Professor Aws Alshamsan, BPharm, RPh, PhD, Saudi Arabia

- *Professor of Pharmaceutics, King Saud University, Saudi Arabia*
- *Dean, King Abdullah Institute for Nanotechnology, King Saud University, Saudi Arabia*
- *Dean (2014–2017), College of Pharmacy, King Saud University, Saudi Arabia*
- *Consultant, Saudi Food and Drug Authority*

GaBI Scientific Meetings

2nd MENA Stakeholder Meeting on **Regulatory Approval, Clinical Settings, Interchangeability and Pharmacovigilance of Biosimilars**

10 October 2018, Le Meridien Dubai, United Arab Emirates

Biosimilars Regulatory Considerations in Saudi Arabia

Professor Aws Alshamsan, BPharm, RPh, PhD, Saudi Arabia

10 October 2018

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

PPCI
Pro Pharma Communications International

MINISTRY OF HEALTH & PREVENTION

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA

Biosimilars Regulatory Considerations in Saudi Arabia

Aws Alshamsan, BPharm, RPh, PhD

Dean and Associate Professor at College of Pharmacy, King Saud University

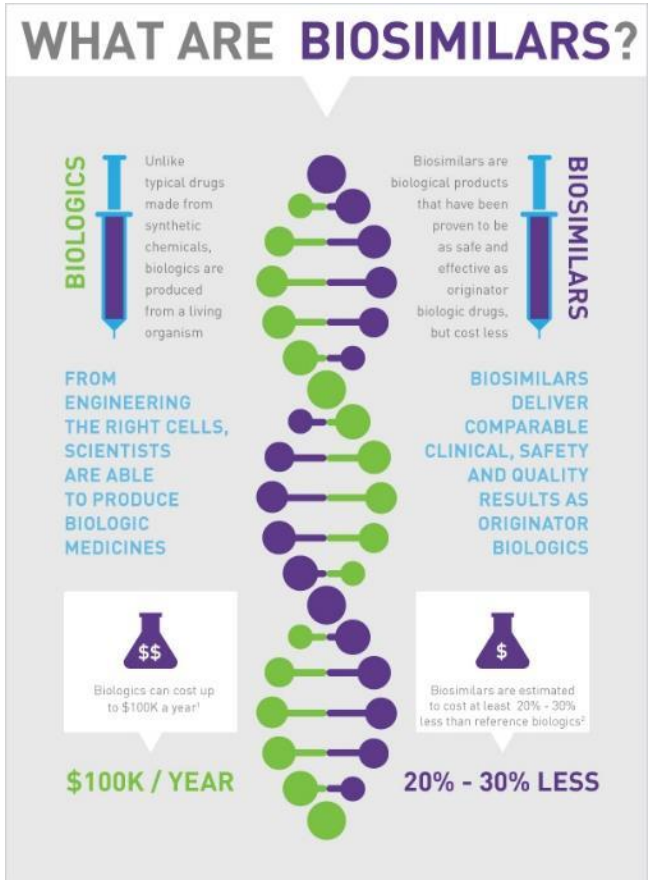
Consultant of the Drug Sector at SFDA

aalshamsan@ksu.edu.sa

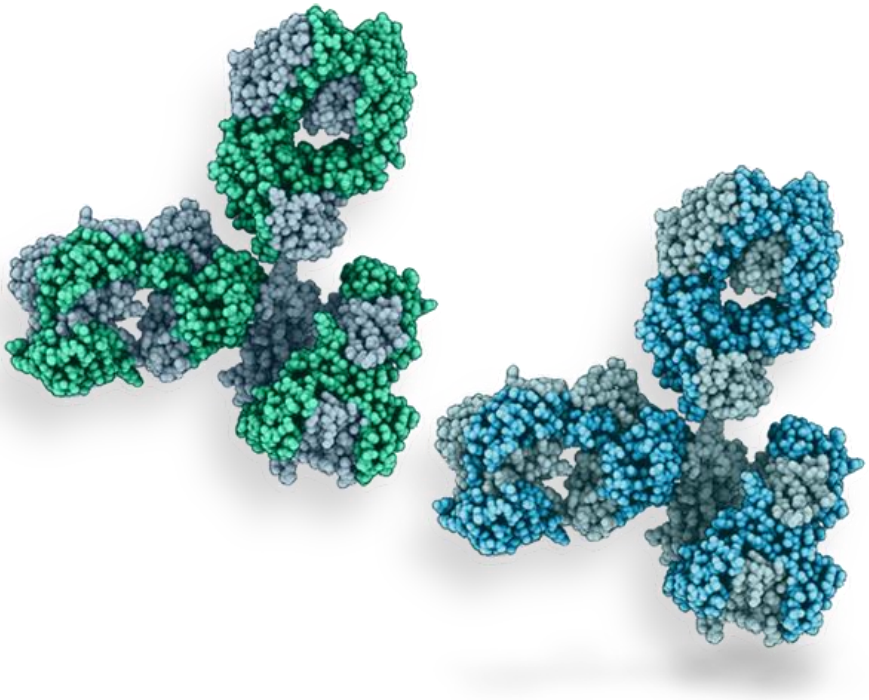
جامعة الملك سعود
King Saud University
1957

