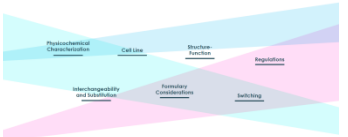


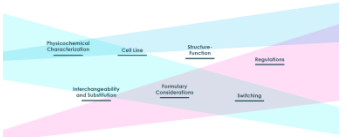
Professor Aws Alshamsan, BPharm, RPh, PhD, Saudi Arabia

- 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

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

20 November 2017, Holiday Inn Izdihar Riyadh, Saudi Arabia



Interchangeability for biosimilars: considerations and concerns

Professor Aws Alshamsan, BPharm, RPh, 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

College of Pharmacy

INTERCHANGEABILITY FOR BIOSIMILARS

Considerations and Concerns

AWS ALSHAMSAN B.Pharm, RPh, PhD
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Saudi Pharmaceutical Society
الجمعية الصيدلية السعودية

INTERCHANGEABILITY

"The possibility of **exchanging one medicine for another medicine** that is expected to achieve the same clinical effect. This could mean replacing a reference product with a biosimilar (**or vice versa**) or **replacing one biosimilar with another**."

- European Medicines Agency -

"Section 351(i) of the PHS Act states that the term *interchangeable* or *interchangeability*, in reference to a biological product that is shown to meet the standards described in section 351(k)(4) of the PHS Act, means that 'the biological product may be **substituted** for the reference product **without the intervention** of the health care provider **who prescribed** the reference product.'"

- US Food and Drug Administration -

"It is generally viewed that **changing or substituting** a protein medicine produced by rDNA technology, whether original (innovator) or a biosimilar, is **the decision of the physician and the patient** when the **treating doctor explains to the stakeholder** the possibility of such substitution and examine the risks versus benefits. **Physicians and pharmacist should discuss** the issue before talking to the patient to prevent inappropriate substitution."

- Saudi Food and Drug Authority -

SWITCHING

"When the **prescriber decides** to exchange one medicine for another medicine with the same therapeutic intent."

- European Medicines Agency -

"For a biological product that is **administered more than once** to an individual, the risk in terms of **safety or diminished efficacy** of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product **without such alternation or switch**."

