



Making Medicines Affordable

EUROPEAN GENERIC MEDICINES ASSOCIATION



EGA HANDBOOK ON BIOSIMILAR MEDICINES



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FOREWORD

The first five **biosimilar medicines** were approved for use in Europe in 2006 and 2007.

This short guide is intended to be the reference source for those who need to understand what these new medicines are; why they are becoming more important; their benefits and questions raised by this emerging type of vital medicine.

It will be particularly useful to:

- Patients and Patient Advocacy Groups
- Clinicians and Prescribers
- Retail and Hospital Pharmacists
- Those responsible for funding health and healthcare on a regional or national basis
- National pricing and reimbursement authorities
- Politicians and advisers
- Policy makers

This handbook provides the background to the emergence of biosimilar medicines, and the clinical and health economic benefits they offer to patients, clinicians and healthcare providers.

It describes the science and technology behind biosimilar medicines; how they are produced and regulated, and also covers the questions surrounding them, namely:

- terminology
- quality, safety and efficacy
- **comparability**
- non-clinical tests and clinical trials
- **pharmacovigilance**
- **immunogenicity**
- access to medicines
- identification and **traceability**
- **interchangeability** and **substitution**

The handbook focuses on the current situation in the European Union (EU) and concludes with a summary of the developments likely to occur in the near future.

A glossary of terms, highlighted in bold in the text, and a list of acronyms or abbreviations are also provided at the back of the handbook.

On behalf of the EGA Board of Directors I believe that this handbook will greatly enhance the knowledge about biosimilar medicines and understanding of their public health contribution.

I thank you for your time in reading this document.

Greg Perry,
Director General
EUROPEAN GENERIC
MEDICINES ASSOCIATION



EXECUTIVE SUMMARY

Generic medicines have made a major contribution to affordable and accessible healthcare for over 20 years, saving the European Union (EU) alone an estimated €20 billion annually.

By 2010 **biopharmaceuticals**, which are defined for the purpose of this handbook as medicines made by or derived from living organisms using biotechnology, are expected to grow 12–15% per year.¹ They represent one of the fastest-growing segments of the pharmaceutical industry, and there are more than 200 of them on the market today. Some 300 more are being investigated in clinical trials.²

Biopharmaceuticals can now also be produced by manufacturers other than the originator when the relevant **patents** have expired. These new biotechnological medicines are most commonly known as 'biosimilar medicines', which will be the term used throughout this handbook. In other texts they may be named 'similar biological medicinal products', 'biosimilars', 'follow-on biologics' or 'biogenerics'. Biosimilar medicines are therefore a subset of biopharmaceuticals, with comparable safety and efficacy to **originator reference medicinal products**. The main difference between the two is that biosimilar medicines will be less expensive.

Biosimilar medicines now offer a major opportunity to provide greater access to affordable healthcare for several life-saving medicines, at least equally significant to the emergence of generic medicines over the past two decades. Biosimilar competition resulting in just a 20% price reduction on five off-patent biopharmaceutical medicines could save the EU over €1.6 billion per year. Since 2004, there has been acceleration in this new field of pharmaceutical development, with the first five biosimilar medicines gaining European regulatory approval in 2006 and 2007.

Biosimilar medicines are approved by the European Commission (EC) through the European centralised procedure, which is overseen by the European Medicines Agency (EMA). The term 'biosimilar medicine' is derived from the EU legislation governing this approval process. As is the case for all medicines, European regulations and guidelines are in place to ensure the quality, safety and efficacy of biosimilar medicines, and also to avoid unnecessary clinical testing. Quality, in this context, means the controls and standards for all manufacturing, preparation and processing of the product.

To gain approval, biosimilar medicines have to demonstrate that they are as safe and effective as the originator reference product. Biosimilar medicines are evaluated for their similarity and comparability with the reference product. This evaluation is customised to each biosimilar product and the **active substance** it contains, together with the methods used for development and the clinical use of the product. One key aspect to be considered is the variation of potency and purity of the product which should be within the limits displayed by the reference product. The biosimilar development process uses the latest analytical and clinical technologies, including some that may have not been available to assess the reference product at the time it was first approved.

Once the medicine is approved, specific monitoring is required for biopharmaceuticals to assure continued safety and efficacy. In addition to the specific monitoring, data is collected through pharmacovigilance activities. The data collected is used to prepare periodic safety update reports (PSURs). These reports review the risk-benefit of medicines, at frequent intervals after the product is first approved and marketed. Pharmacovigilance is not specific to biosimilar medicines but applies to all medicinal products.

Healthcare providers can now work with clinicians and pharmacists to improve the availability and affordability of these important medicines to more patients, confident in the knowledge that they have been scientifically assessed by the EMEA and approved by the European Commission.

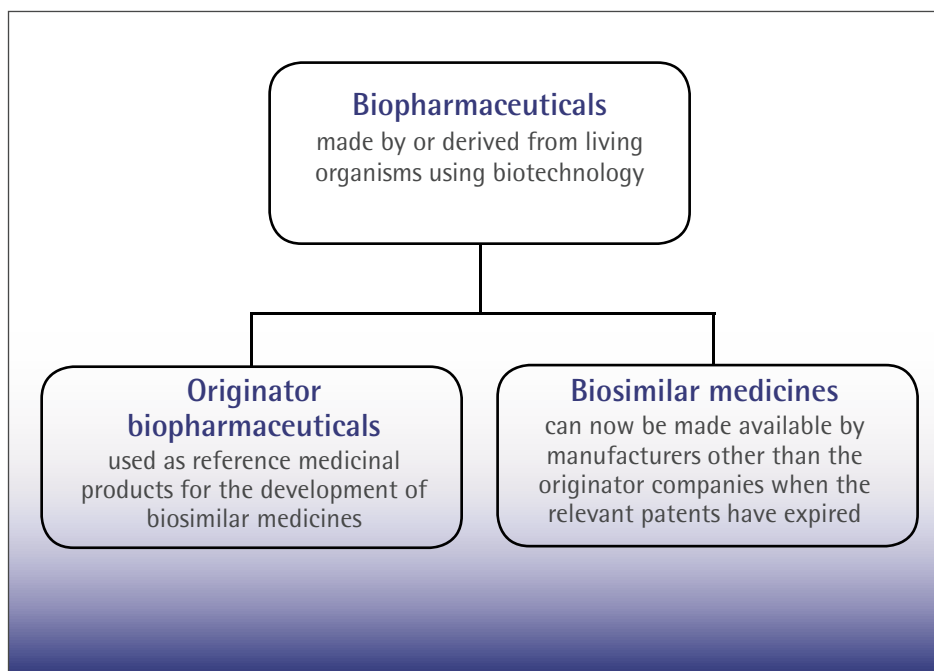
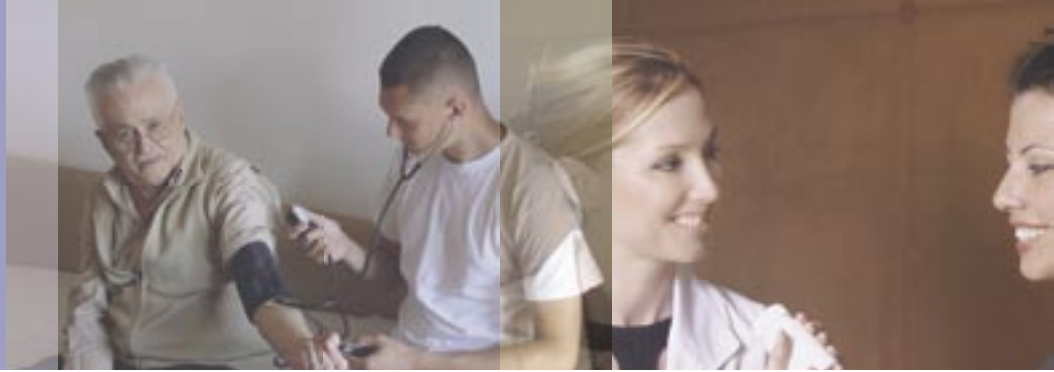


Figure 1: Overview on biopharmaceuticals



WHY ARE BIOSIMILAR MEDICINES IMPORTANT?