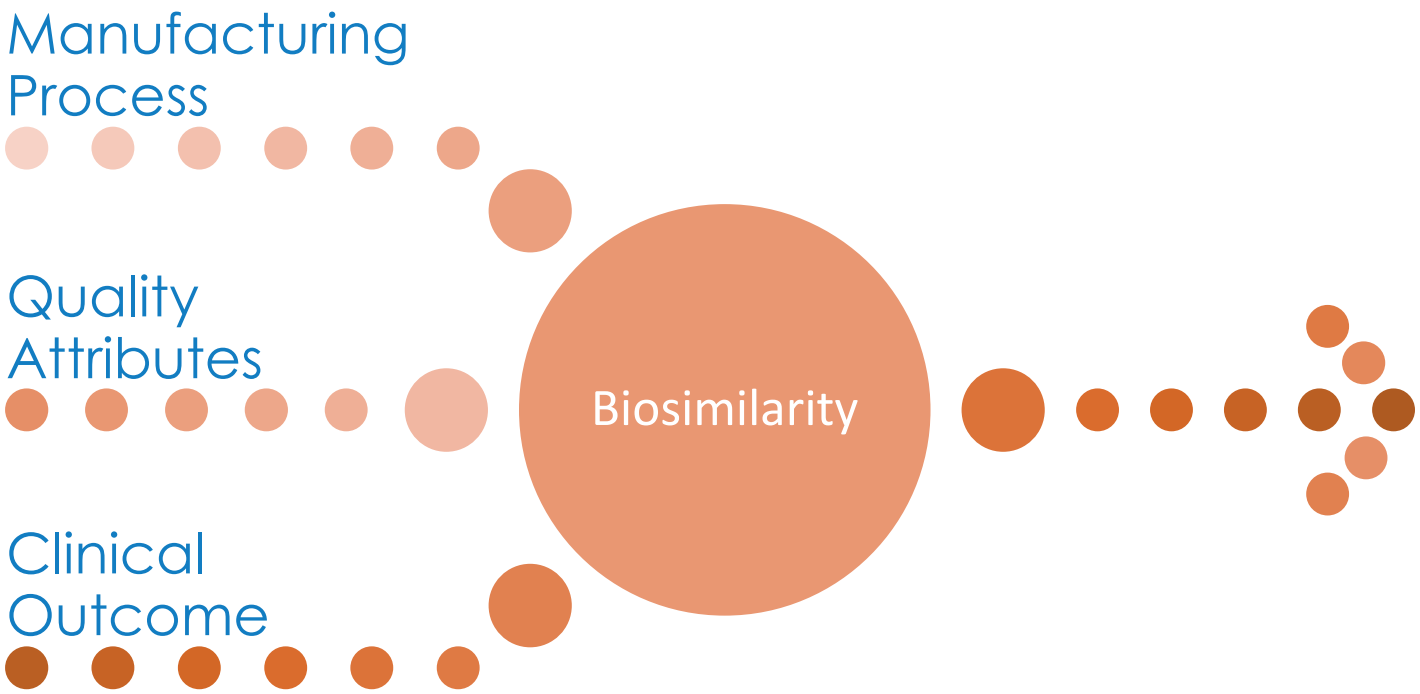
College of Pharmacy

BIOSIMILARS

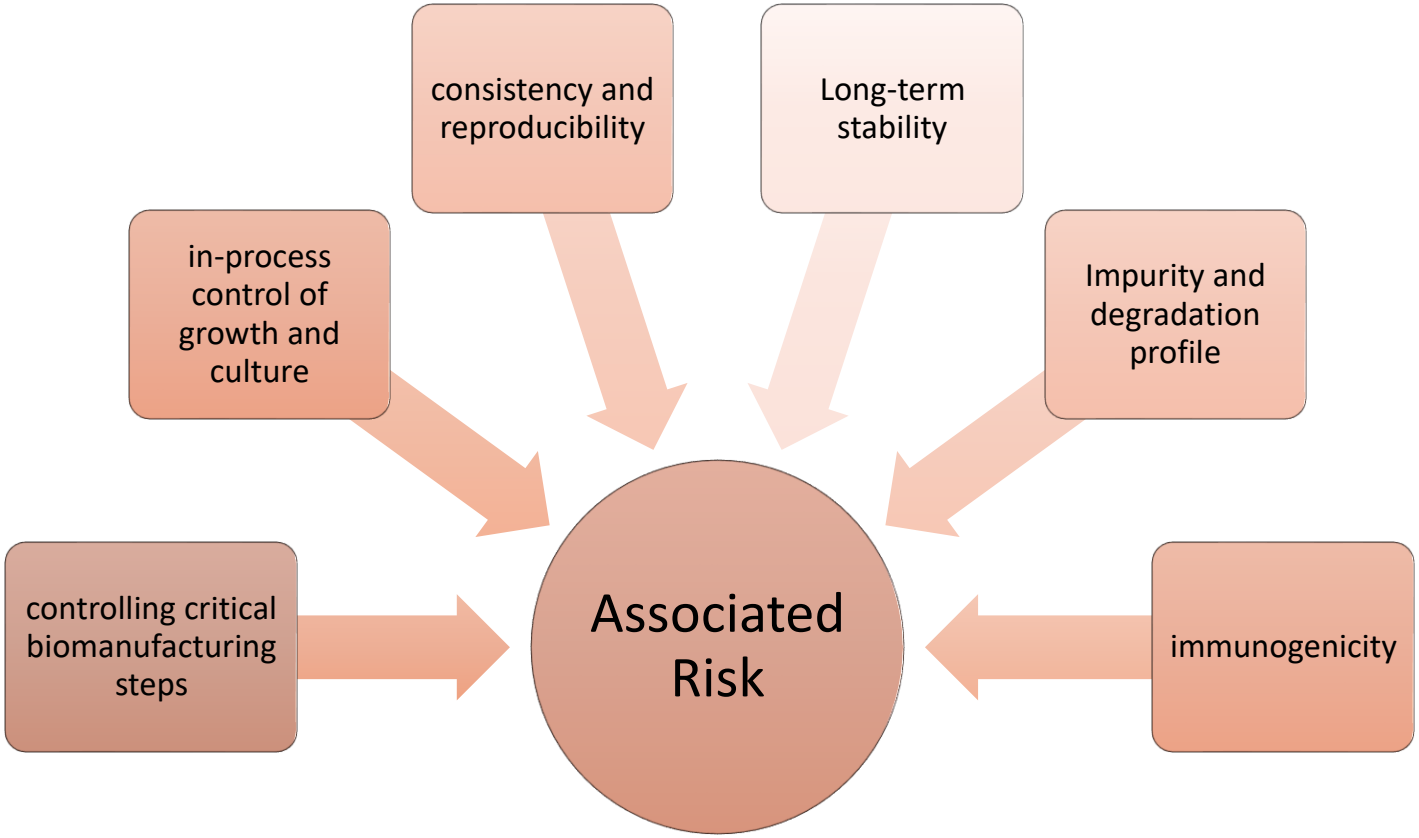


Biological medicinal product that is highly similar to another biological medicine that has already been approved for use




Manufacturing Process
Quality Attributes
Clinical Outcome
Biosimilarity

Associated Risk



BIOSIMILARS

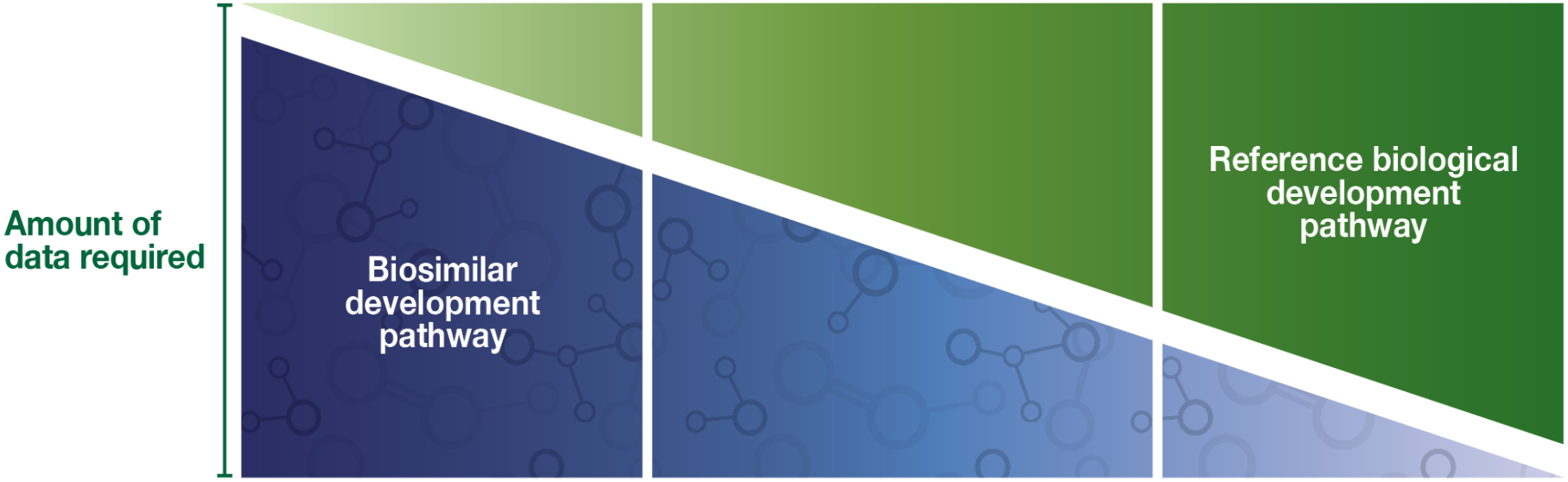
الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA

Pre-clinical assessments

- Analytical characterisation
- Structural
- In vitro functional
- Pharmacokinetic/ pharmacodynamic (animal)
- Toxicology

