GRIFOLS' SOCIAL VALUE

GRIFOLS



INTRODUCTION

GRIFOLS' SOCIAL VALUE THE PROJECT IN DEPTH ADDITIONAL INFORMATION

CONTENT

HAN 110 YEARS 20

Nestill continue to pursue the same goals

"Business investments can be a powerful engine for positive social impact. Corporate investments and social return are not a zero-sum game.

At Grifols, we believe we can achieve solid economic results while generating social value for our donors, communities, patients and society as a whole."

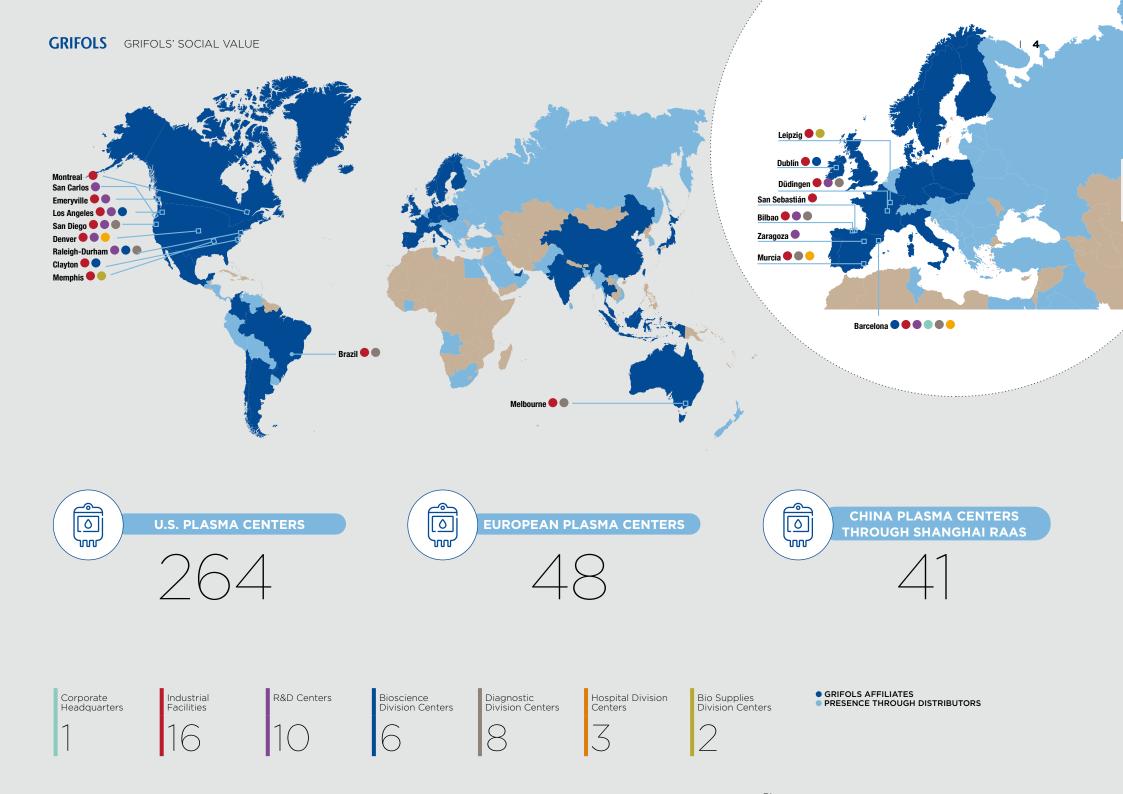
Raimon Grífols Roura, Grifols' Co-CEO

"Engaging with our stakeholders enables us to better understand how our operations impact their lives.

These individual positive impacts – when added altogether – affect society on a global scale."

Victor Grífols Deu, Grifols' Co-CEO





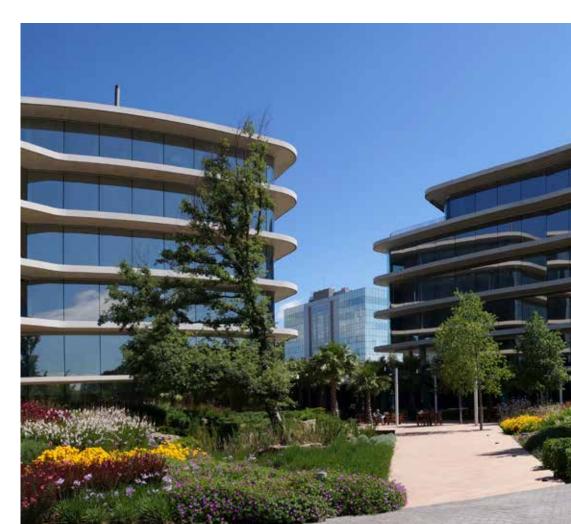
ABOUT GRIFOLS

Grifols, a global healthcare company, committed to improving the health and well-being of people around the world

Established in Barcelona in 1909, Grifols is a global healthcare company committed to enhancing the health and well-being of people around the world. Grifols' business model strives to sustainably create value across its four divisions — Bioscience, Diagnostic, Hospital and Bio Supplies — which develop, produce and market leading-edge solutions and value-added services sold in more than 100 countries.

Pioneers in the plasma industry, Grifols operates a growing network of plasma centers around the world. The company transforms collected plasma into essential plasma medicines to treat chronic, rare and, at times, life-threatening conditions. It is also a recognized leader in transfusion medicine, offering a comprehensive portfolio of solutions to enhance safety from donation to transfusion. The company's offerings also include tools, information and services to help hospitals, pharmacies and healthcare professionals that enhance the delivery of medical care. With close to 24,000 employees in 30 countries, Grifols is committed to its sustainable business model by serving as a beacon of continuous innovation, quality, safety and ethics.

In 2020, Grifols' financial results amounted to EUR 7.5 billion. The company also generated 140,000 jobs, including direct, indirect and induced employment.



