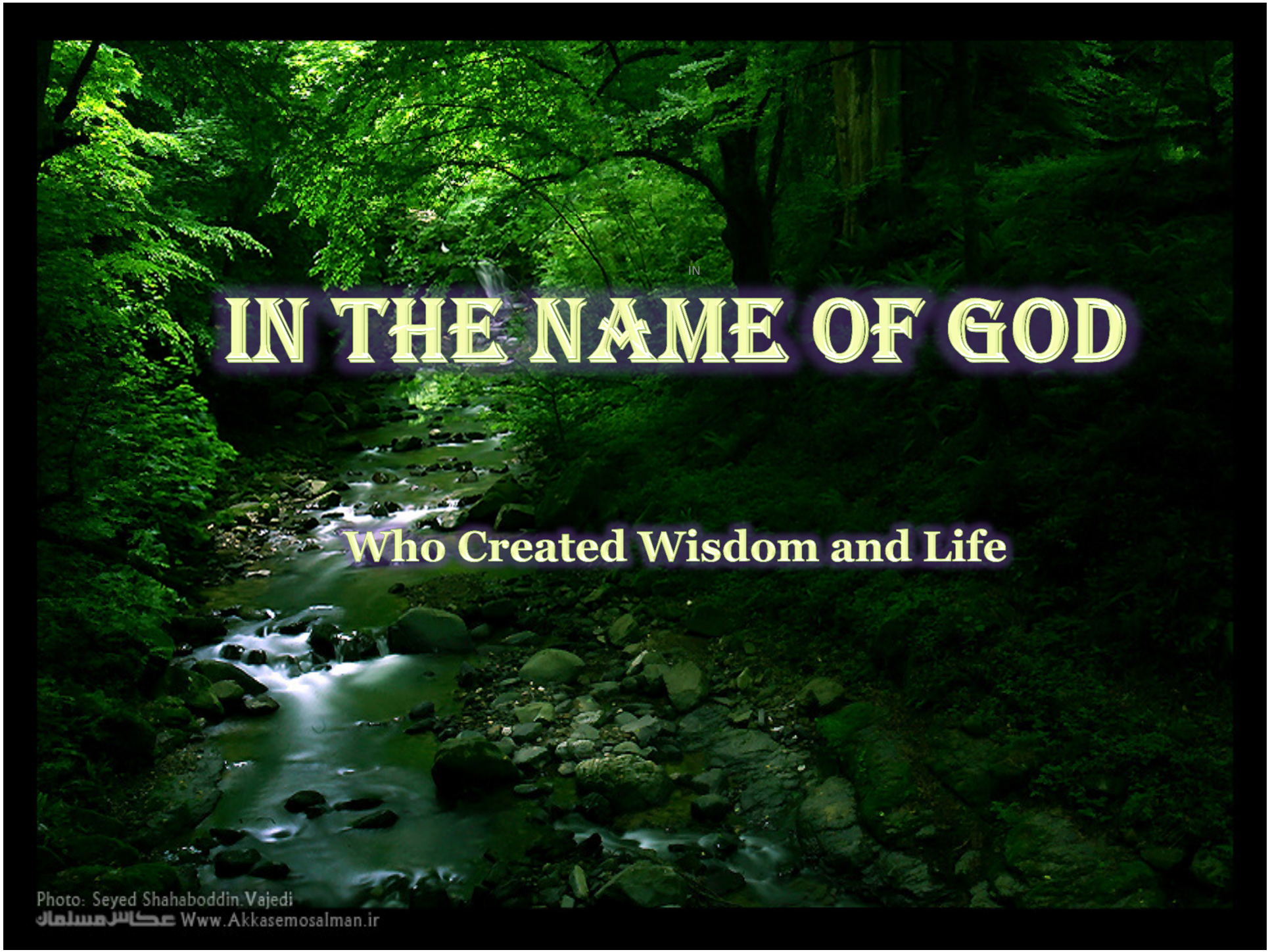
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IN THE NAME OF GOD
Who Created Wisdom and Life
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USE OF GENERIC DRUGS AND DISCUSSIONS WITH THE GOVERNMENT ON DRUG QUALITY

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WHAT ARE GENERIC DRUGS?

A generic drug is a copy of a brand name drug. To be sold, a generic drug must be "bioidentical" to the brand name drug. This means that the generic drug must be proven to be the same as the original brand name drug

IS IT REQUIRED TO SUBMIT CLINICAL DATA REGARDING SAFETY AND EFFICACY FOR GENERIC DRUGS?

- Unlike the approval process for new chemical entities, that for generic drugs allows use of the ANDA, which does not require the submission of clinical data regarding safety and efficacy since this information was already provided for the pioneer product. Since the original active ingredient was already proven safe and effective, the manufacturer must now prove bioequivalence for the pharmaceutically equivalent generic drug product.

