

GRIFOLS

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PRESS BOOK 2013



A **WORLD-LEADING**
MANUFACTURER OF PLASMA-
BASED BIOLOGICAL MEDICINES



Grifols employs almost 11,200 people in 24 countries, who share the mission of improving people's health and well-being through the research, development, manufacture and distribution of plasma-derived medicines, technology for clinical diagnosis and pharmaceutical preparations for hospital use.

Grifols is one of the leading companies in the world in the manufacture of plasma proteins, and the largest European company in this sector. It is one of only a few vertically

A **70-YEAR HISTORY OF**
IMPROVING THE QUALITY
OF LIFE FOR PATIENTS



integrated companies, enabling it to control the entire production cycle, from the collection of raw material in the form of plasma through an extensive network of 150 donor centers in the United States, through to the finished product. Its head office is in Barcelona, Spain.

Grifols embarked on a new era in 2012 following its purchase of North American company Talecris Biotherapeutics in 2011. The success of this operation has doubled the size of Grifols, strengthening its presence in regions such as North America,

A MISSION TO REACH THOSE
PATIENTS WHO DO NOT YET
BENEFIT FROM TREATMENT



and enabling it to expand its portfolio of plasma-derived products for the benefit of patients.

Combining the expertise of both companies in the plasma industry means that Grifols can look to the future with even more ambition and the same entrepreneurial spirit with which it began 70 years ago.

SALES REVENUE OF 2,620 MILLION EUROS IN 2012

- 92% OF INCOME GENERATED IN INTERNATIONAL MARKETS
- STRONG PRESENCE IN THE USA AND CANADA, ACCOUNTING FOR OVER 63% OF SALES, WITH 21% GENERATED IN EUROPE, AND 15% IN OTHER REGIONS

DISTRIBUTION AND SALE OF PRODUCTS IN OVER 100 COUNTRIES

DIRECT GEOGRAPHIC PRESENCE IN 24 COUNTRIES THROUGH WHOLLY OWNED SUBSIDIARIES

MANUFACTURING FACILITIES IN THE UNITED STATES, SPAIN, AUSTRALIA AND SWITZERLAND

150 PLASMA DONOR CENTERS IN THE USA

ALMOST 11,200 EMPLOYEES ACROSS THE WORLD

AROUND 73% OF THE WORKFORCE BASED IN THE UNITED STATES

ONGOING COMMITMENT TO R&D, WITH AN ALLOCATION OF 5% OF ANNUAL INCOME

EXPERTS IN THE MANUFACTURE OF LIFESAVING BIOLOGICAL MEDICINES, INCLUDING:

- **IMMUNOGLOBULINS**, PARTICULARLY INTRAVENOUS IMMUNOGLOBULIN (IVIG), TO TREAT IMMUNOLOGICAL DISORDERS
- **ALBUMIN**, TO REESTABLISH AND MAINTAIN BLOOD VOLUME
- **FACTOR VIII**, INDICATED FOR THE TREATMENT AND PREVENTION OF HEMORRHAGE IN PATIENTS WITH HEMOPHILIA A AND ACQUIRED FACTOR VIII DEFICIENCY
- **ALPHA-1-ANTITRYPSIN**, TO PROTECT AGAINST THE DETERIORATION OF LUNG TISSUES (PULMONARY EMPHYSEMA)





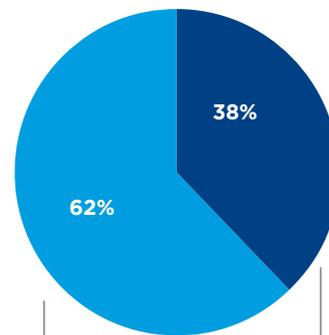
At January 4, 2013, Grifols' share capital amounted to 119,515,205.30 million euros, represented by 213,064,899 ordinary shares (Class A), and 129,827,558 non-voting shares (Class B).

Grifols ordinary shares (Class A) are listed on the Spanish Continuous Market, where they form part of the Ibex-35 (GRF), Spain's leading share index, while its non-voting shares (Class B) are also listed on the Continuous Market (GRF.P) and on the NASDAQ (GRFS) via ADRs (American Depositary Receipts). One Grifols ADR represents one Class B share.

