

BALANCING ACCESS TO BIOLOGICS WITH PATIENT SAFETY AND WELL-BEING

Biotechnology has enabled the discovery of treatments for some of the most serious diseases known to man. Worldwide, the lives of over 325 million people have been transformed by the availability of a growing number of biologic medicines.¹ It is important to provide access for as many patients as possible to the potentially life-changing benefits of biologics; biosimilars can play a part in meeting this goal. An equally and perhaps more important consideration is to protect patient safety and welfare in all stages of the development, approval, and monitoring of originator biologics and biosimilars.

IPHA supports bringing new technology and science to the market and believes that biosimilars have a meaningful role to play in healthcare.

Availability of safe, quality and effective biologic medicines for patients is critical. This should be done while ensuring an environment that maintains adequate incentives for research and development related to the prevention and treatment of diseases that impact patients and society.

It is important for regulators, payers, healthcare professionals, pharmacists, patients and society to understand that a biosimilar is not a direct replica of the originator biologic and therefore cannot be treated like a generic.

IMPORTANT CONSIDERATIONS FOR BIOSIMILARS

SAFETY: All biologics, both originator biologics and biosimilars, like small molecule medicines, are required to track safety throughout the development process and routinely after approval. Tracking possible adverse drug reactions (ADRs) is done, in conjunction with regulatory authorities, through a process called pharmacovigilance. If biosimilars have the same nonproprietary name (INN) as the originator,

it could cause confusion in tracking ADRs for both the originator and its biosimilar.^{2,3}

Therefore successful pharmacovigilance and efficient signal detection, traceability of individual biological medicines (including biosimilars) is essential. The brand name of the medicinal product and the batch number must be specified.²

INTERCHANGEABILITY: In Ireland, interchangeability is the evaluation by the Irish Medicines Board (IMB) of products which have the same qualitative and quantitative composition, same pharmaceutical form and same route of administration, which may be substituted by a pharmacist according to the Health Act 2013; the interchanging of biologic medicines is prohibited under this Act.⁴

Biosimilars are not the same as generics. They are similar but not identical versions of their reference biologic. Unlike chemically-synthesised small molecule generic medicines, it is impossible for biosimilars to be exact copies of the reference biologic medicine.^{5,6,7}

SUBSTITUTION: Substitution occurs when a drug is substituted for another drug without the prescribing physician's knowledge. In Ireland, the *Health (Pricing and Supply of Medical Goods) Act 2013* prohibits the interchanging and therefore the substitution of biologic medicines.⁴

BALANCING ACCESS TO BIOLOGICS WITH PATIENT SAFETY AND WELL-BEING

IPHA supports bringing new technology and science to the market and believes that biosimilars have a vital role to play in healthcare. Availability of safe, effective and quality biotherapeutic products for patients is critical.

Biologic medicines are produced using a complex manufacturing process that takes several months from start to finish.^{1,5} In fact, the manufacturing of a biologic medicine requires twenty times as many quality checks as small molecule medicines.⁸ It is important for regulators, payers, healthcare professionals, pharmacists, patients and other stakeholders to understand that a biosimilar is not a direct replica of the originator product. It cannot be treated like a generic and under the Health Act 2013, cannot be interchanged or substituted.

1. BIOSIMILARS ARE SIMILAR BUT NOT IDENTICAL VERSIONS OF REFERENCE BIOLOGIC MEDICINES

Biosimilars are not the same as generics. They are similar but not identical versions of their reference biologic. Unlike chemically-synthesised small molecule generic medicines, it is impossible for biosimilars to be exact copies of the reference biologic medicine.^{5,6,7}

Biologics are large, complex molecules (as illustrated in Figure 1) that are grown in living cells.

Biologic medicines are produced by living organisms (such as cells, yeast and bacteria) through highly complex processes.^{1,5} Most biologics are proteins and are usually injected or infused. Small molecule medicines are made following an exact chemical formula and are usually taken as a tablet.^{1,8} The manufacturing processes and host cell lines of a biologic are proprietary and unique to a particular company and can't be duplicated.⁵

The characteristics of biologic medicines are largely dependent on the manufacturing process which is a highly complex multi-stage development process.