- In order to receive approval for marketing, a generic drug must meet the same batch requirements for identity, strength, purity, and quality and be therapeutically equivalent to the original product.

- Additionally, the drug must be manufactured according to the same Good Manufacturing Practice regulations required by the FDA.

MYTHS AND FACTS ABOUT GENERIC DRUGS

MYTH	FACT
Generics take longer to act in the body.	The firm seeking to sell a generic drug must show that its drug delivers the same amount of active ingredient in the same time frame as the original product.
Generics are not as potent as brand-name drugs.	FDA requires generics to have the same quality, strength, purity, and stability as brand-name drugs.
Generics are not as safe as brand-name drugs.	FDA requires that all drugs be safe and effective and that their benefits outweigh their risks.

WHAT ARE THE DIFFERENCES BETWEEN COPIED AND GENERIC DRUGS?

- Generic Drugs are produced according to patent regulations and policies; but, copied ones are mostly produced in the countries in which the patent law is not exercised.

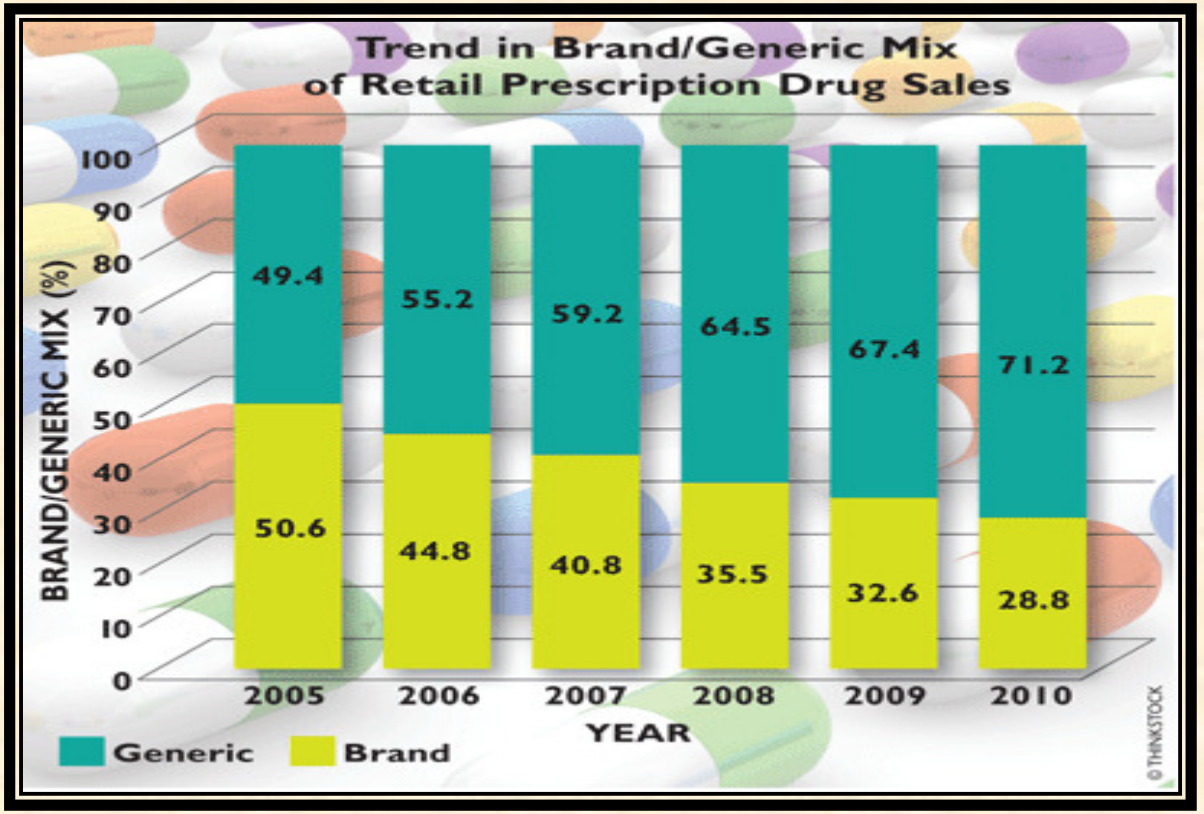
- All information about producing a bioequivalent medicine can be found for generic drugs' production; but, sometimes methods of analysis or evaluation could not be revealed by original makers during patent period. Hence, copy makers should invent the methods and validate them.

WHY USE GENERIC DRUGS?