■ A BUSINESS MODEL BASED ON VERTICAL INTEGRATION

GRIFOLS' VERTICALLY INTEGRATED BUSINESS MODEL GUARANTEES MAXIMUM QUALITY AND CONTROL AT EVERY STAGE OF THE VALUE CHAIN OF ITS FOUR DIVISIONS

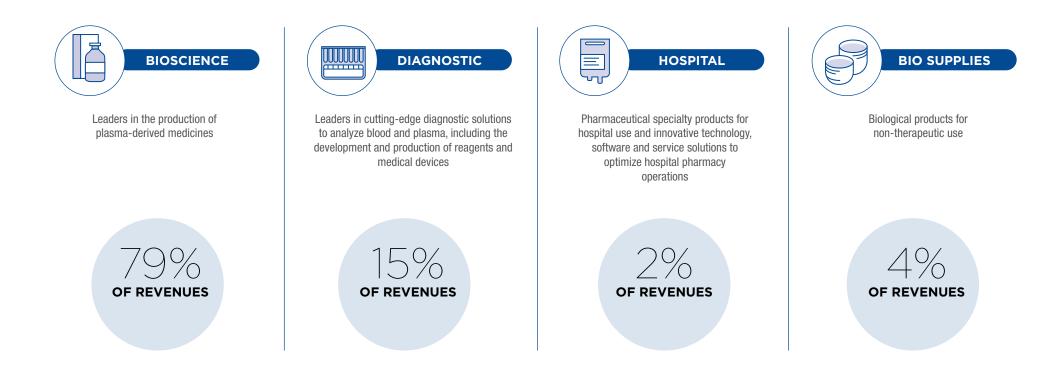
WE PUT DONORS AND PATIENTS AT THE CENTER OF OUR VALUE CHAIN

WE TRANSFORM DONORS' GENEROSITY INTO LIFE-SAVING TREATMENTS FOR PATIENTS AROUND THE WORLD



A BUSINESS MODEL FOCUSED ON SUSTAINABLE VALUE CREATION

Grifols' value creation aims to continuously bolster organizational outcomes and generate new market opportunities across its four main divisions



GRIFOLS' SOCIAL IMPACT: CREATING VALUE BEYOND OUR BUSINESS OPERATIONS

Grifols' Social Value is the estimation of the impact as a result of the company's activities

SOCIAL RETURN ON INVESTMENT (SROI) IS A METHOD TO ACCOUNT FOR VALUE CREATION

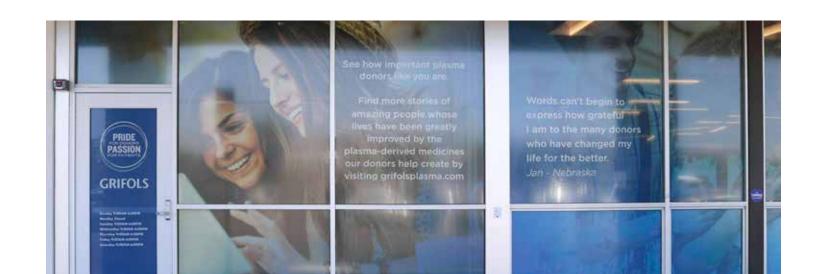
THIS SROI ANALYSIS ENABLES GRIFOLS TO MEASURE ITS NON-FINANCIAL IMPACT ON DONORS, PATIENTS AND LOCAL COMMUNITIES A broader definition of corporate performance has emerged in recent years, extending beyond financial benchmarks to consider the firm's non-financial performance such as its environmental and social impact.

As society embraces a more holistic, purpose-driven definition of corporate performance, global firms face mounting pressure from investors, shareholders and other key stakeholders to consider the value they create – or destroy – beyond just a financial impact of balance sheets and shareholder returns.

Social value, is an intangible, hidden value which is not captured by market prices. As a measurement, social value estimates the change stakeholders perceive in their lives as a result of a company's operations, only some of which is reflected in market prices.

Grifols' long-term sustainable business model is founded on an ethical approach and staunch commitment to creating value for its key stakeholders: patients, donors, donor communities, employees, suppliers, shareholders, investors and society. By measuring its social value, Grifols is able to enhance its awareness of how its operations impact key stakeholder groups and use this insight to better serve them

Thus the Social Return on Investment (SROI) entails a process of understanding, measuring and communicating social, environmental and economic values created by an organization. This method leverages a cost-benefit analysis, providing Grifols' leadership team and investors with an invaluable decision-making framework to assess and optimize the firm's social and environmental impacts.



THE SROI METHOD MEASURES THE VALUE OF SOCIAL BENEFITS IN RELATION TO THE COSTS INCURRED IN OBTAINING THESE BENEFITS OR IMPACTS

THE SROI RATIO IS CALCULATED USING NET PRESENT VALUE OF BENEFITS AND INVESTMENT

THIS METHODOLOGY GOES BEYOND OBTAINING A SINGLE DATA POINT. INDEED, IT DEMONSTRATES A CLEARER CONTEXT FOR UNDERSTANDING THE COMPANY'S IMPACT



THE PROJECT AT A GLANCE

SCOPE

The study analyzed Grifols' Bioscience Division operations, which represented roughly 80% of the company's revenues