For patients: The regulations governing biosimilar approval, developed through extensive consultation and **scientific peer review**, ensure the quality, safety and efficacy of biosimilar medicines. These are now an emerging source of affordable medicines for more patients who have some of the most difficult to treat diseases. Manufacturers other than the **originator companies** have the scientific capability to produce biosimilar medicines, which can take place when the relevant patents of the originator reference products have expired. Information about specific biosimilar medicines is available from a number of sources, including the EMEA, to enable patients, together with their doctor and pharmacist, to have access to the relevant data on the use of these medicines. Patients can have confidence in them because they are approved by the same regulatory organisation – with the same scientific rigour, using the same regulatory systems as the comparable originator products.

For clinicians: Biosimilar medicines, evaluated scientifically by the EMEA and approved by the European Commission, must demonstrate that they have a similar safety and efficacy profile as the reference product. Possible concerns about immunogenicity, which applies to all biopharmaceuticals, both originator as well as biosimilar medicines, are addressed through the pre-clinical and clinical development programmes prior to approval, pharmacovigilance after approval and if appropriate through **Post-Authorisation Safety Studies (PASS)**. Applications for all new biopharmaceuticals, including biosimilar medicines, must also include a **Risk Management Plan (RMP)** in the EU which shows that the company has assumed the responsibility and liability for its medicines, ensuring that all appropriate actions and surveillance will be taken, as considered appropriate and necessary by the EMEA.

Biosimilar medicines offer an affordable alternative to reference products, allowing greater access to these medicines for more patients.

For pharmacists: Pharmacists have a leading role in ensuring that the most appropriate medicines are made available to the right patients in the right way, and at the right time. A prime responsibility is the evaluation and supply of new medicines within their national regulatory and reimbursement framework.

Biosimilar medicines are an emerging source of affordable biopharmaceuticals which pharmacists can critically appraise, referring to data published on the EMEA website, in order to support clinical decisions and health provider (payer) expectations. The very robust regulatory systems now in place in the EU allow full confidence in biosimilar medicines.



For healthcare purchasers and national pricing and reimbursement authorities: Biosimilar medicines offer an equivalent and less expensive alternative to reference products. This means that more patients can be treated within the same limited budget or real savings may be used to fund other treatments, if so chosen.

For politicians, advisers and policy makers: The EMEA is the regulatory body that examines the data for each biosimilar medicine on a case-by-case basis. The European Commission grants a pan-European marketing authorisation based on the EMEA positive scientific opinion. The EMEA is also responsible for the development of guidelines related to biosimilar medicines. These are developed in discussion with many stakeholders including industry, clinicians and patient advocacy groups. Biosimilar medicines provide a means of introducing competition into the biopharmaceutical market, which will allow more flexibility for the uptake of new innovative therapies. The EMEA and the European Commission provide the first and final arbiter of quality to ensure that patient safety is not compromised.





CONTEXT

Healthcare is high on the agenda of every Member State in the EU. People are living longer, but also showing an increasing prevalence of many serious and long-term conditions such as heart disease, cancer, and diabetes. The medical treatment of these patients has to be provided within a finite budget of healthcare resources, so individual governments are developing policies and mechanisms to try and gain the best patient benefit, while controlling costs.

Medicines are a valuable component of healthcare, and a significant element of healthcare expenditure. The latest figures for the EU show that medicines account for an average of around 18% of total healthcare costs, rising for example to 38.5% in the Slovak Republic.³ Healthcare providers across the EU are therefore finding ways to reduce the cost of medicines including measures to increase generic competition.

In essence, there are two types of medicine used to treat human disease. Conventional chemical medicines – called **pharmaceuticals** in this handbook – and biopharmaceuticals, which are medicines made by or derived from living organisms using biotechnology.

Conventional Pharmaceuticals – Generic Medicines

Generic medicines are less expensive versions of conventional pharmaceuticals which have made a major contribution to affordable and accessible healthcare for over 20 years, saving the EU alone an estimated €20 billion per year. They are used very widely in the EU in a large number of therapeutic areas including cancer, cardiovascular disease, diabetes, gastro-intestinal disorders, pain, asthma and infections.

Generic medicines are available at affordable prices to patients and healthcare professionals after the patent protection period of the originator product has expired. As a result, more patients can be treated or savings can be used to fund other therapies, if so chosen. In addition to price competition, the introduction of generic medicines also stimulates the development of new innovative medicines.

Generic medicines contain active substances whose safety and efficacy are well established. New clinical trials are therefore usually not required for their approval. This approach is also in line with ethical principles not to repeat unnecessary tests on animals and humans.

Generic medicines must prove **bioequivalence** with the reference product which broadly means that they need to demonstrate that the same dose of the generic and reference product behave in the body in the same way. Furthermore generic medicines must meet the same quality standard as reference products. Quality means the controls and standards for all manufacturing, preparation and processing of the product. They are consequently therapeutically equivalent to and therefore interchangeable with the reference product in the respective indications.

Biopharmaceuticals – Biosimilar Medicines

Biopharmaceuticals have been available for over twenty years. They fall into different classes:

- Hormone products e.g. growth hormone for growth hormone disorders, erythropoietin for the **anaemia** of kidney disease, and insulin for diabetes
- Immunomodulators e.g. beta-interferon for multiple sclerosis
- Monoclonal **antibodies** (MABs) e.g. trastuzumab for breast cancer
- Blood coagulation modulators e.g. factor VIII and IX for blood disorders such as haemophilia
- Enzymes e.g. for the treatment of metabolic disorders such as **Gaucher disease**
- Vaccines



The development process for biopharmaceuticals is a complex one. The science behind this process is described more fully in the next section.

Manufacturers other than the originator companies have the scientific capability to produce biopharmaceuticals when the relevant patent has expired. In Europe, this new category of medicines is called biosimilar medicines, or sometimes the longer legal term 'similar biological medicinal products' is used. An EU biosimilar medicine has been compared to, and has demonstrated that it matches the reference product in terms of quality (how it is manufactured), safety (e.g. the adverse reactions that can occur) and efficacy or effectiveness (its desired effect in the body). Details on approved biosimilar medicines are available through European Public Assessment Reports (EPARs)^{4,5} which are published on the EMEA and the EC websites.

Biosimilar medicines are a new source of affordable biopharmaceuticals for more patients who have some of the most difficult to treat diseases. As a consequence of the first biopharmaceuticals reaching the end of their patent life, there has been acceleration in this new field of pharmaceutical development since 2004.

