Social Concerns in the Pharmaceutical Supply Chain during a pandemic

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Preface

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Declaration

I declare that this document is an original work of my own authorship and that it fulfills all the requirements of the Code of Conduct and Good Practices of the Universidade de Lisboa.

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Abstract

Sustainability has taken a central role in the 21st century, shaping governments' decisions, companies' management strategies and civil society's choices. Comprising three pillars – economic, environmental and social – it affects the management of supply chains and what its stakeholders prioritize to achieve and report. While economic and environmental goals are vastly tackled in optimization models, there is still a gap when it comes to social aspects. Social concerns undertake especial importance in some industry sectors such as the pharmaceutical, from which people's health is dependent. Disruptions like the COVID-19 pandemic highlighted the vulnerabilities of this sectors' supply chain and its consequences to healthcare systems.

This dissertation analyses the social indicators that optimization models account for and the social performance of six leading pharma companies in 2019. After the 2020 COVID-19 outbreak, a review is performed on the challenges it posed to global supply chains and the pharma supply chain, showing that several actions need to be taken to turn them more agile and resilient. This work also analyses the social challenges that emerged with this pandemic and selects a set of key priority aspects, systematized by the GRI Standards, to be included in the supply chain's stakeholder's annual sustainability reports, suggesting four new reporting disclosures. Quantitative indicators are also included, for these new disclosures, to help decision making on supply chain social performance improvement, namely optimization models. The concept of social resilience is, then, defined with four pillars: Access, Stability, Support and Quality, considered necessary to guarantee the social pillar of sustainability.

The new social concerns brought by the COVID-19 pandemic and the recommendations made to enhance the resilience of supply chain are, finally, compiled into a framework to allow pharma companies improve their supply chain social performance, in times of crisis.

Keywords: sustainability, social resilience, pharmaceutical supply chain, COVID-19, pandemic, GRI Standards, framework, indicators

Resumo

A sustentabilidade tem assumido um papel central no século XXI, moldando decisões de governos, estratégias de gestão de empresas e as escolhas da sociedade civil. Abrangendo três pilares - económico, ambiental e social - afeta a gestão das cadeias de abastecimento e o que os seus intervenientes priorizam para alcançar e relatar. Embora os objetivos económicos e ambientais sejam amplamente abordados nos modelos de otimização, existe ainda uma lacuna no que diz respeito aos aspetos sociais. As preocupações sociais assumem especial importância em certos setores industriais, tais como o farmacêutico, do qual a saúde depende. Disrupções como a pandemia da COVID-19 evidenciaram as vulnerabilidades da cadeia de abastecimento deste setor e as suas consequências para os sistemas de saúde.

Esta dissertação analisa os indicadores sociais que os modelos de otimização contabilizam e o desempenho social de seis empresas farmacêuticas líderes em 2019. Após o surto da COVID-19 em 2020, é feita uma revisão sobre os desafios que colocou às cadeias de abastecimento globais e, em particular, à cadeia de abastecimento farmacêutica, mostrando que é ainda necessário tomar medidas para as tornar mais ágeis e resilientes. Este trabalho analisa também os desafios sociais que surgiram com esta pandemia e seleciona um conjunto de aspetos-chave prioritários, sistematizados pelas normas GRI, a serem incluídos nos relatórios anuais de sustentabilidade dos intervenientes da cadeia de abastecimento, sugerindo quatro novos indicadores. Estes indicadores aparecem com sugestões quantitativas a incluir em ferramentas de tomada de decisão, nomeadamente modelos de otimização, permitindo objetivar a melhoraria do desempenho social da cadeia de abastecimento. O conceito de resiliência social é, então, definido com quatro pilares: Acesso, Estabilidade, Apoio e Qualidade, considerados necessários para garantir o pilar social da sustentabilidade.