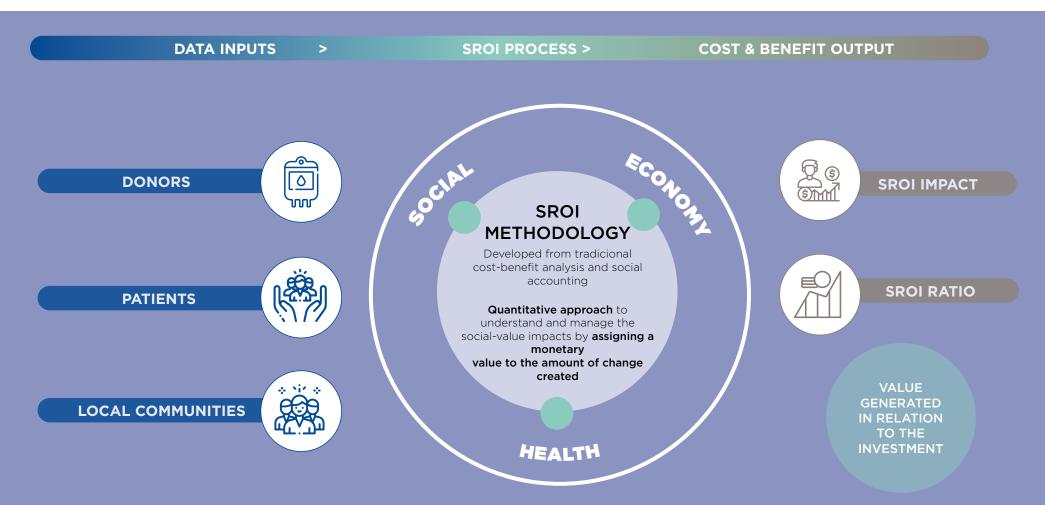


* This SROI analysis was carried out on 2019 data

** IG: immunoglobulin

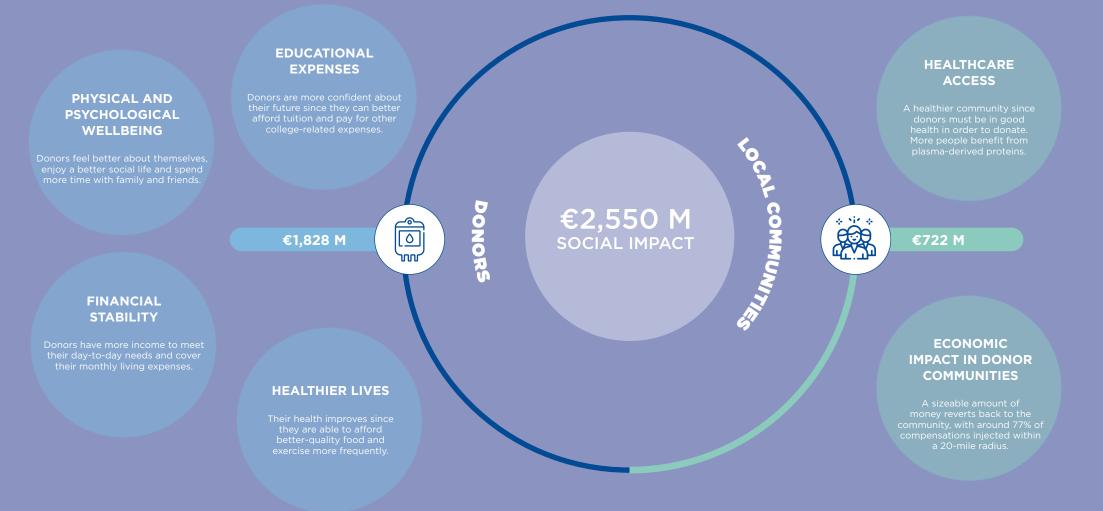
THE SROI METHODOLOGY

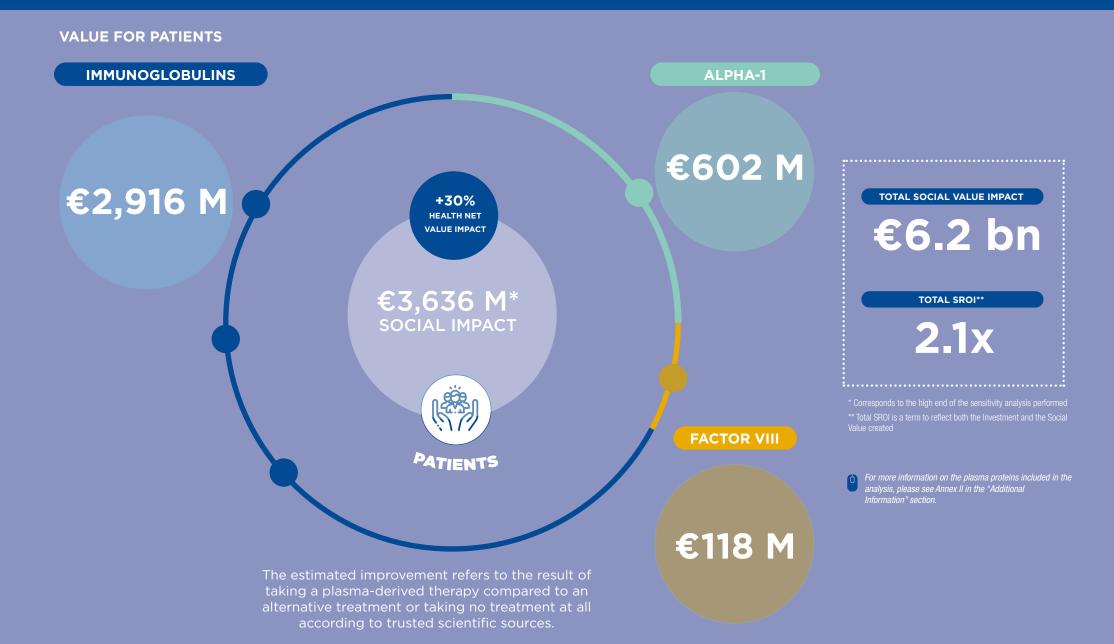
In 2020, Grifols conducted its first Social Return on Investment (SROI) analysis to measure the impact of a portion of its key operations and to better understand the value they generated. The project identified donors, local communities and patients as the main stakeholders. The SROI reflects the change produced by Grifols' operations on each stakeholder group based on individual assessments. These evaluations are subsequently quantified and recorded on an Impact Map to assign a financial value to their social, environmental and economic impact.



GRIFOLS' SOCIAL VALUE KEY FIGURES 2019

VALUE FOR DONORS AND COMMUNITIES





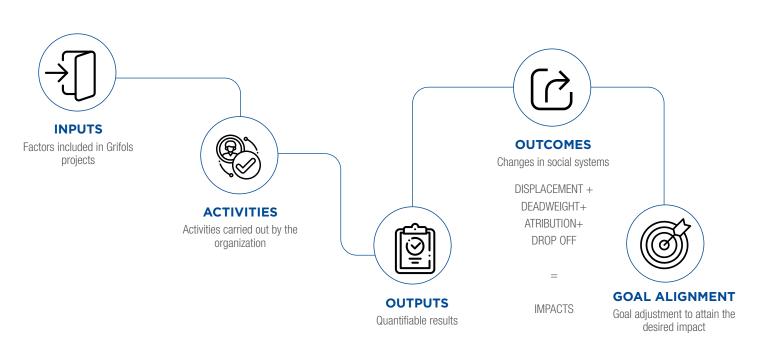




GRIFOLS' SROI ANALYSIS

The first step to calculate Grifols' SROI entails defining a map of impacts, which reflects the impacts noted by stakeholder groups as a result of the company's operations. At the end of the process, a list of impacts is obtained and the SROI ratio is calculated, where the aggregate social impacts or benefits (numerator) are divided by the aggregate resources needed to carry out the project (denominator).

IMPACT VALUE MAP



STAGE 1: DEFINING THE PROJECT SCOPE AND IDENTIFYING STAKEHOLDERS

As mentioned earlier, the SROI analysis focuses on operations carried out by the Bioscience Division. These include the collection of plasma from Grifols' plasma center network, the production of plasma-derived medicines in Grifols' manufacturing installations, and the commercialization of plasma medicines to patients and healthcare professionals.

Since the Bioscience Division has operations throughout the world in various capacities, the scope of SROI Analysis was limited to the following activities:

- Plasma collecting in the US plasma centers
- Patients worldwide treated with Grifols' plasmaderived medicines (IG, alpha-1 and factor VIII)

The first step in calculating the SROI is determining a list of stakeholders who interact with the company. This analysis defined the following stakeholder groups:

- Donors who donate plasma in U.S. centers
- Local communities where plasma centers are located
- Civic associations* that collaborate with Grifols' U.S. plasma centers
- Public authorities* operating in the area where plasma centers are located
- Patients worldwide treated with Grifols IG, alpha-1 and factor VIII plasma-derived medicines
- Grifols as the sponsor of the project
- * These stakeholders are included in order to evaluate how local communities are effected by Grifols' activities.

