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Title: Pioneers and Challengers in the Global Plasma Protein Industry, 1915-2015

Abstract

In the last century the biotech industry has become one of the most dynamic industrial sectors in the world, with average annual growth rates of above 10 per cent. Within the biotech industries, the plasma protein industry has registered a continuous growth since 1910, and an accelerated process of mergers and acquisitions that has led to a concentration of the industry in three companies, in the last decades: Baxter with headquarters in Illinois in the United States (start 1931), CSL Behring in Australia (start 1916) and Grifols in Spain (start in plasma business in 1940). The paper provides a historical overview about the evolution of the industry, and the key pioneering players in the world, and finally tries to explain why and how a challenger like Grifols from a late industrialized country like Spain has crossed entry barriers in the plasma industry, bought many of the pioneering corporations, and established a global leadership position, through a combination of two interactive capabilities: first, an early embedded outward-looking innovative management built while being a small and medium firm (1940-1960); and second, a consistent strategy of alliances with, and acquisitions of, the most innovative pioneering players in the world (1960-2015). Both embedded capabilities have allowed the company to survive crisis, and transform a medium firm into a large company and a global business group.

Key Words: Biotech Industries; Plasma Protein Industry; Grifols; Baxter; CSL

JEL: D22, F23, L65, N60

Introduction¹

Plasma is the liquid portion of blood and constitutes 55% of blood, the remaining 45% being red blood cells. A process named *plasmapheresis* allows the separation of the plasma from the red blood cells, and a process named *plasma fractionation* allows the isolation of the proteins that compose plasma.² The first industrial fractionation process was developed by the Harvard physicists Edwin C. Cohn, to serve needs of the US Army after the Pearl Harbor attack in December 1941.³ The Cohn fractionation process, improved after his death in the 1950s and 1960s, separated proteins into five “fractions”, each fraction containing proteins that are used in hemophilia treatments⁴, and congenital antibody deficiencies (fractions II and III contain intramuscular immunoglobulin)⁵. In the 1970’s, at the plasma fractionation plant of the Swiss Red Cross Blood Transfusion Service in Bern, Switzerland, Kistler and Nitschmann improved the fractionation process to generate higher yields in the production of some proteins. For this reason plasma

¹ Financial support for research and writing of this text came from one of the first *Fundación BBVA I Ayudas en Investigación en SocioEconomía 2014-2016*. Previous presentation of ideas took place in several scientific meetings: at the Universidad de Guadalajara in México the 12th of May 2016, in the *Health and Welfare in the Long Run* at the University of Groningen in the Netherlands the 16th of June 2016, at the *EBHA/World Business History Conference* in Bergen in Norway the 26th of August 2016, in the *Ramón Carande seminar* at the Universidad de Sevilla the 3rd of October 2016, in a seminar at the Faculty of Economics in Nova University of Lisbon the 21st of October 2016, in the Workshop *Innovation and Business in the Health Care Industries in the 20th century* at the Faculty of Economics and Business of the Universitat de Barcelona the 29th November 2016, and in a pre-conference organized in 2017 at the Universidad Complutense de Madrid by José Luis García Ruiz and Jesús M. Valdaliso. Important comments and suggestions received in all these meetings are kindly acknowledged, with the usual disclaimer of responsibility. Also acknowledged is the cooperation of the Grifols corporation in opening their archives and in facilitating interviews with its former CEO Victor Grifols Roura and several managers, particularly two of them who have been extremely generous and kind providing time and comments in the last two years: Nuria Pascual, and archivist director Rosa Avella.

² <http://marketingresearchbureau.com/plasma-industry/current-uses-affecting-the-plasma-industry/> Access online 21/4/2016. The MARKETING RESEARCH BUREAU is an independent market research firm which is the premier supplier of blood and plasma products industry data on a global level. Information for this section comes from their available reports and their website. Their clients include the top 10 world plasma companies. Since 1974 they have published reports of the US market for plasma proteins. Also, each year MRB publishes a market study on the therapeutic plasma proteins market in a region on a rotation basis (Europe, Asia & Pacific and the Middle East, Central and South America). The company’s data spans decades, includes prices, volumes, market shares, historical notes, forecasts, and information about collection, manufacturing, and global distribution.

³ http://www.idi.harvard.edu/news_events/articles/then_and_now_saving_soldiers_lives/

⁴ Factor VIII is used for the therapy of hemophilia type A and Factor IX for hemophilia type B. Both Factors come from cryoprecipitate products.

⁵ The Cohn method allows the obtention of: coagulation factors (from the cryoprecipitate); fibrinogen (from Fraction I); immunoglobulins (from Fractions II and III); alpha 1 antitripsina from fraction IV; albumin from Fraction V. I acknowledge the personal clarifications in this technical description of Rosa Avella, director of the historical archive of the Grifols corporation.

fractionation plants increased scale and scope and fractionate millions of liters of plasma to manufacture a variety of therapeutic products.

The first and most important human plasma protein whose obtention the industry sought in the 1940s, and until the 1980s, was albumin (55-60% of plasma protein), for rapid resuscitation of people from life shocks due to heavy blood loss (Curling, Goss and Bertolini 2015). In the last decades new knowledge has allowed the obtention of new plasma proteins, and the application of plasma proteins to develop new therapeutical products used in a great variety of neurological, autoimmunitary and cardiovascular diseases: reconstituted HDL for acute coronary risk; hepatitis C hyperimmune for hepatitis C; IVIG in various neurological diseases (Multiple Sclerosis, Neuropathic Pain, Chronic Fatigue Syndrome, Post-Polio Syndrome, Dermatomyositis, etc.), Albumin in Stroke, Cirrhosis, Alzheimer's Disease, Malaria and Sepsis; Alpha-1 antitrypsin in Cystic Fibrosis and Type 1 Diabetes; Fibrinogen in cardiac surgery; and Prothrombin Complex Concentrates in the reversal of anti-coagulation agents (such as warfarin). Today the production of albumin and plasma-derived factor VIII (pdFVIII), the two driving proteins of the industry until the 1990s, have a small share of the market (10-15% each). In contrast, in the last two decades intravenous immune globulin (IVIG) has been in higher demand than any other plasma product, and has determined the global industry: IVIG accounts for 40-50% of the global plasma proteins market.⁶ As plasma is the raw material of the industry, the competitiveness of the industry lays in obtaining maximum yields of proteins per unit of plasma, and investing in very expensive research able to produce new knowledge about the therapeutical applications of plasma proteins for new and old diseases (Robert 2015).

The plasma industry has experienced a strong growth, from \$5 billion in global sales in 2000 to over \$14 billion today.⁷ The plasma industry's raw material is expensive (70% total costs), because of the small quantities collected from donors, the costs of the plasmapheresis equipment, the fractionation process, the highly qualified staff, and the

⁶ <http://marketingresearchbureau.com/plasma-industry/current-uses-affecting-the-plasma-industry/> Access online 21/4/2016

⁷ <http://marketingresearchbureau.com/plasma-industry/current-uses-affecting-the-plasma-industry/> Access online 21/4/2016

costs of quality control processes involved in the collection, manufacturing and distribution of the products involved.

There is an abundance of studies about the pharmaceutical industries, and more recently about the biotech industries in the world and for some regions with dynamic creation of start-ups in the last decades like the United States and Spain. Also, there are many monographs and websites with historical information -of diverse degree of quality-, published by business schools, independent economic and financial media, and more often by the corporations.