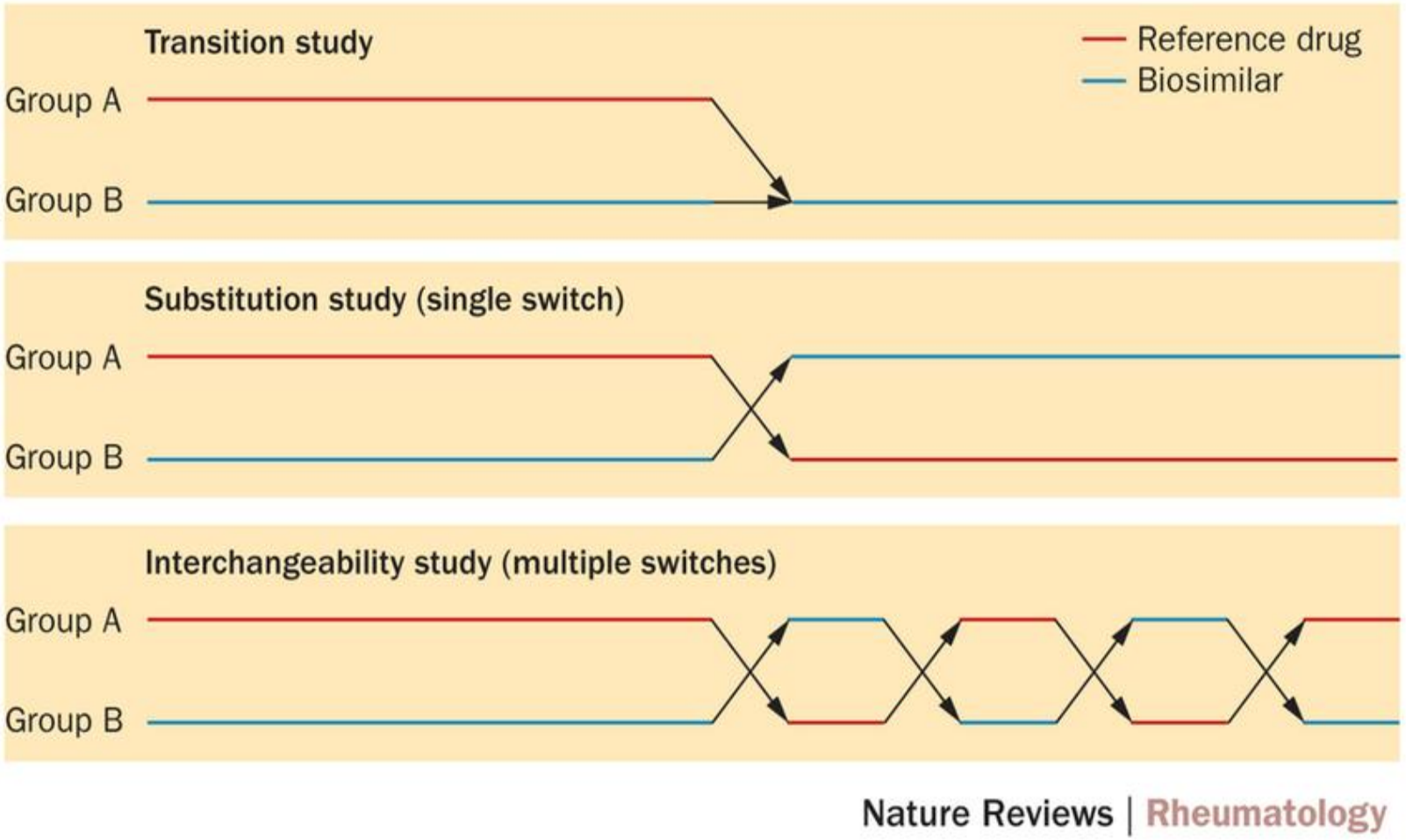
- US Food and Drug Administration -

"(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."

- Saudi Food and Drug Authority -

SWITCHING



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

SUBSTITUTION

"The practice of dispensing one medicine instead of another equivalent and interchangeable medicine at pharmacy level **without consulting the prescriber**."

- European Medicines Agency -

"An interchangeable product may be **substituted** for the reference product **without the intervention** of the health care provider **who prescribed** the reference product."

- US Food and Drug Administration -

"Pharmacists **cannot substitute** biosimilars without […] consultations with **treating physicians**."