As novas preocupações sociais trazidas pela pandemia COVID-19 e as recomendações feitas para melhorar a resiliência da cadeia de abastecimento são, por fim, compiladas num *framework* que permite às empresas farmacêuticas melhorarem o seu desempenho social ao longo da cadeia de abastecimento, em períodos de crise.

Palavras-chave: sustentabilidade, resiliência social, cadeia de abastecimento farmacêutica, COVID-19, pandemia, GRI Standards, framework, indicadores

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
API	Active Pharmaceutical Ingredient
CEO	Chief Executive Officer
CIP	Cleaning-in-Place
CO_2	Cardon dioxide
COVID-19	Corona Virus Disease
DGS	Direção-Geral de Saúde
DNA	Deoxyribonucleic acid
EMA	European Medicines Agency
EFPIA	European Federation of Pharmaceutical Industries and Associations
EU	European Union
FCUL	Faculdade de Ciências da Universidade de Lisboa
FDA	Food and Drug Administration
FFUL	Faculdade de Farmácia da Universidade de Lisboa
FMUL/IMM	Faculdade de Medicina da Universidade de Lisboa/Instituto de Medicina Molecular
GAVI	Global Alliance for Vaccines and Immunization
GDP	Gross Domestic Product
GRI	Global Reporting Initiative
GSK	GlaxoSmithKline
HCP	Healthcare Practitioner
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IQVIA	Quintiles and IMS Health, Inc.
ISA	Instituto Superior de Agronomia
IST	Instituto Superior Técnico
KPI	Key Performance Indicator
LGBT+	Lesbian, Gay, Bisexual, Transgender People
NGO	Non-Governmental Organization
NPD	New Product Development
R&D	Research and Development
RNA	Ribonucleic Acid
RTP	Rádio Televisão Portuguesa
SC	Supply Chain
SCM	Supply Chain Management
SIP	Sterilization-in-Place
SMS	Short Message Service
SNS	Serviço Nacional de Saúde
TBL	Triple Bottom Line
TTL	Triple Top Line

UK	United Kingdom
UN	United Nations
USA	United States of America
VLP	Virus Like Particle
WHO	World Health Organization
WWII	Second World War

1. Introduction

1.1. Context and objectives

Five years ago, in 2015, the United Nations established 17 goals to improve the sustainability of our societies, aimed to be achieved by 2030 – the Sustainable Development Goals of the 2030 Agenda for Sustainable Development (UN, 2015). Goal 3 aims to "ensure healthy lives and promote well-being for all at all ages" and Goal 8 pretends to "promote inclusive and sustainable economic growth, full and productive employment and decent work for all" which set the starting point for this work.

Supply chains ensure that all we need comes to us, being responsible for putting the world "running", as popularly said. Therefore, the way in which supply chains operate has strong impact in our economies, the environment and societies. In 1987, the UN Commission on Environment and Development published the first international statement that world economies development should be sustainable, presenting the concept of sustainability development as the "development that meets the needs of the present without compromising the ability of future generations to meet their own needs" (Brundtland, 1987). Three pillars have been set to support the sustainability concept: the economic, the environmental and the social. While the first two have undoubtedly been tackled in political or management daily decisions, the social one is still dependent on the political ambience of each country or the importance companies give to it. In what concerns supply chain management, social aspects are still addressed by only a few authors, thus, still being a research gap (Barbosa-Póvoa *et al.*, 2018).

Crisis situations cause disruptions in the sustainability agenda, leading governments and supply chain players to prioritize their actions, risking to leave several sustainability aspects to a secondary plan. The COVID-19 pandemic is certainly one of them having had unprecedent impacts due to its consequent lockdowns and movement restrictions. Being a health crisis, the pharmaceutical supply chain plays a decisive role in the response of this pandemic, trying to provide suitable treatments to the new disease and above all, a means to immunization – vaccines – while it is also affected.

As such, this work seeks to study the performance of this sector in this new context, focusing on the social problematics of its supply chain and alert for a set of concerns that should be tackled by its stakeholders in future crisis situations like this pandemic.

