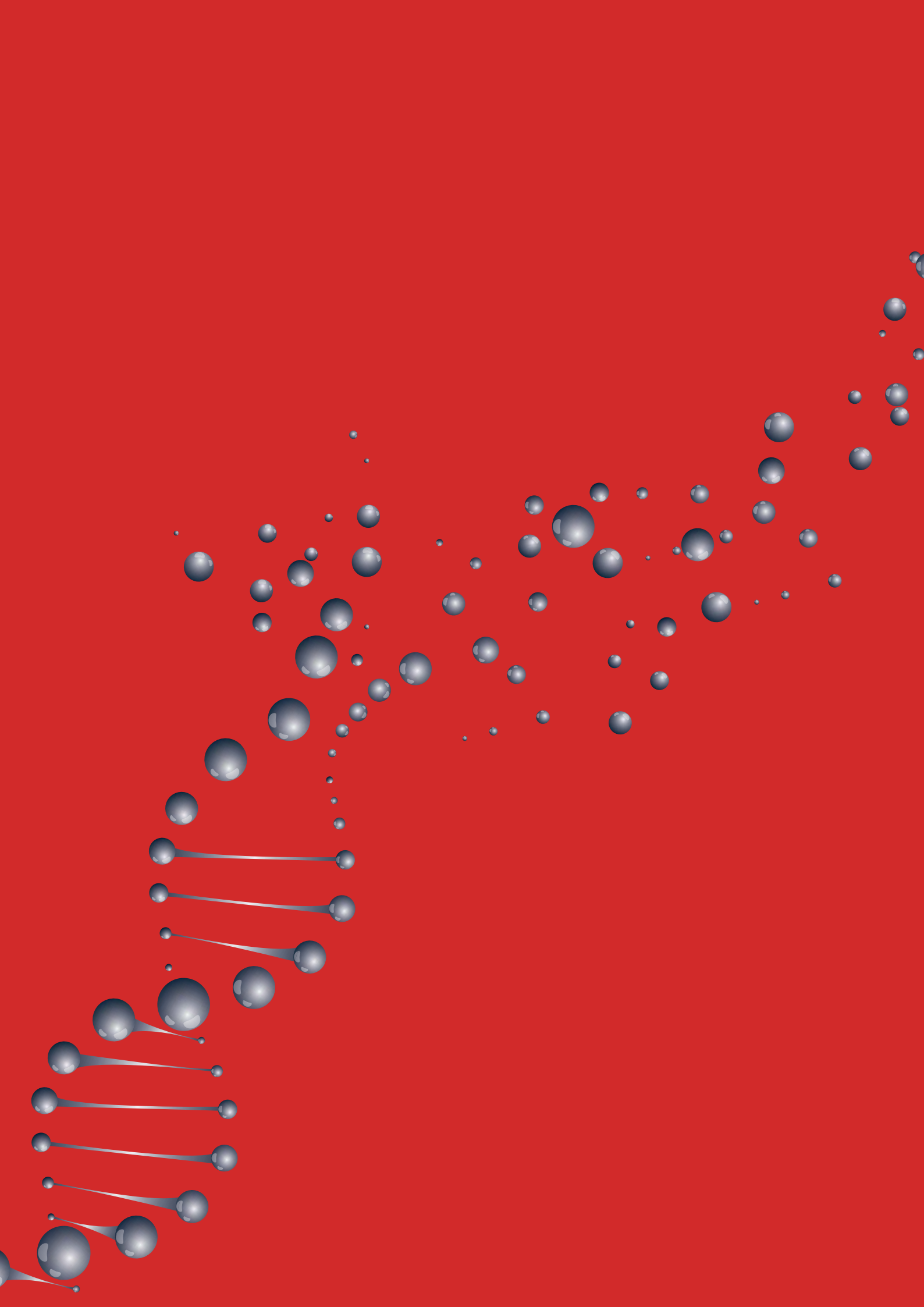
EuropaBio Guide on Biosimilars in Europe

When Science Meets Policy

EuropaBio

The European Association for Bioindustries



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Introduction

As a distinct class of new medicines, biological medicines have opened up new frontiers in the treatment of serious diseases helping patients live longer, and reducing the related social and economic burden of these diseases.

Scientific research and development has also been positively impacted as the share of biological medicines among new treatment options continues to grow. Three decades on after the first biological medicines were launched, exclusivity rights on the early biological medicines have begun to expire, and thus present an opportunity for pharmaceutical companies to consider developing biosimilar medicines of these products. Against this background, and given biosimilars' unique characteristics in comparison to chemically-synthesised small-molecule medicines, European regulatory authorities and national governments (in collaboration with diverse stakeholders) have established a specific regulatory framework for biosimilars which continues to evolve.

EuropaBio brings together small and large biotechnology companies, of which several are developing both novel biological medicines as well as biosimilar medicines. Biosimilars have an important role to play in fostering competition in the market place, and thereby contributing to the sustainability of healthcare budgets. We believe that Europe must continue to be a thoughtful and responsible leader in this regard to ensure that its regulatory framework and practices are of the highest scientific standards and ensure European patients' safety.