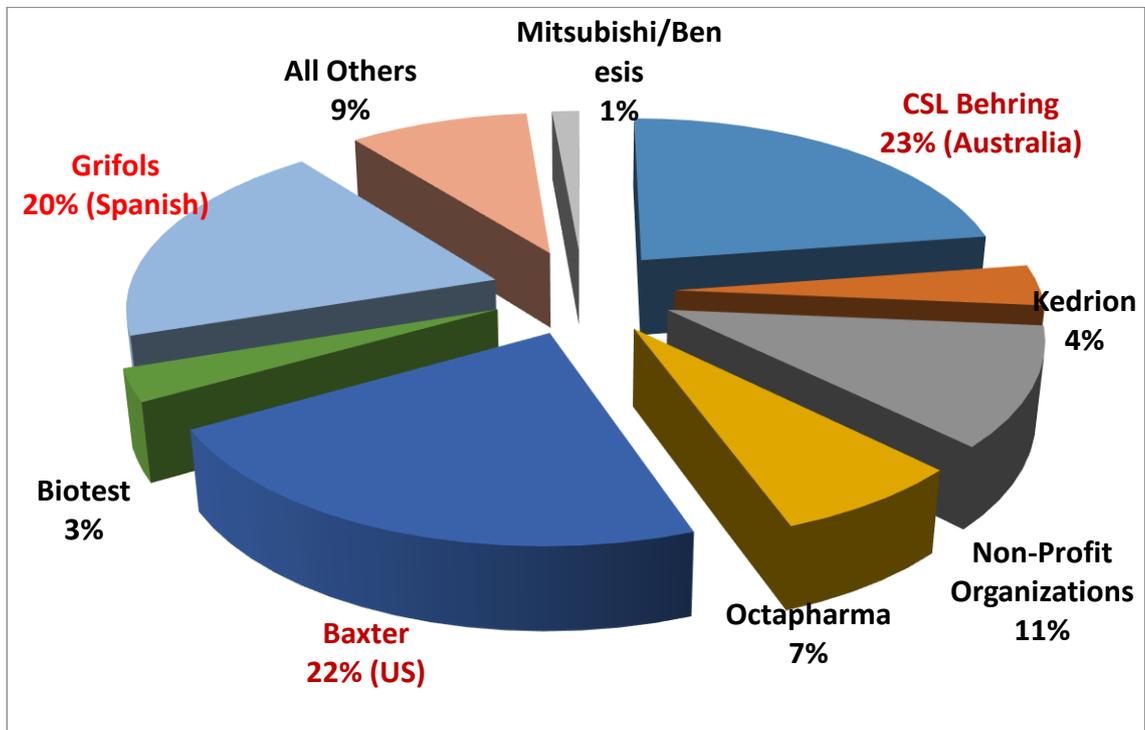
There are very few scientific studies about biotech market niches like the plasma industry from a sectoral or historical point of view, within which analyze and understand the evolution, and the factors of competitiveness, of small start-ups and major players in the industry in developed or developing countries (Curling, Goss and Bertolini 2015). This paper aims to contribute to fill the gap, calling the attention of business and economic historians to study this little known industry. History can shed light about the relevance of the Health industries, and the factors that in late industrialized countries like Spain have slowed down the historical growth and local competitiveness of these industries. In this paper we indicate how innovative start-ups emerged in Spain in a very specialized market niche, very early, in close communication with the pioneering companies that were establishing learning bases of the industry in the US and in Australia or Germany, and how they survived critical times in the industry, and became global.

The Pioneers of the World Plasma Industry

The plasma industry is heavily concentrated. The top seven plasma collectors owned by plasma fractionators collect millions of liters of plasma and are: BioLife (owned by Baxter), BioMat, PlasmaCare and Talecris Plasma Resources (owned by Grifols), CSL Plasma (owned by CSL Ltd.), Octapharma Plasma (owned by Octapharma), Advanced Bioservices (owned by Kedrion SpA). The first three companies

collect over 75% of the total U.S. plasma. Most of the plasma-collecting companies are based in the U.S., as it is the main source of plasma worldwide.⁸

Figure 1. Top World Plasma Fractionators (2014)



Source: Source: Patrick Robert (2014), “Global Plasma Supply and Product Demand”. IPFA/BCA Global Symposium on The Future for Blood and Plasma Donations. Sacramento, California 23-24 September 2014. Market Research Bureau.

http://www.ipfa.nl/UserFiles/File/WS%202014/Symposium%202014%20IPFA%20BCA/Proceedings%20Sacramento%202014/1_5_Robert_IPFA_BCA_2014.pdf (access online 26 April 2016)

The early history of the growth of the industry in the first four decades of the twentieth century is inextricably linked to the history of modern warfare, and the power of imperial armies to spend huge efforts and money from public sources to invest in research and cooperation with private firms. The first blood banks for the massive

⁸ <http://marketingresearchbureau.com/plasma-industry/current-uses-affecting-the-plasma-industry/> Access online 21/4/2016

collection of human blood for transfusion appeared in close connection with World War I (United Kingdom, Russia) and the Spanish Civil War, under the auspices of governments and armies.

Table 1. Pioneers in World Blood Banking (B.B.) and Plasma Fractionation (P.F.)

COUNTRY	PIONEER	DATE B.B.	DATE P.F.
UK	British Red Cross	1921	
USSR	Sergei Yudin	1930	
Spain	Frederic Duran i Jordà	1936	1951 (Grifols)
USA	Edwin Cohn/Armour Labs (later, Baxter)	1940	1940
Germany	Emil von B./ Behringwerke	1939?	1946
Australia	William Penfold/ CSL	1929	1952
Switzerland	ZLB	1939	1949
Japan	Ryoichi Naito / Green Cross	1950	1971
Argentina	Laboratorio de Hemoderivados	1914?	1964/74

Source: Own elaboration with secondary sources from each country and corporation in table, and Curling, Goss and Bertolini (2015)

The blood banks were new organizations that allowed regular and abundant collection of human blood, the raw material from which plasma must be obtained. Plasma extraction was initially very expensive and difficult before the 1940s, and national public health systems with few exceptions had not enough highly qualified scientists able to focus in the long-term research involved in industrializing the production of abundant plasma extraction until after World War II.

The first large public-private agreements signed to finance new industrial ways to produce and distribute safely and in larger quantities, fast, albumin for resuscitation of soldiers in life shock in the battlefield, came after December 1941 and the Pearl Harbor attack in the United States, and continued during World War II. The US Army drew up seven contracts in 1941 with Armour, Lederle, Upjohn Co., Eli Lilly Laboratories, E.R. Squibb, Cutter Laboratories, and Sharp and Dohme to expand fractionation and production of human albumin for the US soldiers. These companies became the first commercial fractionators, and two of them (Armour, Cutter Laboratories) remained in the business in peacetime on the expiry of the 1941 contracts. The others were concerned about availability of plasma and viability of the industry if they did not have a strong (or guaranteed) military demand (Kendrick 1942; Curling, Goss and Bertolini 2015).

Cutter Laboratories was founded in 1897, began plasma fractionation in 1942, becoming the first commercial producer of albumin (Cutter 1975). After completion of its facilities in Clayton (North Carolina) was acquired by the German Bayer AG in 1974, becoming known as Talecris in 2005, which was acquired by the Spanish Grifols in 2011 in what was known as the largest FDI in the pharma industry in the US that year (Grifols 2015; Fernández Pérez forthcoming).

Armour and Company built a manufacturing plant in 1943 under a US Navy contract at Fort Worth (Texas), and was the largest supplier of albumin to the US Army during World War II, establishing after the war a new fractionation plant in Kankakee (Illinois) in 1953. The company was acquired in 1977 by Revlon, Rorer Pharmaceutical in 1986, and merged with Rhône-Poulenc in 1990.

Baxter, the world's largest manufacturer and distributor of hospital supplies and provider of medical specialty products serving over 5,000 hospitals, was founded in 1931 by two Iowa physicians (Ralph Falk and Donald Baxter), opening a plant in Glenview, Chicago, in 1933, with six employees, and selling its products through the American Hospital Supply Corporation (www.baxter.com). Baxter provided blood collection products and intravenous solutions to the US Army during World War II. In the 1950s they expanded in Cleveland, Mississippi, and acquired in 1952 a firm that had produced freeze-dried plasma during the war (Hyland Laboratories of Los Angeles), as well as Flint, Eaton and Company and Fenwal Laboratories of Boston in 1959, and built in 1953 a large new manufacturing plant in Los Angeles (California) to produce a variety of blood

and plasma protein products. Baxter shares began trading on the New York Stock Exchange in 1961 (www.fundinguniverse.com/company-histories/baxter-international-inc-history/)

Courtland Laboratories was founded in 1947, received a license to produce plasma products in 1950, and manufactured animal albumin based products for Max Factor, Merck Sharpe & Dohme, and was acquired by Abbott Scientific Products (a division of Abbott Laboratories) in 1967, and sold in 1978 to the Japanese Green Cross Corporation changed the name to Alpha Therapeutic Corporation. The Spanish Grifols signed a joint venture with Alpha Therapeutic Corporation in 1982 until 1999, and bought Alpha's assets in 2003 establishing the firm Grifols USA that year (Grifols 2015).