Overall, this dissertation tries to answer these questions:

- How do global supply chains account for the social aspects in their optimization strategies?
- What are the new social challenges COVID-19 brought to the pharmaceutical supply chain?
- How can the global supply chains, especially the pharmaceutical one, become more resilient from the social point of view?

1.2. Dissertation methodology

As stated, this dissertation aims to study how pharmaceutical supply chain decision making tools, such as optimization models, quantify the social pillar of sustainability, and to understand the importance of social indicators used. COVID-19 reinforced the significance of this analysis, introducing new social challenges faced by the pharma sector, after the pandemic outbreak. The study led to the proposal of new ways to assess the pharma supply chain's social performance, as well as suggesting new indicators to help decision makers improve its social resilience.

Thus, the followed methodology was this:

1. Review of the social indicators used in supply chain quantitative decision-making tools, namely optimization models aiming to evaluate how these models quantify the social dimension in supply chain management. Forty papers were analysed and the social indicators were grouped in four areas: employment, labour conditions, health and safety, and community development.
2. In order to better understand how the pharmaceutical industry is organized and which challenges are faced by its supply chain, a brief characterization of the sector is done, followed by the analysis of the social performance of the six top ranked companies according to the *Dow Jones Sustainability Index*, based on their annual sustainability reports. The identified social indicators were grouped by the same four areas of the previous review and associated to the Global Reporting Initiative (GRI) standards disclosures, a guidance set of norms to help companies better report on their activity.
3. A few months after the outbreak of the COVID-19 pandemic, global supply chain's challenges were again assessed and a new characterization of the pharmaceutical sector was made, assessing its resilience problematics, with special attention for its social concerns. The review was based on consultancy companies' studies, papers published during the first semester of 2020 and current press articles published in the last months of 2020. The sectors' role in the pandemic was also tackled with emphasis on the vaccine development and its supply challenges.
4. Following the new assessment of the pharmaceutical supply chain social challenges, a set of GRI standards disclosures is selected to be prioritized in sustainability annual reports, related to 2020 and future crisis periods. Four additional disclosures are suggested to report on what GRI does not yet include. Quantitative indicators are also identified, for these new disclosures, that can be included in decision making tools aimed to improve the supply chain social performance.
5. Finally, the concept of social resilience was proposed based on four pillars (access, stability, support and quality), according to the performed reviews, leading to the design of a framework that aims to provide guidance to the pharma supply chain stakeholders on how they can improve their social performance and become more resilient.

Finally, the conclusions obtained from every stage of the work are summarised, followed by future research steps.

1.3. Dissertation outline

This thesis is composed of seven chapters, starting with Chapter 1 that introduces the topic, sets the objectives of this work, provides an overview of the followed methodology and the documents' structure.

Then the following chapters are organized as this:

- Chapter 2 presents the concepts of supply chain, supply chain management and sustainability, emphasising on the social pillar of sustainability, and also includes the review on the social indicators used in supply chain optimization models.
- Chapter 3 highlights the pharmaceutical industry importance, presenting the typical pharma supply chain and the challenges it faced before the COVID-19 outbreak. The social performance of leader pharma companies overview is presented here.
- Chapter 4 contains an analysis of the effects of disruptions in global supply chains, focusing on the COVID-19 pandemic repercussions, ending with recommendations on what companies and their chains can do to be better prepared, as well as how they can respond and recover.
- Chapter 5 shows how the pharma industry has been affected by the COVID-19 pandemic and what it has already achieved regarding the new vaccines' development and supply process.

6. Chapter 6 reviews the social challenges faced by the pharmaceutical supply chain, during the outbreak of the COVID-19 pandemic, and contains the GRI standards disclosures selection, suggested to be reported in the 2020 companies' sustainability reports, including four additional proposed disclosures and their respective quantitative indicators to explore in decision making tools. This chapter also presents the concept of social resilience and the framework to help pharma supply chain stakeholders improve and ensure their good social performance.