Clinical assessments

- Pharmacokinetic
- Efficacy
- Safety



Reference Product

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

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

BIOSIMILARS

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA

Quality

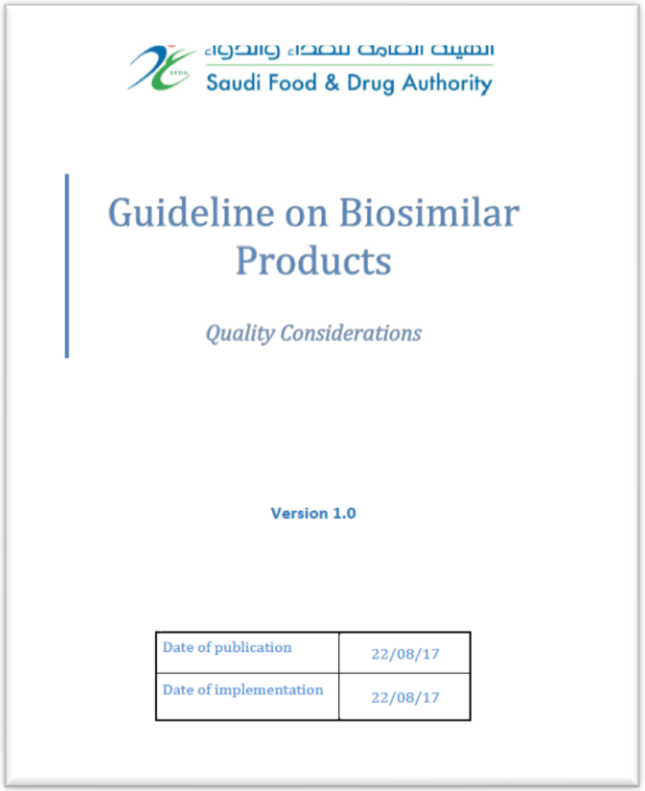
- Drug substance
  - Manufacture
  - Characterisation
  - Control
  - Reference standard
  - Container
  - Stability
- Drug product
  - Description
  - Development
  - Manufacture
  - Control
  - Reference standard
  - Container
  - Stability
- Comparability data
  - Analytical comparison with reference 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 (Study #1)
  - Single dose
  - Repeat dose
  - Special populations
- Efficacy and safety (Study #2)
  - Dose finding
  - Schedule finding
  - Pivotal
    - Indication 1
    - Indication 2
    - Indication 3
    - Indication 4
- Post-marketing studies
  - Safety in larger population
  - Efficacy in other indications
  - Immunogenicity

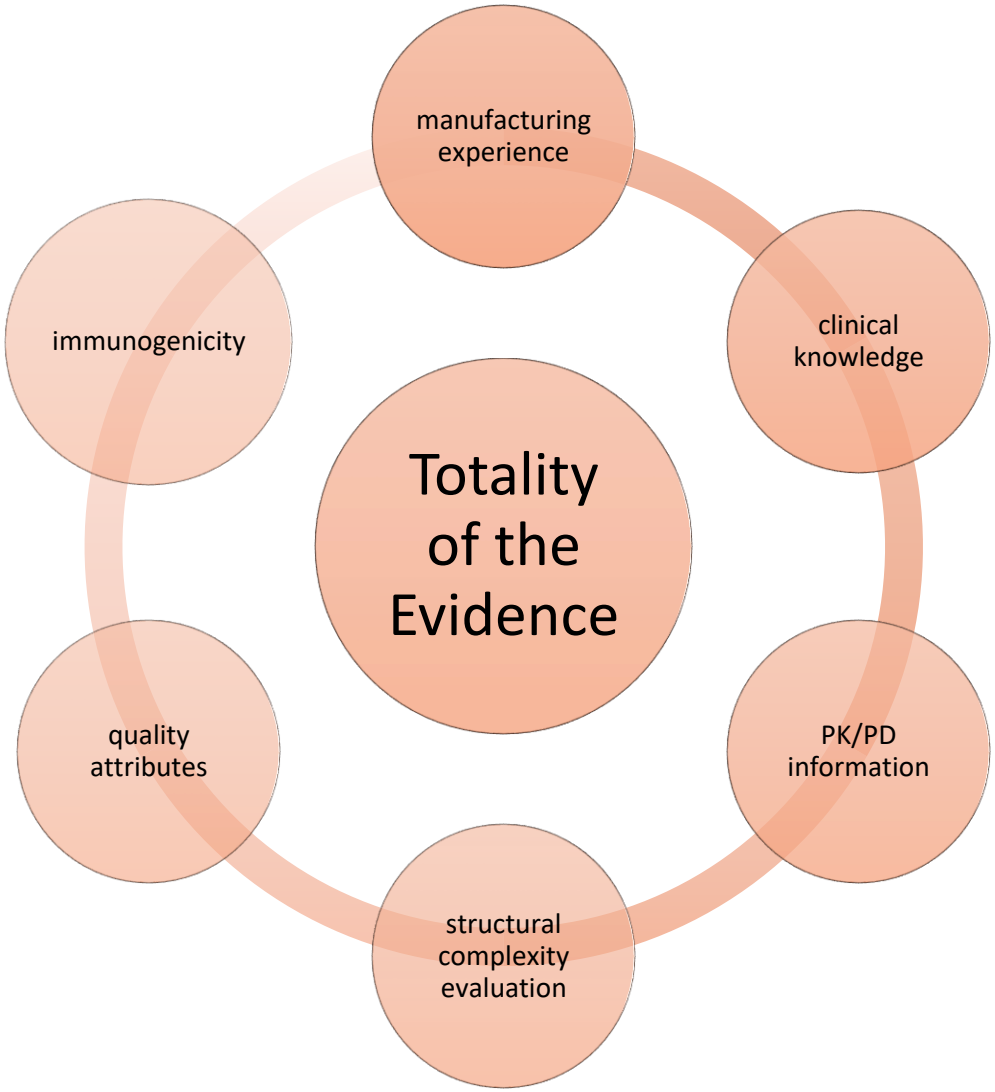

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Guideline on Biosimilar Products