EuropaBio brings together small and large biotechnology manufacturers, many of whom are developing both novel biologics as well as biosimilars. Our members have a stake in ensuring the long-term sustainability of both sectors.

With this brochure, EuropaBio seeks to continue its contribution to the policy debate on biosimilars by generating a better understanding and appreciation of the key issues for European regulators and national policy makers, e.g. the imperative for identification and traceability of biological medicines, with implications for naming and labelling conventions, as well as healthcare systems' sustainability.

The value of healthcare biotech in Europe

With 2,000 companies in Europe ranging from large multinational companies to micro research enterprises, the European healthcare biotech sector is a key contributor to innovation and Europe's competitiveness. The large majority of the European biotech companies are small and medium-size enterprises (SMEs) or micro enterprises. The industry is directly responsible for around 170,000 jobs and EuropaBio estimates that the healthcare biotech industry has been indirectly responsible for approximately 700,000 high-value jobs in 2013. 26% of global manufacturing of biological medicines takes place in Europe[1].

Biologics, including biosimilars: 5 facts you should know

"Biologics" or "biotechnology-derived medicines" are terms used for a range of medicinal products that are produced by processes that depend on living systems. Biosimilar medicines are follow-on versions of original biological medicines (known as the "reference product") which can be introduced to the market once exclusivity rights of the original product have expired. Biosimilars are sometimes incorrectly and inappropriately called "generic" versions of original biological medicines. In fact, unlike generics, which are considered identical copies of chemically synthesised medicines, biosimilars are not the same as the original biological medicines, they can only be highly similar.

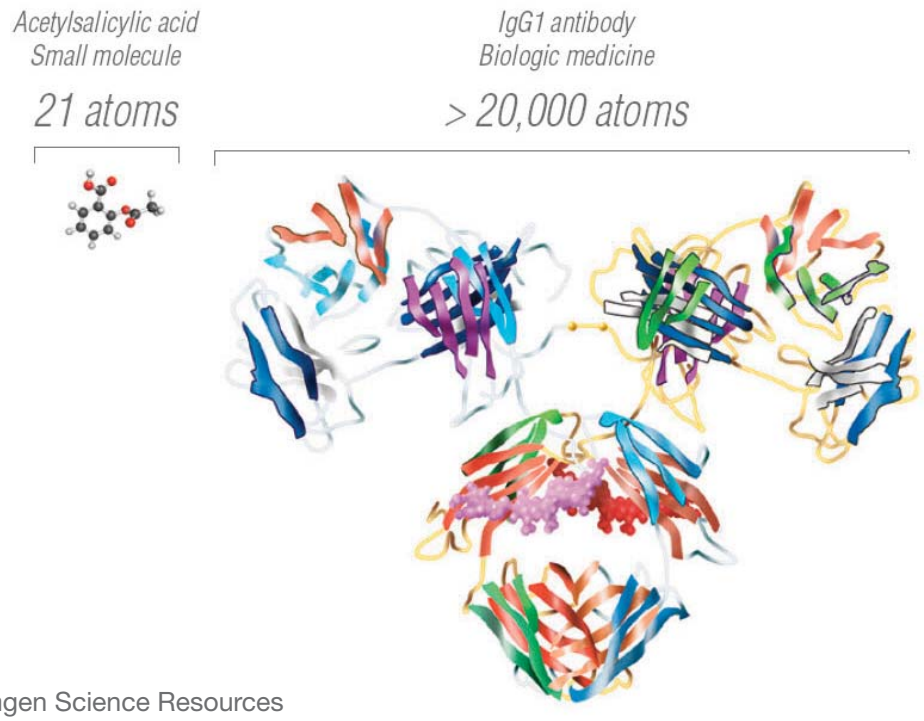
Did you know that...

1

Biological medicines, including biosimilars, are based on proteins, enzymes, antibodies and other substances naturally produced in the human body. Biotechnology uses living systems (plant or animal cells, bacteria, viruses and yeasts) as well as other modern technologies to treat diseases and genetic disorders in humans. Biotechnology in healthcare is primarily used in therapeutic medicines, vaccines and diagnostics. As biotechnology-derived medicines comprise proteins that would be digested and would never reach the site of action when taken orally, biological medicines are typically administered by injection or infusion. Being produced by living systems, biotechnology-derived medicines are highly sensitive to minor changes in their physiological environment, thus meaning that their physicochemical and biological attributes are more variable than traditional small-molecule pharmaceuticals. This makes them more difficult to characterise and replicate.

2

A single molecule of the active substance of a biological medicine is generally 200 – 1000 times bigger than traditional medicines (small molecule pharmaceutical medicine produced by chemical synthesis); they are also structurally far more complex.



Source: Amgen Science Resources

3

Manufacturing biological medicines is complex and requires a highly controlled production process.