- A generic drug is made with the same active ingredients and is available in the same strength and dosage as the equivalent brand-name drug

- The average price of a generic could be around $15 when the average price of a brand-name prescription is between $80 and $100.

SHIFTS IN THE GENERIC-DRUG MARKET



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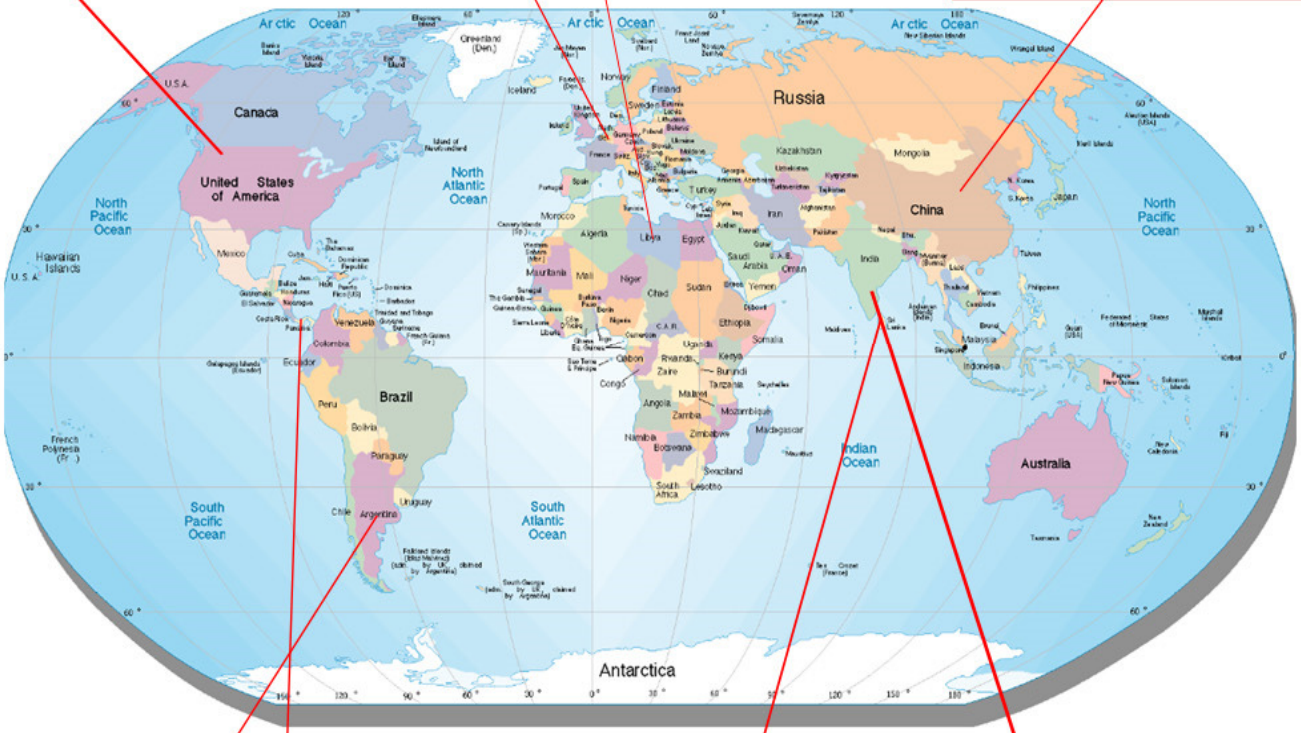
DOES EVERY GENERIC DRUG IN MARKETS MEET STANDARD QUALITIES?

USA (1995): The evidence of three different generic formulations of levothyroxine (used to treat hypothyroidism) were presented. All were more potent than the branded version and varied from one another. One was 12.5% above, another 9% above, and another 3% above the brand name's potency. All had been approved as bioequivalent. Noting that "less than 10% dose intervals make clinical differences," Hennessey told the advisory committee meeting, "These differences are too large."

Aferica (2006): 45% anti-malaria sample tested found to be poor-quality

Belgium (1999): Two babies died. Injected KCl (supposed to be glucose)

China (2007): 200 Patients with serious side effects taking contaminated Methoterexate (nonGMP) and there were a report about Substandard Rabies Vaccine.



Panama (2006): More than 30 died - cough syrup containing diethylene glycol – industrial solvent (in antifreeze) – kidney failure

Argentina (2003): 17% of Clarithromicyn samples tested did not meet criteria for a standard medicine.

Sri Lanka (2010): 4 cases of death were reported due to using substandard deferoxamine.

India (2013): the FDA tested 6,716 samples of drugs sold at various chemists stores across the state and found 392 drugs including vitamin tablets, cough syrups and steroid injections, were not up to the requisite standard.

WHAT CAUSE THE PROBLEM?