Quality Considerations

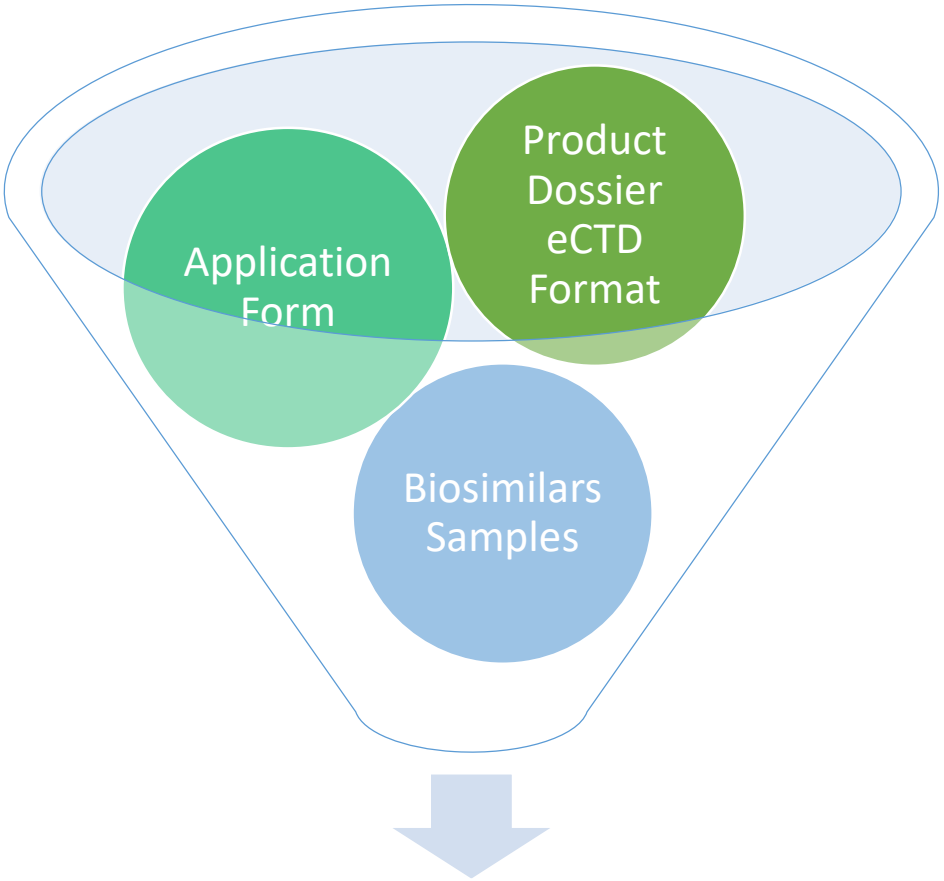
Version 1.0

Date of publication	22/08/17
Date of implementation	22/08/17

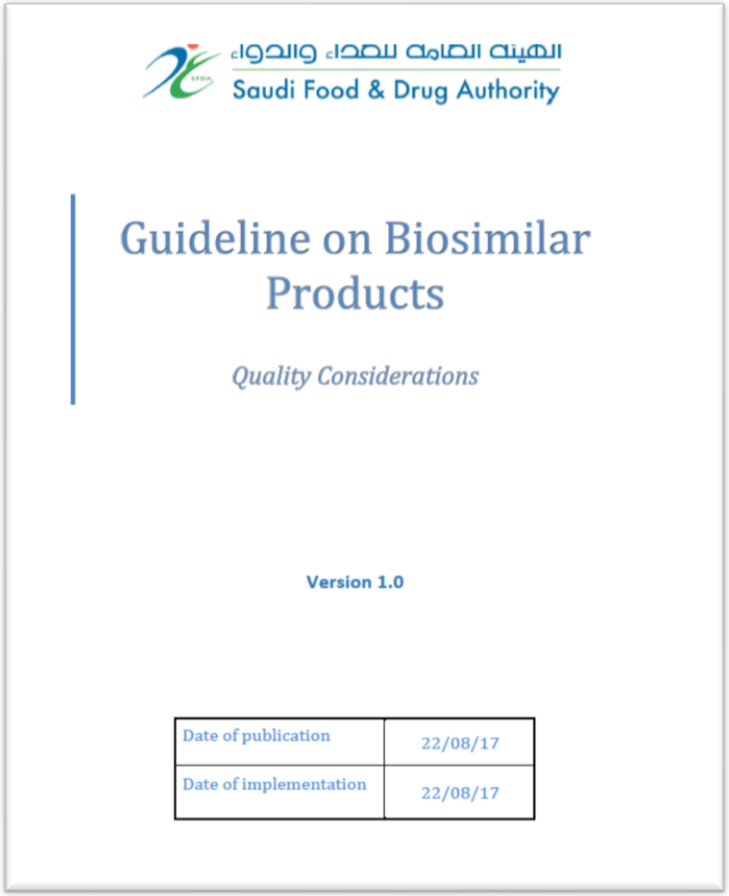

manufacturing experience
clinical knowledge
PK/PD information
structural complexity evaluation
quality attributes
immunogenicity
Totality of the Evidence