INVOLVEMENT AND ENGAGEMENT OF GRIFOLS' STAKEHOLDERS

There are two ways of carrying out an SROI analysis: evaluative and forecast. In this study, the decision was made to carry out an evaluative analysis using verified quantifiable data from 2019 to avoid forecasting and ensure the study remained within its objectivity boundaries. Qualitative data - namely stakeholder interviews - were conducted between November 2019 and May 2020.

Individual surveys were used to collect data from donors, public authorities and civil associations as

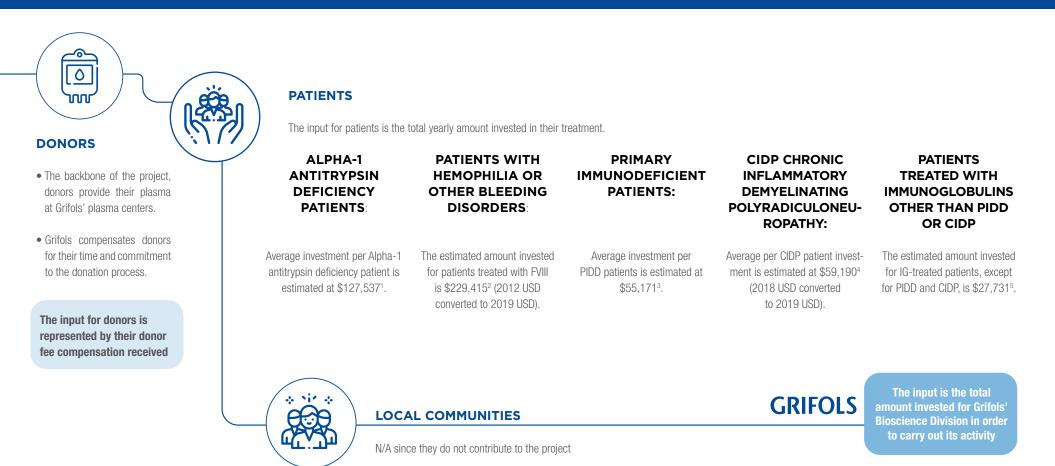
other tools such as group meetings were deemed unnecessary. In the case of patients, data was gathered either through patient associations or via scientific articles.

The surveys contained a series of questions to assess the impact of Grifols' activities on stakeholders' lives. Respondents were guaranteed complete confidentiality and anonymity and the same survey was administered to all members of each group.

In terms of donor surveys, Grifols made sure the participant group was as diverse as possible to attain a representative sample. Researchers employed the "saturation approach," a social-research technique in which data collection is discontinued when interviewees provide no further information to the query posed.

STAGE 2: MAPPING OUTCOMES

IDENTIFICATION AND VALUATION OF INPUTS



| 18

DESCRIPTION OF OUTCOMES



DONORS

- Seniors: enjoy a better social life
- Workers: greater confidence in their future
- Students: greater confidence in their future
- Healthier eating habits
- Ability to spend more time with family
- Donors: improved financial situation to better meet monthly expenses and pay for incidentals and indulgences

LOCAL COMMUNITIES

- Improved economic conditions for area residents: a sizeable amount of money reverts back into the community, most within a 20mile radius
- Build a healthier community: Grifols' plasma centers promote community health since donors must be in good health to donate

OUTCOMES DESCRIBE THE CHANGES EXPERIENCED BY STAKEHOLDERS AS A RESULT OF GRIFOLS' ACTIVITIES, WHICH WERE EXTRACTED BY STAKEHOLDER INTERVIEWS



PATIENTS

- Improved quality of life since receiving Grifols' treatment
- Improved psychological wellbeing in patients participating in "alfacare" programs

STAGE 3: OUTCOMES ARE IDENTIFIED AND VALUED

DEVELOPMENT OF OUTCOMES INDICATORS

As mentioned earlier, outcomes describe the change experienced by stakeholders. These are evaluated and quantified according to indicators, used to measure the changes that have occurred. The study engaged stakeholders to identify an indicator for each outcome.

STAKEHOLDER	OUTCOMES	INDICATORS
DONORS	Senior-age donors: enjoy a better social life	Number of donors who report having a better social life as a result of donating at a plasma center
	Workers: greater confidence in their future	Number of donors who report feelinig more confident about their future since financial compensation provides them funds to invest in their business, visit customers, etc.
	Students : greater confidence in their future	Number of donors who report having more confidence about their future since they can better afford tuition fees and academic materials thanks to financial compensation
	Healthier eating habits	Number of donors who report eating better as a result of receiving financial compensation
	Ability to spend more time with family	Number of donors who report having more time to spend with the family as a result of receiving financial compensation
	Donors: improved financial situation to better meet monthly expenses and pay for incidentals and indulgences	Number of donors who report having an improved financial situation thanks to receiving financial compensation
LOCAL COMMUNITIES	Improved economic conditions for area residents: a sizeable amount of money reverts back into the community, with most compensations injected within a 20-mile radius	Number of donors who spend their compensation in the area
	Build a healthier community: Grifols' plasma centers promote community health since donors must be in good health to donate	Number of donors who visit a plasma center in a year
K	Improved quality of life since receiving Grifols' treatment	Number of patients who report an improvement in their quality of life as a result of receiving treatment
	Improved psychological wellbeing in patients participating in "AlfaCare" programs	Number of patients who report greatly enhanced wellbeing as a result of the psychological support offered in "AlfaCare programs"
PATIENTS	programo	Number of patients who report a higher quality of life as a result of receiving treatment

PUTTING A VALUE ON THE OUTCOME

What makes the SROI method unique is its effort to place a value on outcomes which do not have a market price. Financial proxies were used to estimate the value of non-traded goods for different stakeholders.

LIST OF OUTCOMES AND THEIR VALUATION PERCEIVED BY DONORS

- Senior-age donors: When interviewed, this group of donors (people aged 60 years and up) report an improvement in their social lives as a result of donating plasma at a Grifols' center. This outcome is equated to the cost of four monthly therapy sessions⁶ (\$90 per session).
- Workers: As a result of donating plasma, these donors describe having greater confidence in their future since they have more expendable income for transport costs to grow their business or visit potential customers. This outcome is calculated as 50% of the compensation received per donation since they report spending roughly half of it on gas. The financial proxy is based on a conservative estimate of 8 monthly donations, with an average per donation compensation of \$45⁷.
- **Students:** Students report feeling more confident about their future since the financial compensation helps them meet part of their college tuition fees and pay for academic materials. This proxy is based on the average net salary for recent college graduates (\$55,000) minus the average net salary for employees without college degrees (\$32,000), in the case that they did not finish their degrees. Using this formula, the net salary⁸ is \$23,000.
- Adopting healthier eating habits: These donors reported adopting healthier eating habits thanks to the income provided by donation compensation. This outcome is based on the estimated average yearly amount Americans⁹ spend on fruits and vegetables (\$400).

