ICMRA statement about confidence in biosimilar products (for healthcare professionals)

Purpose:

ICMRA present this statement on biosimilars to provide assurance on the robust regulatory processes for the approval and monitoring of these medicines, and to highlight the benefits they can provide for patients and healthcare systems in terms of increased treatment alternatives, access and cost competitiveness.

ICMRA brings together the heads of 29 medicines regulatory authorities[i] from every region in the world, with the WHO as an observer. Medicines regulators recognize the important role we play in facilitating the provision of access to safe, effective, high-quality products that are essential to human health and well-being. This includes advancing the biology needed to set standards and inform decision-making, as well as maintaining efficient regulatory processes that support the development and delivery of innovative medicinal products while ensuring the benefits of these products outweigh the risks.

Statement:

Biosimilars[1] are biological medicines of proven pharmaceutical quality. Biosimilars are manufactured to the same stringent regulatory standards as other biological medicines. Comprehensive pharmaceutical quality information (chemistry, manufacturing and controls) is required.

Biosimilars are approved after rigorous scientific evaluation by regulatory authorities. The concept of biosimilar development and approval is different from originator biologicals, in that the purpose is to demonstrate that the biosimilar is highly similar to the originator medicine mainly by extensive comparative laboratory testing, and not to re-establish efficacy and safety, as these have already been established for the originator.

As part of the assessment process, biosimilars must demonstrate that they are highly similar to an already approved originator biological medicine[2]. A biosimilar must be shown to be highly similar to the originator in quality and biological activity, with no clinically meaningful differences in efficacy, safety and immunogenicity. The foundation of evidence for similarity is provided by the extensive laboratory comparability studies between the biosimilar and the originator, including physicochemical and structural properties, biological activity and functional *in vitro* studies. Biologicals are often large and complex molecular structures; therefore, comparability studies use highly sensitive state-of-the-art analytical technology that allows robust and extensive examination and comparison of the biosimilar and originator molecules. These comparability studies are required in addition to the comprehensive pharmaceutical quality information.

A full clinical development programme is not necessary when extensive laboratory testing has demonstrated that the biosimilar is highly similar to the originator. The purpose of clinical studies in a biosimilar development programme is to help address remaining questions that require human data to evaluate, such as pharmacokinetics. In addition, a comparative efficacy study is commonly used to confirm that there are no clinically meaningful differences. Once a biosimilar is demonstrated to be highly similar to the originator with no clinically meaningful differences, it can be approved for the same indications as the originator on the basis of the established efficacy and safety of the originator in each indication. This avoids the unnecessary repetition of clinical trials.

Biosimilars have been used safely for many years. The safety of all medicines on the market, including biosimilars, is monitored to protect patients (pharmacovigilance). Regulators have not identified any relevant differences in the type, severity or frequency of side effects between biosimilars and their respective originators.

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1 Biosimilars are also called biosimilar products, biosimilar medicines, similar biological medicinal products or similar biotherapeutic products (SBPs).

2 Originator (original brand product or medicine) is also referred to as a reference product or reference medicine.

Globally, regulators have confidence in the rigour of the scientific review and approval process for biosimilars. Although regulatory pathways for biosimilar licensing differ across countries, the various pathways are robust, as demonstrated by up to 13 years of use throughout the world. Many biosimilars are approved for a wide range of indications, including somatropin, epoetin, filgrastim, pegfilgrastim, follitropin alfa, insulin glargine and insulin lispro, infliximab, etanercept, rituximab, trastuzumab, adalimumab, bevacizumab (not all biosimilars are available in all markets).

Biosimilars enhance competition among biological medicines, providing more treatment alternatives for patients and clinicians. The increased market competition has the potential to reduce pricing of biologicals, enabling improved access to biological medicines for a larger number of patients.

Biosimilars have been increasingly used in clinical practice in most countries. Many regulatory authorities, healthcare providers and clinician associations accept that there are no clinically meaningful differences between biosimilars and originators and that biosimilars are safe and effective treatment options that can be equally prescribed to patients. In particular, changing between originator and biosimilar (i.e., a prescribing healthcare professional transferring a patient on treatment from one medicine to another) is an accepted clinical practice in many countries. Some countries have regulatory frameworks that permit substitution at the pharmacy level (i.e., without intervention by the prescriber) under certain conditions.

NOTES:

The legal and regulatory framework applicable in each country governs biosimilars in that country. However, legal and regulatory differences across countries or regions do not affect the general principles expressed in this statement.

As biosimilars emerge onto the market, healthcare professionals should be aware that advertising and other messaging from industry must respect the laws applicable in each country and should refrain from misrepresenting the quality, efficacy and safety of biosimilars that have undergone rigorous review by regulatory authorities.

There are copy products in some countries that have not been approved on the basis of a robust biosimilar regulatory pathway, as described above. It should be emphasised that these 'copy products' or 'non-comparable biologics' have not gone through extensive comparability studies and cannot be considered as biosimilars. Any questions should be addressed to the National Regulatory Authority for the relevant country.

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[i] ICMRA is an international executive-level coalition of key regulators from every region in the world. It provides a global strategic focus for medicines regulators and gives strategic leadership on shared regulatory issues and challenges. Priorities include coordinated response to crisis situations. Members of the ICMRA include: Therapeutic Goods Administration (TGA), Australia; National Health Surveillance (ANVISA), Brazil; Health Products and Food Branch, Health Canada (HPFB-HC), Canada; China National Medical Products Administration (NMPA), China; European Medicines Agency (EMA) and European Commission - Directorate General for Health and Food Safety (DG - SANTE), European Union; French National Agency for Medicines and Health Products Safety (ANSM), France; Paul-Ehrlich-Institute (PEI), Germany; Health Product Regulatory Authority (HPRA), Ireland; Italian Medicines Agency (AIFA), Italy; Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medical Devices Agency (PMDA), Japan; Ministry of Food and Drug Safety (MFDS), Korea; Federal Commission for the Protection against Sanitary Risks (COFEPRIS), Mexico; Medicines Evaluation Board (MEB), Netherlands; Medsafe, Clinical Leadership, Protection & Regulation, Ministry of Health, New Zealand; National Agency for Food Drug Administration and Control (NAFDAC), Nigeria; Health Sciences Authority (HSA), Singapore; Medicines Control Council (MCC), South Africa; Medical Products Agency, Sweden; Swissmedic, Switzerland; Medicines and Healthcare Products Regulatory Agency (MHRA), United Kingdom; Food and Drug Administration (FDA), United States and the World Health Organization as an observer. Associate members include Austrian Medicines and Medical Devices Agency (AGES), Danish Medicines Agency, Israel Office of Medical Technology, Health Information and Research (MTHIR), Poland Office of Registration of Medicinal Products and Biocidal Products (URPLWMiPB), Russia Roszdravnadzor and Spain Agencia Española de Medicametos y Productos Sanitarios (AEMPS).