Due to the complex processes involved in the production of biologics, it is not possible to create an exact copy of the originator biologic.^{5,9}

As these medicines are created from living cell systems they are subject to micro-heterogeneity and consequently small changes in the production process can lead to changes in the final product which can significantly affect the way a biologic works.^{6,8,9}

EMA'S CHMP GUIDANCE*

Guideline on similar biological medicinal products (CHMP/437/04)¹⁰

'By definition, similar biological medicinal products are not generic medicinal products, since it could be expected that there may be subtle differences between similar biological medicinal products from different manufacturers or compared with reference products, which may not be fully apparent until greater experience in their use has been established.'

*Note: At the time of print the current EMA Guidance is under review and revised guidelines are expected.

2. BIOLOGICS MUST NOT BE SUBSTITUTED BECAUSE THEY ARE NOT DEEMED INTERCHANGEABLE: ONLY THE TREATING PHYSICIAN CAN DECIDE ON THE MOST APPROPRIATE TREATMENT FOR A PATIENT.

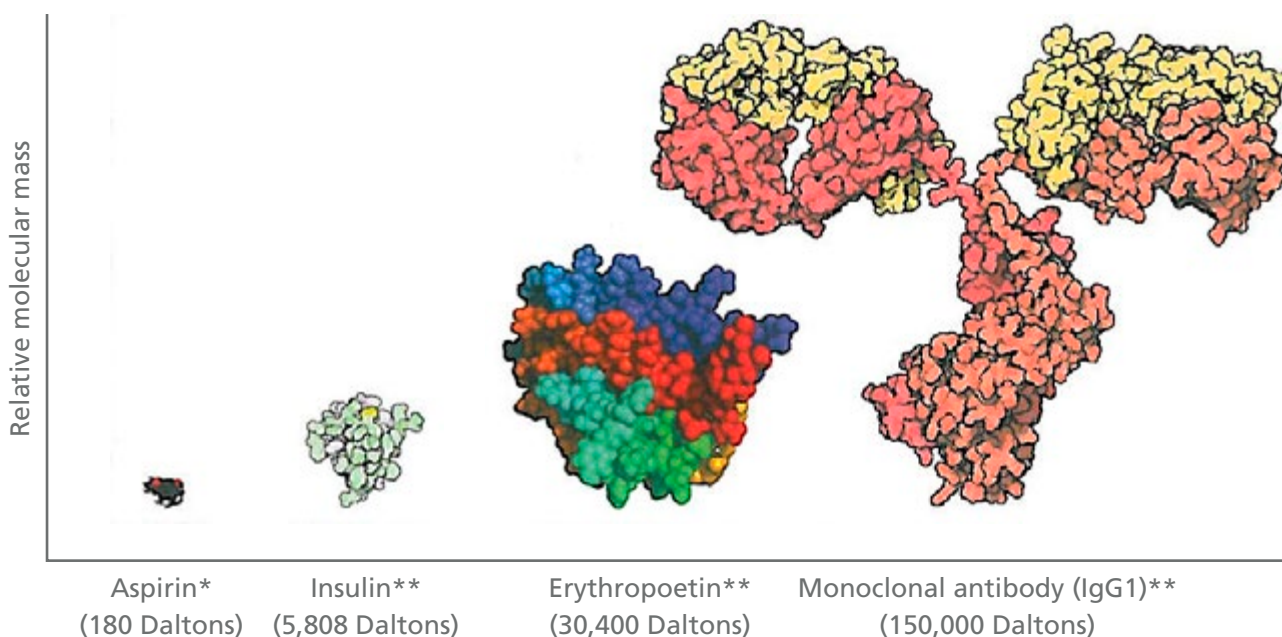
IPHA welcomes and supports the *Health (Pricing and Supply of Medical Goods) Act 2013* which preserves the safety of patients by prohibiting the interchanging and therefore the substitution of biologic medicines.⁴ The Act charges the Irish Medicines Board (IMB) (to be renamed The Health Products Regulatory Authority) to establish and maintain a list of interchangeable medicinal products whereby all of the medicinal products falling within a group will be interchangeable with each other for prescription purposes. The criteria for interchangeable medicines are outlined in the Act.

In this Act biologic and biosimilar medicines **do not meet the criteria and are not interchangeable and consequently cannot be substituted.**

As biosimilars are not deemed interchangeable with the reference biologic under the Health (Pricing and Supply of Medical Goods) Act 2013, the risks of switching a stable, well controlled patient, need very careful consideration.

This should only happen by agreement between the treating physician and the patient, where robust pharmacovigilance data collection and track and trace systems are in place to ensure safe use within the Irish Healthcare System.

