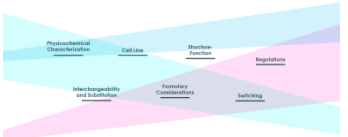


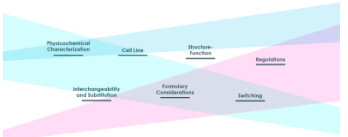
Ali M Alhomaidan, PhD, Saudi Arabia

- Executive Director for Pharmaceutical Products Evaluation, Saudi Food and Drug Authority, Saudi Arabia

GaBI Scientific Meetings

First GCC Stakeholder Meeting on **Approval Process, Interchangeability/Substitution and Safety of Biosimilars**

20 November 2017, Holiday Inn Izdihar Riyadh, Saudi Arabia



Biosimilars regulations in Saudi Arabia

Ali M Alhomaidan, PhD

20 November 2017

GaBi
GENERICS AND BIOSIMILARS INITIATIVE
Building trust in cost-effective treatments

sps Saudi Pharmaceutical Society الجمعية الصيدلية السعودية
PPCI Pro Pharma Communications International

Biosimilars Regulations Saudi Arabia

Ali Alhomaidan Ph.D.
Executive Director
for Pharmaceutical Products Evaluation
The Saudi Food and Drug Authority

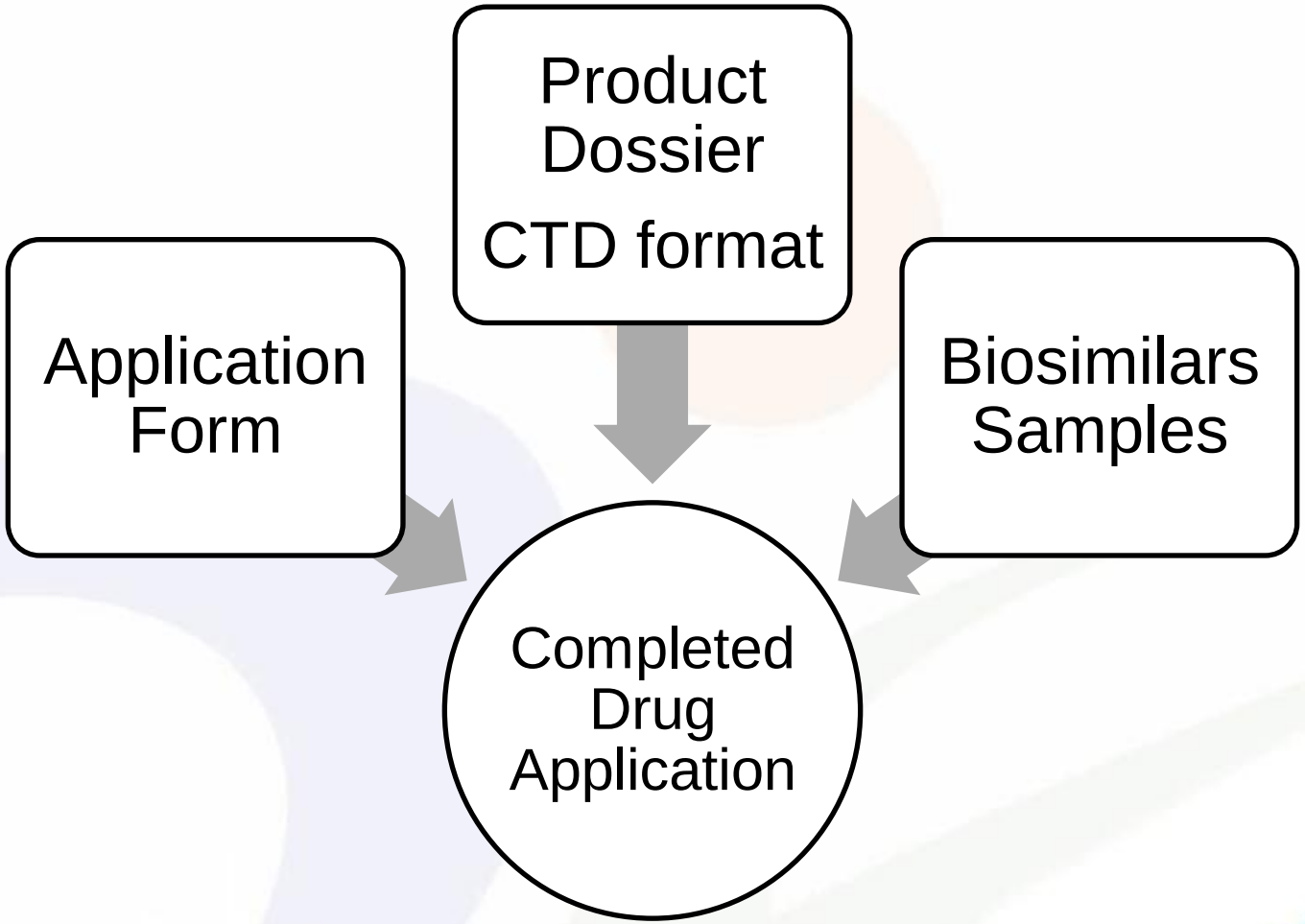
Outline

- Biosimilars Approval Pathway in Saudi Arabia
- Biosimilar products
- Quality, Safety, and Efficacy Considerations
- Pricing
- Interchangeability

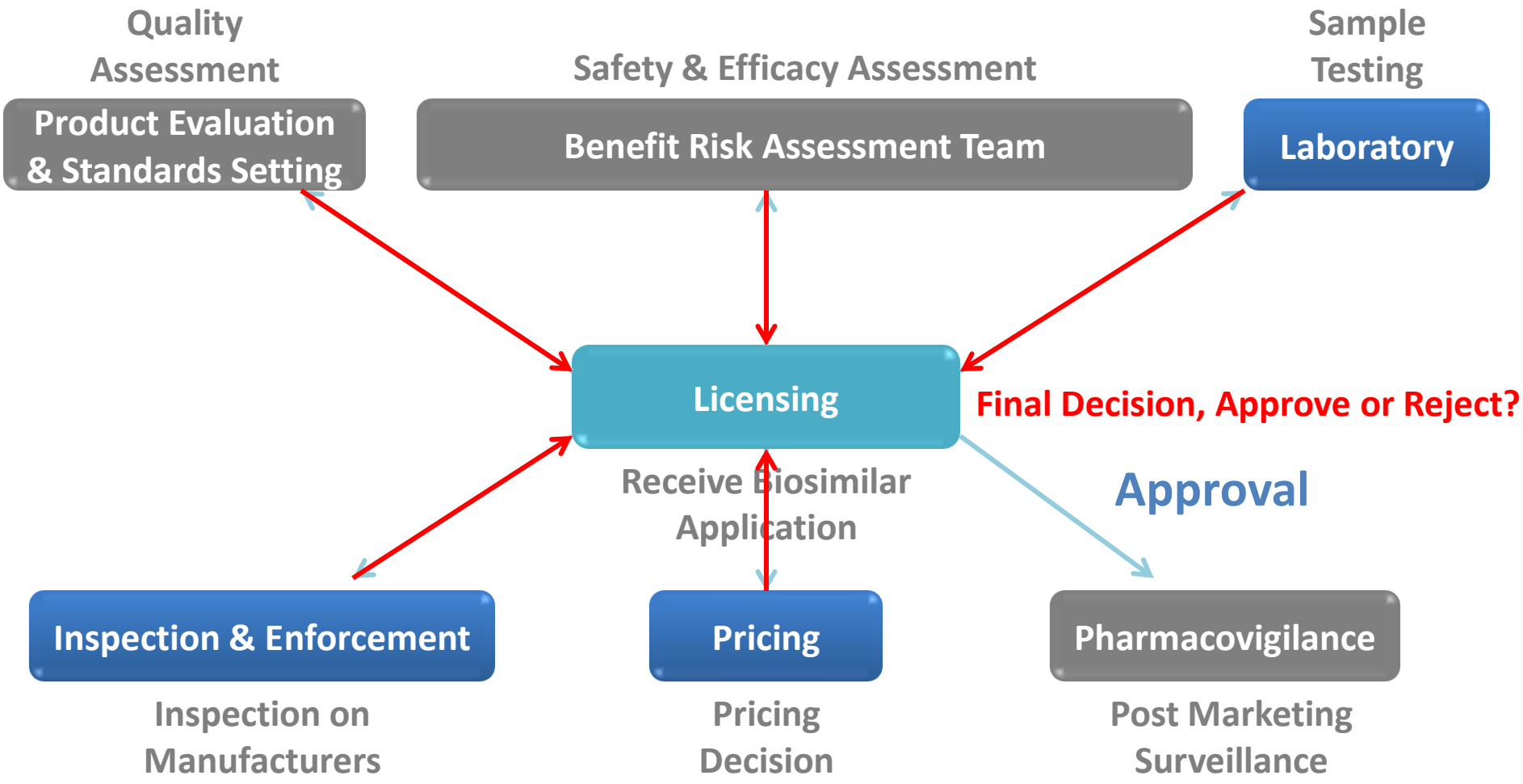
What is a Biosimilar

- Biosimilar Definition: a biological medicine that is similar to another biological medicine that has already been authorized for use.
- Examples:
  - Omnitrope (Growth hormone), Genotropin.
  - Biograstim (Filgrastim), Neupogen.
  - Amgevita (adalimumab), Humira.