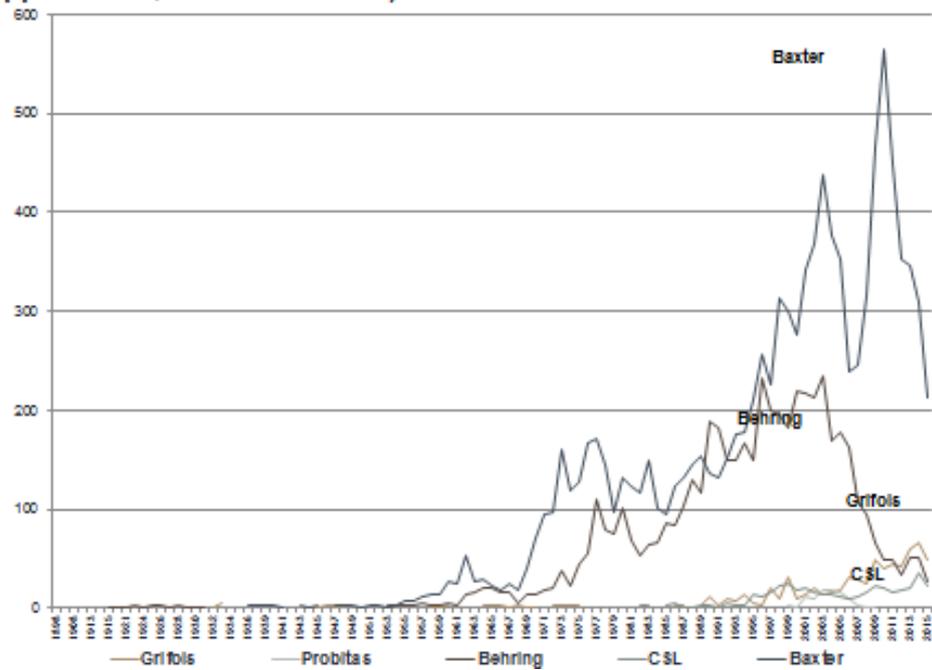
In the early years of the 1950s, in the United States plasma fractionation was a commercial enterprise with very few not-for profit players (American Red Cross, Massachusetts Biological Laboratories), whereas in Europe there was an important not-for-profit plasma sector around national Red Cross societies, and a commercial sector. Among the commercial fractionators the early pioneers in Europe were Behringwerke AG and Biotest in Germany, the Barcelona Blood Service in Spain, Institute Mérieux in France, Berna in Italy, Kabi in Sweden. In Japan, there was a strong commercial private sector as in the United States in the 1950s led by the Green Cross Corporation. In Australia until the 1990s (when CSL was privatized) and in China until today public organizations led research, and plasma collection and fractionation (Curling, Goss, Bertolini 2015; Grifols 2015).

In the 1990s and first decade of the 21st century pioneers like the German Behringwerke or the Swiss ZLB had been acquired by the Australian CSL, and world pioneering leaders of the US like Cutter and Armour had been acquired first by German, Swiss and Japanese competitors, and finally by the Spanish Grifols.

Grifols was a micro family lab in 1940, almost disappeared in 1965 when Spain prohibited plasma exports, and could have disappeared in the 1980s with the AIDS crisis that made big leaders like the Green Cross Corporation of Japan, or Landerlan in Madrid, decline or collapse. It was a corporation whose application of patents to the WIPO was not close to the activity registered by the early pioneers like Baxter or Behring but it

seemed to be above the patent application activity of the Australian CSL, as shown in the figure below.

2.2. Innovation. Patents of Leading Plasma Corporations, 1898-2015 (Applications, WIPO Database)



Source: Own elaboration from WIPO Database.

What competitive factors may help explain that a small company in a late industrialized country like Spain could have challenged the pioneering leaders in a highly concentrated and knowledge intensive biotech industry like the world plasma protein industry? Available literature highlights the organizational and executive capabilities of emerging multinationals from developing economies, and the accelerated process of acquisitions and investments abroad in the last decades (Guillén and Garcia-Canal 2009 and 2010), or their outward-looking networks (Fernández Pérez and Puig 2007; Fernández Pérez and Rose 2010). In knowledge-intensive scientific industries like the plasma protein industry, a long history of early embeddedness and alliances with pioneering leading corporations seems to be the key competitive clue, as shown in the case of Grifols below.

Challengers in the World Plasma Industry after World War II: Grifols

Clinical laboratories with a microscope, and medical instruments for microbiological studies rapidly developed in the Western world after the discoveries of Louis Pasteur and Heinrich Hermann Robert Koch in the last decades of the nineteenth century. Their methods contributed to find vaccines against cholera, and tuberculosis, and many infectious diseases, thus greatly reducing mortality rates in the world. The first clinical laboratories in Catalonia were developed by Jaume Ferran i Clua, and Innocent Paulí i Galceran, after their studies in the library of the Jesuits in the Observatori Astronòmic de l'Ebre in Tortosa. Ferran i Paulí had no studies of Medicine but frequently read the "Comptes Rendues" of the Société Royale des Sciences de Paris, an scientific journal in which Pasteur usually published his findings, in the Observatori Astronòmic de l'Ebre. Ferran studied the findings of the new microbiology there by himself, and wrote an article about paludism. He studied in Marseille the 1884 outbreak of cholera, and studied causes and methodologies of treatment, and recommended in 1887 to open in Barcelona what would become the first municipal laboratory of microbiology to apply his knowledge and experience in the prevention and treatment of infectious massive diseases in the city (Fernández Pérez and Sabaté forthcoming).

Modern clinical laboratories therefore were well established in Barcelona by the late 1880s to help public authorities prevent or control cholera, or paludism. It was in this context that several graduates in Medicine and Pharmacy in the Faculty of Medicine of Barcelona decided to open their own labs to earn their living. One of them was Dr. José Antonio Grifols y Roig, who after finishing his studies of Medicine in 1909 studied in Munich clinical analysis with professors of that University and in German laboratories, and opened in 1909 his Instituto de Análisis Clínicos in Plaza Urquinaona, near Plaza Cataluña, with three colleagues who were doctors or lab specialists (Luis Celis, Ricardo Moragas, and Dr. Gordan former director of the Bacteriology Department in Danzig). The three shared technical and managerial responsibilities as well as ownership until 1923. The Institut carried out biological research with the latest German technologies, elaborating preventive vaccines against typhoidea fever, cholera, Mediterranean fever, and others. Also, clinical tests of Abderhalden and Wasserman for the diagnosis of illnesses like syphilis and other venereal diseases, very common in Barcelona in these decades in patients entering public and religious hospitals (Grifols 2011; Arxiu Hospital Santa Creu i Sant Pau Llibres Majors and Entry Registers of New Patients 1921 and

1935). Their reputation and prestige was soon consolidated and the increase in clients (private doctors, hospitals, patients) encouraged them to invest the profits to move to a larger apartment in Rambla de Catalunya near Provenza street in 1923, the years in which almost 30 new clinics and institutes also moved from downtown to the healthier districts of the Eixample far from the harbor. The success made the three Spanish partners to split and follow individual enterprises. Grifols Roig would be the only owner, director, and technical expert of his new firm, Instituto Central de Análisis Clínicos, Bacteriológicos, y Químicos. He would combine this activity with the direction of the laboratory of Histopathology at the Hospital de Santa Cruz, the teaching of hematology in the Academy of Medical Sciences of Barcelona, and internship in the laboratory of the Faculty of Medicine of Barcelona. The Barcelona House of Ganzer provided him most of the clinical instruments, and most of the clients were doctors who needed a clear diagnosis before recommending treatment to their patients. Grifols employed five doctors and chemists to help him in the technical tasks of the laboratory, four Spaniards and one German (Hellmut H. Hempel). His experience in blood extraction made him start trying, in 1925-26 blood transfusion.⁹ Grifols would preserve his friendship and scientific cooperation with his first partners: Luis Celis Pujol became full professor in the Faculty of Medicine of Barcelona in Histology and Pathological Anatomy in 1923, and Ricardo Moragas was director of the Laboratory of Bacteriology and Serology of Hospital de Santa Cruz and owned his own private laboratory of analysis.

Since 1928 the activity in blood transfusion, collection, and manufacturing of plasma derivatives, would become increasingly the center of the entrepreneurship and innovation of the Grifols company. That year he presented in the Catalan Academy of Medical Sciences a new indirect method of transfusion of blood, in 1929 new studies about blood groups in the Iberian Peninsula, in 1933 he presented in the Vilafranca del Penedés Hospital his new device (“flébula”) for safe transfusions of blood, and in that year and 1934 the leading directors of the public hospitals of Barcelona require his services: Pedro Pons in Hospital Clínica; Dr. Ribas in Hospital de San Pablo; Dr. Clara in the Quinta de Salud La Alianza.¹⁰ His team of experimented professionals, and his

⁹ Historical Archive Museu Grifols in Barcelona. Hemobanco de Laboratorio Grifols SA, Memoria. Reference 6353; Grifols 2011:22-23

¹⁰ Historical Archive Museu Grifols in Barcelona. Hemobanco de Laboratorio Grifols SA, Memoria. Reference 6353. The flébula Device included three patented components: a needle, a glass container, and the container cover.

reputation, was large and he registered between the late 1920s and 1930s many of his new incremental innovations to promote his method of indirect transfusion of blood.