Figure 1: Relative sizes and complexity of small molecule and biologic medicines⁶



Relative molecular masses, expressed in Daltons, are shown in parentheses (A Dalton is the standard unit that is used for indicating mass on an atomic or molecular scale)

* Small molecule medicine

** Biologic medicines

3. THE PRESCRIPTION FOR A BIOLOGIC OR A BIOSIMILAR SHOULD BE WRITTEN BY BRAND AND INTERNATIONAL NONPROPRIETARY NAME (INN)

As biosimilars are considered to be similar but not identical to the reference biological product, all biologics or biosimilars need to be identifiable throughout the prescribing, dispensing and pharmacovigilance processes by a distinct naming convention. IPHA welcomes the EU Pharmacovigilance legislation^{11,12} which supports and recognises the importance of effective pharmacovigilance and imposes an obligation for healthcare professionals to record ADRs for biologic medicines by brand name and batch number.

IPHA recognises significant challenges with traceability. An appropriate mechanism from the point of prescription through to the reporting of an ADR needs to be put in place.

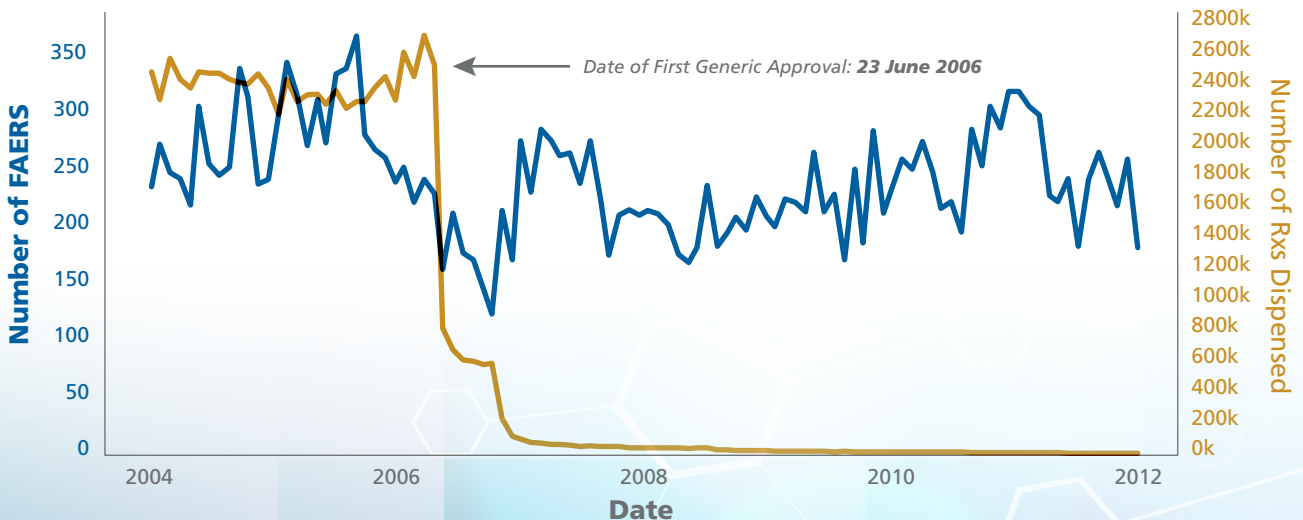
It is important that healthcare professionals be encouraged to use a brand name rather than rely solely on the non-proprietary name when prescribing and reporting ADRs.

This will ensure that any ADRs reported are properly assigned to the correct medicine suspected of having caused the reaction, especially because of the potential risk of adverse immunogenic reactions for biological products in the post-approval period. Challenges with traceability already exist with small molecule medicines as has been described for simvastatin, as seen in figure 2 below. An analysis of ADRs in the US demonstrated that despite loss of intellectual property rights and a substantial decrease in overall sales, ADR data is still attributed disproportionately to the originator medicine after generic introduction.²

In addition, IPHA looks forward to the implementation of the European Cross-border healthcare directive¹³ which specifies the need to indicate the brand name if the prescribed product is a biologic medicine. IPHA therefore recommends that biologic or biosimilar medicines be prescribed by the brand name, INN and other relevant identifiers that may be proposed by the WHO.^{14,15}

Figure 2: Zocor (simvastatin) (oral tablet)

Monthly Number of ADRs for Zocor (simvastatin) submitted to FDA Adverse Event Reporting System (FAERS) between 2004 and 2012 v Monthly Number of Prescriptions Dispensed²