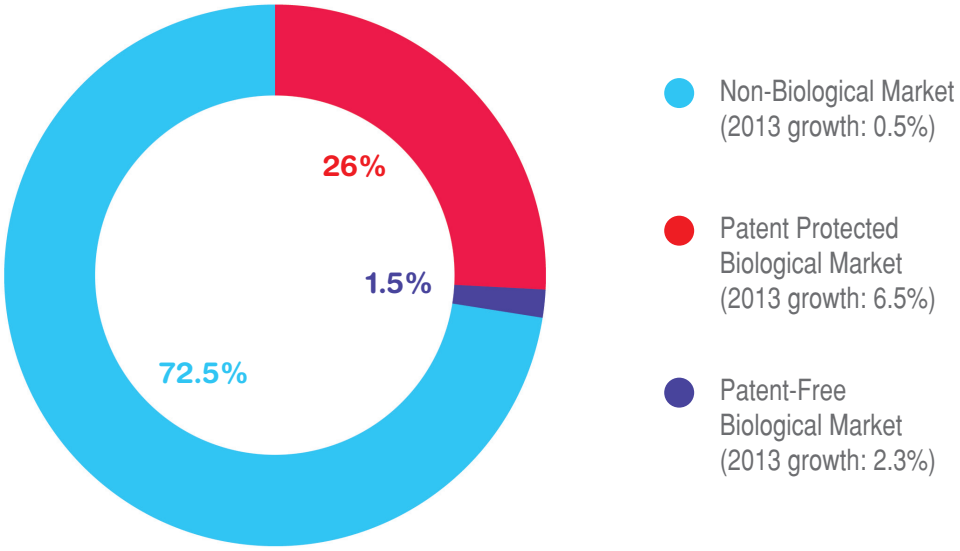
DNA technology is often used to insert desirable genes into host cells. The DNA sequences which encode for the chosen protein are inserted into the host cell enabling it to produce the chosen protein. Genetically modified cell lines are carefully selected and grown in large bioreactors before the biologic medicine is extracted and ultimately purified through complex and lengthy manufacturing processes. Each manufacturer has its own unique cell lines and develops its own distinct manufacturing processes. As even minor variations, for example in temperature, may result in significant changes in the physicochemical and clinical properties of the biological medicine, it is vital to control precisely the manufacturing processes and the environment inside a production facility, to obtain consistent results and to guarantee the safety and efficacy of the medicine. Biological medicines also need special transport and storage conditions as biological material generally degrades quickly when handled inappropriately. Thus, requirements must be established across the entire spectrum of biological medicine development, including standards that assure the product can be produced consistently, with the necessary quality attributes and expected purity and potency.

4

In Europe, all biological medicines, including biosimilars, are assessed and regulated centrally by the European Medicines Agency (EMA). Biosimilars assessed by the EMA are approved if they have demonstrated similar quality, safety and efficacy as the reference medicine[2]. However, their approval does not include any recommendation regarding their interchangeability with the originator product they reference. Decisions of interchangeability and/or substitution rely on national competent authorities, are outside of the remit of the EMA/CHMP and are not a condition to gain marketing authorisation.

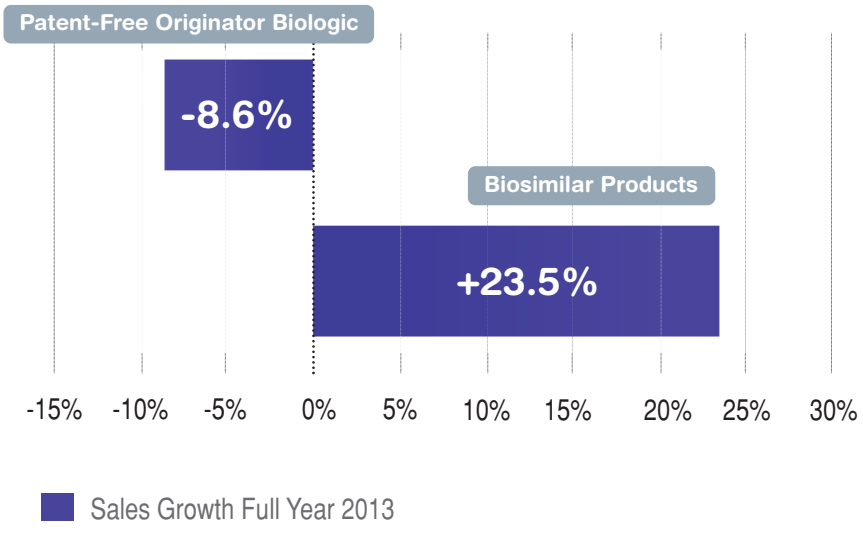
Worldwide, nearly 200 biological medicines have contributed to the understanding and treatment of serious illnesses such as cancer, blood conditions, auto-immune disorders including rheumatoid arthritis and psoriasis, and neurological disorders like multiple sclerosis. Biological medicines are also a promising medical technology for diseases such as HIV/AIDS, Alzheimer's disease, and cardiovascular disease. According to the European Commission, in 2011 biological medicines accounted for 18% of total EU pharmaceutical sales, and 10 of the 30 most often used medicines are biological medicines[3]. In Europe, biosimilars represented about 1.5% of the total EU biological medicines market, and about 23.5% of the EU patent-free biological market in 2013 (see IMS Midas 2013 below).

European Pharmaceutical Market – 2013



Source: IMS analysis / IMS MIDAS

Patent-Free Biological Market – 2013 Growth



Source: IMS analysis / IMS MIDAS

Why Europe needs to continue to maintain high standards for biosimilars

All new biological medicines, including biosimilars, are assessed by the EMA via the centralised procedure. Biosimilars, if deemed highly similar to the reference product by EMA, are recommended for approval by the European Commission.