The laboratory produced new clinical devices with registered patent, vaccines (against tífus, dyarrhea), and nutritional products. German and Spanish experts in clinical analysis and in the production of microbiological products cooperated with Grifols (Dr. Walter Oppenheimer, Dr. Hirsch, Hempel, Cantó, Cuevas). His two sons José Antonio (born 1917) and Victor (born 1919) Grifols Lucas grew up in the lab, and the father taught them since they were very young to help him perform urine or glucose tests, or even the Wasserman test when José Antonio was 17 and Victor 15 (Grifols 2011:40). Soon the two sons were participating in the routine of the family firm. In this context, with two young sons helping in the lab, in 1940 the Institute disappeared and a new family firm was registered, the Laboratorios Grifols S.A., with Grifols Roig and his wife Magdalena Lucas as first shareholders, and the focus on the production of modern clinical services, and the manufacturing of dry plasma, which could multiply the output of each blood donation by several times.¹¹

In 1944 the good expectations of growth made them move to a new building that was considerably larger, making possible the strict division of activities (vaccines, analysis, rabbits) and maintaining the administrative office in the apartment of las Ramblas. Grifols registered several patents with the support of his collaborator Walter Oppenheimer and his sons: after the instrument for indirect transfusion in 1928 and 1929, a process to dry plasma in 1943, table to registre blood groups in 1949; brand “Banco de Sangre y Plasma” in 1950, and several products that improve the extraction and fractionation of blood in patents in 1957, 1961, 1964, 1965, 1966.¹²

Grifols decided then to open the first civil blood bank in Spain in 1945, the Hemobanco.¹³ To maintain the reputation of the lab the father decided that he would be

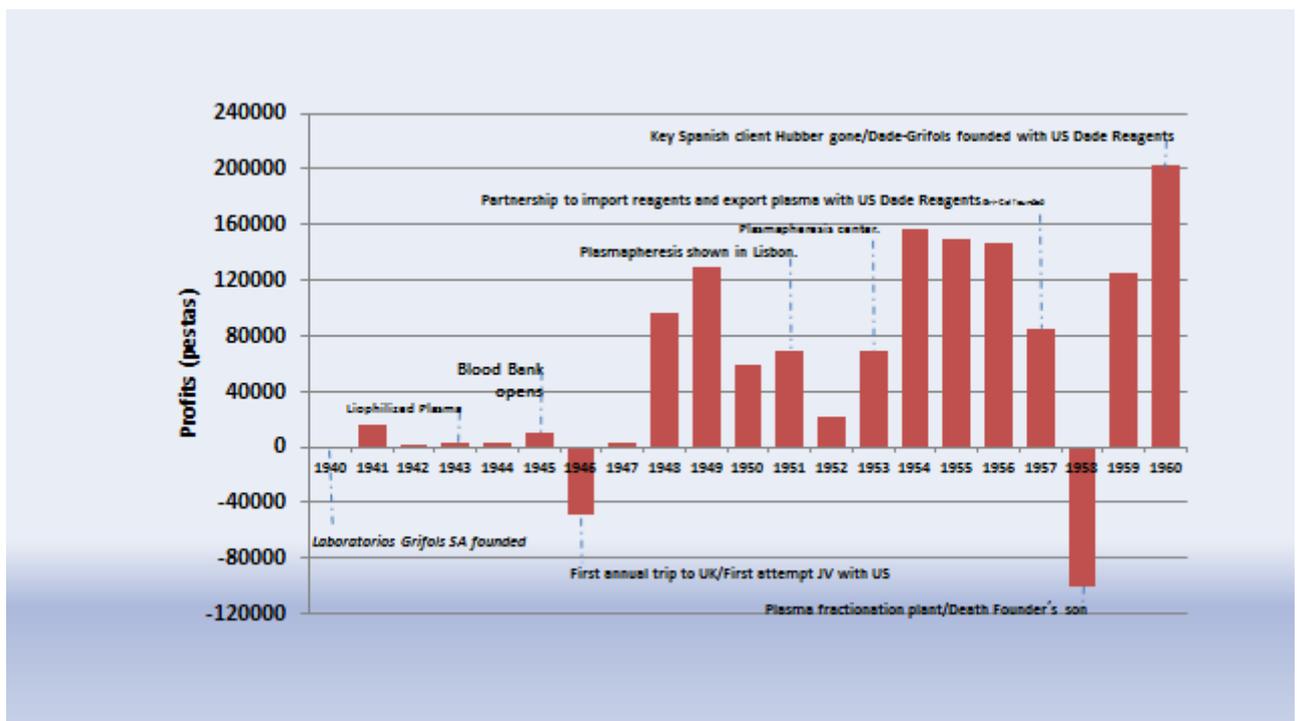
¹¹ Archivo de Protocolos de Barcelona. Not. D. Cruz Usatore y Gracia. Copia de la Constitución de la Sociedad Laboratorios Grifols SA ante el que fue Notario de esta Ciudad Dn Jose Faura Boras en 18 de novembre de 1940. Archivo Museu Grifols. Escrituras. Reference 59763

¹² Historical Archive Museu Grifols in Barcelona. Hemobanco de Laboratorio Grifols SA, Memoria. Patentes relacionadas con la actividad del banco de sangre. Reference 6353

¹³ Historical Archive Museu Grifols in Barcelona. Hemobanco de Laboratorio Grifols SA, Memoria. Reference 6353; and Laboratorios Grifols S.A. Banco de Sangre y Plasma. Funcionamiento económico. Reference 03178

only the manager in Laboratorios Grifols S.A. and that his son José Antonio would be the only manager in the new Blood Bank. Since 1945 until 1960 the blood bank performed around 200,000 blood extractions, a volume that made the family decide to reinvest profits from the two family firms in a new plant of blood extraction in Badalona, a city near Barcelona. The experience in blood collection, preservation, storage, and manipulation, made the scientific father and sons experiment with dry plasma, and with plasma fractionation to obtain and separate proteins with which to produce different plasma derivative products. The method of plasmapheresis was developed and officially presented in 1951 in a scientific congress in Lisbon with presence of Edwin J. Cohn, and a centrifuge Machine to perform plasmapheresis was patented in 1965, soon used for plasma extraction in Spain and in the United States in the context of the joint alliance and agreements between Grifols and the US Corporation Dade Reagents, that led to the foundation of Dade-Grifols.¹⁴

Figure 3. Grifols. Profits, Innovation and Alliances 1940-1960



Source: Own elaboration from Grifols Archives in Barcelona and Sant Cugat del Vallés. Actas Laboratorios Grifols S.A.

¹⁴ Historical Archive Museu Grifols in Barcelona. Hemobanco de Laboratorio Grifols SA, Memoria. Reference 6353

The investments in moving to a larger building, in multiplying the registration of patents of innovations, and maintaining a highly qualified team of experts that now included two adult sons graduated in Medicine and Pharmacy moved José Antonio Grifols Roig to expand the capital of the society and include a client and businessman friend of Grifols, Domingo Brasó, as a new partner. The two young sons also became partners with the father, the mother, and Brasó. From 500,000 pesetas the capital of Laboratorios Grifols S.A. expanded in 1946 to 1,000,000 pesetas with which to finance the expansion of the activities.¹⁵ Brasó and later on his son would remain as enduring shareholders in the business throughout decades, until the early 1990s. The times were very tough in the economy of the country, with scarcities of the post-civil war making difficult the investments or innovation. Grifols was a singular exception of a very small lab developing and investing in innovative activities that had started in the early 1910s. The entrepreneurial attitude of the father was continued by the sons. Victor Grifols travelled to England in 1946, one year after the end of World War II, the same year of the entrance of the new partner into the family firm, to explore new products and potential alliances with British subsidiaries in the UK of North American corporations like British Hayden to jointly produce penicillin in Spain. In that same trip Victor Grifols visited the Royal Society of Pharmacy, distinguished Spanish doctors in the exili like Trueta and Gabarró, and Duran y Jordà, and British houses producing medical instruments and products like Burroughs Welcome and Co.¹⁶

Friendship with the owner of a pharmacy in Barcelona, Ricardo Roca de Viñals, who was a distributor in Spain of the North American company Dade Reagents from Miami, Florida, made possible the beginning in the mid 1950s of conversations towards exporting Grifols serums to the United States in exchange of imports of reagents and other products for the Grifols and the Roca de Viñals firms. Rigid intervention in foreign payments and currency in Spain before 1959 made confidential agreements based on trust necessary, and trustable networks required, to begin the first monthly exports of Grifols plasma derived products during 1957 and 1958 to Dade Reagents in the United States.¹⁷

¹⁵ Historical Archive Grifols in Sant Cugat. Escrituras. Escritura 1.109, de aumento de capital, 9 de mayo de 1946

¹⁶ Historical Archive Museu Grifols in Barcelona. Memoria sobre el viaje a Inglaterra realizado por Victor Grifols del 12 de julio a 22 de agosto de 1946. Reference 05898

¹⁷ Historical Archive Museu Grifols in Barcelona. Letter of J.M. Potts Vice-President of Dade Reagents Inc. To J.A. Grifols-Lucas Hemobanco, 8 January 1958; and Confidential Letters Grifols/Dade Reagents 1957-59. References 2331, 2354, 2357, 02978

The importance of this foreign trade lay more on the qualitative side than in the quantitative value, as the relevant issue was for the Spanish firms to keep in touch with the most updated technology in the 1950s in clinical analysis that was then in the United States, and learn how to establish a win-win alliance with a leading partner of that country. These early contacts provided an early imprinting about how to undertake international activities to the small lab, that would allow further agreements with Dade Reagents and American Hospital Supply Corp, two leading manufacturers and distributors of hospital supply equipment, in 1961, when the joint venture Dade Grifols was established.