Finally, Chapter 7 summarises the conclusions of this work, providing future research suggestions.

2. Social concerns in supply chain optimization

In this chapter, the concepts of supply chain, supply chain management and sustainability are presented, then emphasising on the social pillar of sustainability. A review on the social indicators used in supply chain optimization models is presented here aiming to evaluate how these models quantify the social dimension in supply chain management.

2.1. Supply chain

Supply chain (SC), from a non-expert point of view, is usually associated with the distribution of goods and logistics. However, there are many aspects to account for when a definition is proposed. Supply chain as a concept was firstly purposed by Oliver & Webber (1982) more than thirty years ago, and it has been given several definitions and considerations since then. In its classical form, it can be defined as the network of organizations that are involved, through upstream and downstream linkages, in the different processes and activities that produce value in the form of products and services delivered to the ultimate consumer (Christopher 2011). Lambert *et al.* (1998) established the concept of supply chain as the alignment of firms that bring products or services to market.

According to Mentzer *et al.*, (2001) there are three degrees of supply chain complexity: a “direct supply chain”, and “extended supply chain” and an “ultimate supply chain”. A central organization together with its suppliers and customers comprehends a direct SC while suppliers’ suppliers and customers’ customers are included in the extended SC. The ultimate supply includes all organizations that are involved in all flows of products, services, finance and information from the ultimate supplier to the ultimate customer, as well as intermediaries such as market research firms, financial and logistics services providers. This approach is closer to the nowadays notion of supply chain, wider and as global as possible, considering the more stakeholders as possible.

Chen and Paulraj (2004) stated that a typical supply chain is a network of materials, services and information processing links with the characteristics of supply, transformation and demand, between suppliers and customers, bringing also information into consideration.

It is also viewed as a combination of processes aimed at fulfilling demand and customers’ requests, including all network entities such as suppliers, manufacturers, transporters, warehouses, retailers and customers themselves, taking customers satisfaction at a minimum cost as its main purpose (Simchi-Levi *et al.,* 2007), adding the economic aspect as purpose and an objective.

The products, services and information can circulate in a forward flow in the supply chain, from the first suppliers to the final customer or, in the opposite, a reverse flow. Goods can flow back in the supply chain for different reasons such as service, repair, remanufacturing, recycling or disposal, giving the reverse supply chain an important role in customer satisfaction (e.g. repair of a manufacturing flaw), environmental protection (e.g. collection and treatment of dangerous chemicals) and public safety (e.g. pharmaceutical products market withdrawal).

2.2. Supply chain management

The wider concepts of supply chain involving networks of multiple businesses and relationships are being preferred in the modern business management for a vast range of reasons. Individual businesses cannot compete and thrive as independent entities but rather as active members (Lambert & Cooper, 2000), due to the ever-changing environment and their vulnerability to risks at all levels. This ever-changing landscape can be caused by the huge geographical area in which many supply chains extend (Butner, 2010) or are due to the product customisation, price and level of service, more and more demanding customers, along with the increasing product complexity and offer. Innovation and technological development have been accelerating introduction of new products to the market and, consequently, customers desire to update and replace their products, especially gadgets. External environment is also very dynamic because of several economic and natural factors such as energy prices, raw materials availability, currency exchange rates and extreme weather conditions, natural catastrophes and even health crisis situations.