BIOSIMILARS SUBMISSION GUIDE

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA



Complete Drug Application


الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

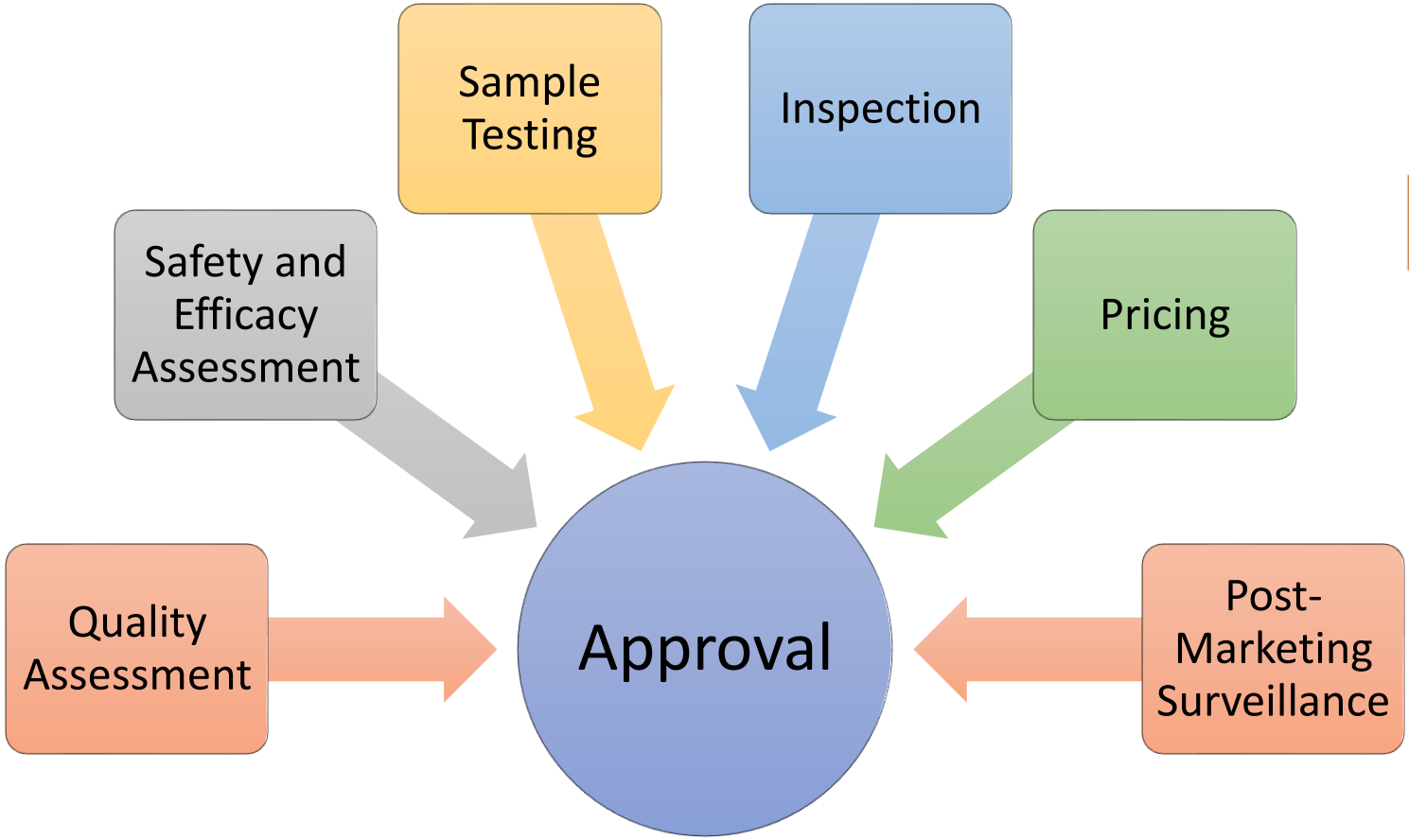
Guideline on Biosimilar Products

Quality Considerations

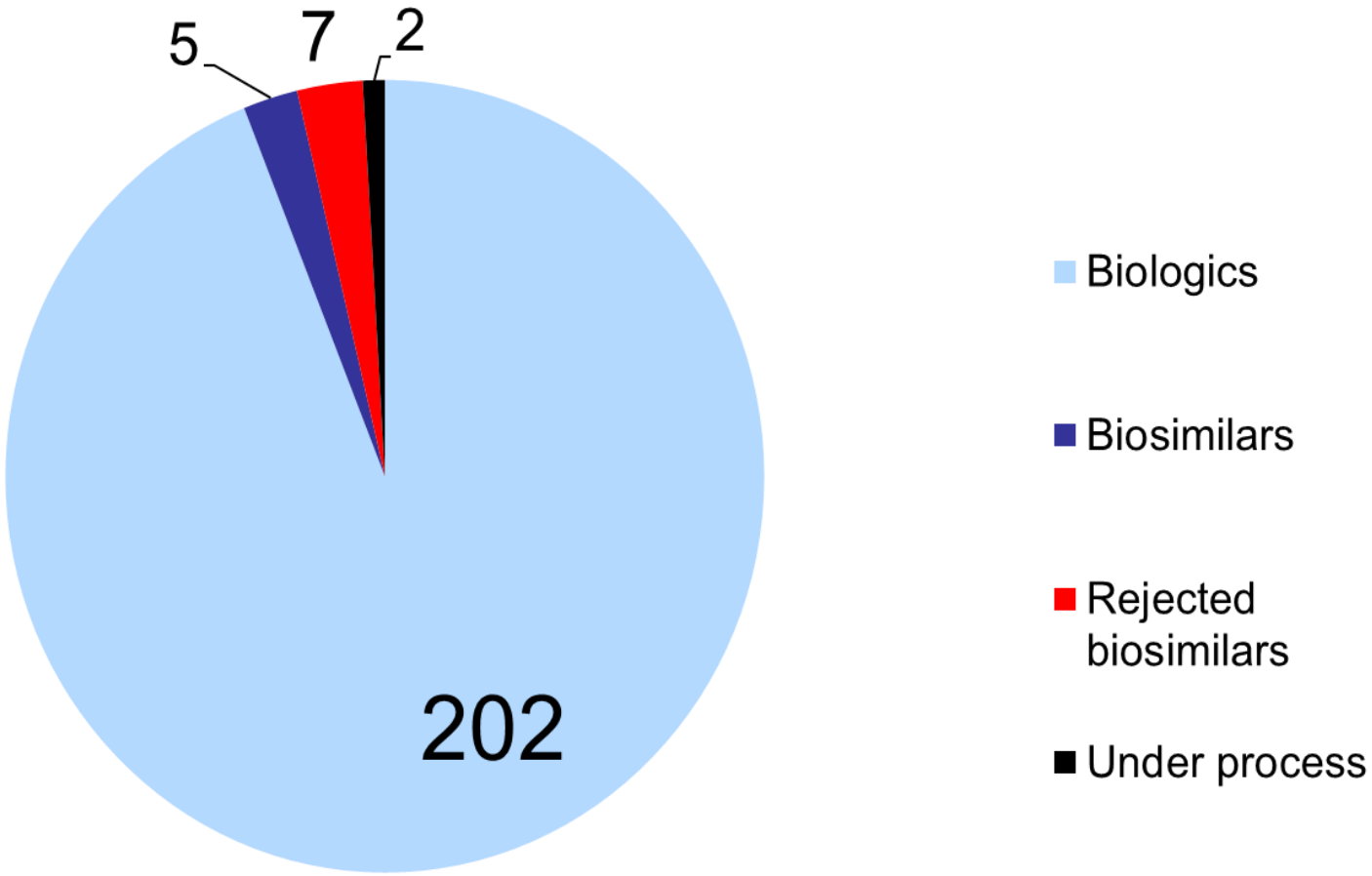
Version 1.0

Date of publication	22/08/17
Date of implementation	22/08/17

Department-Centric Evaluation



290 days


5
7
2
202
Biologics
Biosimilars
Rejected biosimilars
Under process

Examples of Approved Products

- Omnitrope: Recombinant Somatropin 2014
- Remsima: Infliximab 2015
- Zarzio: Filgrastim 2015
- Grastofil: Filgrastim 2017
- Binocrit: Erythropoietin 2017
- The biosimilar on average is 37% cheaper
- Biosimilar Uptake

Examples of Rejected Products

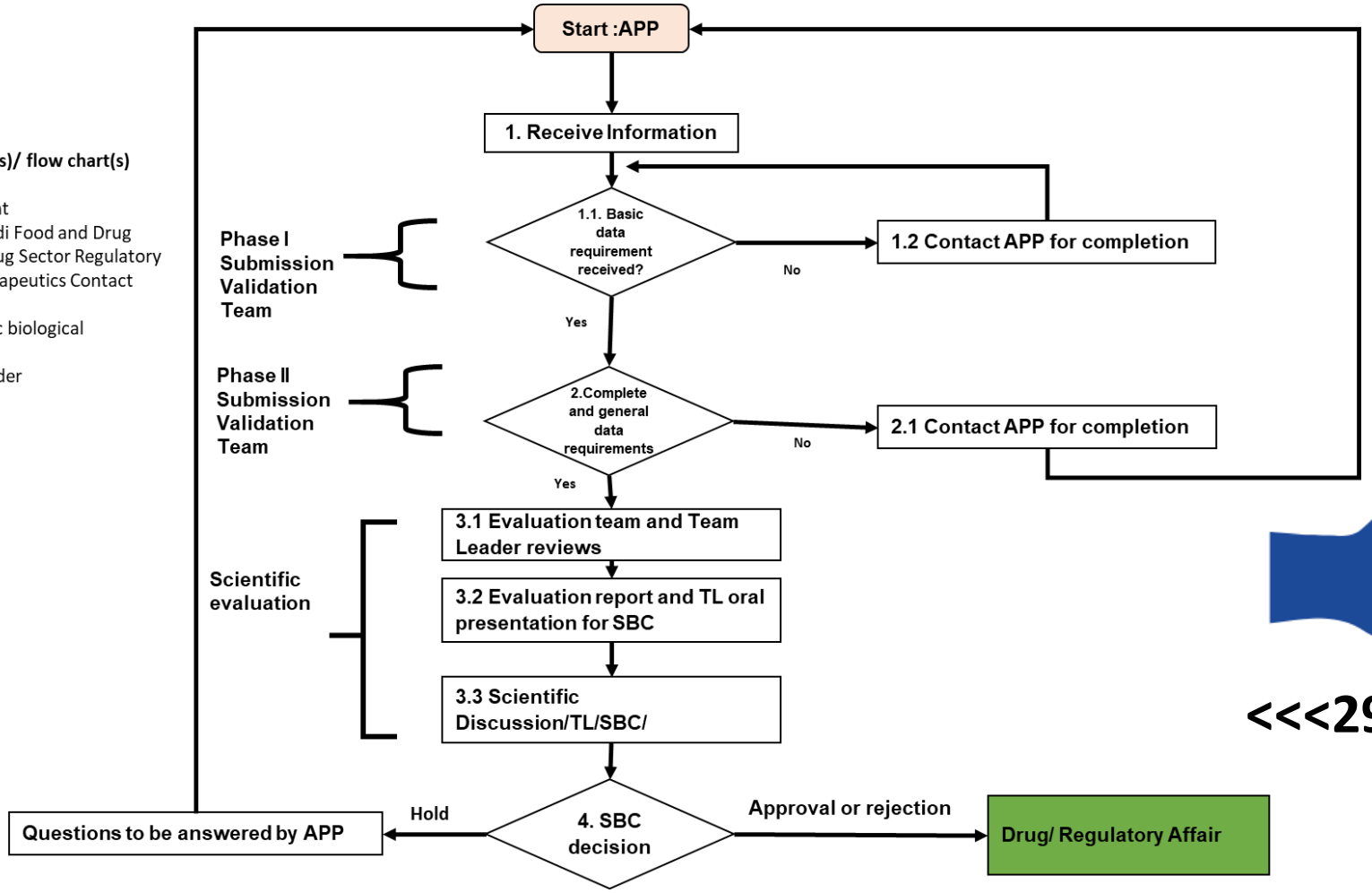
- Follitropin alfa: Failure in Clinical comparability
- 6 Insulins: Failures in quality, safety, and efficacy

Product-Centric Evaluation

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Process map(s)/ flow chart(s)