4. EXTRAPOLATION OF INDICATIONS MUST BE SCIENTIFICALLY JUSTIFIED ON A CASE BY CASE BASIS

Where a biosimilar meets the requirements for licensure for one indication of use that has been approved for the originator biologic, it cannot be assumed that it is appropriate to automatically extrapolate clinical data to support a different condition of use. Any extrapolation of clinical data to additional indications in the originator biologic requires sound scientific justification.¹⁵⁻¹⁷

This justification requires adequate consideration of:

1. Whether the mechanisms of action are the same and are sufficiently understood
2. Whether comparative clinical testing has been done in the setting(s) most sensitive to potential differences in safety, efficacy and immunogenicity

3. The differences in benefit-risk balance between studied and unstudied indications
4. Differences in the patient populations within and between indications.

The complex issues surrounding extrapolation of indications for biosimilar medicines affirm that the biosimilarity exercise and the regulatory review of a biosimilar application cannot be reduced to a technical, analytical exercise – in-depth understanding and consideration of the above principles, and how they apply to a particular product, is needed to warrant extrapolation. Potential risk to patient safety must be considered when evaluating the justification for extrapolation.^{8,18-21}

Biosimilar candidates should undergo full length clinical trials of the most sensitive patient population.

FIGURE 3: SUMMARY OF PATIENT NUMBERS ENROLLED IN BIOSIMILAR INFLIXIMAB CT-P13 (INFLECTRA/REMSIMA) RANDOMISED CLINICAL TRIALS (RCT) COMPARED TO REMICADE INFLIXIMAB²³⁻²⁵

# PATIENTS IN PIVOTAL RCT TRIALS AND YEAR OF APPROVAL FOR EACH INDICATION				
INDICATION	REMICADE		INFLECTRA/REMSIMA	
	#	Approved	#	Approved
<i>Crohn's Disease</i>	1589	1999	Extrapolated	2013
<i>Rheumatoid Arthritis</i>	2516	2000	600	2013
<i>Ankylosing Spondylitis</i>	349	2003	250	2013
<i>PsA</i>	304	2004	Extrapolated	2013
<i>Psoriasis</i>	627	2005	Extrapolated	2013
<i>Ulcerative Colitis</i>	728	2006	Extrapolated	2013
<i>Paed. Crohn's Disease</i>	122	2007	Extrapolated	2013
<i>Paed. Ulcerative Colitis</i>	60	2012	Extrapolated	2013
Total	6295		850	

The clinical trials performed with this example of a Biosimilar Medicine are indicative of clinical requirements for the regulatory approval pathway for Biosimilar Medicines. Please refer to the Q&A section for fuller details on the regulatory approval process.

5. CLINICAL AND PRECLINICAL INFORMATION GENERATED ON BOTH THE BIOSIMILAR AND THE REFERENCE BIOLOGIC SHOULD BE LISTED AND THE SOURCE IDENTIFIED IN THE SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

In order to increase transparency for the prescriber, it is imperative that the SmPC provides easily accessible preclinical and clinical information generated on both the biosimilar and the reference biologic, and identifies the source of this information in terms of what pertains to the original reference biologic, and what relates to information generated on the biosimilar and submitted within the Marketing Authorisation Application.

Currently, regulatory working policy is to duplicate the information on the SmPC for a reference product within the biosimilar SmPC and reserve any specific information on the biosimilar for inclusion in the EPAR only.²⁶

However, this is not such a readily accessible source of information and it would be preferable if the headline data and source were listed in the SmPC allowing the prescriber to access the further detail in the EPAR if required. IPHA is supportive of the EBE position paper on this topic.²⁶

It is imperative that the SmPC highlights that a biosimilar is not the same as the originator biologic. The SmPC should clearly identify what clinical data has been generated in each licensed indication.

6. APPROPRIATE COMPREHENSIVE RISK MANAGEMENT PLANS ARE REQUIRED TO ENSURE POST-APPROVAL SAFETY AND EFFICACY MONITORING

In the European Union (EU), all medicines must have submitted a Risk Management Plan (RMP) to the EMA at the time of application for a marketing authorisation. RMPs are risk mitigation tools for managing known or potential risks associated with a medicine. This is particularly relevant as rare events such as progressive multifocal leukoencephalopathy are unlikely to be detected in a pre-authorisation setting. Therefore, applicants need to propose pharmacovigilance and risk management activities for the post-authorisation phase.¹⁰

Biosimilar RMPs will also be tailored to reflect the needs for further monitoring and review.