ORDINARY SHARES (CLASS A)
INCLUDED IN THE **IBEX-35**,
SPAIN'S LEADING SHARE INDEX

NON-VOTING SHARES
(CLASS B) LISTED ON THE
SPANISH CONTINUOUS MARKET
AND ON THE **NASDAQ**

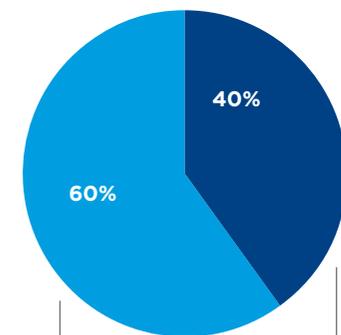
ECONOMIC SHARE STRUCTURE CLASS A AND B SHARES



Class A Shares

Class B Shares

VOTING STRUCTURE - CLASS A SHARES



Institutional / **Freefloat**

Reference Shareholders

THREE DIVISIONS TO MEET THE NEEDS OF PATIENTS AND HEALTH PROFESSIONALS

BIOSCIENCE DIVISION

SPECIALIZING IN PLASMA-DERIVED PRODUCTS FOR THERAPEUTIC USE

ACCOUNTED FOR APPROXIMATELY 88.7% OF INCOME IN 2012

The Bioscience division is Grifols' principal line of business; it draws on the legacy of over 70 years of delivering therapies that improve the quality of life for patients with potentially life-threatening diseases.

The main plasma derivatives are:

- Intravenous immunoglobulin (IVIG)
- Factor VIII
- Albumin
- Alpha-1-antitrypsin (A1-AT)
- Other hyperimmune immunoglobulins

Grifols is currently the world's third largest plasma product company by sales volume and the largest in Europe. In addition, it is the global leader in plasma collection capacity. To achieve this, it has a network of 150 plasma donor centers in the United States, enabling it to obtain more than 6.5 million liters of plasma per year, thereby ensuring a constant and reliable supply of raw material to meet the growing demand for plasma protein treatments.

In order to fractionate and obtain these products, Grifols possesses two plants in the United States and one in Spain; between them, these are able to process up to 8.5 million liters of plasma per year.

HOSPITAL DIVISION

THIS BRINGS TOGETHER NON-BIOLOGICAL PHARMACEUTICAL PRODUCTS AND HEALTH SUPPLIES FOR HOSPITAL PHARMACY

IT GENERATES 4% OF TURNOVER

The division's main products include parenteral solutions (fluid therapy), enteral and parenteral clinical nutrition products, and hospital logistics systems.

Since 2005, the division's plants in Barcelona and Murcia have offered third-party manufacturing services through its Grifols Partnership service. Such arrangements ensure that Grifols maximizes use of its high-tech facilities and makes the company's experience and knowledge of the production of sterile solutions and other health products available to third parties.



DIAGNOSTIC DIVISION

SPECIALIZING IN CLINICAL DIAGNOSTICS

IT ACCOUNTS FOR 5% OF SALES

The Diagnostic division manufactures and develops instrumentation and reagents in three specialist areas: transfusion medicine, immunology and hemostasis. Grifols is one of the leading suppliers of diagnostic tests for transfusion safety. Instrumentation to automate blood typing techniques and donor-patient blood compatibility studies is part of the company's offering for hospital blood banks, transfusion centers and immunohematology labs.

The division's hemostasis line primarily offers instrumentation and reagents for investigating the coagulation status of patients.

Key products in the company's line of automated instruments for diagnostic testing include the WaDiana® and Erytra® immunohematology analyzers, the Triturus® immunology system, and the Q® automatic hemostasis analyzer.

The plasma derivatives produced by the Bioscience division are lifesaving biological medicines used in the following areas:

IMMUNE DISORDERS

Grifols' immunoglobulin range (IVIG) is designed to treat people born with a variety of primary immunodeficiencies, and to provide replacement therapy for patients with chronic lymphatic leukemia or recurrent infections.

PRIMARY IMMUNODEFICIENCIES

Primary immunodeficiencies (PI) encompass a group of 150 diseases that are inherited or caused by genetic errors in the cells that constitute the immune system. As a result, the immune system that protects the body against bacteria or viruses does not function properly. Individuals with an immune deficiency disease are susceptible to infection, both mild and severe, and take longer to recover.

There are different treatments for the different types of primary immunodeficiency. One of the most common treatments is intravenous immunoglobulin (IVIG), which is able to help some patients by temporarily replacing the antibodies needed to fight infection. The IVIG replaces the antibodies that the body should be producing, but does not help the patient's immune system to create more. This is because replacement therapy works by helping to combat infections in patients with immune deficiencies.

NEUROLOGICAL DISORDERS

Gamunex® is the only intravenous immunoglobulin approved by the FDA for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP), a rare neurological disease that causes progressive muscular weakness in the arms and legs.