To survive to such a complex environment, companies must be agile, flexible and prepared to rapidly response to all these challenges. The need to deepen SC understanding, especially how decisions should be made, motivated the development of supply chain management (SCM). Oliver and Webber (1982) defined SCM as "the process of planning, implementing and controlling the operations of the supply chain with the purpose to satisfy customer requirements as efficiently as possible. SCM spans all movement and storage of raw materials, work-in-progress inventory and finished goods from point of origin to point of consumption." Mentzer *et al.* (2001) sets SCM as the systemic, strategic coordination of the traditional business functions and the tactics across these business functions within a particular company and across business within the SC, for the purposes of improving the long-term performance of the individual companies and the SC as a whole. More recently, SCM has been defining a set of approaches utilized to efficiently integrate suppliers, manufacturers, warehouses, and stores, so that merchandise is produced and distributed at the right quantity, to the right locations, and at the right time, to minimize system wide costs while satisfying service level requirements (Simchi-Levi *et al.*, 2007).

Christopher (2011) highlights the cooperation and relationships with suppliers and customers in order to deliver superior value at less cost to the supply chain, focusing supply chain upon the management of relationships in order to achieve a more profitable outcome for all parties in the chain. In some occasions, self-interest of one party may be subsumed for the benefit of the chain as a whole.

SCM includes every decision made about the products or services delivered to customers. There are three levels of decision in SCM: strategic, tactic and operational. SC strategy begins with a long-term decision-making, for several years out, the strategic level, which may be accomplished at an executive management level. Issues such as facilities locations, innovation and long-term improvements are addressed at this level. Strategic SC planning comprehends an holistic analysis of resources acquisition, disinvestment and reconfiguration in a planning horizon of, usually, 1 to 5 years (Barbosa-Póvoa *et al.*, 2018). When it comes to resources allocation, manufacturing, distribution and inventory decisions, a next level of decision-making is required. At the tactical level, the focus is on processes, production schedules, transportation, warehousing and inventory management to meet demand. It is still an holistic

analysis but in a shorter planning cycle, 1 to 12 months. On a daily or weekly basis, planning decisions are made at the operational level, in terms of scheduling, inventory and resource allocation monitoring. At this level, a myopic analysis is performed enabling the control on real time how the SC is running.

Optimization of a supply chain can be a complex task since it has multiple aspects to account and can induce changes in an industry management, suppliers, employees, the environment and even the final consumers. Improving economic performance *per si* can cause harmful consequences to the environment such as pollution or resources exhaustion and reduce the quality of life of a population, since it might, for instance, only take into consideration increasing of production (which may require more raw material and industrial facilities/operations) or cost reduction (decrease of employees, innovation, environmental protection or even safety concerns).

2.3. Sustainability

Population growth, pollution and lack of resources are conducting our modern society to an unsustainable situation. Sustainable development was defined by Brundtland (1987) as the "development that meets the needs of the present without compromising the ability of future generations to meet their own needs". Due to the vagueness that surrounds this definition, the term sustainability has been interpreted in a variety of ways, highly associated to environmental issues. However, as time goes on, a triple line approach is being adopted, valuing not only environmental and economic aspects but also social aspects (Elkington, 2004). In business context, the importance of sustainability has been debated and defined in many ways, of which integrating economic, social and environmental systems has been considered essential for the creation of resilient organizations, since they are better prepared to respond to external and internal shocks. Nowadays, organizations interact globally and deal with a large set or resources, life cycle implications of their decisions have been given more importance and, thus, management of supply chains is receiving increased attention (Ahi & Searcy, 2013).

Sustainability adds complexity to the supply chain that, alongside its subjectivity and lack of consensual measures, has constrained research in the field of sustainable supply chain management (Burgess *et al.*, 2006). Sustainable supply chain modelling is still a research gap with scarcity of models that can simultaneously account for economic, environmental, and social sustainability aspects (Seuring, 2013). The existing studies use a Triple Bottom Line (TBL) approach firstly proposed by Elkington (1998), which accounts for People, Planet and Profit, also referred as 3P. TBL integrates sustainability into the business agenda balancing economic objectives with social and environmental aspects in the existing SCM models, introducing new concerns to the optimization of SC. A similar but different approach has also been proposed, the Triple Top Line (TTL), in which People, Planet and Profit are the three pillars assessed, but on the product level (Mcdonough & Braungart, 2002). TTL follows the laws of nature to give industry the tools to develop systems that safely generate prosperity, for example, having material that can become food for the soil or flow back into the industry forever. Social and ecological value and quality are incorporated in products, facilities and processes since the beginning. TBL intends to minimize impacts of industry slowing down ecological destruction or social negative impacts using the 3P, while TTL designs a new industry itself considering 3P from the start aiming to achieve, in a perfect