IPHA recommends that RMPs consider the potential for greater engagement with Healthcare Professionals on the reporting requirements for any ADRs (by brand name, INN and batch number).

Biologic medicines approved in the EU after 1st January 2011 require additional monitoring for safety and efficacy (denoted by the inverted black triangle symbol ▼). This actively encourages healthcare professionals and patients to report any suspected ADRs observed with the medicine.

▼ What does the black triangle mean?

All medicines are carefully monitored after they are placed on the EU market. If a medicine is labelled with the black triangle, this means that it is being monitored even more intensively than other medicines. This is generally because there is less information available on it than on other medicines, for example because it is new to the market or there is limited data on its long-term use. It does not mean that the medicine is unsafe.

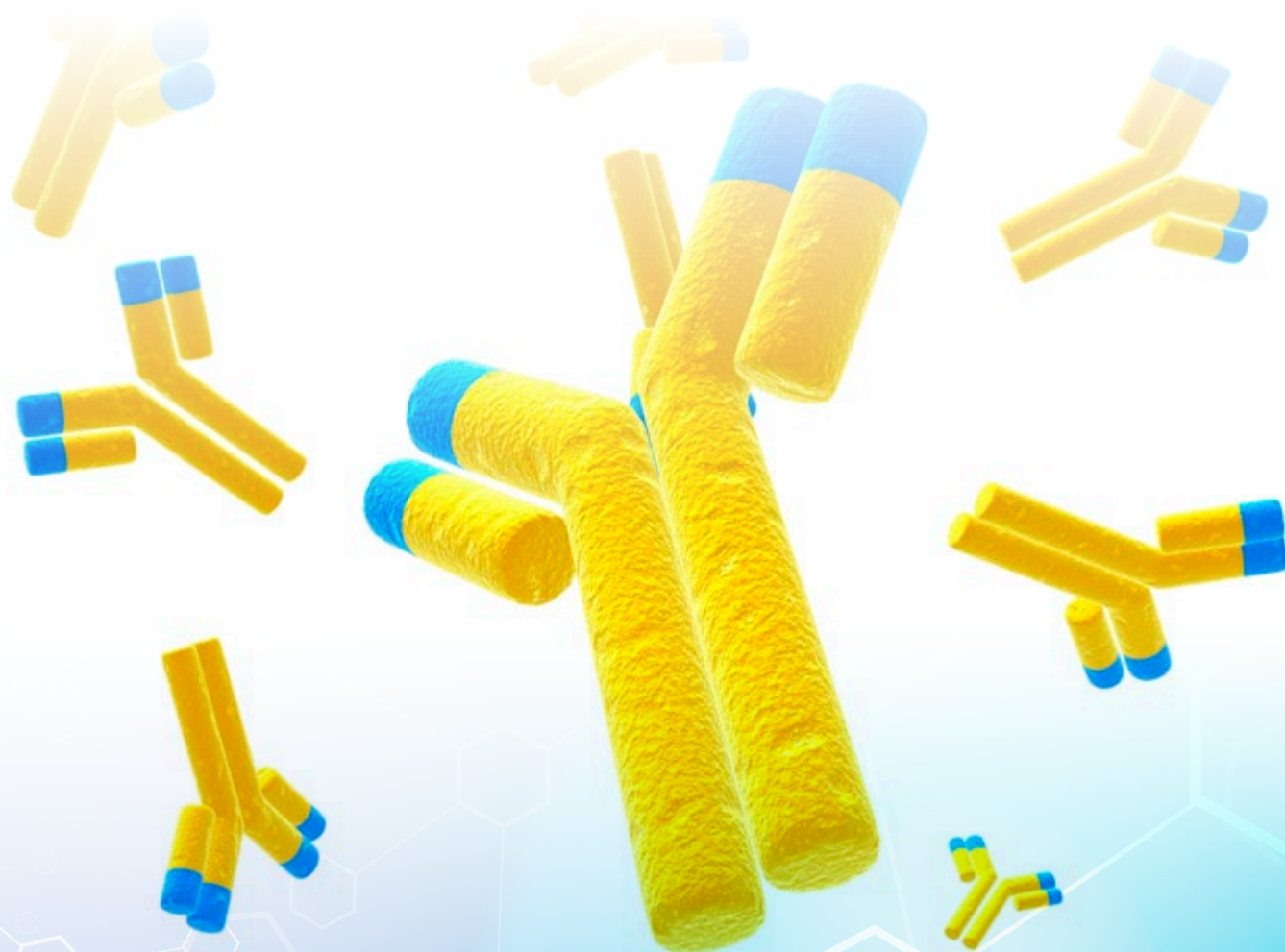
7. CURRENT POLICY AND MARKET MECHANISMS SHOULD BE REVISED FOR BIOSIMILARS

Generic medicines are not subject to comparable levels of pricing & reimbursement assessment to that experienced by originator medicines. The prevailing assumption is that, as exact copies of existing proprietary medicines available at a lower cost, they are automatically cost effective. This cost effectiveness is adjudged against cost minimisation criteria from a payer perspective.

Biosimilars, however, are not identical to originator biologics and therefore pharmacoeconomic assessment requires broader scrutiny, beyond the cost of the medicine.

As biosimilars are not deemed interchangeable with the reference biologic under the Health (Pricing and Supply of Medical Goods) Act 2013, the risks of switching a stable, well controlled patient, need very careful consideration. This should only happen by agreement between the treating physician and the patient, where robust pharmacovigilance data collection and track and trace systems are in place to ensure safe use within the Irish Healthcare System.

Any process for pharmacoeconomic assessment of biosimilars needs to recognise the challenges presented due to the complexity of biologics and the further uncertainty due to extrapolation of indications where there is limited or no data.



QUESTIONS AND ANSWERS

What are biologics?

Biologics are large, complex molecules, usually proteins, that are grown in living cells. They are produced under carefully controlled and monitored conditions, with many steps to refine and produce a consistent medicine. Biologics are almost always given by injection or infusion.^{1,27}

What are some examples of biologics?

Types of biologics include:²⁸