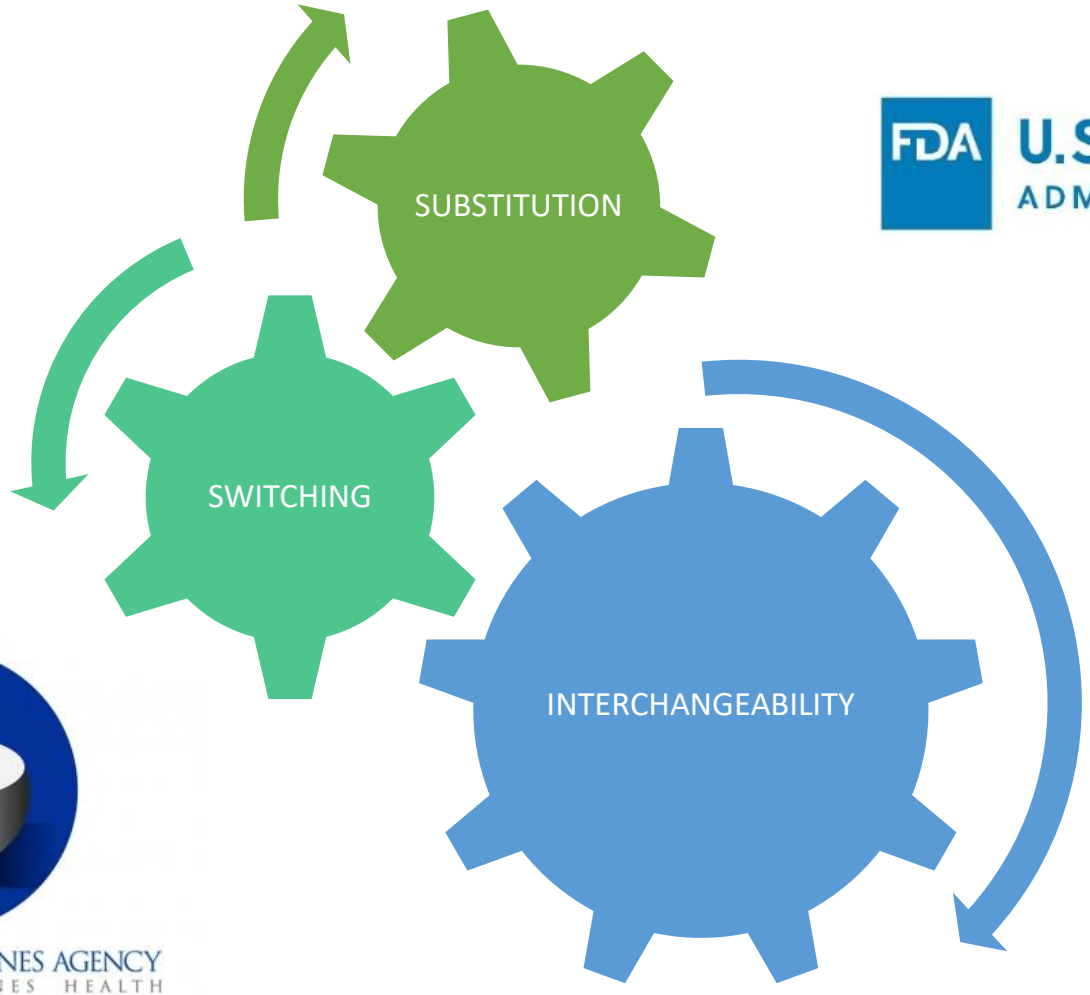
APP: Applicant
RA_BCP: Saudi Food and Drug Authority, Drug Sector Regulatory Affair Biotherapeutics Contact Person
SBC: Scientific biological committee
TL: Team Leader