- More leisure time to spend with their family: Some donors reported having more leisure time to spend with their family thanks to donor compensation. The proxy for this concept is based on a weeklong trip to Florida for 4 people¹⁰ (\$6,716).
- Improved financial situation to better afford monthly expenses, incidentals and indulgences: All donors reported an improved financial situation as a result of receiving compensation for donating plasma. This proxy is based on the average yearly donor compensation¹¹ paid by Grifols.
- SEVERAL FINANCIAL PROXIES WERE IDENTIFIED FOR DONORS WHO ALSO RESIDE IN AREAS WHERE PLASMA CENTERS ARE LOCATED. THE FOLLOWING OUTCOMES AND VALUATIONS WERE DEFINED FOR RESIDENTS AND LOCAL COMMUNITIES
- Improved economic conditions for area residents: A significant portion of donor compensation stays within the local community. According to Grifols' data, 77% of donor reimbursement is spent within a 20-mile radius of plasma centers.
- **Healthier communities:** Grifols' plasma centers help promote the health of local communities since donors must be in good health in order to donate. The proxy is based on the average number of doctor visits that donors make per year (4 times a year¹² at a cost of \$110 per visit¹³).

LIST OF OUTCOMES AND THEIR VALUATION FOR PATIENTS

Outcomes for patients were normally based on the quality of life (QOL) indicator, the most applicable and reliable metric available to assess improvements stemming directly from Grifols' plasma-derived medicines.

Since quality of life is a broad concept, this study instead utilized the quality-adjusted life year metric (QALY) – a generic measure of disease burden that includes both the quality and the quantity of life lived – as the proxy for patients.

Using this metric¹⁴, one QALY equates to one year of perfect health (1 year of life x 1 utility), whereas a less than perfect health year is worth less than 1.

The QALY scale reflects the improvement in the patient's life as a result of Grifols' treatment. As an example, if a healthy person has 0.9 QALY and a cancer patient, 0.2 QALY, the improvement in quality of life would be a significant 0.7 QALY¹⁵.

As mentioned earlier, one use of QALY is to measure quality of life. The formula to calculate a patient's improvement as a result of treatment in monetary terms involves taking the value of a year lived in perfect health (1 QALY) and weighing it with the patient's percentage of improvement.

The most common way to value a QALY – also called the cost-effectiveness threshold – is the standard used by the Boston-based Institute for Clinical and Economic Review (ICER)¹⁶. ICER's latest value assessment framework¹⁷ states a median value of \$100,000 per QALY (with an established lower range value of \$50,000 and an upper range value of \$150,000). Another way of valuing QALYs is 1 to 3 times the gross domestic per capita¹⁸: using the estimated USD GDP per capita¹⁹ in 2019 (\$65,112) would lead to a range between \$65,112 and \$195,335. Finally, a third way to apply a monetary value to a QALY is the one proposed by Braithwaite et al.²⁰ With this study, the authors calculate a QALY value between \$109,000 and \$297,000.

For the purposes of this project, the median average of the three studies mentioned was used (\$144,408), although a sensitivity analysis was carried out in Stage 5 to determine how the analysis performed under different scenarios.

MONETARY VALUE ASSIGNED TO QALYS IN GRIFOLS SROI ANALYSIS

QALY Value	Source	
\$100.000 ICER median value		
\$130.223	Median average 1-3 times per capita	
\$144.408	Median average Three Studies	
\$203.000	Median average Braithwaite Meltzer (BM)	
\$297.000	Upper range BM	



APPLYING QALYS TO TREATED PATIENTS



TREATED WITH ALPHA-1

- Alpha-1 Antitrypsin Deficiency (AATD) patients: Patients report a higher quality of life as a result of receiving Grifols' treatments. For this outcome, the median average of the three studies (\$144,408) was used as a financial proxy. Since it cannot assign the highest score of 1 QALY to these patients, in Stage 4 is calculated for counterfactuals by deducting what could not be attributed to Grifols' treatments.
- **AATD patients participating in "AlfaCare" programs:** Some of AATD patients considered in this study have participated in Grifols' AlfaCare21 programs, an initiative the company describes as "a comprehensive, personalized assistance program that offers training, counselling and a range of other services to AATD patients to encourage new habits and help them better manage the disease." Of these patients, 94% highly value the program's psychological support services. As a result, the proxy for this outcome was calculated based on four monthly therapy sessions²² (\$90 per session).



TREATED WITH FACTOR VIII

• Patients with hemophilia or other bleeding disorders: Patients report a higher quality of life as a result of receiving Grifols' treatments. For this outcome, the median average of the three studies (\$144,408) was used as a financial proxy. Since it cannot assign the highest score of 1 QALY to these patients, in Stage 4 is calculated for counterfactuals by deducting what could not be attributed to Grifols' treatments.



TREATED WITH IMMUNOGLOBULINS

- Patients with primary immunodeficiency (PIDD) syndromes: Patients report a higher quality of life as a result of receiving Grifols' treatments. For this outcome, the median average of the three studies (\$144,408) was used as a financial proxy. Since it cannot assign the highest score of 1 QALY to these patients, in Stage 4 is calculated for counterfactuals by deducting what could not be attributed to Grifols' treatments.
- Patients with chronic inflammatory demyelinating polyneuropathy (CIDP): Patients report a higher quality of life as a result of receiving Grifols' treatments. For this outcome, the median average of the three studies (\$144,408) was used as a financial proxy. Since it cannot assign the highest score of 1 QALY to these patients, in Stage 4 is calculated for counterfactuals by deducting what could not be attributed to Grifols' treatments.
- Patients treated with immunoglobulins with conditions other than PIDDs or CIDP: Patients report a higher quality of life as a result of receiving Grifols' treatments. For this outcome, the median average of the three studies (\$144,408) was used as a financial proxy. Since it cannot assign the highest score of 1 QALY to these patients, in Stage 4 is calculated for counterfactuals by deducting what could not be attributed to Grifols' treatments.