Biosimilars Submission Guidance

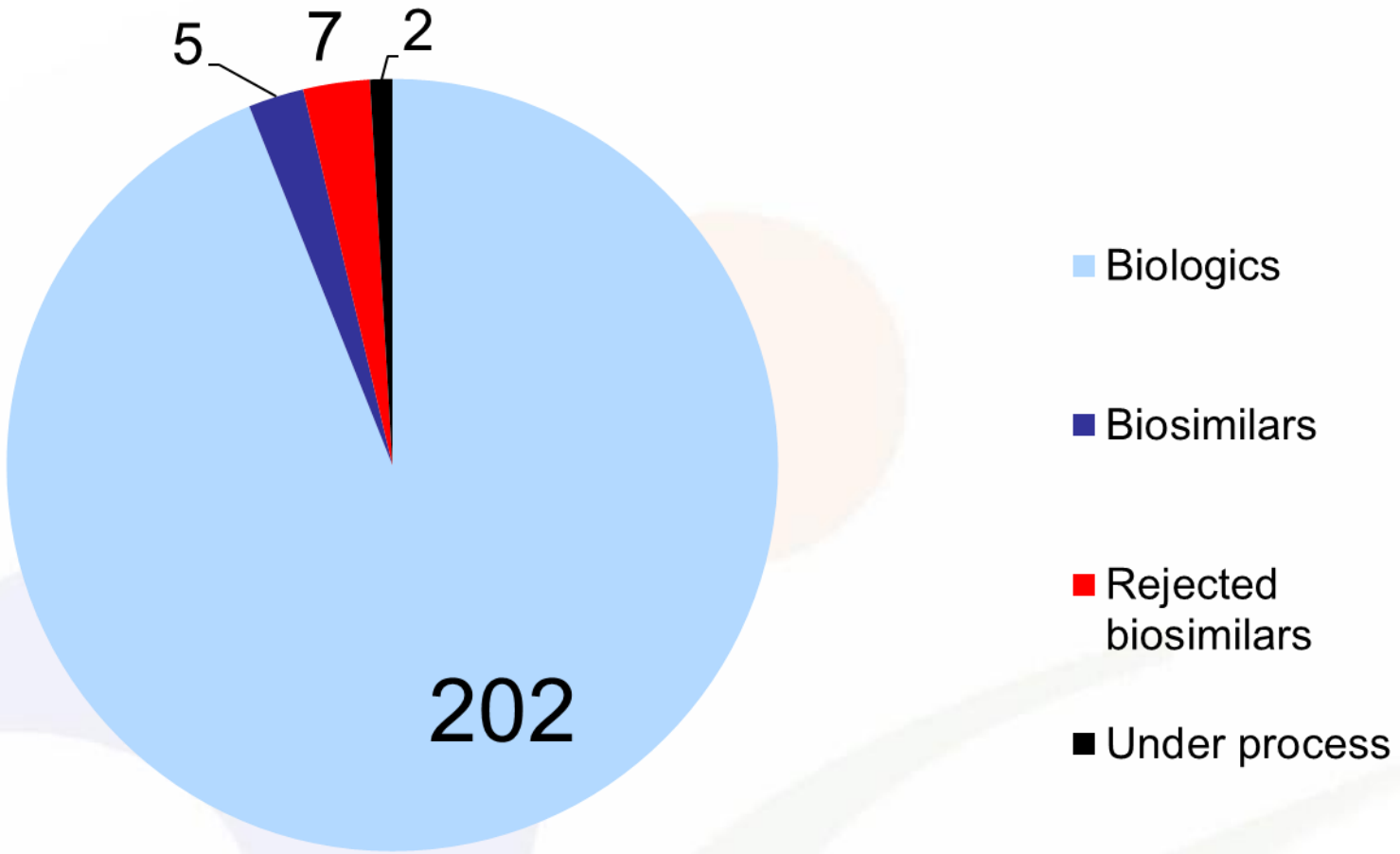


Departments involved in the evaluation of biosimilars



Duration and Fee

Type of Application	Duration	Fee
Biosimilar product	290 days	95,000 SAR About 25,000 USD


5
7
2
202
Biologics
Biosimilars
Rejected biosimilars
Under process

Examples of Approved Products

- Omnitrope: Recombinant Somatropin.
- Remsima: Infliximab.
- Zarzio: Filgrastim.
- Grastofil: Filgrastim.