<<<290 days

INTERCHANGEABILITY

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA



FDA U.S. FOOD & DRUG ADMINISTRATION

SFDA
الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

COMPLEXITY

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

Host cell type

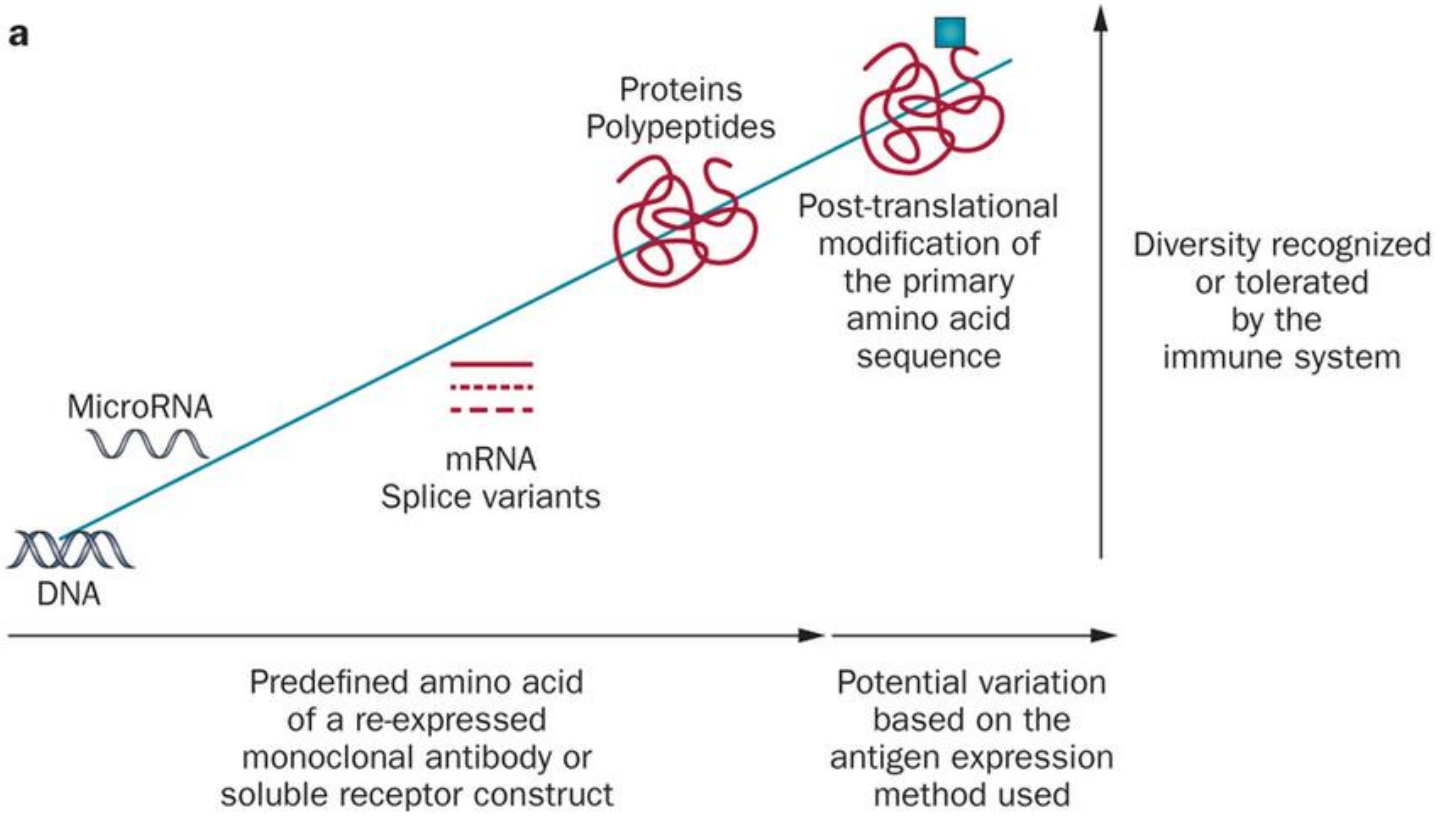
Process applied

Material used

Separation and purification

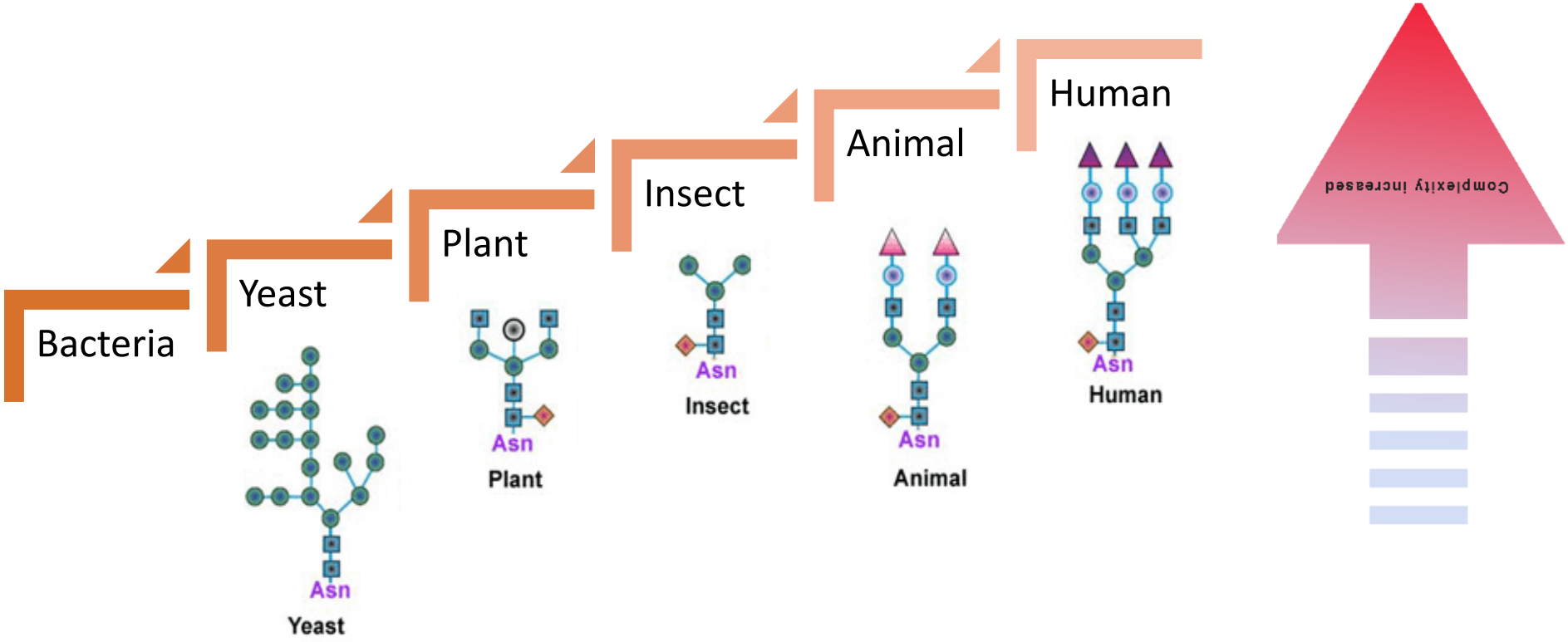
Impurities

Stability



Biosimilars in rheumatology: current perspectives and lessons learnt.
Thomas Dörner, Jonathan Kay
Nat Rev Rheumatol. 2015 Dec; 11(12): 713–724

COMPLEXITY


Bacteria
Yeast
Asn
Yeast
Plant
Asn
Plant
Insect
Asn
Insect
Animal
Asn
Animal
Human
Asn
Human
Complexity increased

AGGREGATION

الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority
SFDA

Journal of Immunotoxicology

http://informahealthcare.com/imt
ISSN: 1547-691X (print), 1547-6901 (electronic)
J Immunotoxicol, 2014; 11(2): 99–109

DOI: 10.3109/1547691X.2013.821564

informa healthcare

REVIEW ARTICLE

Immunogenicity of therapeutic proteins: Influence of aggregation

Kirsty D. Ratanji, Jeremy P. Derrick, Rebecca J. Dearman, and Ian Kimber

Faculty of Life Sciences, University of Manchester, Manchester, UK

Abstract

The elicitation of anti-drug antibodies (ADA) against biotherapeutics can have detrimental effects on drug safety, efficacy, and pharmacokinetics. The immunogenicity of biotherapeutics is, therefore, an important issue. There is evidence that protein aggregation can result in enhanced immunogenicity; however, the precise immunological and biochemical mechanisms responsible are poorly defined. In the context of biotherapeutic drug development and safety assessment, understanding the mechanisms underlying aggregate immunogenicity is of considerable interest. This review provides an overview of the phenomenon of protein aggregation, the production of unwanted aggregates during bioprocessing, and how the immune response to aggregated protein differs from that provoked by non-aggregated protein. Of particular interest is the nature of the interaction of aggregates with the immune system and how subsequent ADA responses are induced. Pathways considered here include 'classical' activation of the immune system involving antigen presenting cells and, alternatively, the breakdown of B-cell tolerance. Additionally, methods available to screen for aggregation and immunogenicity will be described. With an increased understanding of aggregation-enhanced immune responses, it may be possible to develop improved manufacturing and screening processes to avoid, or at least reduce, the problems associated with ADA.

