **excluded**
- **Monoclonal antibodies**
- **Blood products** **natural excluded**
- **Skin substitutes** **excluded**
- **Gene therapy products**
- **Vaccines** **most excluded**
- **[Cell therapy products** **excluded]**

Recombinant products

- **Maintain existing procedures where possible**
  - **stem + prefix**
- **Differentiate from material of natural origin**
- **Different cell systems but ‘same’ product**
- **Modifications of natural sequences (common stem but different prefixes: alteplase, reteplase)**
- **Variability in glycosylation indicated by Greek letter qualifier in full: alfa, beta, gamma, etc**

Family names (stems)

Members of a group of substances identified by a common stem:

- **-kin** **interleukins**
- **-ermin** **growth factors**
- **-plase** **tissue plasminogen activators**
- **-cog** **rDNA blood coagulation factors**

Individual members given unique fantasy prefix

General policies

Unsubstituted proteins – insulins

- **Insulin human - rDNA product**
- **Modified insulins: retain 'insulin' intact with second word indicating structural change**
  - **insulin argine**
  - **insulin aspart**
  - **insulin glargine**
  - **insulin lispro**

General policies

- **Glycosylated proteins**
  - **Identify group with stem (-epoetin)**
  - **Indicate differences from natural amino acid sequence with random prefix (darbepoetin)**
  - **Different manufacturing processes expected to give differences in glycosylation (use of Greek letter: epoetin alfa, beta)**
  - **Greek letters assigned in sequence as applications received**

General policies

- **Transgenic products**
  - **Retain an existing INN and indicate transgenic origin**
  - **Follow scheme for glycosylated products + indicate source in definition**
- **Monoclonal antibodies**
  - **-mab stem**
  - **Indication of origin and target**

Developments in biological nomenclature

- **2002 Consultation to review policies and anticipate developments in biological field**
- **2005 Gene therapy products**
- **2006**
  - **Closed WHO meeting with global regulators for clarification of approaches to biosimilars**
  - **WHO meeting for industry (innovative and generic) to present views on biosimilars**
- **2007**
  - **WHO Meeting to develop regulatory guidelines for biosimilars**
  - **WHO Meeting to review INN policies for biologicals**

Biosimilars - considerations

- **Generic pharmaceuticals retain same INN even if synthesised by different route**
- **The concept of ‘biosimilar’ ‘follow-on’ etc is a regulatory one**
- **Generic substitution and reimbursement are health policy matters**
- **Decisions on interchangeability of products are not made by WHO or regulators**
- **INNs are part of systems for tracing and pharmacovigilance**

Biosimilars

- There is no specific INN policy for biosimilars
- WHO does not receive all information submitted for marketing authorisation
- Decision on name has to be made before full information on product is available
- Non-glycosylated proteins can follow approach for small molecular generics
- Glycosylated proteins from different sources expected to differ in their glycosylation profile so are given distinct names