scenario, in which products and industrial processes designed so they do not need regulations or constraints due to the only positive effects they bring (Mcdonough & Braungart, 2002).

Summing up, sustainability evaluation in SCM considers three pillars: the economic pillar, the environmental pillar and the social pillar. This work focuses on the social pillar since it has been referred as a research gap, trying to analyse how optimization models assess and quantify social concerns.

2.4. Social pillar

Hutchins & Sutherland (2008) investigated social concerns of sustainability in supply chain and proposed a first study on the exploration of measures and how to incorporate them into the decision-making process in a company. Social assessment is one of the most significant research gaps in sustainable SCM modelling (Barbosa-Póvoa *et al.*, 2018; Brandenburg *et al.*, 2014; Seuring & Müller, 2008). In the past, only economic and environmental concerns would be covered in sustainability approaches while social issues (e.g. human rights) were left for the concept of Social Responsibility. Now, these two notions are being integrated, even if still in a not fully consensual way (Pishvaee *et al.*, 2014). Social Responsibility was defined by the Commission of European Communities (2001) as a "concept whereby companies integrate social and environmental concerns in their business operations and in their interaction with their stakeholders on a voluntary basis" and by the World Business Council for Sustainable Development (2000) as "the commitment of business to contribute to sustainable economic development, working with employees, their families, the local community and society at large to improve their quality of life", being the two most used definitions (Dahlsrud, 2008).

The Global Reporting Initiative (GRI) describes the social dimension of sustainability as what concerns "an organization's impacts on the social systems within which it operates". These Sustainable Reporting Guidelines have been used by some authors to develop measures to evaluate social aspects, however, the measures are described as either being subjective and qualitative or based on past occurrences. In what concerns the levels of decision in SCM in which the social pillar of sustainability is given relevance, few authors take it into consideration at the strategic level (Mota *et al.*, 2015). Čuček *et al.*, (2012), in their review of footprint analysis for monitoring impacts on sustainability, list the following social footprints: human rights, corruption, poverty, online social presence, job, work environmental, food to energy and health, a footprint being a "quantitative measurement describing the appropriation of natural resources by humans that describes how human activities can impose different types of burdens and impacts on global sustainability" (Hoekstra, 2008). Houdin (2012) indicates human rights, health and security, governance, working conditions, cultural heritage as the most used indicators. Barbosa-Póvoa *et al.* (2018) identify, in their review, job creation, poverty, safety, number of working hours, discrimination, health and satisfaction as the most used indicators. Some of these indicators, however, are difficult to assess, such as for instance human rights or corruption, due to inherent value judgements surrounding the terms of violation and corruption as well as the lack of readily available evidence. (Stamford & Azapagic, 2011). As Yue *et al.* (2014) have noticed, the evaluation methodology of social concerns is still immature, and the formulation of indicators is still under debate. One indicator that presents consensus as being one of the most important in the social dimension is employment, so it is the first indicator addressed studied in this work.

2.4.1. Optimization and the Social Pillar

As decision problems in supply chains are complex for achieving the benefit of the chain as a whole, fundamental optimization models are crucial tools to support sustainable supply chain decisions (Barbosa-Póvoa *et al.*, 2018). Therefore, it is important to understand how different SC optimization models assess the social dimension of sustainability, specifically which indicators are used and their quantification parameters. The literature materials collection was performed in the *Web of Science* database in December 2019. Only papers in English were chosen, with no date range restriction applied. Table 2.1. summarises the keywords selected for the search and the results obtained.