- **Authority: In some developing countries the authority does not outline perfect and unshakeable norms and standards for drug production**

- **Different Sources of ingredient: During recession, a few companies switch into cheaper and more available ingredients which may be more impure.**

- **Change in the process of production: The process of formulation could be changed deliberately or due to error in quality control.**

LEGAL APPROVAL BY FDA, EMA, AND SOME DEVELOPING COUNTRIES

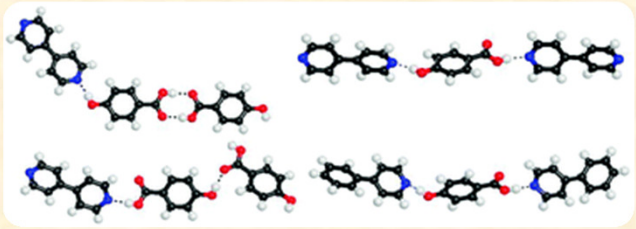
Registration requirements for Generics by authorities that are usually used as a reference (examples)	*FDA*	*EMA*	Some Developing Countries
Bioavailability and bioequivalence testing with sound scientific methodology and ethical committee surveillance	√	√	Not a common requirement, in some not required at all
Evaluation of active ingredient quality including identification and quantification of impurities (e.g. genotoxic impurities)	√	√	
Pre and post approval when source of active ingredient changes	√	√	
Identification and qualification of degradation production in medicines, not just stability testing	√	√	Not a requirement
Strict cGMP and field inspections of plants	√	√	Just a few countries require
Actual laboratory testing of finished product, not stamping and paper work	√	√	Not a requirement in most

IMPURITIES IN THE DRUG SUBSTANCES MAY HAVE PHARMACOLOGICAL EFFECTS

- Quality of drug substances is the key for clinical outcome and safety

- Action of a pharmaceutical formulation may be severely impaired by impurities

- Different polymorphs (= a different drug substance)



POOR QUALITY DRUGS = RX FOR DEATH?!

- Increased mortality and morbidity
- Enhancement of drug resistance and the loss of medicine efficacy
- Adverse effects from incorrect active ingredients

POOR QUALITY DRUGS = WASTE OF RESOURCES?!

- Economic loss for patients, their families, health systems, and the producers and traders in good-quality medicines

- Waste of enormous human efforts and financial burden on development of medicines.

POOR QUALITY DRUGS = RX FOR SMASHING TRUST?!

- Loss of confidence in health systems and health workers
- Fall in patients' compliance to suggested treatments
- Increased burden on health workers, medicine regulatory authorities (MRAs), customs officials, and police officers

WHAT IS WHO DOING TO HELP THE COUNTRIES?

- **Normative functions: Setting norms and standards Including GMP, providing technical and scientific support**

- **Capacity building: Ensuring that international norms and standards are applied all through the process including assessment, inspection (GMP, GCP, GLP) and quality control**

- **Prequalification Programme: Priority Essential Medicines**

World Health Organization

WHAT CAN NGOS DO TO COMBAT THE PROBLEM

- Urging for medicine regulatory authorities and independency (MRAs) to be strengthened.
- Improving quality of production by using post marketing studies.
- Fighting for both the availability of drugs and relatively inexpensive drugs

WHAT CAN POST MARKETING STUDIES REVEAL ABOUT GENERIC DRUG QUALITY?

- In post marketing studies, physicians and professionals in the field of Clinical Pharmacy could compare generic drugs with original ones in terms of efficacy, potency, and side effects.

- In post marketing studies, each change in the production process which causes clinical effects can be reported by health professionals

WHAT ROLES DO NGOS PLAY IN POST MARKETING STUDIES?

- In some countries especially developing ones, new information about drugs are not promulgated; hence, it is within the scope of activities of NGOs to demand clarifications.

- In underdeveloped and developing countries, it is too hard for patients to access original drugs and accordingly there is no way to compare the original drugs with generic ones; thus, it is a prioritized duty for NGOs to demand for ramping up the access to original drugs.

WHAT ROLES DO NGOS PLAY TO SECURE THE CONSTANT QUALITY FOR EACH DRUG

During recessions or pharmaceutical companies' financial problems, a few companies change their ingredients or the process of production. So, there is an urgent need for a study with the sufficient sample size with random sampling design to reliably estimate the quality of medicines.

WHY SHOULD WE LISTEN TO THE PATIENTS?

- WHO defines drug promotion to include all efforts and interventions initiating from production extending to distribution, marketing, sales, and the use of medicines. Thus, making satisfaction is an undivided part of drug promotion.

- Patient-centered care supports active involvement of patients and their families in the design of new care models and in decision-making about individual options for treatment.

THANK YOU