PLASMA VOLUME REPLACEMENT THERAPY

Human albumin is one of the essential proteins and is the largest single component of blood. In intensive care it is used as a treatment to reestablish plasma volume in patients who have suffered from shock or trauma with a significant loss of blood. Grifols biological medicines such as albumin are administered to reestablish and maintain blood volume.

CLOTTING DISORDERS

Grifols also manufactures biological medicines indicated for the treatment and prevention of diseases that cause excessive bleeding or abnormal clotting, including hereditary diseases such as hemophilia, von Willebrand's disease and anti-thrombin deficiency.

An absence of factor VIII produces hemophilia A, while the lack of factor IX causes hemophilia B. Grifols produces specific clotting factors to meet the needs of patients suffering from deficiencies of either of these plasma proteins.

ALPHA-1 ANTITRYPSIN DEFICIENCY

Also known as AATD or alpha-1, this is a hereditary disorder that causes a significant reduction in the naturally occurring protein, alpha-1-proteinase. Alpha-1 is the most common cause of genetic emphysema in adults, and the most common cause of liver disease in children. People who suffer from this deficiency often develop chronic obstructive pulmonary disease (COPD), leading to incapacity and early death.

Grifols is the world's leading producer of alpha-1 proteinase inhibitor, used to provide replacement therapy for alpha-1-antitrypsin deficiency (AATD) in patients with pulmonary emphysema.

FATAL INFECTIONS

Grifols produces a range of hyperimmune immunoglobulins that provide rapid, temporary immunity against a series of potentially fatal infections such as rabies, tetanus, hepatitis B and Rh incompatibility.

PRESENT IN OVER 100 COUNTRIES, AND WITH SUBSIDIARIES IN 24 COUNTRIES

During recent years, Grifols has consolidated its presence in the United States, and its subsidiary Grifols Inc. is the parent company for the group's subsidiaries in that country. Grifols took its first steps towards consolidating its business structure in the North American market with the acquisition, in March 2002, of its first 48 plasma donor centers. Through a combination of acquisitions and the opening of new centers, this network now consists of 150 centers.

Other corporate operations, including the acquisition of Talecris, have seen Grifols' presence in the United States grow steadily, together with the incorporation of Canada as a major new market with its own subsidiary. Approximately 85% of sales are concentrated in Europe and the United States, although other emerging areas such as Latin America and the Asia-Pacific region are gradually gaining in importance. Grifols has a strong presence in Latin America, with subsidiaries in Argentina, Chile, Mexico, Brazil and Colombia. In Europe it has subsidiaries in Spain, Portugal, France, the United Kingdom, Italy, Germany, the Czech Republic, Slovakia, Poland, Switzerland and Scandinavia, and in the Asia-Pacific region it has established subsidiaries in Japan, Thailand, Malaysia, Singapore, China and Australia.

INTERNATIONAL EXPANSION CONTINUES TO BE ONE OF THE STRATEGIC DRIVERS OF GROWTH



MANUFACTURING FACILITIES IN EUROPE AND THE UNITED STATES

GRIFOLS

GRIFOLS' PLASMA DERIVATIVES, HEALTH PRODUCTS AND CLINICAL DIAGNOSTICS PRODUCTS SHARE A SINGLE PURPOSE: TO SERVE THE NEEDS OF MILLIONS OF PATIENTS AND TO SUPPORT THE WORK OF HEALTH PROFESSIONALS

AT ALL OF ITS MANUFACTURING PLANTS, GRIFOLS APPLIES THE HIGHEST QUALITY AND SAFETY STANDARDS

INVESTMENT IN MANUFACTURING FACILITIES WILL TOTAL OVER 400 MILLION EUROS DURING THE PERIOD 2012-2015



MANUFACTURING PLANTS: PLASMA-DERIVED MEDICINES

The manufacture of plasma-derived medicines is a highly technological process. Grifols has a track record of improving and modernizing its facilities for the fractionation and purification of the various therapeutic plasma proteins in order to maximize the safety and efficacy of these products.

Production plants:

PARETS DEL VALLÈS

(BARCELONA, SPAIN). ONE OF THE LARGEST PLASMA FRACTIONATION PLANTS IN EUROPE. CAPACITY TO FRACTIONATE 2.1 MILLION LITERS OF PLASMA PER YEAR.

LOS ANGELES

(CALIFORNIA, UNITED STATES). CAPACITY TO FRACTIONATE 2.2 MILLION LITERS OF PLASMA PER YEAR.

CLAYTON

(NORTH CAROLINA, UNITED STATES). CAPACITY TO FRACTIONATE 3 MILLION LITERS OF PLASMA PER YEAR.