Table 1: Timelines for emergence of biosimilar medicines:

The first patents protecting biopharmaceuticals expired	2001
The notion of 'biosimilar medicine' or the concept of 'biosimilarity' was introduced into EU legislation in June 2003 and further developed with the adoption of the 'EU Pharmaceutical Review' on 31 March 2004 ⁶	2003/4
EMA receives first three biosimilar medicine applications ⁷	2004
The EMA published an overarching guideline describing the concept of biosimilar medicine and the basic principles to be applied ⁸	2005
The EMA finalised two guidelines for biosimilar medicines (quality and non-clinical / clinical issues) ^{9,10}	2006
EMA produced four product specific guidelines covering Granulocyte Colony Stimulating Factor (G-CSF), insulin, growth hormone and erythropoietin) outlining non-clinical/clinical requirements for comparability of biosimilar medicines ^{11,12,13,14}	2006
EMA receives three more applications for biosimilar medicines ⁷	2006
European Commission approved the first two biosimilar medicines, Omnitrope® and Valtropin®, which are both human growth hormone products for the treatment of growth hormone deficiency ¹⁵	2006
Twelve applications for initial evaluation of biosimilar medicines have been received by the EMA ¹⁶	2007
The European Commission, on the basis of the positive scientific opinion by the EMA, approved three biosimilar medicines (based on one development): Binocrit® (Epoetin alfa) from Sandoz GmbH, Epoetin alfa Hexal (Epoetin alfa) from Hexal Biotech ForschungsGmbH and Abseamed® (Epoetin alfa) from Medice Arzneimittel Pütter GmbH & Co KG ¹⁵ . (These are all erythropoietins)	2007
EMA published a 'Questions and Answers' document on biosimilar medicines (similar biological medicinal products) ¹⁷	2007
The EMA adopted positive scientific opinions for the biosimilar medicinal product Silapo® (Epoetin zeta), from Stada Arzneimittel AG, and Retacrit® (Epoetin zeta), from Hospira Enterprises B.V. ¹⁸ These are erythropoietins. The European Commission approvals follow the positive EMA opinion.	2007
More biosimilar medicine applications and approvals are anticipated	2008–2010

WHY HAS THE TERM 'BIOSIMILAR MEDICINE' BEEN CHOSEN?

The European Commission and the EMA chose the term 'similar biological medicinal product' more often called 'biosimilar medicine' to reflect the approach of approving a biological medicine which is similar to an already authorised reference biological medicine. Typically a more extensive and very expensive development programme, including more registration data, is required for biosimilar medicines compared to generic medicines to demonstrate that the therapeutic performance of the biosimilar medicine is comparable to the reference product. This explains why the term 'biosimilar' was chosen over the term 'biogeneric'.

All biopharmaceuticals are inherently variable due to the fact that they are produced from living organisms. This variability exists within batches, from batch to batch, and when production processes are improved or changed or differ between manufacturers. The variability of biopharmaceuticals is greater than that typically observed for conventional pharmaceuticals and applies to originator biopharmaceuticals as well as to biosimilar medicines. This also explains why the term 'bio-identical' cannot be used.

Biosimilar medicine is (to date) a term derived from the nature of the medicine and from the EU regulatory and legal route for approving these medicines, rather than an agreed terminology that will be used globally.

SCIENCE AND TECHNOLOGY BEHIND BIOSIMILAR MEDICINES

Biopharmaceuticals contain much larger **molecules** than conventional pharmaceuticals, and each has a set of characteristics naturally subject to some variability. They are usually **proteins or polypeptides**. The variability includes the 'shape' of the molecule (folding) and the type and length of any sugar or carbohydrate groups that may be attached to it (**glycosylation**).

All biosimilar medicines are biopharmaceuticals. Biopharmaceuticals, including biosimilar medicines, are produced in, and isolated from, living organisms. The end product has to be purified from the thousands of other biomolecules present in a living cell or living organism, therefore the production process requires sophisticated and validated technologies, and the pharmaceutical company developing the biosimilar medicine needs to have the associated scientific capability.

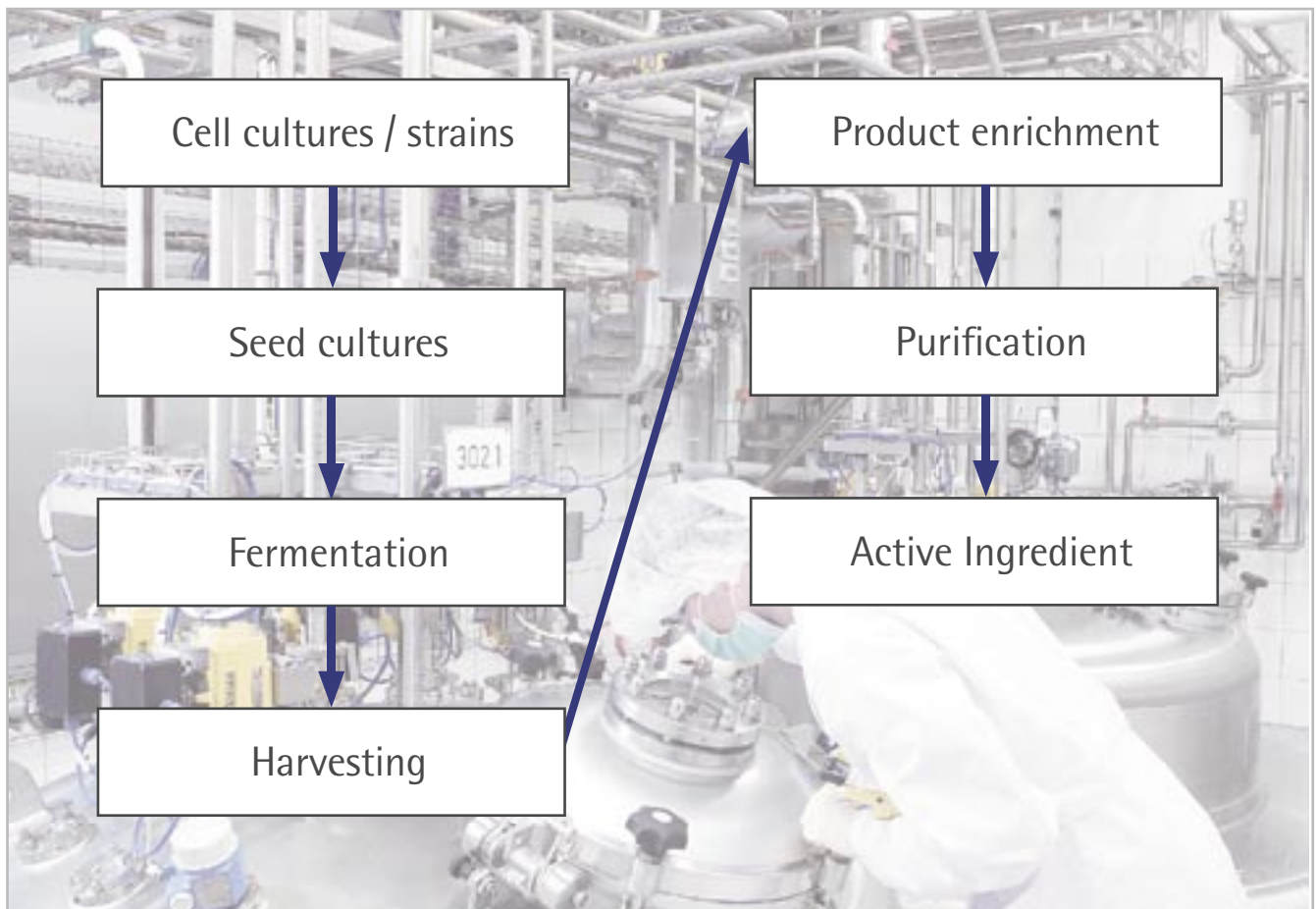




How are biopharmaceuticals developed?