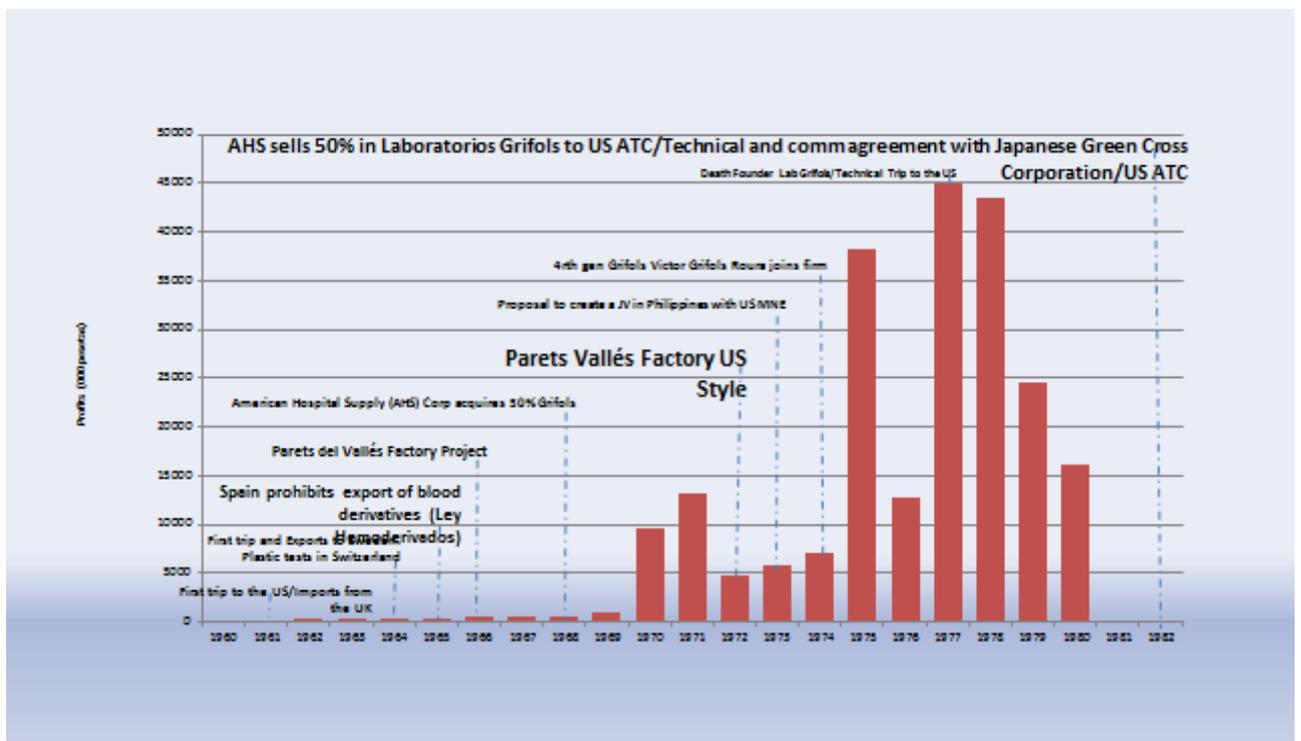
In a long six-pages letter signed the 29th of March of 1969 by Victor Grifols Lucas addressed to Joe Potts of Dade Reagents Inc., Grifols explained that in 1965 the Barcelona company Hubber (founded 1951 by Felix Gallardo Carrera), who had been in the last ten years the most important local client of the plasma produced by Grifols, started investments to integrate vertically the production of plasma in their own factory, reducing to half the amount the quantities of plasma bought to Grifols, and formally pressing the Ministry of Health in Spain to forbid plasma exports. Grifols felt this was a threat. He shared with Potts his concern that this could be an strategy of Hubber to integrate the industry in Barcelona, and get rid of Grifols collapsing them in the domestic market (half of the sales in Spain went to Hubber in the early 1960s and Hubber's size was not easy to be substituted by an alternative client absorbint stocks of plasma in Spain) and in the international markets (where more than half the total sales of Grifols went, a sign of their competitive entry in tough and sensible health care markets of Europe and the US). Grifols had been exporting more than half of their total sales before 1965, right the year when according to the letter "the Spanish Ministry, doubtlessly influenced by Hubber's complaints published the decree of prohibition of export of plasma ... Hubber S.A. has a great influence in the Dirección General de Sanidad as well as in other regulatory centers of the politics of this country".¹⁸ Be for this reason, or for others, Grifols complains in the letter that in 1969 they have problems with their main Spanish client, that due to the governance of the blood Banks (regular paid donations and regular tests on the Health of donors) they were accumulating blood and stocks, they could not export their surplus from their network of blood banks for the ban to blood exports of the government of 1965,

¹⁸ Historical Archive Museu Grifols. Letter of Victor Grifols to Joe Potts of Dade Reagents Inc. 29 March 1969, p. 2. Reference 869

and that they had losses and had to increase holidays of their employees in the blood bank to reduce stocks and losses.

Grifols could have right then withdrawn from the business but decided a counter-cyclical strategy: to enter the business of their main local competitor Hubber and manufacture plasma derivatives, integrating vertically forward, and investing in a US style factory that could produce FDA products authorized to be sold in the US in the future. The plans were indeed visionary, in times of decline of sales and tough regulatory problems, and involved convincing US partners to enter with them into a joint venture to help them grow in scale and scope, and internationalize products of higher added value in the blood industries. The dream was expensive, but the Grifols family suggested studying sharing ownership, and management, to the big Corporation that had recently bought Dade Reagents in the US: American Hospital Supply Corporation. The joint venture with them was signed in 1961, and would lead to the construction in the late 1960s of the new modern US style factory of Parets del Vallés, one of the leading factories in the world today in the plasma industry.

Figure 4. Grifols. Profits (current 000 pesetas) and Alliances, 1960-1982



Source: Paloma Fernández's own elaboration with data from Historical Archives of Grifols in Barcelona and Sant Cugat del Vallés, Balance of Accounts 1940-1960.

Dade Reagents Inc. (DR) of Miami, Florida, was a relatively medium-sized corporation that was very innovative in the United States. It had been founded in 1949 by John Elliott, a military officer and scientist who had participated in the creation of one of the first North American blood banks (the Dade County Blood Bank) during World War II. DR produced blood serums and solutions and their exclusive distributor in the United States in the 1950s was American Hospital Supply (AHS). When Elliott suddenly died in 1955, AHS's CEO, Foster G. Mc Gaw, made a formal proposal to merge to Elliott's widow and heirs and on 1 July 1956 DR became a subsidiary of AHS Corporation at a purchase price of 90,000 dollars.

Grifols' contact with DR, and through it with AHS, was made possible as we mentioned above thanks to Ricardo Roca de Vinyals, a well-known pharmacist from Barcelona acquainted with the Grifols family and a distributor of DR products. Roca de Vinyals was also acquainted with the representative of DR in pre-revolutionary Cuba, Dr. Guillermo Anido, who was well connected with the Cuban Institute of Tropical Diseases and the La Habana Faculty of Medicine, where he and his brother had been very actively innovating in the field of clinical analysis and quality control in labs. In 1957, Roca de Vinyals offered to help connect Grifols with DR to obtain reagents, and then mediated to help Grifols import reagents and solutions directly from DR. During 1958 and 1959, a continuous flow of imports is reported in letters and confidential invoices preserved in the Grifols archive. There were also some exports. Problems in handling, storing, sending, and maintaining the small glass containers with blood derivative products in their long journey with Iberia airlines from Spain to Switzerland and then to the United States had to be solved and constituted very valuable training for the future.