Grifols' fractionation capacity currently stands at 8.5 million liters of plasma per year. Future plans provide for this to increase to over 12 million liters by 2016.



MANUFACTURING PLANTS: PHARMACEUTICAL PREPARATIONS AND HEALTH PRODUCTS

Grifols is one of the leading Spanish manufacturers of enteral and parenteral solutions in flexible and glass containers.

It manufactures products for intravenous therapy in accordance with the highest quality standards, and its plants hold environmental, quality and workplace safety certification: ISO 9001, ISO 14001, ISO 13485, OHSAS 18001.

These are as follows:

PARETS DEL VALLÈS
(BARCELONA, SPAIN). PRODUCTION PLANT FOR INTRAVENOUS SOLUTIONS FOR PARENTERAL NUTRITION IN GLASS CONTAINERS.

LAS TORRES DE COTILLAS
(MURCIA, SPAIN). MANUFACTURING FACILITIES FOR THE PRODUCTION OF INTRAVENOUS SERUM IN FLEXIBLE CONTAINERS AND BLOOD CONSERVATION BAGS. HOLDS FDA HEALTH PRODUCT APPROVAL.

DEVELOPMENT AND MANUFACTURING PLANTS: DIAGNOSTIC PRODUCTS

PARETS DEL VALLÈS
(BARCELONA, SPAIN). DIAGNOSTIC PRODUCTS MANUFACTURING PLANT.

DÜDINGEN
(SWITZERLAND). MANUFACTURING PLANT FOR MDMULTICARD® RAPID BLOOD GROUP TYPING CARDS.

MELBOURNE
(AUSTRALIA). DG GEL® CARD MANUFACTURING PLANT.

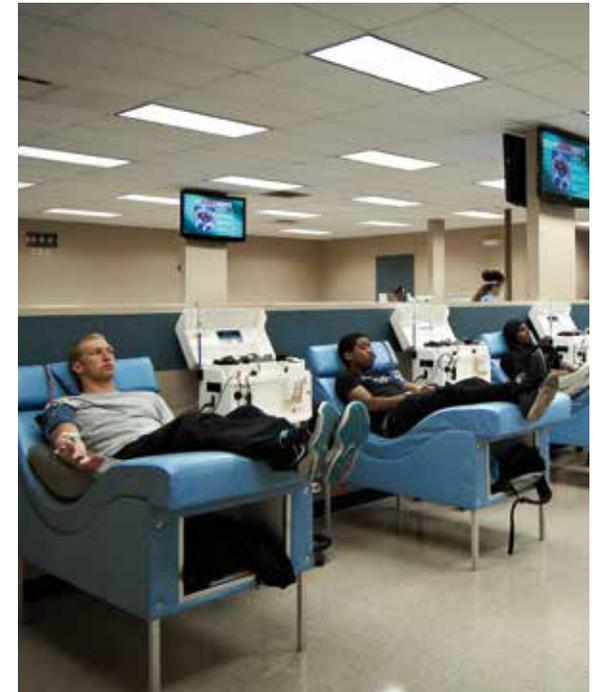
PLASMA SUPPLY

The production of plasma-derived medicines depends on a supply of high quality plasma. Grifols is the world's leading plasma supplier, and has built up an extensive US-based organization, Grifols Plasma Operations, consisting of:

150 PLASMA DONOR CENTERS DISTRIBUTED THROUGHOUT THE UNITED STATES, WHICH PROVIDED GRIFOLS WITH 5.8 MILLION LITERS OF PLASMA IN 2012.

TWO CENTRAL PLASMA ANALYSIS LABORATORIES IN THE UNITED STATES: SAN MARCOS AND AUSTIN (TEXAS).

PLASMA LOGISTICS:
3 CENTRAL WAREHOUSES FOR THE STORAGE AND DISTRIBUTION OF PLASMA TO THE DIFFERENT MANUFACTURING CENTERS.



RECONCILING MANUFACTURING WITH THE NEEDS OF THE ENVIRONMENT

The increased production of plasma derivatives by the Bioscience division, Grifols' main area of activity, has been achieved on a responsible basis that minimizes the potential environmental impact. This has been made possible by applying the company's environmental policy and objectives, the key features of which are set out in the Corporate Plan for strategic action on energy 2010–2012.