Biopharmaceuticals are developed using a variety of mechanisms, but representation of a 'standard' biotechnological process is shown in Figure 2.

Figure 2: Technical development and production of a biopharmaceutical





The development goals for both reference and biosimilar medicines are safety, quality (of production), reproducibility and efficacy.

The development of a biosimilar medicine is based on at least ten years of clinical and regulatory experience with the reference product. This wealth of knowledge provides information to develop and produce the biosimilar medicine, and defines the testing needed to assure biosimilarity with the reference product.

Biosimilar production starts either with the cloned cell-line (copies of host cells with the target gene in place) or the seed culture ready to be fermented (*Figure 2*). The cell-line or culture can be developed by the manufacturer; purchased from another company or developed in partnership with a company who has the required expertise and capability. In this way manufacturers of biosimilar medicines can reduce the time for development by up to two years in comparison to the originator manufacturer (*Figure 3*).

Each biosimilar medicine has a validated process of development to ensure that it matches its reference product in terms of quality, safety and efficacy. A development programme may include:

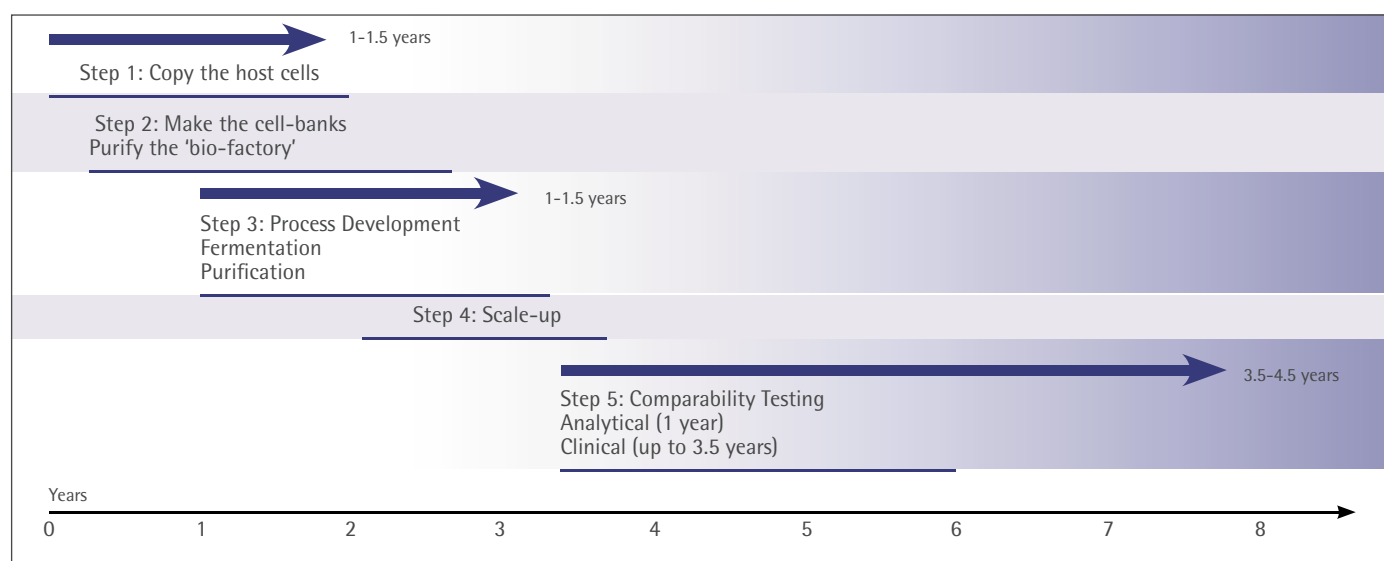
- A thorough characterisation programme to compare the purity of the potential biosimilar medicine with the reference product. This is done using a large series of different state-of-the-art analytical tests, as no single method can characterise all aspects of a product.
- If there are significant differences found on analyses, the development process is modified until the product generated has a profile which matches the profile of the reference product.
- This modification continues at every stage of the development process so that the final biosimilar medicine matches the reference product by every criterion required by the EMEA when the file is submitted for assessment and marketing approval.

The stages in development of a biosimilar medicine are summarised in *Figure 4*.

Regulatory authorities have the expertise and the data to decide whether comparability has been demonstrated between a biosimilar medicine and its reference product.

The cost of developing a biosimilar medicine is at least ten times greater than for generic medicines. These costs do not include building specialised manufacturing plants or very expensive Post-Authorisation Safety Studies (PASS).

Figure 3: Timeline for development of a biosimilar medicine





How are biopharmaceuticals produced?

Both originator reference products and biosimilar medicines are made under carefully controlled conditions to ensure the products are consistent, and manufactured to the required quality. This is known as Good Manufacturing Practice (GMP).

In the European Union, GMP inspections for all biopharmaceuticals (both originator and biosimilar medicines) are coordinated by the EMEA and performed by National Regulatory Agencies. There are three levels:

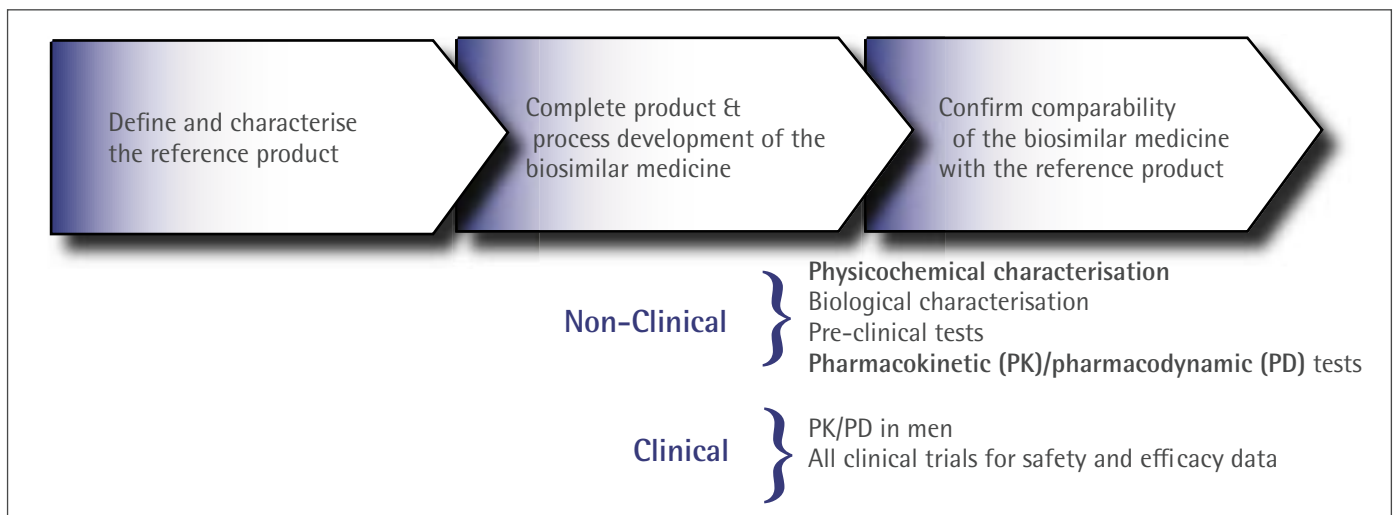
- Routine GMP inspections of manufacturing sites to ensure that medicines are produced safely and correctly
- **Pre-Approval Inspections (PAI)** for GMP compliance prior to the approval of new medicines for marketing if there are specific issues identified during the approval process
- Unannounced inspections