STAGE 4: DETERMINATION OF THE IMPACT

DEADWEIGHT AND DISPLACEMENT

After conducting stakeholder interviews, only these two cases were encountered deadweight:

- 1. 25%* deadweight among donors who report feeling more confident about their future since they are able to visit more customers.
- 80%* deadweight among donors who report having more time to spend with their families as a result of receiving financial compensation.
 *Based on donor interviews.

The study found no displacement.

ATTRIBUTION

In the study, among student donors, there was a 91% attribution rate since financial compensation only covers about 9% ²³ of the total annual academic costs.

With regard to patients, the following attributions were discovered:

- **AATD patients:** The study found²⁴ a 24.7% improvement in the quality of life of patients treated with plasma-derived medicines compared to patients who did not receive this treatment (75.3% attribution).
- Patients with hemophilia or other bleeding disorders: The study found²⁵ an 8.66% improvement in the quality of life of patients treated with plasma-derived medicinal products (PDMPs) compared to patients who did not receive this treatment (91.34% attribution).

- **PIDD patients:** The study found²⁶ a 9.1% improvement in the quality of life of patients treated with PDMPs compared to patients who did not receive this treatment (90.9% attribution).
- **CIDP patients:** The study found²⁴ a 34.5% improvement in the quality of life of patients treated with PDMPs compared to patients who did not receive this treatment (65.5% attribution).
- Patients not affected by PIDD or CIDP: The attribution of this group was based on a weighted average between CIDP and PIDD quality-of-life improvement rates. The study found an 18.11% QOL improvement (81.89% attribution).

DROP-OFF

Drop-off is the deterioration of outcomes as a result of a variation, modification or change over time. The analysis found no drop-off effect.

MEASURING THE IMPACT

As previously mentioned, the Impact Map contains an overview of the estimated impact, which includes the total value of each change per stakeholder group. The impact is calculated as follows:



STAGE 5: CALCULATING THE SROI

CALCULATION OF THE SROI RATIO

UPPER RANGE			AVERAGE RANGE		
SUM OF IMPACTS	SROI RATIO	TOTAL SROI	SUM OF IMPACTS	SROI RATIO	TOTAL SROI
€6.2 BN	1: 1.1	2.1x	€4.4 BN	1: 0.7	1.7x

This means that for every $\in 1$ invested in the project, a social value of approximately $\in 1.1$ was created. In other words, the company returns to Society $\in 1.1$ for every $\in 1$ invested.

This means that for every $\in 1$ invested in the project, a social value of approximately $\in 0.7$ was created. In other words, the company returns to Society $\in 0.7$ for every $\in 1$ invested.

SENSITIVITY ANALYSIS

As mentioned earlier, Stage 3 leveraged three different approaches to assess patients' quality of life. In order to calculate the total social value impact, the median value of these methodologies was used (\$144,408). This table summarizes the different monetary valuations for the impact on patients measured according to the changes experienced in their quality of life (QALY) as established by three sources with their respective methods (ICER, Braithwaite Meltzer and average per capita). The SROI ratio may vary according to each one of them as follows:

	QALY VALUE	VALUE CREATED FOR PATIENTS	SROI RATIO	TOTAL SROI
ICER median value	\$ 100,000	1,240 M€	0.6	1.6x
Median average 1-3 times per capita	\$ 130,223	1,607 M€	0.7	1.7x
Median average Three Studies	\$ 144,408	1,780 M€	0.7	1.7x
Median average Braithwaite Meltzer (BM)	\$ 203,000	2,493 M€	0.9	1.9x
Upper range BM	\$ 297,000	3,636 M€	1.1	2.1x

CONCLUSIONS



This study analyzed the SROI impact of the main activities carried out by Grifols' Bioscience Division, associated with the collection of plasma and manufacturing of plasma-derived medicines. As plasma cannot be created in a laboratory or produced synthetically, only the generosity of volunteer plasma donors makes these medicines possible, with Grifols' at the heart of these activitities, helping others to lead better lives and contributing to generating a positive impact. Therefore, this analysis aimed to measure the change or modification that donors, local communities and patients experienced as a result of their interactions with Grifols' operations. A detailed analysis of social impacts for each stakeholder group was created and summarized on an Impact Map. Based on the study's findings, the operations analyzed at Grifols' Bioscience Division generate an impact ratio of 1:0.7. In other words, the company returns to Society €0.7 for every €1 invested, so Grifols' total SROI amounts to €1.7. This social value manifests itself in a number of ways: enhanced social lives among donors, better financial conditions in local communities and healthier residents in areas where plasma centers are located. And perhaps most importantly, the enhanced quality of life of patients treated with Grifols' plasmaderived medicines.

Furthermore, the more than \in 4.4 billion of social impact that has emerged as a result of this analysis should be added to and complement the company's financial results.

This study was prepared in accordance to the principle of prudence and thus, the SROI method takes into account both positive and negative impacts. Although, no negative outcomes were found in the analysis.

As a result of the current context of a global pandemic in which the importance of plasma has come to the forefront, the need to conduct a report in 2020 based on the values of 2019 proved essential. In fact, the appeals for people who recovered from COVID-19 to donate their plasma has been steady. This hyperimmune plasma contains specific antibodies to SARS-CoV-2, and using it to treat infected patients could be a promising treatment for producing a specific medicine - hyperimmune immunoglobulins. Therefore, today more than ever, plasma centers and donors are essential.

Hugo Narrillos Roux

ABOUT HUGO NARRILLOS ROUX

A specialist in social value, Hugo Narrillos Roux is the author of *Economía Social: Valoración y medición de la inversión social (método SROI)* (Social Economy: Valuation and Measurement of Social Investment (SROI method)) and a holder of a doctorate degree in Economics with Honors from the Complutense University of Madrid (Spain). His thesis was titled, "Social Return on Investment: A Good Method to Measure the Social Value Created by Social Firms."

Mr. Narrillos Roux is recognized as an Accredited SROI practitioner from Social Value International, a member-led network focused on social impact and social value. He teaches at several universities and consults for leading global firms to help them evaluate their social impact.



REFERENCES

1. Sieluk, Jan, Levy, Joseph, Sandhaus, Robert, Silverman, Henry, Holm, Kristen and Mullins, C. Daniel. "Costs of Medical Care Among Augmentation Therapy Users and Non-Users with Alpha-1 Antitrypsin Deficiency in the United States." Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation, (2019), Vol. 6(1):6-16: doi: https://doi.org/10.15326/ jcopdf.6.1.2017.0187.

2. Thorat, Teja, Neumann, Peter and Chambers, James. "Hemophilia Burden of Disease: A Systematic Review of the Cost-Utility Literature for Hemophilia." Journal of Managed Care & Specialty Pharmacy (2018) Vol. 24(7):632-42.