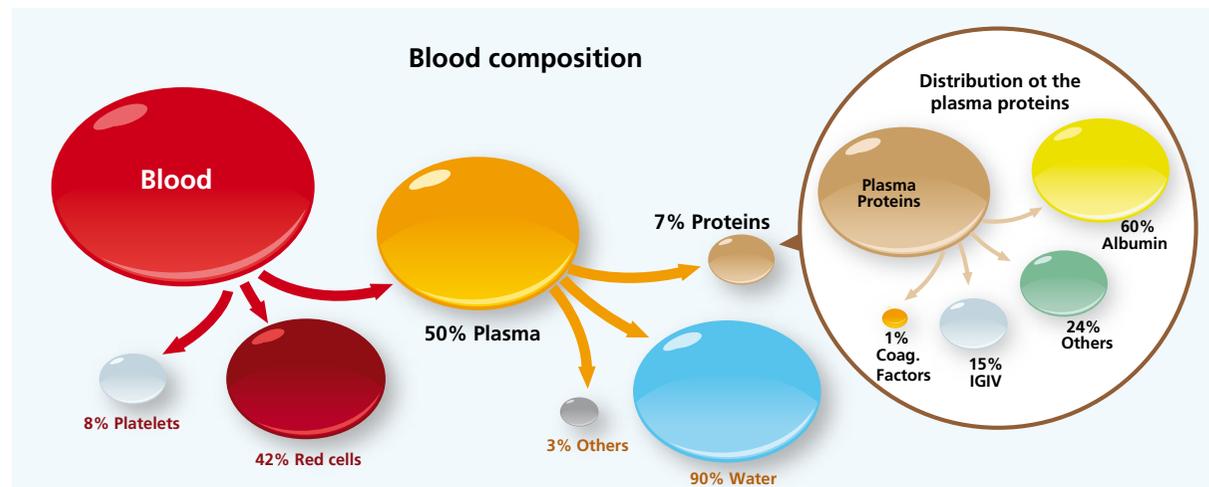
At all Grifols' manufacturing facilities, key objectives focus on recovering compounds, as in the case of ethanol, increasing the recycling of waste, both general and plastic, through more efficient separation, and reducing atmospheric emissions. Grifols participates in the Carbon Disclosure Project (CDP), an initiative designed to recognize the measures adopted by various companies to reduce emissions and mitigate the risks of climate change. In 2012, the company obtained a score of 88 out of 100, making Grifols the 14th highest placed company of the 125 largest companies in Spain and Portugal, and the leading company in the health sector.



Plasma is the liquid component of human blood. Around 90% of plasma consists of water, and approximately 7% of the remainder consists of essential proteins and antibodies that help maintain the vital functions of our body. These are what are called plasma proteins.

A deficit of any of these proteins, such as albumin or the immunoglobulins, causes diseases that can only be treated through the administration of plasma-derived products. Proteins converted into medicines are the standard treatment for millions of people who need them to stay alive. Grifols develops and produces these blood-derived treatments and distributes them in almost 100 countries across the world.

Some of the most important biological medicines obtained from plasma include albumin, clotting factors (such as factor VIII), intravenous immunoglobulin (IVIG) and alpha-1-antitrypsin.



In order to produce the necessary quantities of these lifesaving proteins, a considerable quantity of human plasma is required as raw material, because not all of the proteins are present in the same proportion in plasma.

From collection of the plasma unit until distribution of the final product takes between 9 and 11 months. This cycle is managed by Grifols from start to finish, and the company's integrated production model enables it to guarantee every stage of this complex process.

PLASMA COLLECTION

Plasmapheresis is the process most widely used to obtain donated plasma. This is a method by which plasma is separated from the other blood components (red blood cells, platelets and other cells), which are injected back into the donor during the donation process. For this reason, we always talk about plasma donations, not blood donations.

Plasmapheresis was developed by Dr. José Antonio Grifols Lucas in 1951, and is the most effective system for obtaining the amounts of plasma needed to extract the different therapeutic proteins through industrial fractionation.

Grifols has 150 donor centers in the United States, and these provide almost all of the plasma it then fractionates to obtain each protein for therapeutic use.

Grifols has also fractionated excess plasma from Spanish hospitals for over 20 years. Spanish plasma is converted into plasma-derived products for use by the Spanish health system. Similar agreements exist with hospitals in Canada, the Czech Republic and Slovakia.

PLASMA FRACTIONATION AND PROTEIN PURIFICATION

After the plasma has been collected, it is subject to careful controls to ensure its quality. It is then fractionated or separated to obtain each of the different therapeutic proteins. Fractionating the plasma involves subjecting it to various changes of temperature and pressure, among other procedures, causing each protein to separate out.

Once it has been separated, each protein undergoes a rigorous process to inactivate any infectious agents, and is purified before being filled under sterile conditions to maintain its therapeutic properties.

Grifols' manufacturing facilities in the United States and Spain are licensed by the FDA and by the health authorities of the European Union. All the processes are performed in accordance with Good Manufacturing Practice for Drugs (GMP).