On 1 May 2007 the EMEA launched a new database designed to facilitate the exchange of information on compliance with GMP within the European medicines network. The database, called EudraGMP, can be accessed by national competent authorities, the European Commission and the EMEA.

Biosimilar medicines are made by specialist organisations. They may be a dedicated but separate part of a large pharmaceutical company, a stand-alone biotechnology company, or a partnership between the two, which has benefits in terms of reducing development costs. The development and manufacture of these products is a complex field which is expensive, requires particular expertise and carries a degree of commercial risk.

Not all biopharmaceuticals will necessarily become available as a biosimilar medicine. The cost of development, production, and also the size of the market (number of patients) have to be taken into account by a potential manufacturer. Industry must be able to develop and produce the biosimilar medicine at a cost that allows them to market competitively at lower prices than the reference product.

Figure 4: Stages of development of a biosimilar medicine





REGULATION OF BIOSIMILAR MEDICINES

Many of the questions around biosimilar medicines were also raised about generic medicines when they first became widely available about 20 years ago. The experience gained in the development, regulation and use of generic medicines, together with extensive regulatory and clinical experience with originator biopharmaceuticals, has led to the introduction of new legislation and guidelines to regulate biosimilar medicines.

The idea of a 'biosimilar medicine', with the concept of "biosimilarity", was introduced into EU legislation in 2003 and further developed with the adoption of the 'EU pharmaceutical review' and new legislation in 2004. Europe is leading in the development of a robust regulatory framework for biosimilar medicines; it has been described as arguably one of the most complex issues that the European Commission has faced in the area of pharmaceuticals in the last five years.¹⁹

Scientific guidelines related to all medicines have long been produced by the EMEA over many years, usually after consultation with all the relevant stakeholders. These stakeholders include national regulatory bodies, industry, clinicians, and patient groups.

In the past few years the EMEA, together with the Committee for Medicinal Products for Human Use (CHMP), the Biotechnology Working Party (BWP) and the Working Party on Similar Biological Medicinal Products (BMWPP), and all the appropriate stakeholders, has developed a new series of specific guidelines dealing with all aspects of the development, production, testing and regulation of biosimilar medicines.

Quality, safety and efficacy

In order for any medicine to be marketed, it must be approved by the relevant regulatory body. All manufacturers of medicinal products have to demonstrate that the medicines are:

- of a specific and reproducible quality;
- safe for patients to take (i.e. the risk of potential side effects is considered acceptable when compared to the benefits);
- guaranteed to produce the desired clinically beneficial effect (efficacy).

In order to obtain a marketing authorisation, companies are required to supply data covering all these areas. These data are evaluated by the EMEA and its experts which will include staff from EU national agencies. If all these data are assessed as being satisfactory then the medicine will be approved and will receive a marketing authorisation from the European Commission which will allow the company to launch and market the medicine in Europe.

Pharmacovigilance

All European pharmaceutical companies are legally required to monitor the use and effects of all their medicines. They must have systems in place to detect, assess, understand and communicate any adverse reactions or any other medicine-related problem. This science and activities of these processes are known as 'Pharmacovigilance'.

As part of pharmacovigilance, each pharmaceutical company must provide a detailed description of their pharmacovigilance system in the marketing authorisation application. In addition, for every new medicine, including biosimilar medicines, a **Risk Management Plan (RMP)** must be submitted and agreed by the EMEA. The RMP describes what is known about the safety of the medicine and outlines how the manufacturer will further monitor and fill any gaps in knowledge as well as any measures needed to minimise any risk from the medicine. This plan is published in the European Assessment Report (EPAR) and needs to be updated throughout the lifetime of the medicine.



Once the medicines are marketed, pharmaceutical companies must also continuously evaluate the information on the benefits and risks of their medicines. Therefore post-marketing surveillance (PMS) activities are important. This involves:

- Spontaneous reporting of possible adverse reactions from the medicine by the patient, or by health care professionals e.g. the pharmacist or clinician.
- The preparation of regular reports to review all available safety data. These are known as Periodic Safety Update Reports (PSURs).
- Post-Authorisation Safety Studies (PASS, sometimes called Phase IV studies)

These studies are considered as a relevant part of the Risk Management Plan.

The EMEA is also responsible for the development and maintenance of the EU pharmacovigilance database – **EudraVigilance** – that holds details of all suspected serious adverse reactions to medicines observed in the EU. All pharmaceutical companies must now submit information on serious adverse reactions to the EMEA electronically.

On a larger scale, the EMEA and **Heads of Medicines Agencies (HMA)** from the national regulatory authorities evaluate the implementation of the European Risk Management Strategy (ERMS) which concerns all medicines available in the EU.²⁰ Further improving the operation of the EU Pharmacovigilance System and strengthening the science that underpins the safety monitoring of medicines are two main areas covered by the ERMS.

Immunogenicity

Immunogenicity is the capability of a specific substance to induce the production of antibodies in the human body. It is important to discuss immunogenicity in the context of biosimilar medicines. All biopharmaceuticals, in contrast to conventional pharmaceuticals, demonstrate a greater capacity to elicit such an **immune reaction**, because they are polypeptides or proteins. In many patients, such a response does not lead to any clinical consequences. However, the potential exists for general immune reactions e.g. allergy, **anaphylaxis**. In addition, they may cause reactions which lead to a loss of effect from the medicine or rarely reactions which cause an enhancement of activity. The type and level of **immune response** will be examined during the development process, and after the product is authorised and marketed as part of the pharmacovigilance activities, e.g. in the PSUR.

Immunogenicity may be influenced by factors relating to the medicine itself e.g. manufacturing process and **formulation**, and also by factors related to the patient and the disease and the treatment e.g. route of administration or depressed immune response in cancer patients.²¹ These factors are carefully evaluated during the development and assessment of all biopharmaceuticals, including biosimilar medicines.

Substantial guidance for immunogenicity assessment is incorporated in the various guidelines for biosimilar medicines today.