- The biosimilar on average is 37% cheaper.

- Biosimilar Uptake.

Examples of Rejected Products

- Follitropin alfa: Failure in Clinical comparability.

- 6 Insulins: Failures in quality, safety, and efficacy.

Under Process

- Follitropin alfa
- Filgrastim
- Insulin glargine

Under Process

- Follitropin alfa
- Filgrastim
- Insulin glargine

Registration requirements (Original)

Quality	Nonclinical	Clinical

• Drug substance
  • Manufacture
  • Characterisation
  • Control
  • Reference standard
  • Container
  • Stability
• Drug product
  • Description
  • Development
  • Manufacture
  • Control
  • Reference standard
  • Container
  • Stability
	• Pharmacology
	  • Primary pharm.
	  • Secondary pharm.
	  • Safety pharm.
	  • Interactions
	• Pharmacokinetics
	  • ADME
	  • Interactions
	• Toxicology
	  • Single dose
	  • Repeat dose
	  • Genotoxicity
	  • Carcinogenicity
	  • Reproduction
	  • Local tolerance
		• Pharmacology
		• Pharmacokinetics
		  • Single dose
		  • Repeat dose
		  • Special populations
		• Efficacy and safety
		  • Dose finding
		  • Schedule finding
		  • Pivotal
		  • Indication 1
		  • Indication 2
		  • Indication 3
		  • Indication 4
		• Post-marketing studies

Registration requirements (Biosimilar)

Quality

- Drug substance
  - Manufacture
  - Characterisation
  - Control
  - Reference standard
  - Container
  - Stability
- Drug product
  - Description
  - Development
  - Manufacture
  - Control
  - Reference standard
  - Container
  - Stability
- Comparability data
  - Analytical comparison with reference product

Nonclinical

- Pharmacology
  - Primary pharm.
  - Secondary pharm.
  - Safety pharm.
  - Interactions
- Pharmacokinetics
  - ADME
  - Interactions
- Toxicology
  - Single dose
  - Repeat dose
  - Genotoxicity
  - Carcinogenicity
  - Reproduction
  - Local tolerance

Clinical

- Pharmacology
- Pharmacokinetics
  - Single dose
  - Repeat dose
  - Special populations

Study #1

- Efficacy and safety
  - Dose finding
  - Schedule finding
  - Pivotal
    - Indication 1
    - Indication 2
    - Indication 3
    - Indication 4

Study #2

- Post-marketing studies
  - Safety in larger population
  - Efficacy in other indications
  - Immunogenicity

Follitropin alfa

- Quality:
  - Stability:
    - Long-term stability data at 2-8° C are available up to 36 months for three production batches.
  - Process validation:
    - Traditional approach, comprising the successful manufacture of three validation batches.

Follitropin alfa

- Quality II:
  - Process and product-related impurities properly justified and controlled.
  - Specification:
    - Release and shelf-life specifications include:
      - FSH content, biological activity,
      - purity, oxidized forms,
      - bacterial endotoxin,
      - sterility, identification,
      - content, visual appearance, visible and sub-visible particles.

Follitropin alfa

- Quality III: Comparability Exercise with Gonal-f:
  - The primary sequence of Biosimilar and Gonal-f has been verified by proteolytic cleavage and ESI-ion trap-MS/MS analysis.
  - Peptide mapping, CD-spectroscopy and Proton Nuclear Magnetic Resonance.
  - SDS-PAGE, SEC-HPLC, Western blotting …etc.

Follitropin alfa

- Safety:
  - Single dose and Repeat-dose toxicity.
  - No studies on genotoxicity, carcinogenicity, reproductive and developmental toxicity or other toxicity were conducted, which is considered acceptable.

Follitropin alfa

- Efficacy:
  - One pivotal Phase III study (FIN3001) was conducted in 410 patients
  - Randomized, assessor-blind, multi-national, multi-center, controlled, parallel group equivalence trial.
  - The primary endpoint: Number of oocytes retrieved.
  - Biosimilar: 10.85 oocytes Gonal-F: 10.58 oocytes
  - The equivalence margin for the primary endpoint ‘number of oocytes retrieved’ was -2.9 and +2.9

Pricing

Interchangeability

Thank You
Questions or Comments

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