BIOSCIENCE DIVISION: FINISHED PRODUCTS

The main plasma derivatives manufactured by Grifols are intravenous immunoglobulins, coagulation factor VIII, albumin and alpha-1-antitrypsin.



BIOSCIENCE DIVISION: FINISHED PRODUCTS

INTRAVENOUS IMMUNOGLOBULIN (IVIG)

Intravenous immunoglobulins are regarded as the most important plasma derivatives. These are the purified plasma fraction containing the antibodies that provide the body with its immune defenses. They are currently the most widely consumed plasma proteins.

IVIG is generally indicated for the treatment of primary immunodeficiencies, certain secondary immunodeficiencies, various autoimmune diseases and in allogenic bone marrow transplant.

Grifols produces the first and, to date, only IVIG approved in the United States and Canada to treat chronic inflammatory demyelinating polyneuropathy (CIDP), a neurological disorder characterized by progressive weakening and deterioration of the sensory function in the arms and legs. This immunoglobulin is also registered in the United States for subcutaneous use in the treatment of primary immunodeficiencies.

ALBUMIN

Albumin is indicated for reestablishing and maintaining blood volume in situations due to traumatic shock or hemorrhage. Replacing human albumin can speed up recovery and increase the survival rate of intensive care patients.

COAGULATION FACTOR VIII

Factor VIII is indicated for the treatment and prevention of hemorrhage in patients with hemophilia A and acquired factor VIII deficiency. Future market growth for factor VIII is ensured due to the rise in prophylactic treatments, combined with the large number of hemophiliacs who still do not receive treatment. According to the *World Federation of Hemophilia*, only around 20% of the world's hemophiliacs receive treatment with factor VIII concentrates.

One of the versions of factor VIII produced by Grifols is the first and only high-purity concentrated factor VIII/von Willebrand factor complex to incorporate a double inactivation stage in its production process. It has been approved by the FDA for use in the treatment of congenital von Willebrand disease.

ALPHA-1-ANTITRYPSIN

Alpha-1-antitrypsin is a protease inhibitor that is indicated as a replacement therapy for people with alpha-1-antitrypsin deficiency, which is a genetic disorder that can cause chronic obstructive pulmonary disease (COPD) such as emphysema and chronic bronchitis.

OTHER HYPERIMMUNE IMMUNOGLOBULINS

Grifols' portfolio of plasma derivatives includes various specific hyperimmune immunoglobulins for the treatment of potentially fatal infections such as rabies, tetanus, hepatitis B and Rh incompatibility.

HOSPITAL DIVISION PRODUCTS

Through its Hospital division, Grifols supplies standard parenteral solutions for intravenous therapy, preparations for clinical nutrition, and a wide range of sterile products and medical devices. In addition, the division provides technological platforms for hospital logistics management, designed to ensure that citizens receive safe, high-quality healthcare. These include cutting-edge products for the management of medicines.

AREAS OF SPECIALIZATION

FLUID THERAPY: SOLUTIONS FOR INTRAVENOUS THERAPY

The intravenously administered therapeutic solutions to restore or maintain fluid and electrolyte balance that Grifols offers to hospital pharmacy services are available in a range of pharmaceutical forms. The company also develops systems for the preparation of intravenous solutions under sterile conditions, such as the Misterium®-Modular Clean-Room and the Grifill® 3.0 filling device.

CLINICAL NUTRITION

Clinical nutrition affects patients' quality of life and contributes to their rehabilitation. Grifols produces a full range of special diets and formulations for parenteral nutrition and enteral (oral or nasogastric) nutrition.

MEDICAL DEVICES FOR INTERVENTIONAL THERAPY

This line includes advanced instrumentation, medical devices and disposable material for a range of hospital services, including hemodynamics, urology, anesthesiology and cardiovascular surgery.

HOSPITAL LOGISTICS

The Grifols model for the integrated management of medicines consists of a wide range of high-tech products that cover every stage of the medication process, from the central pharmacy all the way through to individualized registration of administration to patients at the bedside. This model is designed to ensure maximum quality and safety of patient care.

The range includes the BlisPack® system, which automates the preparation and electronic identification of medicines and can prepare 85% of solid medicines for use in a unit dose setting and in hospital units, and the Pyxis® system, used to automate the control of stocks of medicines and health material on the ward.

DIAGNOSTIC DIVISION PRODUCTS

Grifols' diagnostic products division manufactures and develops devices, instrumentation and reagents for clinical analysis, such as blood typing tests or donor–recipient compatibility tests prior to transfusion. Diagnostic products are aimed at blood banks, donor centers and the clinical laboratory sector. During recent years, Grifols has made significant investments in its transfusion medicine line, making it a major player in this sector.