- Vaccines
- Insulin
- Fusion receptors
- Growth hormones
- Colony Stimulating Factors
- Erythropoietin
- Monoclonal antibodies

What are biosimilars?

Biosimilars are biologics developed to be similar to an already licensed biologic, known as the originator or reference biologic upon patent expiry. As the name suggests, biosimilars are similar to the originator biologic, but **not the same**.^{7,8,10}

Are biosimilars the same as generics?

No. Generics have active ingredients that are identical to the originator medicine. **Biosimilars are not generic originator biologic medicines because it is impossible to produce an exact copy of a biologic medicine.** Each biologic is unique because the manufacturing processes and host cell lines – that are proprietary and unique to a particular company – cannot be duplicated.^{7,8}

What are small molecule medicines?

Small molecule medicines are chemicals which are made by combining certain molecules in a defined series of chemical reactions using a formula. Because these molecules are smaller and involve fewer process steps than biologics, they are much easier to duplicate. These medicines are usually taken orally, most often in tablet form.⁸

What is substitution?

Substitution occurs when a drug is substituted for another drug without the prescribing physician's knowledge. In Ireland, the Health (Pricing and Supply of Medical Goods) Act 2013 prohibits the substitution of biologic medicines.⁴

What is interchangeability?

In Ireland, interchangeability is the evaluation by the Irish Medicines Board (IMB) of products which have the same qualitative and quantitative composition, same pharmaceutical form and same route of administration, which may be substituted by a pharmacist according to the Health Act 2013; the interchanging of biologic medicines is prohibited under this Act.⁹

Are pharmacists permitted to substitute a reference biologic medicine with a biosimilar?

No. The *Health (Pricing and Supply of Medical Goods) Act 2013* prohibits the interchanging and therefore the substitution of biologic medicines.⁴

How are biosimilars approved?

Regulatory bodies around the world agree that the process for approving generic small molecule medicines are not adequate for biosimilars. The number and size of the trials may not necessarily be the same as for the originator biologic.^{10,18,22,30,31}

The approval process for originator biologics involves several phases of controlled clinical trials, starting with animal studies and ending with large scale trials in humans, often called Phase III trials. Typically, at least two Phase III trials are required in each indication for which a biologic is approved.^{32,33}