Originator biologics need to provide a complete dataset which includes chemistry, manufacturing and control (CMC), pre-clinical data together with clinical data in each clinical indication for which the biologic is to be approved.

For biosimilars the EMA regulations allow a reduced dataset to be provided since biosimilar sponsors can partly refer to data previously generated for the originator product to support approval. Indeed, since 2003[4], a legal and regulatory "biosimilar pathway" aimed at establishing "biosimilarity" between the reference product and the biosimilar medicine has been created. This allowed the first placing of a biosimilar on the European market in 2006. So far, 19 biosimilars have been centrally approved by EMA´s Committee for Medicinal Products for Human Use (CHMP) and have received marketing authorisations from the European Commission. 17 biosimilars are currently available on the market.

Europe was the first region to set up a legal framework for approving biosimilars

Biosimilars are developed in a step-wise approach to be highly similar to the reference product with regards to quality, safety, and efficacy. The foundation of biosimilar development is the definition of the molecular characteristics and quality attributes of the target product profile of the biosimilar and its comparability with the reference product. The developer then proceeds with a biosimilarity exercise performed in three steps[5]:

"Structural or process related differences between a biosimilar and the reference product could potentially lead to clinical impacts on the effectiveness and safety of the biosimilar. This is especially the case for more complex biological medicines – such as monoclonal antibodies – since the mechanisms that make these medicines so successful may not be fully known. Similarly, different patient groups may respond differently to the same biological medicine, due to differences in age, gender, sex, co-morbidities, or other medications taken. Thus, appropriate evaluations of similarity of efficacy, safety and immunogenicity should be conducted in the patient population(s) that is most sensitive to differences in these parameters"[6].

The EU framework has served as a reference for many other regulators around the globe. The issuance of the first EMA guidelines on biosimilars in 2005 was followed by the adoption of similar principles by the World Health Organisation (WHO). Other countries around the world, such as Australia, Canada, Japan, Korea, South Africa, Saudi Arabia, Switzerland and many more, have implemented biosimilar pathways, often with reference to the European framework. In the US, the FDA published its first draft guidance in 2010.

As the development of new biosimilar medicines continues and as the number of biosimilar medicines seeking regulatory approval within Europe and around the globe continue to increase, the understanding of these medicines will evolve. Therefore it will be critical for Europe to continue to adopt new insights and to adjust existing guidelines and practices as appropriate.

Identifying biological medicines – Why it is critical to patient safety

Europe has developed strict principles regarding patient safety. Manufacturers have to put programmes in place to monitor the safety of their medicines once they have been approved, in order to detect any safety issues. This monitoring requirement is highly dependent on the ability to identify and track individual medicines at the time they are prescribed by the physician, the time they are dispensed by the pharmacist and, ultimately, the time they are taken by the patient.

A global naming standard to ensure patient safety

Upon request from the international medical/pharmaceutical community, the WHO has put in place International Non-proprietary Names (INN) since 1950, namely "a single name of world-wide acceptability for each active substance" used in a pharmaceutical and biological product. This international nomenclature plays a key role in the "clear identification, safe prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide".

The WHO is currently assessing a proposal for a biologic qualifier[7] which "would help link a biosimilar to its reference product and to other biosimilars, which in turn would contribute to decreased mis-prescribing and improved pharmacovigilance"[8].

The INN system is a voluntary global system, and some manufacturers of biosimilars have chosen not to request an INN but instead make use of the originator's INN. In practice, the EMA has not asked biosimilar developers to approach the WHO's INN Expert Group to request an INN for their biosimilar molecule. Two or more distinct medicines (the original biologic medicine and all approved distinct biosimilars) can share the same INN, whether they have structural differences or not. Product identification and collection of monitoring data can therefore be challenging where different products make use of the same INN.

Globally or within the EU, two or more biologic medicines can share the same INN. As a result, identification and monitoring data might be significantly compromised to the detriment of patient safety and the quality of pharmacovigilance systems.

In order to address the challenge above, the new EU framework for pharmacovigilance, which came into force in July 2012, requires that all biologicals be identified by the trade name and batch number and not by the INN (International Non-proprietary Name). However, more measures should be undertaken to reinforce both the identification and traceability of all biologics from prescribing, through dispensing, recording and reporting.

Recent research has shown that prescribing of biologics is often done by INN and that batch numbers are not generally included in the reporting of adverse reactions[9]. Furthermore, in the event of a reported adverse drug reaction for which naming information beyond the INN is not available, these incidents are usually referred to the originator and will be recorded in the originator's adverse event database. This means that adverse events are attributed to the wrong manufacturer and that the collected pharmacovigilance data has the potential to be misleading or inaccurate[10].