AREAS OF SPECIALIZATION

TRANSFUSION MEDICINE

Instruments and reagents for pretransfusion tests. The DG Gel® blood group typing gel card reagent has established a new standard in immunohematology. In the instrumentation area, the WaDiana® and Erytra® analyzers offer the possibility of automating test techniques. Erytra® is the latest addition to this range, offering a higher sample processing capacity, together with functional improvements. The line is completed by other products such as devices for the extraction and conservation of blood.

HEMOSTASIS

Hemostasis investigates a patient's clotting status or coagulation disorders. The Q® hemostasis analyzer is an instrument that performs coagulation tests and is compatible with a complete line of in-house reagents.

IMMUNOLOGY

The Triturus® analyzer is aimed at clinical laboratories that need to perform a large number of different tests using ELISA techniques for infectious serology, autoimmunity, hematology or immunochemistry. The system can be used with a wide range of associated reagents.

GRIFOLS PROMOTES INNOVATION THROUGH RESEARCH INTO NEW THERAPEUTIC PLASMA PROTEINS AND THE INVESTIGATION OF NEW INDICATIONS FOR EXISTING PROTEINS

In 2012, Grifols invested 124.4 million euros in R&D, confirming its commitment to the research and development of therapeutic alternatives designed to contribute to both scientific and social development. Grifols currently has 12 clinical trials under way for new products and new indications.

DURING 2012, GRIFOLS INVESTED 124.4 MILLION EUROS IN R&D, A FIGURE THAT REPRESENTS 5% OF SALES REVENUE

THE INTEGRATION OF TALECRIS HAS SEEN GRIFOLS EXPAND ITS PORTFOLIO OF PROJECTS UNDER DEVELOPMENT



PRINCIPAL RESEARCH LINES

INTEGRATED ALZHEIMER'S RESEARCH STRATEGY

Grifols' Alzheimer's research strategy aims to provide an integrated approach to this degenerative disease, including treatment with plasma derivatives, early diagnosis, and prevention and protection through the use of vaccines.

2012 saw the start of the AMBAR study (*Alzheimer Management by Albumin Replacement*). This multi-center trial, building on two previous studies, involves combining hemapheresis treatment with the administration of albumin and intravenous immunoglobulin (IVIg), two of the main plasma derivatives, at different intervals and in varying doses. It involves approximately 350 participants, from both Spain and the United States.

This strategy is also pursued through Araclon Biotech, a Grifols group company. Its research lines focus on the validation of a diagnosis kit and on the development of a vaccine against Alzheimer's disease that would make it possible to combat the disease during the asymptomatic/pre-clinical stages. The vaccine has passed the animal experimentation stage and is pending approval by the Spanish Medicines Agency for the start of clinical trials in humans.

ALBUMIN IN HEPATOLOGY

Clinical study to evaluate the effects of the prolonged administration of human albumin on cardiovascular and renal function in patients with advanced cirrhosis and ascites.

ANTI-THROMBIN IN CARDIAC SURGERY

Clinical study to demonstrate the clinical efficacy of Anbinex[®] anti-thrombin (AT) in patients undergoing heart surgery.

FIBRIN BIOLOGICAL GLUE

Biosurgery represents a new specialist research line, pursued as an interdisciplinary R&D project. Research is focusing on the development of a hemostatic and tissue sealant for vascular, liver, soft tissue and connective tissue surgery. Four clinical trials are currently under way: two in vascular surgery, and two in liver and soft tissue surgery, in Europe, Canada and the United States.

OTHER STUDIES

Study to obtain efficacy data for IVIG Flebogamma[®] 5% DIF in the pediatric population; projects investigating the use of plasmin in cases of acute peripheral arterial occlusion; and the start of phase II of the clinical trial to evaluate the safety and tolerance of treatment of cystic fibrosis with an inhaled formulation of alpha 1-antitrypsin.

NEW RESEARCH FIELDS

GRIFOLS PROMOTES BIOTECHNOLOGY INITIATIVES THROUGH ITS PARTICIPATION IN BIOTECH COMPANIES SUCH AS NANOTHERAPIX, VCN BIOSCIENCES, ARACLON BIOTECH AND PROGENIKA BIOPHARMA

Grifols itself is not a biotechnology company, as Grifols' plasma-derived medicines are manufactured from extracted plasma, and not as a result of biotechnological processes. However, Grifols' pioneering spirit and its commitment to patients have led the company to pursue a presence in biotechnology projects.