Table 2.1. – Search results on social supply chain sustainability in *Web of Science* database, in December 2019.

SC Keywords		Social Keywords	Papers obtained
supply chain (sustainability OR sustainable) social	**AND**	job OR employment OR unemployment OR poverty	89
		health OR injury OR illness OR safety OR fatality OR death	137
		salary OR "working hours" OR human rights OR discrimination OR "labor conditions"	29
		solidarity OR humanitarian	13
		TOTAL[1]	**243**

[1]The total number of papers obtained does not match the sum of the number of papers obtained for each social keywords group, since there are some papers that address more than one social indicator.

These publications were subject to a content analysis, being excluded if they did not satisfy all the following criteria:

1. The paper is written in English and was published in a peer-reviewed journal;
2. The paper has a quantitative approach, developing a supply chain optimization model;
3. The paper is not a review.

A considerable portion of the retrieved documents was excluded because it only tackled social dimension issues qualitatively not proposing quantitative indicators and quantifiers for social aspects. The material collection performed was not exhaustive as other databases were not included. Thus, it is possible that some relevant papers were not considered. A small number of additional papers, which were not retrieved in the *Web of Science* collection, was also considered. A final set of 41 papers was analysed (a detailed table of these papers and the information retrieved can be consulted in Annex A).

Based on the content analysis of the performed literature review on the different ways used to quantify social aspects in SCM, indicators were studied in the following groups:

- Employment
- Labour Conditions
- Health and Safety
- Community Development

This work also identifies the industry sector and management level decision of the models analysed.

2.4.2. Employment

Employment is unquestionably a driving force in social welfare of a family, community or even a country. Companies are great contributors for job creation in a certain region since they require employees to install and operate their facilities as well as to perform several services such as transportation, therefore playing a crucial role in local economies. Choosing factories location properly may promote local development and generate work sources in regions with a higher unemployment rate and encourage industrial activity in places with a lower economically active population or a lower GDP, eventually alleviating poverty (Meyer *et al.*, 2019). Thus, SC models can have a great impact on the social welfare if employment parameters are included.

Several optimization models analysed in this work propose a mono-criteria objective function applying employment as their social criteria, usually the third function of the model, while economic and environmental are the first and second ones. Maximization of new job opportunities created is the most common option (Habib *et al.*, 2019; Heidari *et al.*, 2019; Jafari *et al.*, 2017; Martínez-Guido *et al.,* 2016; Miret *et al.*, 2016; Mota *et al.*, 2015; Pedram *et al.,* 2017; You *et al.*, 2012) while some authors choose to, instead, minimize social impacts related to employment due to alterations or reconfiguration of their supply chain such as employee dismissals when the delocalization/closing of facilities is suggested by the model (Günther *et al.*, 2015; Kannegiesser *et al.*, 2015).

For this maximization, the number of jobs must be estimated, and it can be done through different ways. This number can represent the persons that work directly on the plants (Direct Jobs), but also take into account jobs created or supported by all the firms impacted, namely subcontractors (Indirect Jobs) and even new employees in the local community due to their (and their families) consumption in the local economy (Induced Jobs) (Chazara *et al.*, 2017; How & Lam, 2018; Miret *et al.*, 2016). Jobs can also be divided in fixed jobs (essential staff to factories, distribution centres and warehouses and managers) and variable jobs (staff required for inspections or specific seasonal tasks, as well as staff contracted depending on the production volume and demand) (Darbari *et al.*, 2019; Sahebjamnia *et al.*, 2018).