Table 2: Information required in dossiers submitted to the EMEA (called also marketing authorisation applications)

Quality data	<p>The quality dossier for biosimilar medicines meet the same standard as the reference product. It includes all the necessary data to establish quality for example:</p> <ul style="list-style-type: none"> ■ Definitions and descriptions of the manufacturing process, and associated control tests and standards ■ Data on the consistency of manufacture (quality control of the process) ■ Data on analytical tests (molecular structure; potency and purity/impurity profile)
Pre-clinical data	<p>Dossiers for biosimilar medicines include pre-clinical data. The amount of pre-clinical data required is specific to the product, and will be determined on a case-by-case basis. The data is generated through an abbreviated programme of <i>in vitro</i> and <i>in vivo</i> tests (which may include some animal testing).</p>
Clinical data	<p>Dossiers of biosimilar medicines also include clinical data, the results of trials in patients and healthy volunteers. Due to the clinical experience accumulated over many years with the use of the reference product, the same extent of clinical testing needed for a new active substance is not required. The design of the clinical trial programme takes into account the nature and the characteristics of the medicine and its intended use; and how comparable the profile of the biosimilar medicine is to that of the reference product. The closer the profiles of the medicines are, and the more the similarity has been demonstrated with appropriate comparative quality and pre-clinical tests, the more an abbreviated clinical trial programme can be accepted by the regulators. This means the very high development costs can be reduced. Abbreviated clinical trials also help to ensure that unnecessary human testing does not take place. However, for most biosimilar medicines, extensive trials have been or are required, often including several hundreds of patients.</p> <p>Companies applying for a marketing authorisation must submit all the results from their trials, both positive and negative, which will be assessed on their own merits. A summary of this information is available to the public through EPARs, produced by the EMEA and published on their website when the product is approved by the European Commission.</p>
Pharmacovigilance	<p>Biosimilar medicines, like all medicines, are carefully monitored in the clinical setting after the medicine has been made available. This will be achieved by pharmacovigilance and post-marketing surveillance (see next section). Information about how this will be achieved is included in the application in the description of the Pharmacovigilance Systems and also in the Risk Management Plan.</p>



ACCESS TO BIOSIMILAR MEDICINES

Access to medicines

The World Health Organisation (WHO) states that access to medicines depends on four factors.²²

- Rational selection and use of medicines
- Affordable prices
- Sustainable financing
- Reliable health and supply systems

Most European countries have or are developing strategies to address each of these factors.

Strategies to increase the affordability and availability of medicines to more patients include promoting competition and enhancing the availability of generic medicines. Biosimilar medicines need to be included in these strategies. Since a clear legal and regulatory environment has been established, a clear market pathway for biosimilar medicines needs to be established in each individual Member State to enable access to these medicines as soon as possible after their marketing approval.

Indeed, the way countries determine which medicines are selected and used needs to be adjusted to ensure biosimilar medicines are made fully available.

Factors include marketing authorisation approval, agreement on price and on how the biosimilar medicines are reimbursed and gaining the acceptance of clinicians and patients in using biosimilar medicines as part of their practice and treatment. Access for patients to biosimilar medicines is not automatic; it requires proactive steps to be taken by all relevant stakeholders.

Health economics

The use of medicines increases as people age, with those over 60 years using on average three to four times more medicines than when they were 30. It is estimated that the European population aged over 60 will increase from under 22% to more than 25% between 2000 and 2015.²³ This equates to an additional 50 million people in Europe aged over 60.

Current estimates for Europe show that the related expenditure on medicines is growing at more than twice that of the growth of GDP (Gross Domestic Product).²³ Not surprisingly, the effective management of healthcare costs is key for all governments.

Biopharmaceuticals are some of the world's most expensive medicines. On average, they cost much more per patient as conventional pharmaceuticals. They cost many thousands of euros or more per patient per year for the whole life treatment of some rare metabolic disorders. They are also often used to treat long-term conditions such as diabetes, cancer, anaemia of chronic kidney failure and multiple sclerosis, with a corresponding impact on clinical practice. As a consequence, payers must try to fund the treatments considered best for the patient by their clinicians, while ensuring value for money and the management of finite resources.

These budgetary pressures can result in patients not being treated in accordance to national guidelines. For example, in France, around two-thirds of pre-dialysis patients would be expected to be on erythropoietin (EPO), but figures show that less than half receive the treatment.

The improved affordability of healthcare that could result from the use of biosimilar medicines is real. It has been estimated that 20% reduction in price of five biopharmaceuticals off patent, or imminently off patent, would save the EU over €1.6 billion per year.²⁴

The price differential between a reference product and a biosimilar medicine will depend on the relative development costs. Biosimilar medicines can be expected to be offered at a price below that of the reference product, partly as a result of production process efficiencies, and partly because of the reduced costs of a streamlined development programme. The greatest savings are likely to result from the clinical trial programme, since a biosimilar medicine, containing a known and well-used substance, usually requires less clinical data to support its approval.

The price differential and consequential savings are also likely to increase as biosimilar medicines expand their volume share and it becomes standard practice to use biosimilar medicines amongst healthcare professionals and patients.

These additional savings differential should lead to significant and much-needed release of healthcare funds.



Identification

As required by law for all medicines in the EU, every biosimilar medicine will either have an invented or brand name, or the name of the active substance together with the company name. Every biosimilar medicine is consequently clearly identified by its unique name, which has to be formally accepted by the EMEA prior to its approval.

The first two biosimilar medicines in Europe bear invented names (Omnitrope® and Valtropin®). Both contain the same active substance, somatropin. Somatropin is the scientific name for this active substance. The scientific name is usually called the **INN (International Non-proprietary Name)** or generic name. The INN is also approved by the EMEA during the scientific evaluation of the biosimilar medicine.

The name of a medicine and the name of its active substance are very important for the clear identification, safe prescription and dispensing as well as for monitoring the safety in use of the medicine.

Traceability

All pharmaceutical and biopharmaceutical manufacturers use a variety of techniques to be able to trace their medicine at all times. This includes unique labelling, batch numbering and packaging. Effective traceability also covers systems which track the way medicines reach the patient via the supply chain, and how medicines taken by or administered to patients are recorded and can be traced back in case adverse reactions occur during the treatment.

Interchangeability

Interchangeability refers to the medical/pharmaceutical practice of switching one medicine for another that is equivalent, in a given clinical setting. The regulatory scientific data, published via the EPAR (European Public Assessment Report), should guide the decisions regarding interchangeability.

If an **originator company** changes its manufacturing process of their product, interchangeability between the pre and post-change products is presumed so long as it is supported by comparability data. For scientific consistency, the same approach should be taken for biosimilar medicines.

It is important to reiterate that biosimilar medicines match their reference product in terms of quality, safety and efficacy. A demonstration of therapeutic equivalence is required in order to adopt the posology (dose recommendations) of the reference product.²⁵

The extensive comparability and post-marketing data will therefore demonstrate that it is safe and efficacious to switch dose for dose from the reference product to the biosimilar medicine.

Substitution

Substitution is a national administrative rule which requires or permits the switch from one medicine to another medicine proven to have the same quality, safety and efficacy. Substitution can take place at the retail pharmacy level, or at hospital pharmacies. It is governed by laws for generic medicines which vary from country to country and take various scientific and non scientific parameters into account. As of August 2007, this did not apply to originator and biosimilar medicines.

A 2006 EGA internal survey²⁶ has shown that while 71% of EU countries legally allow generic substitution, in most cases this can be opposed by both the clinician and the patient. Only 7% of EU physicians are legally obliged to prescribe using the INN name only. In the UK, medical students are taught to write prescriptions using INN but physicians are not compelled by law to do so, and pharmacists are obliged to dispense exactly what is written on the prescription. For 18% of EU countries, it is compulsory for pharmacists to substitute a generic medicine if one is available. Such an obligation is called automatic substitution.