EuropaBio and its members believe that a distinguishable non-proprietary name for all biological medicines, including biosimilars, would further enhance effective pharmacovigilance and patient safety. The WHO's current development of a proposal for a biological qualifier for biological medicines (including biosimilar medicines) is an important step that, if designed appropriately, should strengthen the EU pharmacovigilance system. Distinguishable non-proprietary names contribute to the "clear identification, safe prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide"[11]. In this respect, Europe, as a global pioneer in the approval of biosimilars, has an important role to play in taking leadership to deliver policies on naming and product-level traceability for biological medicines that will benefit patients within and outside Europe.

Biosimilar labelling conventions – Why transparency will build confidence with physicians

EuropaBio is of the opinion that transparent labelling is important to ensure that physicians and patients have readily available information about each distinct biosimilar. This will allow them to make an informed decision on which drug to choose, and to understand which drug has been dispensed.

As for all medicines, biosimilars' labelling is governed by the EMA's QRD (Quality Review of Documents) guidance[12] which does not distinguish between biosimilars, generics and hybrid products in terms of labelling.

A new labelling regime for biosimilars would facilitate physicians' and patients' understanding and acceptance of biosimilars

The current approach foresees that the labelling of a biosimilar should be identical to that of the reference product (unless otherwise justified). Concerns have been raised that this approach does not reflect the specificities of biosimilars and lacks consistency. It is important to understand how the biosimilarity exercise was built up and which additional data were generated to show that previously proven safety and efficacy of the reference product also apply to the biosimilar. For this reason, and since the development of each distinct biosimilar requires generating specific preclinical and clinical data, we believe that a specific label should better reflect the outcomes of this data. The label must provide the information needed for prescribers to understand the technical and scientific context under which the product was approved to ensure its safe and effective use[13].

A biosimilar's label should include information on the biosimilar as well as information on the reference product clearly and without ambiguity. Ultimately, we believe that a new and transparent labelling regime for biosimilars will contribute to facilitate physicians and patients' understanding and acceptance of these products.

Cost-savings and competition – Why these two objectives go hand in hand

Focus on intellectual property for healthcare

Innovative medicines benefit from a certain period of intellectual property protection, via patents and other exclusivity rights. Patent rights give the patent holder the right to prevent others from manufacturing, selling, using and importing a follow-on product (i.e. generic or biosimilar) and from using a specific process, or selling a product made by that process during a limited period of time.

Most drugs are granted patent protection for a much shorter time period than other products. This is due to the regulatory requirements which are associated with the development activities as well as the mandatory completion of clinical trials before regulatory approval can be sought[14].

Intellectual property protection is critical for innovation as it enables companies to recoup their investments and further spend in the research and development of new medicines. Intellectual property tools, such as patents, benefit both companies and society at large, as they enable important scientific information, which might otherwise remain hidden, to be made publicly available.

Biosimilars enhance existing market competition in the EU. By offering an alternative to existing biological medicines that have lost their exclusivity rights, they enhance competition which may offer potential economic benefits to healthcare systems. However, cost savings achievable with biosimilars are not expected to be as great as it has been experienced with small molecule generics. The European Commission's Consensus Information Document stresses that "price differentials […] between biosimilar medicinal products and their reference medicinal products have not been as substantial as experienced in the classical small-molecule generic medicine market"[15].

Unlike with generic medicines, biosimilar manufacturers need to invest in an extensive biosimilarity exercise. The amount of additional data to be generated depends on the outcome of each step in this exercise but will usually comprise a clinical trial in at least one indication of those indications for which the originator biologic has been approved. In addition, biosimilar manufacturers are required to establish and sustain manufacturing and post-approval safety monitoring programmes similar to those of the originator companies. According to IMS Health[16], the cost of developing a generic small molecule is around $1-4 million, whereas biosimilars have been estimated to cost between $100-250 million to reach approval, largely due to the time and investments needed for development.

A balanced approach serving both the sustainability of Europe's biotech industry as well as its healthcare systems' must be achieved

The biosimilar market to date has been growing steadily and is expected to continue to grow above the pharmaceutical market growth rate as numerous leading biologic medicines will lose their exclusivity rights over the coming years. In this context, the European Commission's 2013 Consensus Information Document has confirmed that the pharmaceutical market in Europe is functioning and that "further information about the concept of biosimilar medicinal products […] directed to decision makers […] is necessary"[17]. Furthermore "information to patients, including patient organisations, may be crucial as well to facilitate uptake of biosimilar medicinal products"[18].

EuropaBio believes that a balanced approach serving both the sustainability of Europe's innovative biotech industry as well as its healthcare systems' must be achieved. Whilst we understand and support the need for Member States to manage their health expenditures, policies must carefully balance the value of a healthy population and workforce, budgetary requirements and the sustainability of the EU's excellence in healthcare biotech.

Unless otherwise specified, all EMA positions in this glossary have b
Consensus Information Document on biosimilars in theEuropean

Determining the terms of use for biological medicines including biosimilars in patient care

Physicians' prescribing authority should be respected

In the EU, decisions regarding (automatic) substitution at pharmacy level and prescription incentives lie within the responsibility of each Member State. In its scientific evaluation of the quality, safety and efficacy, the EMA assesses the similarity of a biosimilar to its reference product, but does not assess nor conclude whether the products are interchangeable.