3. Vaughan, Leslie. "Managing Cost of Care and Healthcare Utilization in Patients Using Immunoglobulin Agents." The American Journal of Managed Care, (2019), Vol. 25: S105-S111.

4. Divino, Victoria, Mallick, Rajiv, DeKoven, Mitch and Krishnarajah, Girishanthay. "The Economic Burden of CIDP in the United States: A Case-Control Study." PLOS One (2018), Vol. 13(10): e0206205: doi.org/ 10.1371/journal.pone.0206205.

5. Average yearly cost of primary and secondary immunodeficiency treatments weighted by the number of patients treated in each group.

6. "How Much Does Therapy Cost." Thervo website. thervo.com/costs/ how-much-does-therapy-cost. Accessed on December 1, 2020.

7. Plasma compensation varies depending on the location, although typically averages \$45 per donation based on information obtained from Business Insider.

8. Bonnie Conrad. "The Average Yearly Income for High School Graduates Vs. College Graduates." Career Trend website, September 28, 2017. careertrend.com/the-average-yearly-income-for-high-school-graduates-vs-college-graduates-12460627.html. Accessed on December 1, 2020.

9. "Spending Fruits and Vegetables Under Trend." The Packer website. September 11, 2018. www.thepacker.com/article/spending-fruits-and-vegetables-under-trend. Accessed on December 1, 2020.

10. "How Much Does It Cost to Go to Orlando?" Budget Your Trip website. www.budgetyourtrip.com/united-states-of-america/orlando. Accessed on December 1, 2020.

11. Total donor compensation amount paid by Grifols based on 2019 data

12. Niall McCarthy. "Americans Visit Their Doctor 4 Times A Year. People In Japan Visit 13 Times A Year." Forbes website, September 4, 2014, www. forbes.com/sites/niallmccarthy/2014/09/04/americans-visit-their-doctor-4-times-a-year-people-in-japan-visit-13-times-a-year-infographic. Accessed on December 1, 2020.

13. "Healthcare Costs in the USA." InternationalInsurance.com website, 2020, www.internationalinsurance.com/resources/healthcare-costs-in-the-usa.php. Accessed on December 1, 2020.

14. Prieto, Luis and Sacristán, José A. "Problems and Solutions in Calculating Quality-Adjusted Life Years (QALYs)." Health and Life Quality Outcomes (2003), Vol. 1, art. 80.

15. Joshua T. Cohen, Daniel A. Ollendorf and Peter J. Neumann. "Will ICER's Response to Attacks on the QALY Quiet the Critics? CEVR-Tufts website, December 18, 2018, cevr.tuftsmedicalcenter.org/news/2018/ will-icers-response-to-attacks-on-the-qaly-quiet-the-critics. Accessed on December 1, 2020.

16. ICER Institute for Clinical and Economic Review website, icer-review. org. Accessed on December 1, 2020.

17. "ICER 2020-2023 Value Assessment Review." icer-review.org/ wp-content/uploads/2019/05/ICER_2020_2023_VAF_013120-1.pdf. Accessed on December 1, 2020.

18. Paul Revill et al. "Cost-Effectiveness Thresholds: Guiding Health Care Spending for Population Health Improvement," November 2015, www.idsihealth.org/wp-content/uploads/2015/01/CE-Thresholds-iDSI-Working-Group-Final-Report.pdf. Accessed on December 1, 2020.

19. "Economy of the United States." Wikipedia website, en.wikipedia. org/w/index.php?title=Economy_of_the_United_States. Accessed on December 1, 2020.

20. Braithwaite, R. Scott, Meltzer, David, King Jr., Joseph, John, Leslie, Douglas, and Roberts, Mark S. Medical Care, Vol. 46, No. 4 (April, 2008), pp. 349-356.

21. "Grifols Introduces AlfaCare in Spain, the First Support Program for Patients with Alpha-1 Antitrypsin Deficiency (AATD)." Grifols corporate

website, November 15, 2018, www.grifols.com/en/view-news/-/news/ grifols-lanza-en-espana-alfacare-el-primer-programa-de-soporte-apacientes-con-deficit-de-alfa-1-antitripsina-daat. Accessed on December 1, 2020.

22. "How Much Does Therapy Cost." Thervo website. thervo.com/costs/ how-much-does-therapy-cost. Accessed on December 1, 2020.

23. "The Cost of Studying at a University in the United States." The World University Rankings website, May 27, 2020, www.timeshighereducation. com/student/advice/cost-studying-university-united-states#survey-answer. Accessed on December 1, 2020.

24. Luisetti Maurizio et al. "Italian Registry of Patients with Alpha-1 Antitrypsin Deficiency: General Data and Quality of Life Evaluation." COPD: Journal of Chronic Obstructive Pulmonary Disease, Vol. 12 (S1): 52-57 (2015): doi: 10.3109/15412555.2015.1023393

25. Royal, S. et al. "Quality-of-Life Differences Between Prophylactic and On-demand Factor Replacement Therapy in European Haemophilia Patients." Haemophilia (2002): doi: 10.3109/15412555.2015.1023393.

26. Routes, John et al. "Health-Related Quality of Life and Health Resource Utilization in Patients with Primary Immunodeficiency Disease Prior to and Following 12 Months of Immunoglobulin G Treatment." Journal of Clinical Immunology (2015). Published online April 18, 2016: doi: 10.1007/s10875-016-0279-0

27. Cirillo, Giovanni, Todisco, Vincenzo and Ricciardi, Dario and Tedeschi Giacchino. "Clinical-Neurophysiological Correlations in Chronic Inflammatory Demyelinating Polyradiculoneuropathy Patients Treated with Subcutaneous Immunoglobulin." Muscle Nerve (2019) 60(6):662-667: doi: 10.1002/mus.26669