For a biosimilar, a stepwise approach starting with characterisation of quality attributes of the product, non-clinical physio-chemical and biological characterisation studies will be conducted to investigate similarity and differences both on structural and functional grounds. Despite such significant improvements in analytical techniques, current analytical methodology may not be able to detect all relevant structural and functional differences between two proteins. Preclinical and clinical trials to assess pharmacodynamics (how the drug acts in the body) and pharmacokinetics (how the body acts on the drugs) will be conducted. The approval process for biosimilars also involves clinical trials in patients for at least one indication of the already licensed reference biologic medicine. All other indications are then considered for approval by extrapolation.^{10,18}

Additional Requirements

In addition to clinical trials, many other factors must be carefully examined to ensure efficacy and patient safety before a biosimilar medicine can be approved:³⁴

- Manufacturing process
- Host-cell expression system
- Pharmacokinetics
- Pharmacodynamics
- Immunogenicity

In order to authorise a biosimilar product and to ensure that only products considered to be of appropriate standards of quality, safety and efficacy it's important to acknowledge that the EMA requires comprehensive and justified

comparability studies between the biosimilar and the reference products in the quality, non-clinical, and clinical data. Due to the complexity and diversity of the biologic products the approval pathway of biosimilar products in the EU is based on case-by-case reviews.

What is indication extrapolation?

Indication extrapolation means that biosimilar approval may be extended to multiple indications for which the originator biologic is approved based on evidence from approval in just one indication.¹⁸

Extrapolation of indications should be scientifically justified on a case by case basis.

How long does it take to manufacture a biologic?

Biologics are produced using a complex manufacturing process that takes several months from start to finish.^{5,9} In fact, biologic manufacturing requires 20 times as many separate quality checks as small molecule medicines.³⁵

How will safety be tracked for biosimilars?

All biologic manufacturers must commit to tracking safety in order to be approved for use. This is the same for originator biologics and biosimilars.

Tracking possible Adverse Drug Reactions (ADRs) is done through a process called 'pharmacovigilance.' If biosimilars have the same INN name as the originator biologic, however, it could compromise the tracking of ADRs for both the originator biologic and its biosimilar.⁷

The European Cross-Border Healthcare Directive¹³ specifies the need to indicate the brand name if the prescribed product is a biologic medicine. Each member state has a legal obligation to ensure traceability.

What is a manufacturing change comparability?

Manufacturing change comparability is the mechanism of comparing post-change product to pre-change product where manufacturing changes are made by a single manufacturer.³⁶ Manufacturing changes are highly regulated and validated. While some of the methods of comparison may be similar, the overall requirements and goals for the biosimilar comparability exercise versus manufacturing change comparability are different.³⁷

Are the requirements for a Biosimilar to prove comparability not the same as a manufacturing change?

No. Manufacturers of biotechnological/ biologic medicines frequently make changes to manufacturing processes of medicines both during development and after approval. Reasons for such changes include improving the manufacturing process, increasing scale, improving product stability, and complying with changes in regulatory requirements. When changes are made to the manufacturing process, the manufacturer evaluates the relevant quality attributes of the medicine to demonstrate that modifications did not occur that would adversely impact the safety and efficacy of the medicine. Such an evaluation should indicate whether or not confirmatory nonclinical or clinical trials are appropriate.³⁸

The EMA is clear that the comparability exercise for a biosimilar versus the reference biologic is an additional element to the normal requirements of the quality dossier and should be dealt with separately when presenting the data.³⁷

The EMA states that the Biosimilar guidelines do not address the comparability exercise for changes introduced in the manufacturing process of a given medicine (i.e. changes during development and post-authorisation), as addressed by ICH Q5E.³⁸

Furthermore, the FDA has qualified this by stating that: *“Demonstrating that a proposed product is biosimilar to a reference product typically will be more complex than assessing the comparability of a product before and after manufacturing changes made by the same manufacturer.”* This is because a manufacturer who modifies its own manufacturing process has extensive knowledge and information about the product and the existing process, including established controls and acceptance parameters.³⁹



GLOSSARY

Active ingredient

The component of a medicine that provides medicinal value. Many medicines combine several active ingredients, and the interaction between these ingredients may be critical to the function of the medicine.

Biologic medicines

Medicines whose active ingredients are proteins or are derived from proteins (such as growth hormone, insulin, antibodies) and other substances produced by living organisms (such as cells, viruses and bacteria). They are larger and more complex than chemically synthesised medicine and their characteristics and properties are typically dependent on the manufacturing process itself.

Biosimilar

A medicine that is similar, but not identical, to an already authorised originator biologic medicine, with demonstrated similarity to the latter in terms of quality, safety and efficacy assessed through a direct (or head-to-head) comparison.