Many difficulties arose from the loss of their most important client (Laboratorios Hubber, which decided to produce its own plasma) and the deflationary Plan de Estabilización designed by the government. In addition, there were concerns that the Franco authorities could at any time block the commercial interaction and payments because foreign currency was scarce. But the relationship with DR went ahead and a joint venture, Dade Grifols, was forged in 1960. The partners on the Spanish side of the agreement were the Grifols, Braso, and Dr. Roca de Vinyals, who died shortly before signing the notarized documents of the new firm.

In 1961, Víctor Grifols Lucas travelled for the first time to Miami and stayed for several months. There he met the Cuban Dr. Anido, who had been distributing DR products in Cuba before the revolution and with his contacts he was able to negotiate with the new owners (AHS) to get a job in Dade County when he arrived in 1961 after escaping from purges among the staff of clinical centers and medical faculties in Cuba. He was hired as medical manager of the corporation and as manager in charge of organizing international clinical quality control conferences with other big corporations in the United States and in Switzerland, frequently attended by owners and managers such as Grifols. Grifols Lucas and Anido met in Miami at a very difficult time in the life of Anido and became friends and colleagues until the end of the twentieth century.

This friendship became extremely important in the history of Grifols in subsequent decades. Anido and other Cuban technical managers in AHS served as hybrid bridges for the Grifols firms, transferring know-how in a more affordable way about the standards of the Food and Drug Administration for registering patents and products in the United States, about how to deal with the US corporation, and about who was who for potential future partnerships and collaborations in the global plasma and hospital equipment industries.

The association with DR and the new joint venture Dade Grifols facilitated regular imports of much-needed reagents and solutions and hospital and clinical supplies, and the beginning of regular exports of plasma products from the Grifols blood bank and Laboratorios Grifols to the United States and Sweden up until the late 1960s. Between 1961 and 1966, exports represented more than half the total sales of the Grifols firms. The good times ended abruptly due to a regulatory change. In 1965, a Spanish law prohibited the export of human blood products and Grifols exports to the United States and Europe gradually declined and disappeared after 1968—the prohibition lasted until the end of Francoism.

The alliance with the owner of DR (AHS) since 1956 served to keep Grifols' expansion going. It sold a huge variety of hospital supply equipment from most of the North American manufacturers involved in the industry and was expanding in the late 1960s beyond the United States, changing its organization into that of a large professional corporation, integrating backwards, launching its own production and factories, and planning its own internationalization. In this context, in 1968, AHS fully acquired the

Grifols shares formerly owned by its subsidiary and more visibly and directly became the lab's US partner, increasing the number of exclusive products distributed through Grifols among the growing number of Spanish hospitals.

We have to keep in mind that AHS was founded in 1921 by an experienced salesman, Foster G. Mc Gaw, and a business angel from the construction sector, Harry L. Drake, to create and connect the previously fragmented market of the hospital supply business in the United States. They offered their commercial services to hundreds of small manufacturers dispersed throughout the country, offering to sell their products—on commission—to distant hospitals that were sprinkled across the United States. They began production only in the 1960s, with backward vertical integration, and were tremendously innovative in the organization and training of their salesforce and their technical staff thanks to the leadership, experience, and organizational ideas of Mc Gaw (Sturdivant 1970).

AHS had plenty to sell and to teach to the small though ambitious Grifols lab. The abundance of products sent to Dade Grifols, particularly cardiovascular products and a diversity of supplies for hospital needs, required the Grifols staff to learn many new procedures: how to keep track of the movement of products in storage; how to maintain the products; how to write the invoices in a standardized way; how to train the sales staff; how to deal with staff in hospitals; and how to handle logistics in the transportation and storage of products to reduce losses. The few preserved records of sales of AHS products through Dade Grifols reveal that in the 1970s sales and profits from Dade Grifols in some years represented up to ten times those obtained in the other firms in the Grifols network (the blood bank, Laboratorios Grifols, and Gri-Cel (producer of lab instruments)).

The growth in sales and staff was so successful that, finally, it necessitated a new building outside the city of Barcelona, big enough to organize Grifols' large-scale production and commercialization. The factory in Parets del Vallès was launched in 1972 by CEO Víctor Grifols Lucas. Land was bought in 1966 for this purpose and authorizations were obtained. The factory was completed in 1970 and began operating with all the necessary licenses in 1972. It had been designed to closely follow North American standards of quality control in production, under the supervision and in close coordination with AHS's technical staff. Víctor Grifols Lucas, from the third generation of the Grifols family, and his son Víctor Grifols Roura, from the fourth generation,

together learned how a modern factory in the biopharmaceutical industries was built. More professional routines in accountancy were adopted, computers were introduced, and human resources began to be more efficiently organized. In Dade Grifols, women with degrees in Chemistry and Pharmacy occupied top managerial and technical positions.

There were not many competitors in the Grifols' niche market—Laboratorios Hubber, Laboratorios Leti, Landerlan, Llorente, and the Spanish subsidiaries of the German Behringwerke and the US Baxter were the most important ones—but all of them were expanding fast as they also perceived the same opportunities for growth.

MAJOR MANUFACTURERS IN THE PLASMA INDUSTRY IN SPAIN BY 1975 (in * manufacturers that have survived the 1980s-90s crisis)

BARCELONA	MADRID	VALENCIA
Grifols *	Landerlan	US Baxter's subsidiary *
Hubber	Llorente	
Leti *		
German Behring's subsidiary		

Sources: Own elaboration from Grifols Archive in Museu Grifols in Barcelona and Sant Cugat; Corporate Websites of CSL Behring and Baxter

Therefore, besides innovation in production, the young Víctor Grifols Roura, when he joined the company in 1973, took it upon himself to dramatically improve the informal personalistic routines of the previous generation of commercial managers. Antonio Ruiz, who had been in the company managing the commercial and administrative functions of the lab in close connection with the Grifols owners since 1951, retired and died in the early 1980s and Grifols Roura took over these responsibilities with new energy.

He was able to create a new generation of commercial agents with whom he put together a team in charge of developing a sales network in Spain. For this, he employed

the sales representatives as salaried staff and started organizing general meetings in 1981 to homogenize sales strategies. Coinciding with the radical organizational shift that took place after 1982, the firm Movaco was created to organize and create commercial offices with salaried employees devoted exclusively to Grifols products in different Spanish provinces—Valencia, Seville, Madrid, Barcelona, Bilbao, and A Coruña. Movaco was established at the same time as the Grifols Group holding was formed (1987) and its purpose was to overcome past inefficiencies in the coordination of sales and production, to organize the professional training of the sales workforce, and to increase efficiency in selling the diversity of exclusive products from their North American suppliers to Spanish hospitals.

The context changed in the country and the company after 1975 with the transition from dictatorship to democracy that came after Franco's demise and with the rapid integration of the country into European institutions and markets since 1986. Formerly scarce strategic resources could be more easily introduced into the country and the lab in this period, transforming the company into a global corporation. Víctor Grifols Roura, from the fourth Grifols generation, joined the company and, following the family traditions of strategic alliances with leaders in their field, sealed a new alliance with Alpha Therapeutic Corporation (ATC), the North American subsidiary of the Japanese global Green Cross Corporation. After 1975, and particularly after 1982, mass production techniques, global channels of distribution, long-term capital invested by foreign banks and investors, and professional managers in business administration were introduced very rapidly. It was indeed a Chandlerian revolution, with dramatic changes taking place in three areas: improvement and increase of the production capacity following the US Food and Drug Administration's standards; organization of the sales force at home and foreign direct investments abroad; and the creation of the Grifols Group, a formal business group managed by a team of Spanish, North American, and Japanese professionals in business administration who shared top managerial responsibilities in the coordination of investments, production, and sales with a global perspective.

In management, three changes took place one after the other between 1975 and 1985 that made the previous growth in scale and scope in production and distribution possible: the reorganization of the sales departments; the improved organization of internationalization; and the creation of a formal business group with functional divisions and business lines (hospitals, solutions, and diagnostics). All three changes took place

during a time that in most family businesses is conflictual; a period of generational transition. The founder of Laboratorios Grifols, José Antonio Grifols Roig, died in 1976, three years after his grandson, Víctor Grifols Roura, of the fourth generation, had joined the company in the sales department, and only four years after the opening of the new US-style factory in Parets del Vallès in 1972. The emotional attachment to the family business and the shared long-term values focused on seriousness and professionalism in a very special business sector help explain the peaceful and very positive coexistence of the third (Víctor Grifols Lucas) and fourth (Víctor Grifols Roura) generations of the Grifols family in the top management, representing half of the shares owned in the different joint ventures with North American and later also Japanese partners.