ANNEX I: STAKEHOLDERS INCLUDED IN GRIFOLS' SROI ANALYSIS

STAKEHOLDERS	HOW THEY AFFECT OR ARE AFFECTED BY THE ACTIVITY	REASON FOR INCLUSION	HOW DATA WAS COLLECTED
DONORS	Donors play a pivotal role in the plasma industry as their plasma is critical in the production of life-saving plasma- derived medicines. Grifols compensates donors for their time and commitment to the donation process		One-on-one interviews with donors in November 2019 (Pittsburgh, PA) and January 2020 (Florida)
RESIDENTS IN THE COMMUNITIES WHERE PLASMA CENTERS ARE LOCATED	They are affected in two distinct ways: (i) they experience the reinvestment of the donor's compensations, and (ii) the activity of donating plasma promotes the health of donors, who live in the area	Key stakeholder	Interviews with the following departments: Grifols' plasma center managers in Penn Hills (PA), Pittsburgh (PA), DeLand (FL) and South Orlando (FL) and Public Affairs, which are based in Washington D.C.
CIVIL ASSOCIATIONS	They work in collaboration with plasma centers in order to enhance Grifols' involvement in the community and encourage the center's philanthropic activities		Interviews to 6 associations: 2 in Penn Hills, Pittsburgh, PA (Penn Hills Rotary Club, Barber National Institute), 2 in Pittsburgh, PA (Pittsburgh North Side Rotary Club, The Institute of Medical and Business Careers), 1 in Deland, Florida (Main Street DeLand Association) and 1 in South Orlando, Florida (South Orlando YMCA)
PUBLIC AUTHORITIES	They work on community outreach activities in neighborhoods where plasma centers are located		Interview to Gina Grone, Executive Director of North Side/Shore Chamber of Commerce, Pittsburgh
	Alpha-1 Antitrypsin Deficiency Patients treated with Grifols Alpha-1		Interview to Miriam O'Day, CEO of the Alpha 1 Foundation in the U.S. Interview was carried out using written surveys which were prepared in advance. Additionally, searched for evidence of social impact in scientific articles
PATIENTS	Patients with hemophilia or other bleeding disorders treated with Grifols' factor VIII		Interview to Michelle Rice, Chief External Affairs Officer of the National Hemophilia Foundation in the U.S. Interview was carried out using written surveys which were prepared in advance. Additionally, searched for evidence of social impact in scientific articles
	PIDD patients treated with Grifols' IG		Interview to John Boyle, Chief Executive of the Immune Deficiency Foundation in the U.S. Meeting with Fred Modell, Vicki Modell and Vanessa Tenembaum of the Jeffrey Modell Foundation. Interviews were carried out using written surveys which were prepared in advance. Additionally, searched for evidence of social impact in scientific articles
	CIDP patients treated with Grifols' IG		Interview to Lisa Butler, Executive Director GBS-CIDP Foundation International. Interview was carried out using written surveys which were prepared in advance. Additionally, searched for evidence of social impact in scientific articles
	Rest of the patients treated with Grifols' IG		Gathered Grifols' internal information on this field. Additionally, searched for evidence of social impact in scientific articles
GRIFOLS	The company is the sponsor of the project		Interviews to the following departments: Grifols' plasma center managers in Penn Hills (PA), Pittsburgh (PA), DeLand (FL) and South Orlando (FL) ; Public Affairs, Washington D.C.; Medical Affairs; Scientific and Medical Affairs

ANNEX II: INFORMATION ABOUT MAIN PLASMA-DERIVED THERAPIES

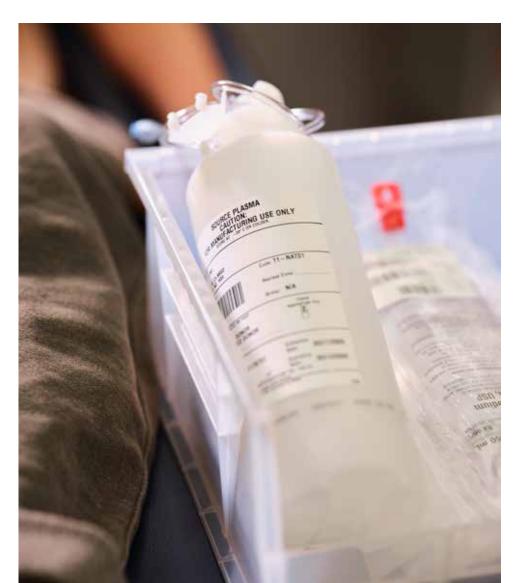
This study includes an analysis of the social impact on patients treated with the main plasma proteins manufactured by Grifols: immunoglobulins (IG), alpha-1 antitrypsin and factor VIII (FVIII). The social impact represents the benefit that patients receive as a result of these plasma-derived medicines. Its valuation is calculated using their perceived improvement in their quality of life.

Immunoglobulin therapy is used for a variety of conditions, many of which involve decreased or abolished antibody production capabilities. When the cause of this deficiency is hereditary or genetic, it is called a primary immunodeficiency disease (PIDD). In these situations, immunoglobulin infusions confer passive resistance to infection in their recipients by increasing their quantity/quality of IgG.

Immunoglobulin therapy is also used for several other conditions, including in neurological diseases and disorders, chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy, stiff person syndrome, multiple sclerosis and myasthenia gravis. It is also used to treat autoimmune disorders such as Guillain–Barré syndrome, immune thrombocytopenia and Kawasaki disease, among others. For the purposes of this study, immunoglobulin therapies have been segmented into three major categories: Primary immunodeficiency (PIDD), chronic inflammatory demyelinating polyneuropathy (CIDP), and other not PIDD nor CIPD, including secondary immunodeficiencies such as some autoimmune disorders (i.e. as immune thrombocytopenia and Kawasaki disease).

Augmentation therapy using alpha-1 antitrypsin protein in Alpha-1 Antitrypsin Deficiency: Alpha-1 Antitrypsin Deficiency (Alpha-1) is a genetic (inherited) condition which may lead to serious lung disease in adults and/or liver disease at any age. The specific therapy for the treatment of alpha-1related lung disease is augmentation therapy, also called replacement therapy. Augmentation therapy is the use of alpha-1 antitrypsin protein (AAT) from the blood plasma of healthy human donors to augment (increase) the alpha-1 levels circulating in the blood and lungs of alphas diagnosed with emphysema.

Factor VIII in hemophilia: Hemophilia is a disease that prevents blood from clotting properly after a cut or injury. In factor VIII deficiency (hemophilia A), the body doesn't make enough factor VIII, one of the substances needed to form a clot. Although the disease can't be cured, it can be managed. To prevent bleeding episodes, patients with more serious cases of hemophilia often get regular shots of the factor that their body lacks. This is known as clotting factor replacement therapy.



ANNEX III: BREAKDOWN OF OBJECTIVES AND SOURCES FOR EACH STAGE

Stage	Objective	Developments
Stage 1	Defining the project scope and identifying stakeholders	• Information provided by Grifols
Stage 2	Mapping outcomes	 Information provided by Grifols Survey information provided by Donors, Local Authorities, Civil Authorities and Patients' Associations Various scientific articles Various websites
Stage 3	Outcomes are identified and valued	 Information provided by Grifols Survey information provided by Donors, Local Authorities, Civil Authorities and Patients' Associations Various scientific articles Various websites
Stage 4	Determination of the impact	 Information provided by Grifols Survey information provided by Donors, Local Authorities, Civil Authorities and patients' Associations Various scientific articles Various websites

GRIFOLS

www.grifols.com