EVOLVING LANDSCAPE OF BIOSIMILAR MEDICINES

The period from 2007 to 2010 will see more developments in relation to biosimilar medicines, and healthcare professionals and healthcare purchasers need to ensure that they are aware of what is happening in this rapidly changing environment.

A large number of patents of originator reference products have lost their protection since 2001.

More biosimilar medicine applications are under assessment by the EMEA, with a number of additional applications in the manufacturers' pipeline. They mainly concern epoetins, interferons, insulins and granulocyte-colony stimulating factors (G-CSFs).¹⁹

The EMEA guidelines not yet finalised by September 2007 covered:

- Therapeutic specific annex to the overarching guideline - for recombinant alpha-Interferons.²⁷
- Guideline for the immunogenicity assessment of biological / biotechnology-derived proteins²¹ (which applies to both originator and biosimilar medicines).
- Guidance note on comparability after a change in the manufacturing process (which applies to both originator and biosimilar medicines).²⁸
- Guideline on similar biological medicinal products containing low molecular weight heparins.²⁹

To keep ahead of the evolving landscape, further developments can be monitored via the EMEA web site.

In order to support all those interested in biosimilar medicines, this handbook will be followed by updates on the EGA website.

Table 3: Some examples of active substances of originator reference products

Scientific Name of the Active Substance	Main Treatment Area
imiglucerase	Gaucher disease
human insulin	diabetes
interferon alpha 2a interferon alpha 2b	various cancers, viral hepatitis B & C
interferon beta-1a interferon beta-1b	multiple sclerosis
somatropin	growth hormone deficiency
epoetin alfa epoetin beta	anaemia associated with chronic kidney failure
alteplase	heart attack
filgrastim (granulocyte-colony stimulating factor, G-CSF)	neutropenia (in cancer patients)



FURTHER INFORMATION

More information on the issues summarised in this short guide can be found at the following links:

Table 4: Useful website links

European Medicines Agency (EMA)	http://www.emea.eu.int/
European Commission, Enterprise and Industry	http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm
World Health Organisation (WHO)	http://www.who.int/en
European Generics medicines Association (EGA)	http://www.egagenerics.com/

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Disclaimer:

The information in this handbook contains the views of the EGA, and not the views of the EMEA or any national regulatory agency.



Making Medicines Affordable

GLOSSARY

Active substance:

Active ingredient or molecule which goes into a specific medicine and which provides this medicine with properties for treating or preventing one or several specific disease(s)

Anaemia:

Low red blood cell count

Anaphylaxis:

Acute and severe allergic reaction in humans

Antibodies:

Large proteins used by the immune system to identify and neutralise foreign objects e.g. bacteria, viruses

Adverse reaction:

Any unexpected or expected reaction following the administration of a given medicine that is harmful to the patient

Biopharmaceuticals:

Medicines made by or derived from living organisms using biotechnology

Biotechnology:

Technology which manipulates living organisms so that they reproduce human hormones e.g. insulin

Bioequivalence study:

Assessment of the comparative behaviour in the body of two medicines

Bioequivalent:

Two medicines are considered bioequivalent if they are shown to behave in the body in the same way

Biosimilarity:

Capacity of a medicine to show similarity in terms of quality, safety and efficacy to a reference biological medicine to which it has been compared

Biosimilar medicine:

Medicine which is approved by the regulatory authorities to be similar in terms of quality, safety and efficacy to a reference biological medicine with to which it has been compared

Comparability:

The scientific evaluation of a comparison of two medicinal products to determine equivalence and any detectable differences at the level of quality, safety and efficacy

Formulation:

The recipe and presentation of a medicine

Gaucher disease:

Rare inherited disorder; people with this disease do not have enough of a specific enzyme called glucocerebrosidase

Generic medicine:

Medicine which has the same composition in active substance (s) and the same pharmaceutical form as the originator reference medicine, and whose bioequivalence with the originator reference medicine (i.e. the same behaviour in the body) has been demonstrated by appropriate bioavailability studies

Glycosylation:

The type and length of any sugar or carbohydrate groups attached to a given molecule

EudraVigilance:

Data processing network and management system for reporting and evaluating suspected adverse reactions during the development and following the marketing authorisation of medicinal products in the European Economic Area (EEA)

EU Pharmaceutical Review:

European legislative process which adopted a new EU pharmaceutical legislation on 31 March 2004

INN (Internationally Non-proprietary Name):

Scientific or generic name of an active substance. INNs for new active substances are allocated by the World Health Organisation (WHO) in Geneva. The INN is a unique and universally accessible name. For generic and biosimilar medicines cross-referring to reference products, it is the regulatory authority who decides whether the INN of the active substance as submitted for the generic or the biosimilar medicine is scientifically acceptable

Immune response/reaction:

Production of antibodies by the human body in reaction e.g. to viruses and substances recognized as foreign and possibly harmful

Immunogenicity:

Capability of a specific substance to induce the production of antibodies in the human body which is also called an immune response/reaction.

Interchangeability:

Refers to the medical/pharmaceutical practice of switching one medicine for another that is equivalent, in a given clinical setting

In vitro:

Biological or chemical work done in the test tube (*in vitro* is Latin for "in glass") rather than in living systems

In vivo:

Experiments or tests carried out in living organisms (as opposed to the laboratory)

Heads of Medicines Agencies:

Grouping of Heads of Member States Competent Authorities who deal with the System of Medicines Regulation, and who provides a forum for the exchange of views on issues of Community interest

Molecule:

Compound made by atoms in a definite arrangement held together by strong chemical bonds

Originator Company:

Company first to develop and produce a specific medicine (biopharmaceutical or pharmaceutical)

Patent:

Set of exclusive rights granted to a company for a set period of time in exchange for the disclosure of its invention

Phase I study or trial:

Study determining that a medicine is safe in healthy humans and helping to predict the dosage range for the medicine. These are often conducted in healthy volunteers

Phase III study or trial:

Study involving a larger group of patients which helps to determine if the medicine can be considered both safe and effective in a real clinical setting

Pharmaceuticals:

Conventional or traditional chemical medicines

Pharmacodynamic tests:

Study of the action/effects of a medicine over a period of time

Pharmacokinetic tests or studies:

To determine how medicines are absorbed, distributed, metabolised and eliminated by the body

Pharmacovigilance:

Defined by the World Health Organization as the science and activities relating to detection, assessment, understanding and prevention of any adverse effects or any other medicine-related problem

Physicochemical characterisation:

Test to determine the properties of a molecule or active substance e.g. molecular size/weight, chemical structure, purity

Polypeptides:

Molecules made up of chains of amino acids, which may have activity in the human body. They contain less amino acids, and hence have lower molecular weights than proteins

Post-Authorisation Safety Study:

Clinical trial carried out in accordance with the terms of a marketing authorisation and conducted with the aim of identifying or quantifying a safety hazard relating to an authorised medicinal product

Pre-approval inspection:

Any inspection (e.g. of the manufacturing plant) performed by a regulatory authority before the medicine receives its marketing authorisation

Proteins:

Large molecules made of amino acids arranged in a chain. E.g. erythropoietin is a protein