At the point in time of publication of the consensus information paper in 2013, "no country has explicitly authorised the substitution of biological products from different manufacturers, and a number of EU Member States have put legal, regulatory, and political provisions in place that prevent this practice"[19]. Furthermore, several countries have adopted specific regulatory guidance on the use of biological medicines including advice on brand name prescribing and procurement. Physician's supervision is particularly relevant, as not all biosimilars will necessarily have all of the same indications, or the same administration devices as their reference medicine. "For questions related to switching from one biological medicine to another, patients should speak to their doctor and pharmacist"[20].

Focus on the Alliance for Safe Biologic Medicine's physician survey in Europe (2013):

At the end of 2013, the Alliance for Safe Biologic Medicine (ASBM) surveyed 470 European physicians from various specialties about their prescribing habits and understanding of biosimilars. Key findings of the survey highlight European physicians' insufficient knowledge of biosimilars, as well as the need for distinguishable International Non-proprietary Names (INNs) for all biological medicines as a mean to further strengthen and facilitate patient safety through effective pharmacovigilance. The survey also provides important information regarding substitution. 72% of prescribers consider it "Critical" or "Very Important" to have the authority to decide whether a patient should receive an innovator biologic medicine or a biosimilar.

Patient information and involvement

The European Commission's Consensus Information Document underlines the importance of dialogue between patients and physicians: "The relationship between patient and healthcare professional is key to ensuring the best treatment/care decisions and health outcomes for each patient. Patients often do not receive enough information from healthcare professionals that they understand, whereas many health professionals overestimate the amount and quality of information they provide. It is crucial that all available therapeutic options are discussed thoroughly and that healthcare professionals ensure that patients understand the options, relative benefits and risks."

The Package Information Leaflet is an important source of information for patients. For this reason, the leaflet for biosimilars should indicate that the medicine is:

1. Approved as biosimilar to a reference product for stated indication(s) and route of administration(s);
2. Or has not been determined to be interchangeable with the reference product[21].

With regards to substitution, it is important that for stable and well-treated patients the specific therapeutic needs of the patient should always be considered, and the potentially negative consequences on efficacy and safety of changing treatment should always be taken into consideration.

EuropaBio's call for action

The European biotech industry has taken on commitments to be a contributor to patients' safety and a sound regulatory environment for all biological medicines:

- Taking part in the further development of EMA's guidelines on biosimilar;
- Enhancing stakeholder education on the specificities of biosimilars and their complexity compared to chemically-synthesized small molecule generic medicines; and
- Producing evidence supporting policy recommendations with regards to all biological medicines.

We call on EU policy-makers, national regulators, physicians, other healthcare providers and patients to contribute to a better understanding of biosimilars in Europe and to the further development of a policy framework which takes into account the specificities of biosimilars and their specific requirements, in particular when compared with chemically-synthesized small molecule generic medicines:

What can the European Union do?

1. Further strengthen measures to support accurate adverse event reporting in particular the correct attribution of an adverse event to a product in order to ensure patient safety and to contribute to global pharmacovigilance;
2. Share best practise for the identification and traceability of biological medicines;
3. Ensure transparent labelling for biosimilars;
4. Enhance the education of physicians, healthcare professionals and patients on the specificities of biosimilars and their complexity compared to chemically-synthesized small molecule generic medicines.

What can national regulators Union do?

1. Take into account the specificities of biosimilars (alongside originator products and generic medicines) in the regulatory frameworks in Europe;
2. Prevent non-medical substitution;
3. Make sure that the continuity of patients' treatments and physicians' authority to prescribe take precedence over austerity policy measures;
4. Involve all interested parties (physicians, patients, and industry) in any policy debate related to the uptake of biosimilars;
5. Issue guidance/organise trainings recommending physicians to prescribe all biologics including biosimilars by brand (trade) name only;
6. Enhance the education of physicians, healthcare professionals and patients on the specificities of biosimilars and their complexity compared to chemically-synthesized small molecule generic medicines.

What can physicians and other healthcare providers do?

1. Make sure that patients are prescribed medicines that best suit their needs;
2. Ensure that patients understand the specifics of biological medicines, including biosimilars;
3. Prescribe all biological medicines, including biosimilars, by brand (trade) name to make sure that patients receive the medicine intended for them;
4. Maintain physicians' prescribing authority;
5. In case of adverse events, report the brand name, the batch number and the INN of the biological medicine.

What can patients do?

1 Pay attention that the biological medicine delivered by the pharmacist always corresponds to the specific product prescribed by a physician throughout all phases of the treatment.

2. Contact your national patient group(s) to obtain further information on biosimilars. Alternatively, study the patient Q&A section of the European Commission's Consensus Information Document and/or IAPO's (International Alliance of Patients' Organisations) Information and Advocacy Toolkit on Biological and Biosimilar Medicines.

Glossary of key terms

Unless otherwise specified, all definitions in this glossary have been taken from European Commission Consensus Information Document on biosimilars in the European pharmaceutical environment, April 2013

Adverse event/side effect: Any unintended or unfavourable event following the administration of a given medicine.

Accessible market: The "accessible market" is defined by the market of originator medicinal products, which have been referenced in biosimilar applications, and originator medicinal products, which have lost their market exclusivity, but have not yet been referenced.