On the other hand, there was a substantial shift and tensions among the managers on the board representing the North American shareholders in the Grifols firms. AHS—through its subsidiary DR and later alone—was on the managing board of Dade Grifols, Gri-Cel, and Laboratorios Grifols from 1960 until 1976. With AHS suffering the impact of powerful competitors at home, and the negative effects of the late-1970s crisis on sales, it decided to sell its 50 percent of the shares in Laboratorios Grifols. AHS invited Grifols to choose the company it would sell its shares to in order to avoid damaging its interests. Dr. Guillermo Anido's advice was important in this regard; he suggested the name of ATC, a North American subsidiary of the Japanese Green Cross Corporation (a global player in the blood industries). In a later interview, the Japanese CEO indicated that they liked doing business with the small Spanish lab because it had a long-term conservative attitude, typical of a family business, and they preferred a partner like this over an aggressive short-term dividend-oriented North American or Western European company.

The Grifols accepted the suggestion from their Cuban colleague—with whom they would maintain a long-term friendship despite the termination of the joint venture with AHS—and signed a commercial and technical cooperation agreement with ATC in 1982, placing managers from ATC on the managing board. AHS still retained half of the shares in the Dade Grifols joint venture. However, just three years later, in 1985, Baxter Travenol, a traditional competitor of AHS in the United States, suddenly bought AHS and the 50 percent shares it had in Dade Grifols. This was considered a threat to the interests of Grifols' future expansion in global markets and in Spain. The Spanish shareholders of Dade Grifols decided to sell their 50 percent to Baxter, abandon their flagship company that had generated such huge profits in the 1960s and 1970s, and concentrate on their new

partner and a new generation of managers in control of the future of Laboratorios Grifols. The holding company Grupo Grifols was created in 1987 with the remaining firms and new firms (Laboratorios Grifols, Movaco, Instituto Grifols, Diagnostic Grifols, and Logister). ATC turned out to be a great “business school” during their partnership (1982–1999), teaching Grifols how to become a global leader and to initiate exports and acquisitions on a large scale.

In 1958 and 1959, the Spanish lab had exported plasma to the United States and Switzerland, but in quite reduced amounts and of limited value. Between 1960 and 1966, exports to the United States continued and small quantities were also sent to Sweden and Germany, until the Spanish government’s 1965 prohibition on exporting human blood products. The prohibition was lifted in the early 1970s and in 1974 Víctor Grifols Roura, who had just joined the company as the first member of the fourth generation with managerial responsibilities, met a commercial agent with whom agreements to export products to the then Portuguese Angola were signed. Angola became independent soon after and some limited exports were sent to Denmark. The partnership with ATC represented a radical change in the company’s international department. Víctor Grifols Lucas and his son, Víctor Grifols Roura, travelled to China in 1983, the first year of the partnership, to start exports in a country where they had no idea how to do business. The Green Cross Corporation, owner of ATC, asked Grifols to export their plasma products together with Grifols’ own products to China—at that time Japanese blood products were forbidden in China. From 1983 to 1985, the Grifols entrepreneurs learnt how difficult it was to find even a secretary through the embassy to start the paperwork to establish a commercial representative and to export to China, and experienced great organizational difficulties of every kind. After 1982, when news of the AIDS epidemic started to spread, with recommendations from the Food and Drug Administration to heat blood stocks, China soon increased controls and reduced and later stopped imports.

Grifols became leader in the supply of key plasma proteins for the Spanish market in the 1980s, as shown in the table below

Hemoderivatives, Spain, 1987. Total and Percentage represented by Grifols on total Spanish imports, exports, and total Spanish foreign trade of hemoderivatives

No.	PRODUCT	UNIT	SALES		%	EXPORTS		%
			SPAIN	GRIFOLS		SPAIN	GRIFOLS	
2	HEMOFACTOR	UI	7995540	3188500	39.9	860000	0	0.0
5	FACTOR VIII	UI	67665750	28488000	42.1	6934000	995750	14.4*
15	GAMMA ANTI-D	MMCG	29449	10200	34.6	3105	0	0.0
16	GAMMA ANTI-H	ML	36820	29978	81.4	16000	0	0.0
22	GAMMA ANTI-T	MUI	724021	313548	43.3	158544	6710	4.2
27	GG POLIV.	G	223958	152500	68.1	292328	37442	12.8
33	PPL	L	9029	9029	100.0	1243	1243	100.0
35	ALBUMINA	G	3134859	1052140	33.6	8194914	2400400	29.3
36	ATIII	UI	0	0		3899500	2329000	59.7

Source: Paloma Fernández elaboration from "ESTUDIO COMPARATIVO HEMODERIVADOS AÑO 1987. VENTAS GRIFOLS VS TOTAL VENTAS, SEGÚN ESTADÍSTICA FACILITADA POR EL MINISTERIO DE SANIDAD (OCTUBRE 1988)". A copy in Archivo Histórico Grifols, Barcelona.

In 1989, the name of the joint venture was established as Alpha Grifols. ATC is also very significant for understanding two key elements of the 1980s and 1990s (the relationship ended in 1999): the fast speed of the joint venture's acquisitions and foreign direct investment; and its privileged contacts with foreign banks that provided huge amounts of external capital with which to finance international expansion and modernization in production, distribution, and the managerial professionalization of the group. As the statistical information indicates, it was during the joint venture with ATC that three new focuses were added to the Grifols Group's previous trajectory: (i) long-term capital endowment from outside sources; (ii) huge investments in Europe, America, and Asia; and (iii) a rapid decline in the percentage of sales represented by the Spanish market in the structure of the group's total sales (Figure 5).

New premises, companies, and acquisitions evolved as follows: Portugal (1988), Argentina (1991), Mexico (1993), Germany/Italy/United Kingdom (1997), Brazil (1998), and Slovakia/France (1999). In 1999, ATC and Grifols ended their joint venture due to a combination of problems related to a broader crisis affecting the Green Cross Corporation in Japan and its subsidiaries in Europe, and to disagreements about how to manage the uncertainty of the first years of the AIDS epidemic in the industry (from a technical point of view). After their friendly separation, Grifols felt strong enough and with enough

resources and know-how to go it alone and invested in subsidiaries in the United States (ATC's factory) and Malaysia in 2003, in Poland in 2004, and in the United States in 2006, in representative offices in Japan in 2006 and in China in 2007, and in more subsidiaries in Switzerland in 2009 and in Colombia and Nordic countries in 2010. 2011 was the year of their large acquisition of Talecris in the United States for around 3,000 million US dollars, which was followed in 2014 with assets from Novartis Diagnostics and in 2015 by the purchase of 45 percent of Alkahest, both also in the United States. In recent years, beyond the United States (acquisition of assets of Hologic in 2017), Grifols has increased its presence in Canada and Ireland.¹⁹

Information from the corporation reveals that long-term sources of external capital played an increasingly relevant role in financing, innovations and patents, and acquisitions abroad. Internal resources became insufficient and syndicated bank loans, with a combination of local and foreign banks, made their appearance. After 2006, when Grifols was listed in the Spanish stock market, more dispersed investors contributed external capital to the group from all over the world.

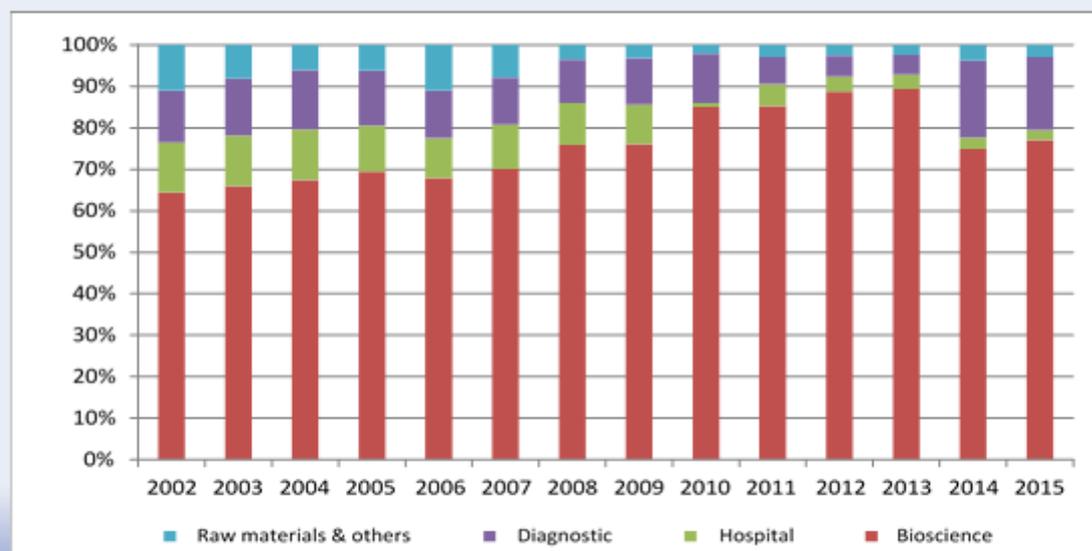
As a result of the speed and extent of the Grifols Group's internationalization, exports rapidly increased, representing 95 percent of total sales in 2016 in comparison to only 4 percent of total sales in the early 1980s. It was a radical change in the structure of the destination market for the business's sales. Also, the partnership with ATC granted Grifols leadership in the Spanish blood derivatives market in the 1980s, which coincided with a process of concentration of human blood industries in Spain. These industries had six major local companies producing during Franco's time in the early 1970s, mostly located in the Catalan region. Among them, Laboratorios Hubber had been one of the most modern, internationalized companies in plasma fractionation until its decline after the owner Félix Gallardo, a very sick widower, sold the company shortly before his death to the Spanish holding RUMASA to protect the future of his daughters who had no professional interest in managing the lab. The mid-1980s was therefore a time of decline for their major local competitor, just when Grifols had a new huge factory operating in Parets del Vallès and a new foreign partner and resources with which to expand and

¹⁹ Detail of acquisitions and financial information kindly provided by Nuria Pascual, from Grifols, by email to author 09/07/2017

internationalize the Grifols business. It was an opportunity not just to export but also to concentrate the Spanish plasma fractionation industry and to lead it.

