Generic, biosimilars, copies, substandard drugs: efficacy, efficiency, sustainable quality? What is the difference?

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What do the various terms mean?

- **"Generic" product**
  - different meanings in different jurisdictions
  - may be marketed either under the approved nonproprietary name (INN) or under a brand (proprietary) name
  - marketed in dosage forms and/or strengths different from those of the innovator products
  - usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after expiry of the patent or other exclusivity rights

- → **multisource pharmaceutical product** preferred
INNs
... "Generic medicines therefore offer the potential to achieve equivalent health outcomes at lower cost, provided their quality is assured." ....

In: Millennium Development Goal 8, MDG Gap Task Force, Report 2011
Underlying basic principles for generics – interchangeability

- Products are **consistently produced with same quality**, according to quality assurance principles, including:
  - Compliance with Good Manufacturing Practices
  - using quality active pharmaceutical ingredients
  - meeting specifications, etc

- **Variations** made by the manufacturer are **controlled** by national medicines regulatory authority
"Substandard medicines are pharmaceutical products that do not meet their quality standards and specifications.

Each pharmaceutical product that a manufacturer produces has to comply with quality assurance standards and specifications, at release and throughout its shelf-life, according to the requirements of the territory of use. Normally, these standards and specifications are reviewed, assessed and approved by the applicable national or regional medicines regulatory authority before the product is authorized for marketing."

Ref: 45th WHO Expert Committee on Specifications for Pharmaceutical Preparations 2010
A biosimilar is a **biological product** that is **highly similar to a licensed reference biological product** notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

*Ref:* slightly adapted from [http://gabionline.net/Biosimilars/General/FDA-definitions-of-generics-and-biosimilars](http://gabionline.net/Biosimilars/General/FDA-definitions-of-generics-and-biosimilars)
World Health Organization

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EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 19 to 23 October 2009

GUIDELINES ON EVALUATION OF SIMILAR BIOOTHERAPEUTIC PRODUCTS (SBPs)
Or in other words….

**Similar biotherapeutic product (SBP)**

- A biotherapeutic product which is *similar in terms of quality, safety and efficacy to an already licensed reference biotherapeutic product*.

**Reference biotherapeutic product (RBP)**

- A reference biotherapeutic product is used as the *comparator for head-to-head comparability studies with the similar biotherapeutic product in order to show similarity in terms of quality, safety and efficacy*. Only an originator product that was licensed on the basis of a full registration dossier can serve as a RBP. It does not refer to measurement standards such as international, pharmacopoeial, or national standards or reference standards.
WHO Definition of a "counterfeit" medicine (1992)

A product that is:

- deliberately and fraudulently mislabeled with respect to source and/or identity.

Counterfeiting can apply to both

- generic and branded products.
Counterfeiting: increasingly sophisticated business

Well crafted hologram - with ‘GUILIN PHARMA’ written below the waves but in an abnormally large font

‘Guilin Pharma’ legend present but the letters are of larger font than those on the genuine hologram and can be read with the naked eye. Letters are ~ 0.3 mm high.

The blister pack seen with this fake hologram is printed with:

Code = ‘000801’
Date of ‘manufacture’ = ‘08/00’
Date of expiry = ‘08/09’.
Note the abnormally long interval between ‘manufacture’ and expiry.

Wellcome Trust SE Asian Tropical Medicine Research Units
With very many thanks to the numerous people who assisted with this project
12th January 2005
Please distribute: Copies available from
paul@tropmedres.ac or arjen@tropmedres.ac
Usual perceptions in making judgements

Appearance

Smell

Taste
What is special with medicines, compared to other goods/commodities?

- Patients are not able to make independent judgement about of the QUALITY, SAFETY and EFFICACY

- Health professionals have difficulties, unless they are specially trained
Rationale for Government's role

- Governments *are obliged* to intervene in the activities of the pharmaceutical sector due to public health and safety concerns;

- In this context, medicines regulation is a public policy that *restricts private sector activities* in order to attain social goals identified by the State;

→ Medicines regulation in the countries is performed through *National Medicines Regulatory Authorities (NMRAs)*
In a broad sense medicines regulatory authority means a network (institution) that administers the full spectrum of drug regulatory activities, including at least the following functions:

- Marketing authorization for new products and variation of existing authorizations;
- GMP, GCP, GLP inspections;
- Licensing and post-license control of manufacturers, wholesalers and other distribution channels;
- Quality control laboratory testing;
- Adverse drug reaction monitoring;
- Provision of drug information and promotion of rational drug use;
- Enforcement operations;
- Monitoring of Drug Utilization, etc.
Which factors may encourage "bad quality" medicines globally? (I)

- Social value of medicines not given priority consideration when defining national medicines policies
- Manufacturing without GMP compliance
- Poor storage and distribution condition
- Presence of unregulated markets, manufacturing & distribution outlets
Which factors may encourage "bad quality" medicines globally? (II)

- High prices and price differentials, health care providers and patients looking for cheaper sources

- Scarcity or erratic supply of medicines

- Lack of government commitment to create strong medicines regulation:
  - Weak legislation
  - MRAs week in terms of resources, expertise, and enforcement
Which factors may encourage "bad quality" medicines globally? (III)

- International aspect of manufacture and supply of pharmaceuticals -> difficult to control → multi-jurisdictional

- New trade arrangements
  - opening of boarders for trade
  - trade through free ports
  - trade through several intermediaries
  - promotion and trade through Internet
.. From active ingredient to finished product (FPP)..

APIs

Source 1
Source 2
Source X

Process1
Process2
Process X

Today
Past

World Health Organization
Quality of medicines remains a problem
Defining extent of counterfeiting and substandard medicines is difficult for many reasons:

- Variety of information sources, including national medicines regulatory authorities, enforcement agencies, pharmaceutical companies and nongovernmental organizations, ad hoc studies on specific geographical areas or therapeutic groups
- Different methods used to produce reports and studies
WHO's work in medicines area: strategies

1. **Providing tools, international norms, standards** and guidelines to assist that medicines circulating in national and international commerce are safe, efficacious and of good quality

2. **Providing support to Member States** to build national regulatory capacity

3. **Developing global activities**

4. **Providing means enabling exchange of information**
WHO’s medicines quality assurance provides more than 70 international standards for:

- Development
- Production
- Quality Control
- Quality related regulatory guidelines
- Inspection
- Distribution

→ For full life cycle of medicines from manufacture to delivery to patient
Prequalification of Medicines for UN procurement

- **Partners**
  - UNAIDS
  - UNICEF
  - UNFPA
  - WHO
  - With the support of World Bank

- **WHO role**
  - *Technical assistance based on WHO norms and standards, plus other standards, where applicable*
  - Open to both innovators and multisource/generic manufacturers
What can patients' organizations do?

- Support governments in establishing and maintaining an efficient medicines regulatory system to protect patients.
- Promote the importance of implementation of current good practices and international standards from development to distribution to ensure quality, safety, and efficacy of medicines.
- Encourage patients to purchase from reliable sources.
- Inform patients what to do in case of "suspect" medicines.
- Collaborate with international and national networks in case of serious events related to medicines.
What to recommend to patients?

- **Buy** medicines from licensed pharmacies, reliable sources
- **Examine** the package to see if sealed
- **Check** the label for: name, manufacturer, expiry date and instructions of use
- **Avoid** buying loose tablets, capsules or injections
- **See** your doctor/pharmacist if symptoms persist
- If you suspect something is wrong, **report** to your pharmacy and healthcare provider or medicine regulatory authorities
Safe quality medicines

- Thank you for your attention!