Grifols has a presence in the biotechnology field through:

- Its pharmaceutical engineering company, Grifols Engineering, specializing in the development of industrial biotechnology (also known as white biotechnology).
- The acquisition of shares in companies and R&D projects in fields of medicine lying outside the scope of its main activities.

GRIFOLS ENGINEERING IS GRIFOLS' PHARMACEUTICAL ENGINEERING OPERATION, SPECIALIZING IN THE DEVELOPMENT OF INDUSTRIAL BIOTECHNOLOGY

Grifols primarily channels its part-ownership of biotech companies through Gri-Cel, a group company that manages and coordinates research in gene and cell therapy conducted by spin-off companies such as Nanotherapix or VCN Biosciences.



Grifols is involved in the following fields and biotechnology companies:

In the field of **advanced therapies**, an innovative and important area with strong potential for the treatment of diseases for which there is currently no effective treatment:

NANOTHERAPIX

Nanotherapix is a biotechnology company specializing in the field of gene therapy (human gene-based medicines). Its main project is the development of a platform based on the use of adenoviruses as vectors to introduce genes into cells. Nanotherapix uses the latest generation of adenoviral vectors to increase the safety and efficacy of this class of treatment.

The Nanotherapix project grew out of collaboration between researchers at the Autonomous University of Barcelona and the Hospital Germans Trias in Badalona.

VCN BIOSCIENCES

VCN Biosciences is dedicated to the research and development of new therapeutic approaches to tumors for which there is no effective treatment, using a technological platform based on oncolytic adenoviruses. Its most advanced project is the VCN-01 adenovirus, which has been designated as an orphan drug by the European Medicines Agency (EMA) to treat pancreatic cancer. The clinical phase is due to start in 2013. VCN Biosciences grew out of the Virotherapy Group of the Catalan Oncology Institute (ICO).

Within the **health technology** field, a field of biotechnology with significant growth potential:

ARACLON BIOTECH

A biotechnology company specialized in the research and development of therapies and diagnosis methods for degenerative diseases, principally Alzheimer's disease (AD). Its activities currently focus on two lines of research: early diagnosis of AD, for which it has developed blood diagnostic kits (ABTest), and treatment of the disease through immunotherapy, in particular by developing a series of patented vaccines.

Araclon Biotech does not currently have any products at market, although its ABtest is available to the scientific community for use in research studies. Araclon Biotech was founded in 2004 as a spin-off from the University of Zaragoza.

PROGENIKA BIOPHARMA

Biotechnology company specializing in the development of technology for personalized medicine. It focuses on the design and manufacture of *in vitro* genome-based tests for the diagnosis and prognosis of diseases, and to predict and monitor the response to pharmacological treatment. It has also developed its own technology for the production of molecular-based diagnostic and prognostic tests, and is an international leader in this field. In particular, Progenika is a global pioneer in the development of molecular biology tests for the performance of transfusional compatibility studies.



ALBUMIN

Is one of the most important plasma proteins, together with intravenous immunoglobulin and clotting factors.

APHERESIS

This consists of the extraction of a limited amount of plasma from the patient (up to 800 ml) and its replacement with albumin or intravenous immunoglobulin (IVIG).

FOOD & DRUG ADMINISTRATION (FDA)

Official name of the US government agency that regulates food and medicines.

HEMOTHERAPY

Treatment of an illness using blood, blood components or their derivatives.

INTRAVENOUS IMMUNOGLOBULIN (IVIG)

Antibody-rich plasma protein, with multiple applications in the treatment of infectious diseases and immunodeficiencies.

INTRAVENOUS SOLUTION

Medicine or homogeneous mixture of a substance in liquid, enabling it to be infused into the circulatory system through a needle.

PARENTERAL SOLUTION

Homogeneous mixture of a substance in liquid, enabling it to be infused into the intravenous system through a needle.

PARENTERAL

Intravenous administration of medicines.

PLASMA DERIVATIVES

Are purified plasma proteins with therapeutic properties, obtained by fractionating human plasma. Plasma-derived products have become essential medicines, capable of saving lives and improving the quality of life and life expectancy of patients with chronic illnesses for which there are no alternative treatments.

PLASMA

Liquid part of the blood, consisting of a mix of a large number of proteins in solution.

PLASMAPHERESIS

Method developed by Dr. Grifols in 1949 and that continues to be the most widely used method in the world for the collection of plasma. The first plasmapheresis center was opened in Barcelona in 1953. This process enables blood to be extracted and immediately separated into its cellular components, which are then injected back into the donor, with the plasma being retained.