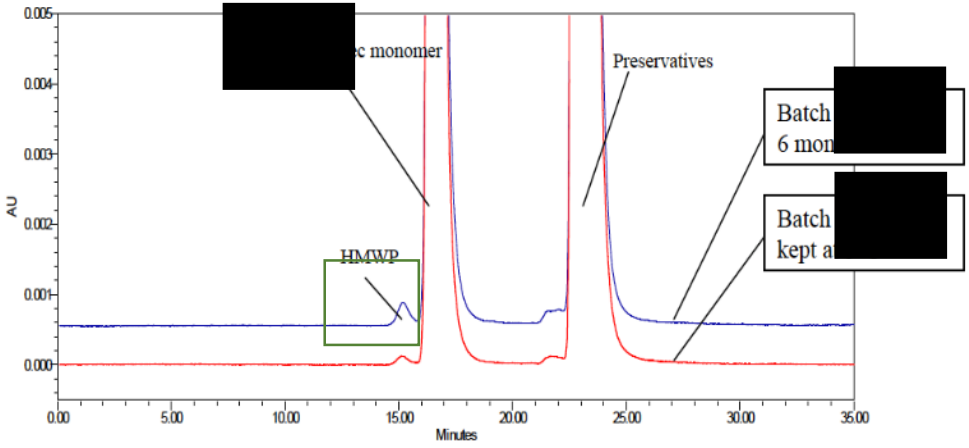
Keywords

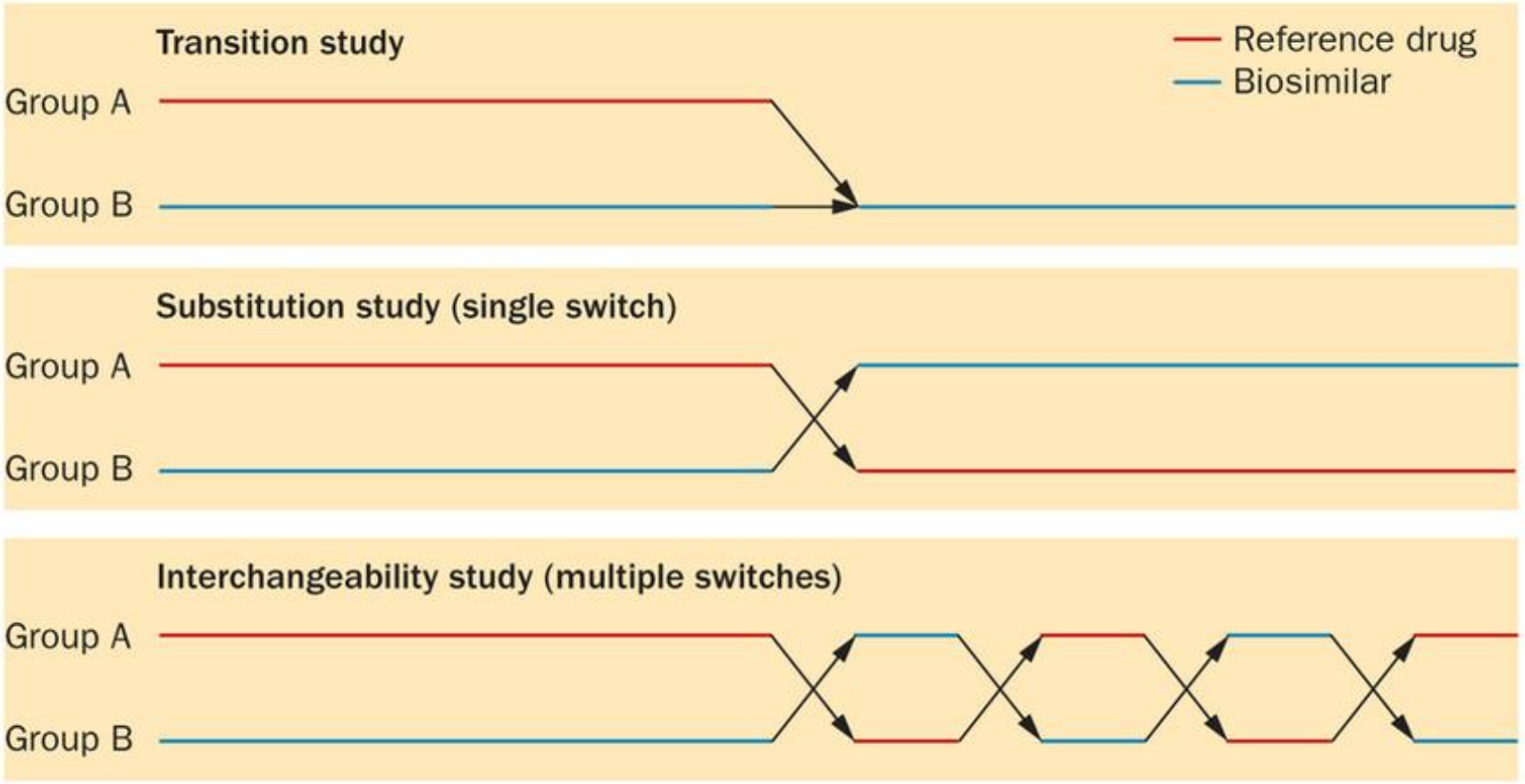
Aggregation, anti-drug antibodies, bioprocessing, biotherapeutic, immunogenicity

History

Received 30 May 2013
Revised 26 June 2013
Accepted 28 June 2013
Published online 6 August 2013

Section 3.2.S.3 Characterization of Impurities





Biosimilars in rheumatology: current perspectives and lessons learnt.
Thomas Dörner, Jonathan Kay
Nat Rev Rheumatol. 2015 Dec; 11(12): 713–724

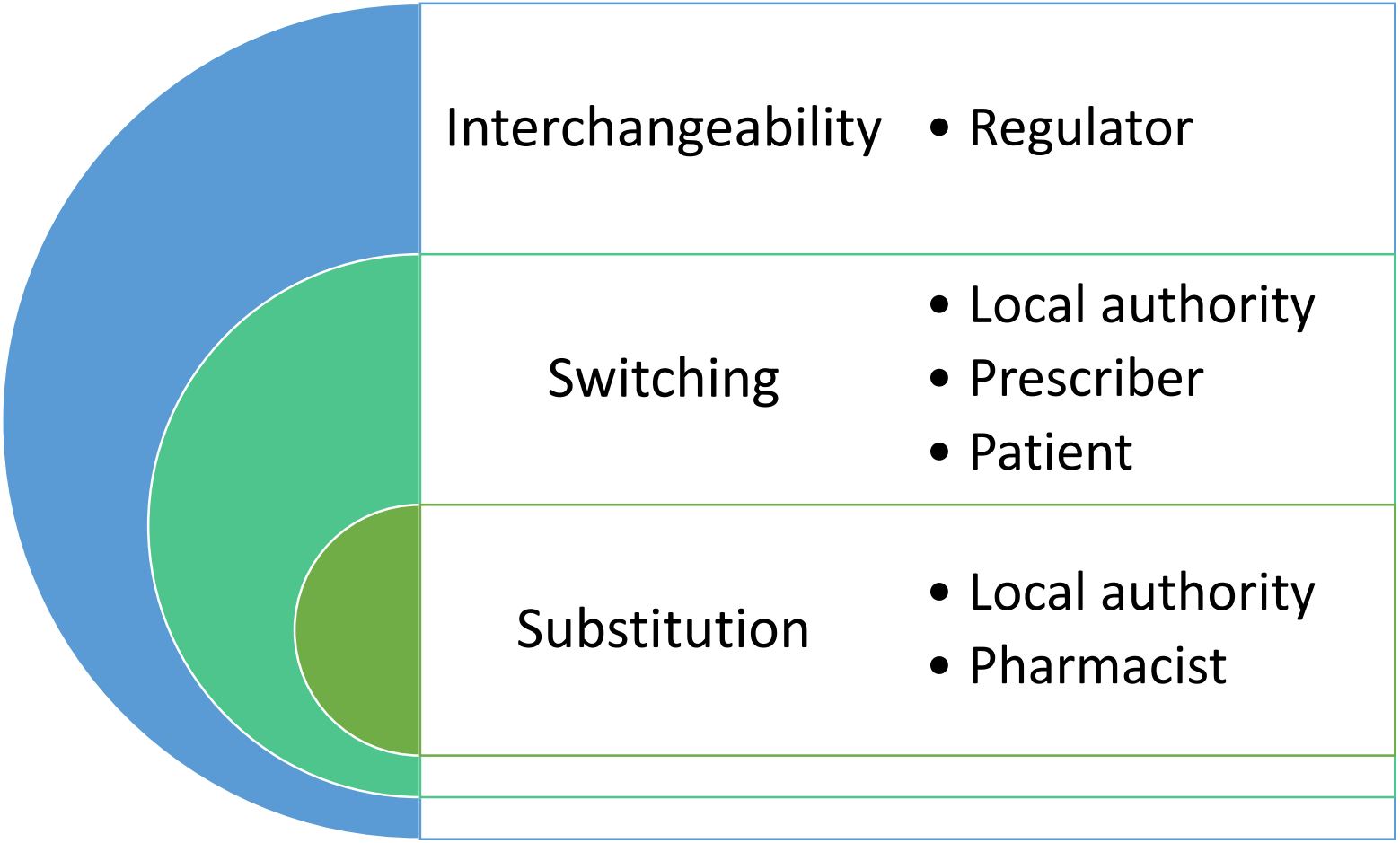
(1) Changing **from an innovator drug to a biosimilar drug** which used that **same innovator drug as its RMP** for comparability (**or vice versa**) can be accepted after physician and patient discussion.

(2) Changing **from a biosimilar drug to another same biosimilar drug** from a different manufacturer can be accepted **after physician and patient discussion** only if they both used **the same RMP** for comparability purposes."

(3) Pharmacists **cannot substitute** biosimilars without […] consultations with **treating physicians**

- Saudi Food and Drug Authority-

LEVELS


Interchangeability
• Regulator
Switching
• Local authority
• Prescriber
• Patient
Substitution
• Local authority
• Pharmacist

Biosimilar Celebrities