- Saudi Food and Drug Authority -

COMPLEXITY

Host cell type

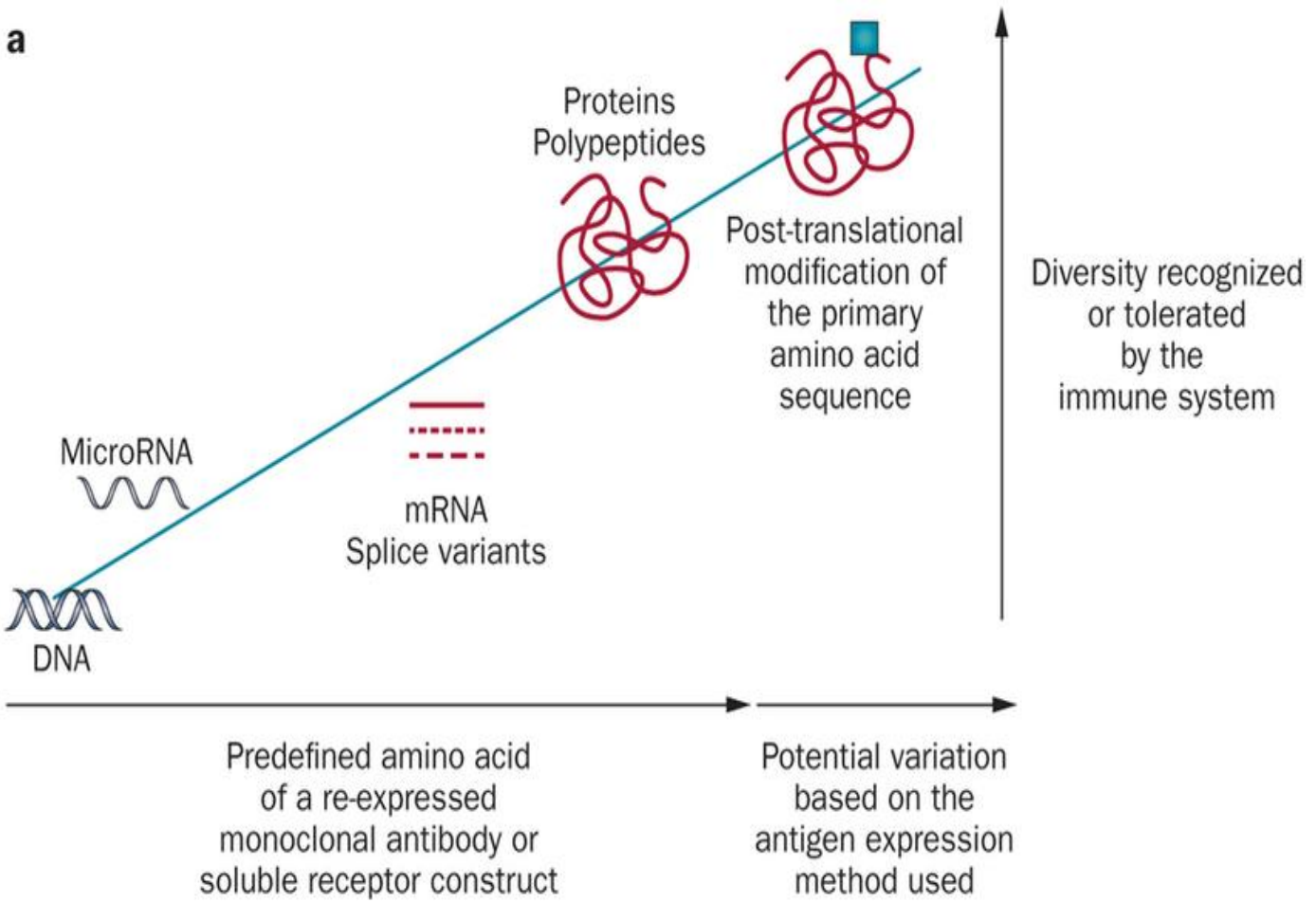
Process applied

Material used

Separation and purification

Impurities

Stability



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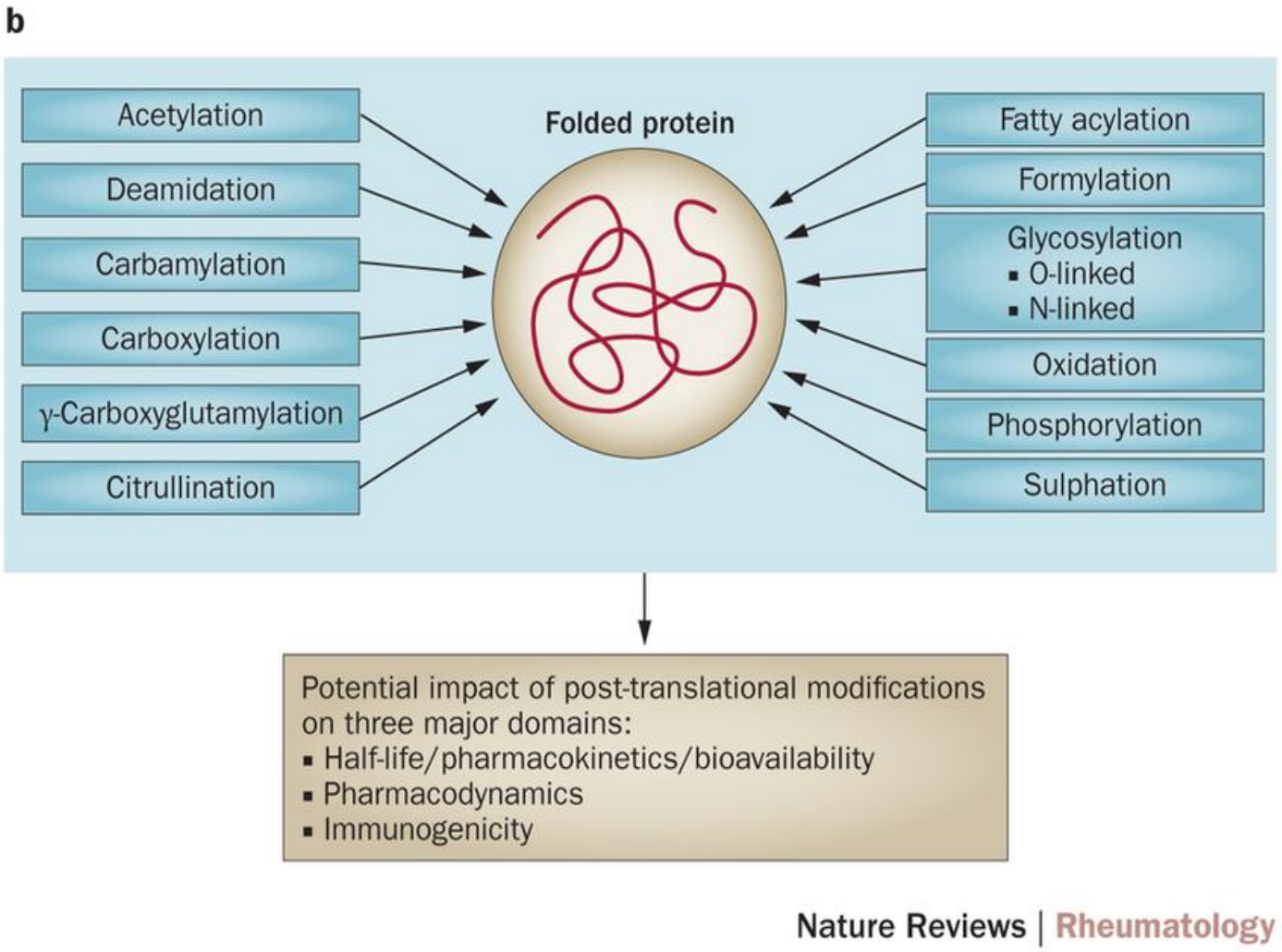
COMPLEXITY