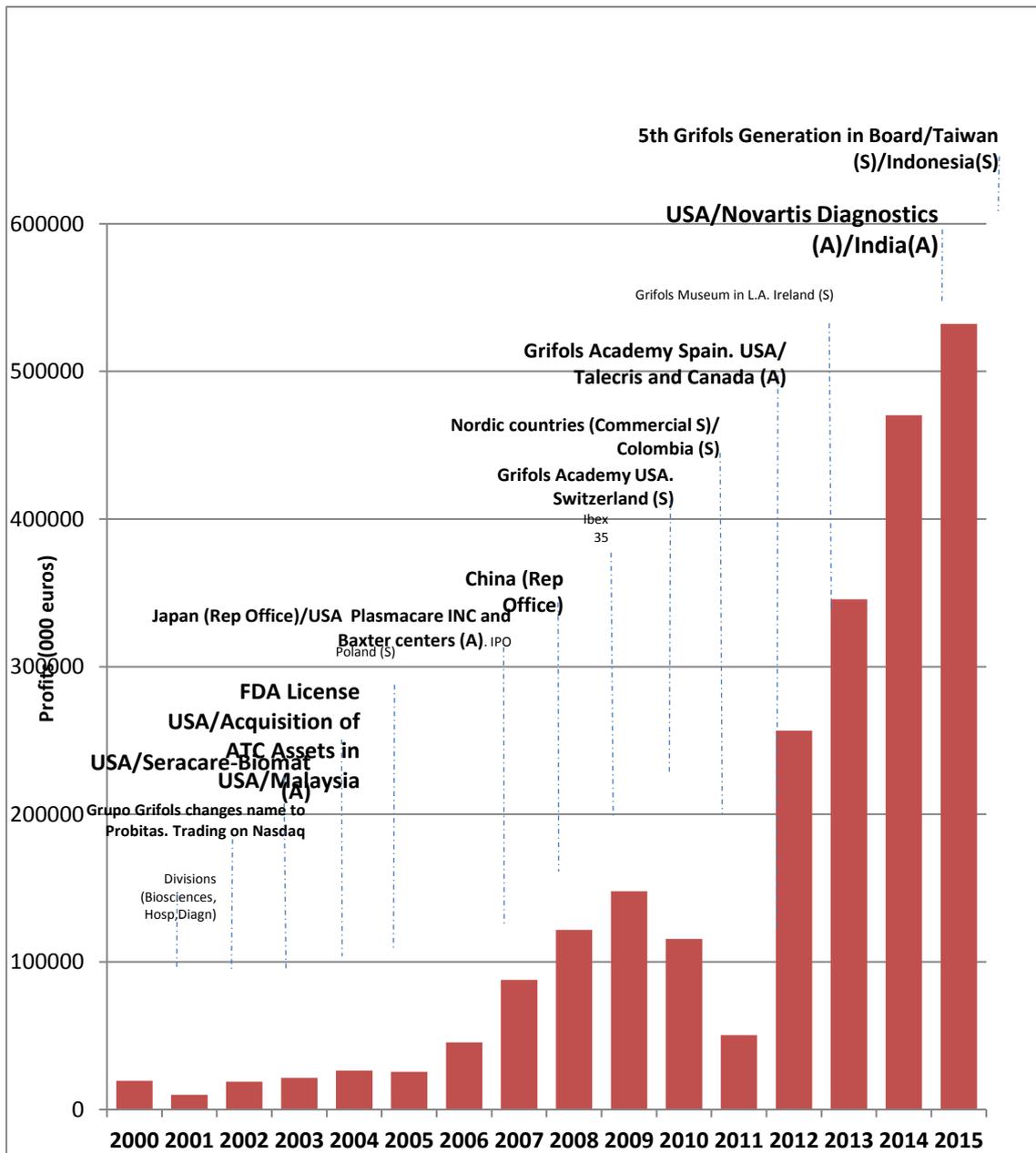
The partnership with ATC ended in 1999, but the Spanish financial and commercial departments of Grifols had by then learnt how to operate as a global corporation. During the first 15 years of the twenty-first century, staff graduated in business and economics in local institutions received fast practical training in how to export worldwide, how to operate with European and North American corporations, and how to obtain licenses in the toughest pharmaceutical markets of the world where the highest return on investments could be obtained. The accumulation of lessons and resources among Grifols' human capital also meant a capacity to deal with global sources of financing for internationalization, right during the years when deregulation and the globalization of finances offered many opportunities for global investment and funding (García Ruiz and Fernández Pérez forthcoming). Grifols had enough strength to take advantage of the new abundance of opportunities to access capital and to invest in tough markets, and it did so in the biotech industry in Western Europe and the United States first and later also in Asia.

Grifols. Sales by Division 2002- 2015



Source: Group annual consolidated accounts, auditors' report. October 1-23, 2015; April 28/2016.
<https://www.grifols.com/en/web/international/investor-relations/annual-report-and-annual-audited-account>

Note: Updated sales for 2016 from Nuria Pascual of Grifols when this paper was finished were: Bio: 79.7%; Diagnostic: 16.4%; Hospital: 2.4%; Raw Materials and Others: 1.5%



Source: Grifols Corporation. Museu Grifols in Barcelona and Sant Cugat Headquarters. Acquisition of assets from Hologic of the USA in 2017 to be included.

Conclusions

After the first third of the twentieth century the large corporations driving innovation in the pharmaceutical and chemical industry started to have complex learning bases and structures that made the future of the pharma and chemical industry in the world take individual pathways. Large biomedical industries would grow up in the second half of the twentieth century, some linked to historical large pharmaceutical leaders, and some created with new organizational foundations. In some late industrialized economies like

Italy and Spain many small firms in the pharmaceutical business sold nutritional and medical products manufactured by the large companies. However, a few innovative scientists and entrepreneurs well connected to pioneering innovations before World War I like Cesar Serono in Italy (1906), or José Antonio Grifols in Spain (1910), created embryonic small biomedical laboratories and maintained close contacts with leading scientists and firms of Switzerland, the UK, USA, and Germany. This paper analyzes with the story of the Grifols business in Spain how to have a small size, lack of institutional support, the competition from local and foreign competitors, or scarcity of financial resources, were problems that could be overcome through a century old history of: research and innovation, international alliances, and specialization in market niches far from the core activities monopolized by the big pharma or biomedical players.

The opportunity to supply specialized products (not provided by large public and private companies) to the increasing number of public and private hospitals in Spain after the 1960s required new resources: technology, organizational know-how, and capital. These resources were sought among leading corporations in the United States, with whom the small lab signed joint venture agreements and technological and commercial alliances in 1960 (Dade Reagents, a subsidiary of American Hospital Supply Corporation since 1956) and in 1968 (American Hospital Supply Corporation). Internal and external threats suffered in the 1970s—the death of the founder of the lab, generational transition, changes in the top management, more powerful competitors in Spain and in the United States, and the decision of the US partner to leave the partnership creating important financial and organizational difficulties—were solved by seeking a partner that was a world leader in plasma fractionation technology: the North American Alpha Therapeutic Corporation—a giant with up to 50 times the production capacity of Grifols—which was a subsidiary of the Japanese Green Cross Corporation.

The new partners served as a type of business school for Grifols, helping it go beyond exports and to decisively start ambitious foreign investment activity in Europe, Latin America, North America, and Asia after the 1990s. The established historical reputation of the Grifols Group was a guarantee for the new North American and Japanese corporations of the reliability of their smaller Spanish partner. It was Grifols' reputation that made it possible for it to work with global corporations

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Grifols Archive in Headquarters of Sant Cugat del Vallés

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