Biotechnology

The collection of processes that involves the use of biologic systems. For some industries, these processes involve the use of genetically engineered organisms.

Comparability exercise

The head-to-head comparison of a biotherapeutic product with a licensed originator medicine, with the goal to establish similarity in quality, safety, and efficacy.

Drug product

A pharmaceutical product type that contains a drug substance, generally in association with an excipient.

Drug substance

The active pharmaceutical ingredient and associated molecules that may be subsequently formulated, with excipients, to produce the drug product. It may be composed of the desired product, product-related substances, and product- and process-related impurities. It may also contain other components such as buffers.

Generic medicines

A medicine that contains an exact copy of the active pharmaceutical ingredient (API) of a reference chemically-synthesised small molecule originator medicine. Once these identical copies are proven to be bioequivalent to the originator medicine, their approval relies on the safety and efficacy of the reference medicine.

Immune response

The way in which the body recognises and defends itself from foreign substances.

Immunogenicity

The potential or ability of a substance or antigen to cause an immune reaction/response.

INN

An official international nonproprietary or generic name given to a pharmaceutical substance, as designated by the World Health Organisation (WHO).

Insulin

Human insulin is a relatively small protein; it contains 51 amino acids arranged in two chains, and is absolutely essential for the metabolism of carbohydrates.

Non-clinical evaluation

The comparing of the biosimilar and the reference biologic medicine in relevant in vitro and, if necessary, in vivo models. This step is required before proceeding to any clinical trials in humans.

Originator medicine

A novel medicine which has been licensed by the national regulatory authorities on the basis of a full registration dossier, i.e. the approved indication(s) for use were granted on the basis of full quality, safety and efficacy data.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of ADRs or any other drug-related problem.

Reference biologic medicine

The comparator for head-to-head comparability studies with the similar biotherapeutic product in order to show similarity in terms of quality, safety and efficacy. Only an originator product that was licensed on the basis of a full registration dossier can serve as a reference biologic medicine.

Similarity

The absence of a relevant difference in the parameter of interest that is studied.

Small molecule medicines

Medicines produced through a step-by-step chemical synthesis process. They are characterised by a small molecule composition and are relatively simple organic compounds containing few functional molecular groups.



SUMMARY

IPHA Position

Summary

Biosimilars are similar but not identical versions of reference biologic medicines.

By definition, biosimilars are not generic medicinal products, since it could be expected that there may be subtle differences between biosimilars from different manufacturers or compared with reference products, which may not be fully apparent until greater experience in their use has been established.

Biologics must not be substituted because they are not deemed interchangeable: only the treating physician can decide on the most appropriate treatment for a patient.

A generic small molecule medicine may be deemed interchangeable with the brand name drug it copies because its active ingredient is an exact copy. This is more complex in the case of biosimilars as the active ingredient is not an exact copy of the brand name drug and is therefore not deemed interchangeable. This is captured under the Health (Pricing and Supply of Medical Goods) Act whereby biologics and biosimilars do not satisfy the criteria for interchangeability and therefore cannot be substituted.

The prescription for a biologic or a biosimilar should be written by brand name and international non-proprietary name (INN).

It is important that healthcare professionals be encouraged to use a brand name rather than rely solely on the non-proprietary name when prescribing and reporting ADRs.

Extrapolation of indications must be scientifically justified on a case by case basis.

Where a biosimilar meets the requirements for licensure for one indication of use that has been approved for the originator medicine, it cannot be assumed that it is appropriate to automatically extrapolate clinical data to support a different condition of use. Any extrapolation of clinical data to additional indications in the originator product requires sound scientific justification.³⁶⁻³⁸

Clinical and preclinical information generated on both the biosimilar and the reference biologic should be listed and the source identified in the summary of product characteristics (SmPC)

It is imperative that the SmPC highlights that a biosimilar is not the same as the originator biologic. The SmPC should clearly identify what clinical data has been generated in each licensed indication.

Comprehensive risk management plans are required to ensure post-approval safety and efficacy monitoring.

IPHA recommends that RMPs consider the potential for greater engagement with Healthcare Professionals on the reporting requirements for any ADRs (by brand name, INN and batch number).

Current policy and market mechanisms should be revised for biosimilars.

Any process for pharmacoeconomic assessment of biosimilars needs to recognise the challenges presented due to the complexity of biologics and the further uncertainty due to extrapolation of indications where there is limited or no data.

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