PAHO Regional Meeting on regulation of biotechnological products

SIMILAR BIOTHERAPEUTIC PRODUCTS:

Situation in selected countries

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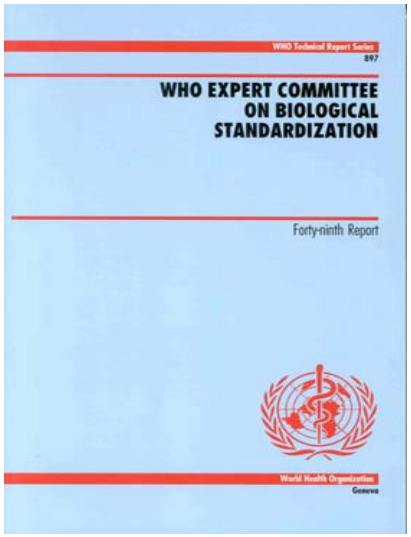
World Health Organization

Outline

- Implementation of WHO guidelines for evaluation of SBPs
- Role of NRAs in assuring Q, S and E of biologicals
- Experience in countries where SBPs are under development
- Challenges

WHO Written Standards
A tool for harmonization of specifications worldwide



National Pharma-Copeias

OR

NRA/NCL

NRA/NCL

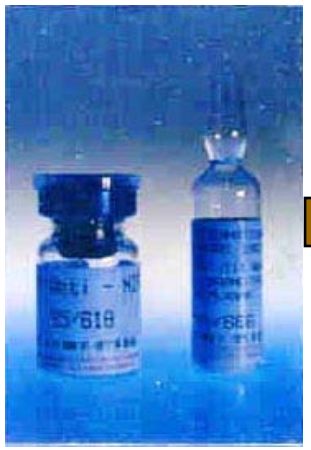
Manufacturers

Product Users

World Health Organization

WHO Biological Reference Preparations
A tool for comparison of results worldwide

WHO IS/IRP



2nd Ref. Material

Specifications to prepare and characterize WHO IS: WHO TRS 932 (2006)

National Control Laboratory

Manufacturers

Product Users

World Health Organization

Role of NRAs in the regulation of SBPs

- One of the responsibilities of an NRA is to set up appropriate regulatory oversight for the licensing of SBPs that are developed and/or authorized for sale in their country
- Decision making regarding the licensing of SBPs should be based on scientific evidence
- Stepwise approach: Comprehensive characterization and comparison at the quality level are the basis for possible data reduction in the non-clinical and clinical development
- The reduction in data requirements is only possible for the non-clinical and/or clinical parts of the development program
- Significant differences between the SBP and the RBP during the comparability exercise would be an indication that the products are not similar

Experience in countries where SBP are under development

- Regulators and manufacturers from EU, Canada, USA, Japan, India, China, S. Korea, Thailand, Cuba, Brazil, Iran and other countries provided input to previous WHO meetings;
- Variety of approaches in evaluating SBPs are in place;
- In most countries comparability in terms of quality and non-clinical assessment could be done BUT no comparability in clinical evaluation;
- Example from a large country in great expansion: "None-innovative new drug study approach" – product developed through stand alone approach with some comparability in physico-chemical parameters.

Need for strengthening expertise in designing and evaluating data from CTs;

Reports from countries in 2009

1. EU: 13 biosimilars licensed based on 6 products (gGH, EPO-α & -z, G-CSF)
2. Canada: Submission requirements for SEBs developed; revised in 2009; 1st SEB approved in April 2009
3. Japan: Guidelines approved in March 2009; different nonproprietory names given; 1st biosimilar approved in June 2009 (Somatropin, Sandoz)
4. Cuba: Position paper on SBPs issued on March 2009; new version of Rules is being developed; specific legislation for SBPs, so-called "known biological products" (category C)
5. USA: Recently signed bill (March 2010); the legislation would give the US FDA the authority to approve generic biologics but branded drug makers would be given a 12-year data exclusivity period
6. China: huge market, 95% of biopharmaceuticals; an abbreviated pathway of reducing NC and C data for "non-innovative new drug"; insulin, rhG-CSF, INF, EPO, IL-2, mabs; only two companies are working towards WHO and ICH standards;

Report from countries in 2009 cont.

7. India: no specific regulation for SBPs; head-to-head comparison with the originator in Q, NC and PK/PD studies; a confirmatory single arm stand alone efficacy study; clear regulatory pathway expected in 2010;

8. Rep of Korea: Biosimilar pathway implemented in June 2009; list of RBPs to be published;

9. Malaysia: Guidelines for registration of SBPs in July 2008;

10. Thailand: "similar nomenclature biologicals"; more than 40 brands of EPO, insulin, IFN, G-CSF and growth hormone have been licensed; EPO registry project for PRCA monitoring;

11. Singapore: introduced a new guideline for registration of biosimilars in Aug 2009; biosimilar should first be approved by at least one of HAS's reference agencies (TGA, HC, EMEA, US FDA);

12. Taiwan: Four product specific guidelines issued in Nov 2008: somatropin, insulin, G-CSF, EPO;

13. S. Africa: Guidelines under development.

Challenges

1. Regulatory framework for biotherapeutics: diversity of approaches
2. Lack of expertise for clinical evaluation of biotherapeutics at NRAs
3. Conduct of comparability studies with RBP and the interpretation of the data
4. Additional responsibilities of NRAs and other national authorities:
    1. IP issues
    2. Interchangeability and substitutability
    3. Labelling and prescribing information
5. PhV system in many countries: need to be developed/ improved

Questions for the audience

- **Regulatory requirements for licensing SBPs in Latin American and Caribbean countries**

  Survey in 2009 (Pombo et al. Biologicals 2009) in 17 countries identified:

  - 75% of countries have regulation for biologicals;
  - 12% of the countries with licensed biosimilars: rh insulin, coagulation factors (II, VII, VIII, IX, X, XII), plasma activating factor, fibrinogens, immunoglobulins, human albumin, streptokinase, urokinase, sodium enoxaparine, hr EPO (alpha, beta), filgrastim, lenograstim, IFN, G-CSF etc.
  - Argentina, Brazil, Chile and the Bolivarian Rep of Venezuela do not support the term of similarity between biological products;

  Is the situation still the same? If not, what has been changed?

- **Experience with the Reference Product (RBP)? Examples? Criteria for choosing an appropriate RBP?**