Batch: A batch of a medicinal product is an entity which comprises all the units of a pharmaceutical form which are made from the same initial quantity of material and have undergone the same series of manufacturing and/or sterilisation operations or, in the case of a continuous production process, all the units manufactured in a given period of time[22].

Biological medicine: A medicinal product or a vaccine that consists of, or has been produced by the use of, living organisms. Recombinant DNA (a combination of DNA sequences that do not exist naturally in order to establish new functions) often forms the basis for biotechnologically manufactured products.

Biosimilar: A similar, but not identical, version of an existing biological medicine made following the patent expiry of the original product.

Biotechnology: Any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.

Brand name: It "may be either an invented name not liable to confusion with the common name, or a common name or scientific name accompanied by a trade mark or the name of the marketing authorisation holder"[23].

Deoxyribonucleic acid (DNA): DNA is a molecule that encodes the genetic instructions used in the development and functioning of all known living organisms.

Extrapolation of indications: The decision whether to extend the efficacy and safety data from an indication (a medical condition, disorder or disease) for which the biosimilar has been clinically tested to other conditions for which the branded product is approved, is known as "extrapolation".

Generic (medicine): A medicine that is developed to be the same as a medicine that has already been authorised (the "reference medicine"). According to Directive 2001/83/EC "generic medicinal product" is a product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. A generic medicine can only be marketed after the loss of market exclusivity of the reference medicine.

Immune reaction: A defence mechanism by the body that leads to the production of antibodies by the human body in response to an invading substance (i.e. antigen) e.g. to viruses and substances recognized as foreign and possibly harmful.

Immunogenicity: The potential or ability of a substance or antigen to cause an immune reaction/response (see above).

Indication: A medical condition, disorder or disease.

INN: International Non-proprietary Name which identifies pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognized and is public property. A non-proprietary name is also known as a generic name. (Source: WHO Guidance on INN, www.who.int).

Interchangeability: The medical practice of changing one medicine for another that is expected to achieve the same clinical effect in a given clinical setting and in any patient on the initiative, or with the agreement of the prescriber.

Patent: A patent is a set of exclusive rights granted by a state to an inventor or their assignee for a limited period of time in exchange for public disclosure of an invention.

Patient Information Leaflet: Document that is primarily intended to summarise information on the medicine for patients. It is also contained within each pack of the medicine.

Pharmacovigilance: Science and safety control procedures to which medicines are subject before, during and after their approval by regulatory authorities with the aim of detecting, assessing and understanding the benefit: risk profile of a medicinal product. Pharmacovigilance activities cover the whole life-cycle management of medicines in relation to safety.

Recombinant protein: Recombinant protein is a manipulated form of protein, which is generated in various ways to produce large quantities of proteins, modify gene sequences and manufacture useful commercial products. The formation of recombinant protein is carried out in specialized vehicles known as vectors[24].

Reference product: A medicinal product which has been granted a marketing authorisation by a Member State or by the European Commission on the basis of submitted quality, pre-clinical and clinical data, to which the application for marketing authorisation for a generic or a biosimilar product refers.

Substitution: Practice of dispensing one medicine instead of another equivalent and interchangeable medicine at the pharmacy level without consulting the prescriber. Terms such as 'non medical substitution' and 'automatic substitution' can also be used.

Summary of Product Characteristics (SmPC): Legal document approved as part of the marketing authorisation of each medicine. It provides information for healthcare professionals on how to use the medicine. This information is updated throughout the life-cycle of the product as new data emerge.

List of acronyms

ASBM	Alliance for Safe Biologic Medicines
CMC	Chemistry, Manufacturing and Control
DNA	Deoxyribonucleic acid
EMA	European Medicines Agency
EU	European Union
GMP	Good Manufacturing Practices
INN	International Non-proprietary Name
WHO	World Health Organization

Notes & References

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[3] European Commission, What you need to know about Biosimilar Medicinal Products, , Consensus Information Document 2013 p.20 - http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf

[4] Annex 1 of the Directive 2003/63/EC on the Communicty code relating to medicinal products for human use recognises biosimilars

[5] European Commission (2013), "What you Need to Know about Biosimilar Medicinal Products. A Consensus Information Document", p. 12.

[6] European Medicines Agency (2013), draft Guideline (EMEA/CHMP/BMWP/42832/2005 Rev. 1) on "similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues"

[7] For further details about the WHO programme, please refer to the Executive Summaries available on the WHO website: http://www.who.int/medicines/services/inn/meetings/en/

[8] 57th Consultation on International Nonproprietary Names for Pharmaceutical Substances Geneva, 22-24 October 2013, INN Working Document 13.340, Dec 2013, page 6.

[9] Market Research, Biosimilars Study, Market Research Report (2014), Hertfordshire UK, Medix Limited: 37 pages.

[10] Cf. Heads of Medicine Agencies (HMA), Guideline on good pharmacovigilance practices (GVP) – Module VI – Management and reporting of adverse reactions to medicinal products, 20 February 2012, p. 24 - http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129135.pdf : "With regard to the collection and recording of reports of suspected adverse reactions, marketing authorisation holders responsibilities apply to reports related to medicinal products (see VI.A.2.2) for which ownership cannot be excluded on the basis of one the following criteria: medicinal product name, active substance name, pharmaceutical form, batch number or route of administration".