Reference (originator) product:

Medicine, which has been developed and produced by an originator company, and which has been approved by the national regulatory authorities or the European Commission on the basis of a full registration dossier

Risk Management Plan:

Plan which describes what is known about the safety of the medicine and outlines how the manufacturer will further monitor and fill any gaps in knowledge as well as any measures needed to minimise any risk from the medicine

Scientific peer review:

Scientific review and validation of documents or data performed by peers, who are independent scientists with suitable qualifications and experience

Substitution:

Refers to a national administrative rule which requires or permits the switch from one medicine to another medicine proven to have the same quality, safety and efficacy. Substitution can take place at retail pharmacy level, or at hospital pharmacies. It is governed by laws for generic medicines which vary from country to country and take various scientific and non scientific parameters into account

Traceability:

Refers to the ability to trace every batch of a medicine in the distribution and supply chain as well as to trace back which medicine has been taken by or administered to a patient

REFERENCES

¹ IMS MIDAS, Therapy Forecaster, Market Insights, Sep. 2006

² Scrip-World Pharmaceutical News-17 September 2007 (Ref. S00970766)

³ OECD Health Data 2006, OECD, Paris June 2006 (OECD in figures 2006-2007) - ISBN 9264022635

⁴ European Public Assessment Report: Valtropin (Doc. Ref.: EMEA/H/C/602, approved on 24 April 2006)

⁵ European Public Assessment Report: Omnitrope (Doc. Ref.: EMEA/H/C/607, approved on 12 April 2006)

⁶ Directive 2004/27/EC of the European Parliament and Council of 31 March 2004 amending Directive 2001/83/EC on the Community Code relating to Medicinal Products for Human Use; and Regulation (EC) 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

⁷ EMEA Annual Report 2006 (Doc. Ref.: EMEA/MB/24167/2007/EN/Final), page 23/134

⁸ Guideline on Similar Biological Medicinal Products (Doc. Ref.: EMEA/CHMP/437/04, London, 30 October 2005)

⁹ Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Quality Issues (Doc. Ref.: EMEA/CHMP/BWP/49348/2005, London, 22 February 2006)

¹⁰ Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues. (Doc. Ref.: EMEA/CHMP/BWP/42832/2005, London, 22 February 2006)

¹¹ Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues - Guidance on Similar Medicinal Products Containing Recombinant Granulocyte-Colony Stimulating Factor (Doc. Ref.: EMEA/CHMP/BWP/31329/2005, London, 22 February 2006)

¹² Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues - Guidance on Similar Medicinal Products Containing Recombinant Human Soluble Insulin (Doc. Ref.: EMEA/CHMP/BWP/32775/2005, London, 22 February 2006)

¹³ Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues - Guidance on Similar Medicinal Products Containing Somatropin (Doc. Ref.: EMEA/CHMP/BWP/94528/2005, London, 22 February 2006).

¹⁴ Annex to Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: Non-clinical and Clinical Issues - Guidance on Similar Medicinal Products Containing Recombinant Erythropoietins (Doc. Ref.: EMEA/CHMP/BWP/94526/2005 Corr., London, 22 March 2006).

¹⁵ The community register of medicinal products, European Commission, Enterprise and Industry

¹⁶ Work Programme for the European Medicines Agency 2007, adopted by the Management Board on 19 December 2006 (Doc. Ref.: EMEA/MB/428793/2006/EN/Final)

¹⁷ Doc. Ref.: EMEA/74562/2006

¹⁸ EMEA Press Release of 18 October 2007 (Doc. Ref. EMEA/479200/2007)

¹⁹ Personal testimony of Nicolas Rossignol (European Commission) at the Hearing before the Senate Help Committee on 'Follow-On-Biologics' (March 2007) (Introduction, page 1)

²⁰ Public Status Report on the Implementation of the ERM Strategy /Reporting Period Mid 2005–Mid 2007)(Doc. Ref.: EMEA/168954/2007)

²¹ Draft Guideline on Immunogenicity Assessment of Biotechnology-derived Therapeutic Proteins (Doc. Ref.: EMEA/CHMP/BMWP/14327/06, London 24 January 2007)

²² World Health Organization website (Globalization, trade and health/Access to medicines)

²³ UN Population division, OECD 2001

²⁴ Oldham, T. *Strategies for entering the biosimilar market*, in: Biosimilars – Evolution or Revolution? (November 2006). Biopharm Knowledge Publishing, London

²⁵ Report of WHO Informal Consultation on Regulatory Evaluation of Therapeutic Biological Medicinal Products (19 – 20 April, 2007). The report contains the collective views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization

²⁶ 2006 (Internal) MARKET REVIEW: The European Generic Pharmaceutical Markets. EGA, Brussels

²⁷ Annex to the Guideline on Similar Biological Medicinal Products containing Biotechnology-derived Proteins as Active Substance: (Non) Clinical Issues – Concept paper on similar biological medicinal products containing recombinant alpha-interferon (Doc.Ref.: CHMP/BMWP/7241/2006, London, 26th April 2006)

²⁸ Draft Guideline on Comparability of Biotechnology-derived Medicinal Products after a Change in the Manufacturing Process – Non-clinical and clinical issues (Doc. Ref.: CHMP/BMWP/101695/2006, London 24 January 2007)

²⁹ A concept paper on similar biological medicinal products containing low molecular weight heparins – (non) Clinical Issues (Doc. Ref.: EMEA/CHMP/BMWP/496286/2006).

ACRONYMS AND ABBREVIATIONS

BMWP	Working Party on Similar Biological Medicinal Products (EMA)
BWP	Biotechnology Working Party (EMA)
CHMP	Committee for Medicinal Products for Human use (EMA)
EC	European Commission
EEA	European Economic Area
EGA	European Generic medicines Association
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ERMS	European Risk Management Strategy
EPO	Erythropoietin
EU	European Union
G-CSF	Granulocyte-Colony Stimulating Factor
GDP	Gross Domestic Product
GMP	Good Manufacturing Practice
HMA	Heads of Agencies
INN	International Non-proprietary Name
MAB	Monoclonal Antibody
NCA	National Competent Authority
PAI	Pre-Approval Inspections
PD	Pharmacodynamics
PK	Pharmacokinetics
PASS	Post-Authorisation Safety Studies
PMS	Post-Marketing Surveillance
PSUR	Periodic Safety Update Reports
RMP	Risk Management Plan
WHO	World Health Organisation

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Making Medicines Affordable

Formed in 1993, the EGA is the official representative body of the European generic pharmaceutical industry, which is at the forefront of providing highquality affordable medicines to millions of Europeans and stimulating competitiveness and innovation in the pharmaceutical sector.

The EGA and its members work with European national governments and the EU institutions to develop affordable solutions for pharmaceutical care and to increase Europe's competitive strength in the global pharmaceutical market

L'EGA, créée en 1993, est le représentant officiel de l'industrie pharmaceutique générique européenne, au premier rang de la production de médicaments de haute qualité et abordables pour des millions d'européens stimulant ainsi la concurrence et l'innovation dans le secteur pharmaceutique.

L'EGA ainsi que ses membres, oeuvrent avec les gouvernements nationaux européens et les institutions européennes au développement de solutions économiques pour la santé et au renforcement de la concurrence européenne sur le marché pharmaceutique au niveau mondial

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