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PHARMACIST PRACTICE

"The decision on whether to allow interchangeable use and substitution of the reference biological medicine and the biosimilar is **taken at national level**."

- European Medicines Agency -

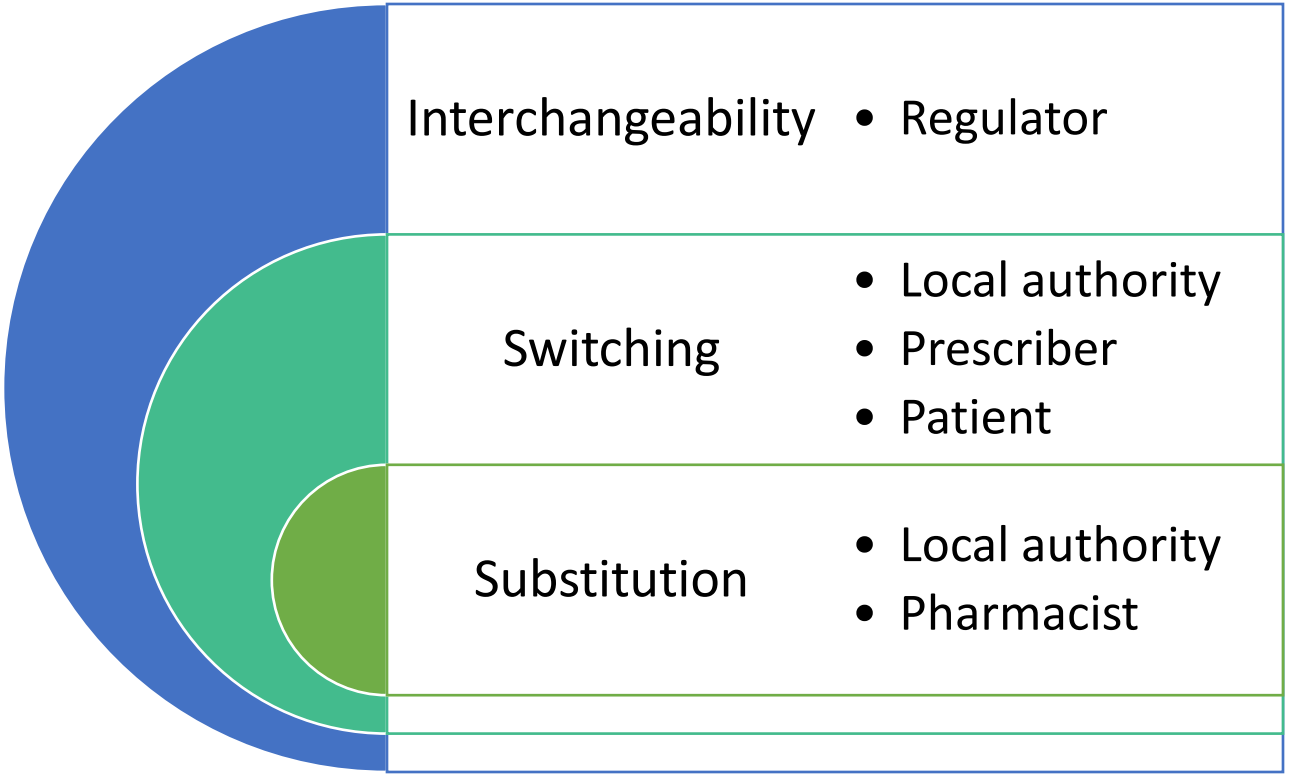
"Once interchangeable biological products are available in the United States, some **states may permit** an **interchangeable product to be substituted** for the reference product – a practice commonly called pharmacy-level substitution.."