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[14] EuropaBio, Biotechnology - How intellectual property rights promote innovation and create economic and societal value, p. 11 http://www.europabio.org/sites/default/files/report/how_intellectual_property_rights_promote.pdf

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[21] Davies G. C., Bowker G. M., Labeling Standards for Biosimilar Products, Therapeutic Innovation & Regulatory Science, 2014 48: 36, p. 368 - http://dij.sagepub.com/content/48/3/367

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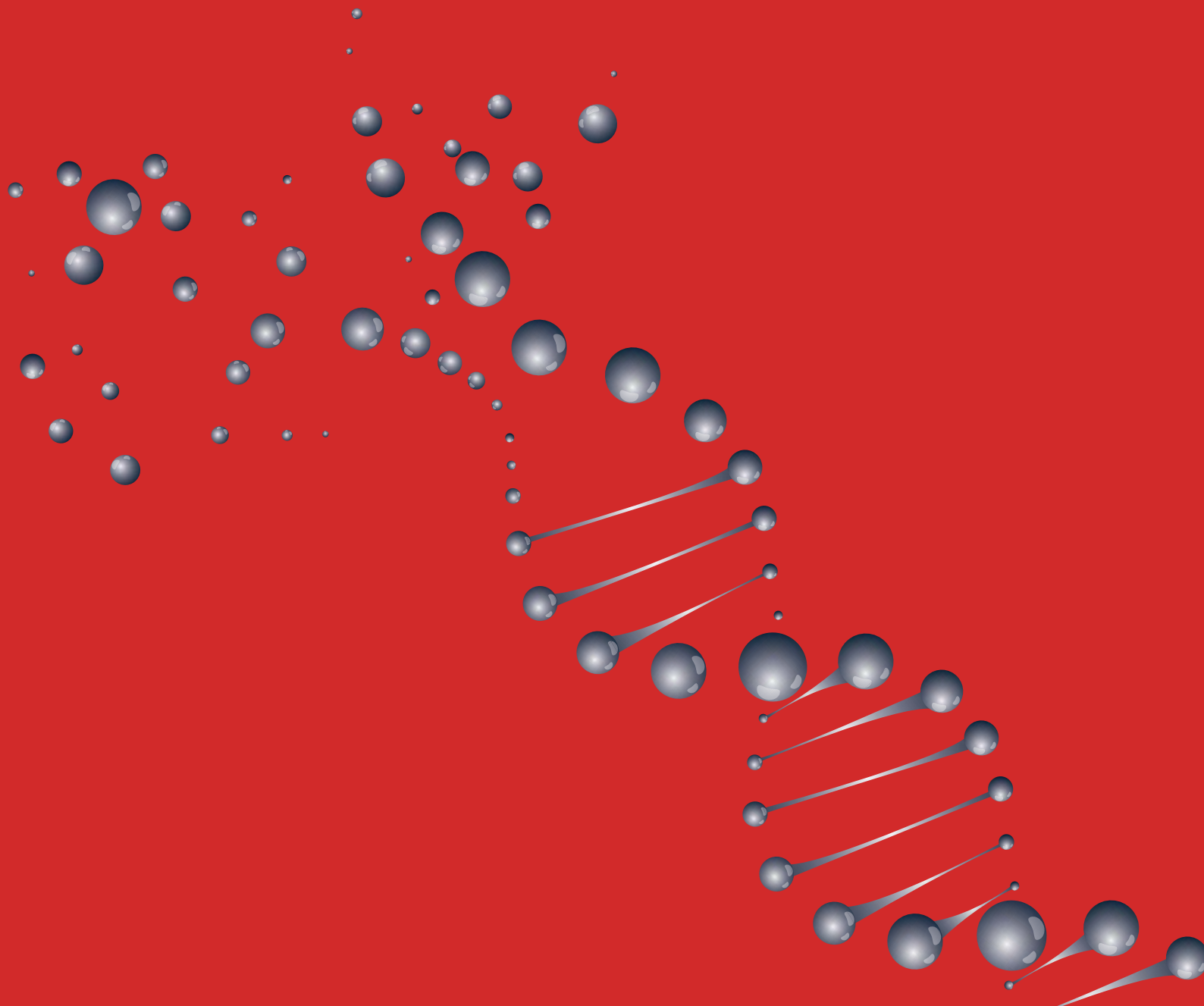
[24] www.recombinant-protein.com/recombinant-protein-definition

EuropaBio's mission is to promote an innovative and dynamic biotechnology base in Europe. Our membership includes a wide range of corporate members and industry associations involved in biotechnology throughout Europe. EuropaBio has 55 corporate and 15 associate members and BIO Regions and 17 national biotechnology associations – representing some 1800 small and medium sized enterprises across Europe.

The latest information on biosimilars and EuropaBio may be found on EuropaBio's website at **www.europabio.org**.



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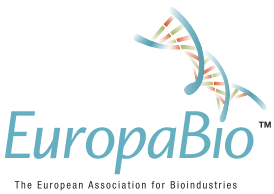

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