- US Food and Drug Administration -

"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

The biosimilar product has been determined by the United States Food and Drug Administration to be **interchangeable** with the prescribed product **for the specified indicated use**.

The prescribing practitioner **does not specifically indicate** in the practitioner's own handwriting "brand medically necessary" on a written prescription, does not expressly indicate that an oral prescription is to be dispensed as communicated, or has not taken a specific overt action to include the "brand medically necessary“ language with an electronically transmitted prescription.

The **pharmacist informs the individual** receiving the biological product that the biological product may be substituted with a biosimilar product and that the **individual has a right to refuse** the biosimilar product selected by the pharmacist and the individual chooses not to refuse.

The **pharmacist notifies the prescribing practitioner** in writing or via electronic transmission within 24 hours of the substitution.

Physicians have the **authority to specify "do not substitute"** for biological products and that specification overrides any policy – e.g. by payers or state law – that would have substitution be the standard or default practice.

Physicians and pharmacists should **work collaboratively** to ensure that the treating physician is aware of the exact biologic – by manufacturer – given to a patient in order to facilitate patient care and accurate attribution of any adverse events that may occurs.

The **timing of the notification** process must not impose an undue burden on the pharmacist and **need not be in advance of a substitution** being made but must be timely enough to facilitate accurate record keeping and attribution of adverse events by the physician.

CONCERNS

"**Experience** with manufacturing changes of biological medicines suggests that switching from pre- to post-manufacturing change versions will **very rarely trigger adverse reactions**."

"**There are no studies** on sources of variance in comparative studies investigating biosimilars and their reference products. However, it seems likely that, as for generics, **intra-subject variability** rather than product-related variation plays a crucial and decisive role in the variation of drug exposure."

"Biosimilars are **highly similar** to their reference products, and the active substance of most currently approved biosimilars **mimic closely or at least partly endogenous substances of the body to which there is an immunological tolerance**. Therefore, **it is not unexpected** that the licensed biosimilars were shown to exhibit immunogenicity comparable with their reference products."

"The **observations** that switching between products containing structurally different active substances, even between high-risk products, or in ADA-positive/susceptible patients did not enhance immune responses suggest that the risk of exaggerated immune reactions as a result of switching between a biosimilar and its reference products is **substantially overrated**."

Interchangeability of Biosimilars: A European Perspective. Pekka Kurki, Leon van Aerts, Elena Wolff-Holz, Thijs Giezen, Venke Skibeli, Martina Weise. BioDrugs. 2017 Jan 24

CHALLENGES

- Extrapolation of indications to diseases only studied for the reference drug
- Ethical and medical-legal aspects
- Strategies for adequate pharmacovigilance to monitor biosimilars after marketing approval
- Effective pricing policy that distinguish high-quality products

جامعة الملك سعود
King Saud University

Thank you!