Jobs have been measured as equivalent jobs, for example as a full-time equivalent for one year (You *et al.*, 2012), by facility opened (Pedram *et al.*, 2017), in terms of wages (Gao *et al.,* 2019) or hours of work (Cambero & Sowlati, 2016). Kristianto & Zhu (2017) estimate job creation per million gallon of product after the optimization of their SC network, although they do not include a social objective function. One study created its own metric *employee-period* as a work input unit, to work with the social objective (Arampantzi & Minis, 2017). In a similar way, Jiang *et al.*, (2018) create a social welfare coefficient that considers job creation and regional GDP per capita. Job creation is then measured in terms of opportunities created by a facility (depending on its capacity) and affected by a weight factor based on the unemployment rate of each location and then summed to a regional score based on it GDP. Barbosa-Póvoa *et al.* (2018) develop a social indicator in which the number of jobs created is quantified for the different work force needs (opening the facility, operations and transportation) and is also affected by a relative regional factor based on GDP statistics, that assumes value 1 for the EU GDP per capita in ppp (purchasing power parity). Social objective functions that consider GDP information

end up promoting equality in supply chains, since they aim to reduce discrepancies in regions wealth and give job opportunities to those who live in less developed areas.

As for the minimization of job redundancies, Günther *et al.* (2015) calculate the number of dismissals caused by production processes over all periods and locations, based on the process quantities and the respective labour requirements. Dismissals result from the delocalization of process capacity, being perceived as a negative social impact since it causes instability in employees' life and their families. Avoiding dismissals turns out to be the social objective of this model. The same authors propose another model that seeks to minimize the time period until the reaching of sustainability in which they aim to reach a steady state in job redundancies, limiting to 5% in all locations (Kannegiesser *et al.*, 2015).

Multi-criteria social objective functions are also a common practise among SC modelling, considering other criteria such as safety and health (tackled in the following topics of this work) besides job creation (Arampantzi & Minis, 2017; Charmondusit *et al.*, 2014; Darbari *et al.*, 2019; Devika *et al.*, 2014; How & Lam, 2018; Pishvaee *et al.*, 2014; Sahebjamnia *et al.*, 2018; Tsao *et al.*, 2018).

2.4.3. Labour Conditions

Besides job creation opportunities, having a good working ambience and conditions is also a social well-being important factor. Assessing employee satisfaction can include a variety of aspects such as having an adequate number of working hours, stability, healthy environment, not facing discrimination or harmful behaviour and, of course, having a reasonable salary. This topic considers issues that influence labour quality and conditions of the employees, and ultimately human rights, including not only what immediately makes employees satisfied but also education and training, but excluding health and security which are tackled in the next topic.

Not many SC models include labour conditions terms in their objective functions and when so, they are usually combined with job creation or employment criteria. Hahn & Brandenburg (2018) model, was the only one found that uses a social mono-criteria objective function focused on this type of indicators, minimizing overworking hours, which of course are not beneficial in hazardous working environments such as the chemical process industries.

Hiring local employees seems to create jobs and stimulate local economies. However, its benefit can go much further than that, as Boukherroub *et al.* (2015) state when they include proximity of employees to production sites in their multi-criteria social objective function. Closeness to work location promotes employee well-being since it reduces time spent in either public or private transport. Their model minimizes the total travelled distance multiplied by the total flow of employees.

Job stability is another major employee concern, tackled by Boukherroub *et al.* (2015) social objective function which favours the transfer of employees between production sites instead of dismissing or laying-off them. Lay-off can happen if one facility does not need to produce in a certain period due to lack of demand, not contemplating salary payment in that period. Employee transfer might be preferred by both workers and the company, since they avoid the loss of their jobs and reduces hiring and lay-off burdens, respectively. Moreover, it can enhance the trustworthy relationship between the company and the employees preventing an instability feeling.

Idle labour, *i.e.*, significant work periods when the employee is not producing or being useful leads to lower job satisfaction, according to (Arampantzi & Minis, 2017) whose model tries to minimize.

Finally, education and training can also be decisive job condition improvers because when training is offered, employees can perform tasks with better knowledge and confidence. It stimulates the feeling that employees are important assets to the company since it is investing on them. Darbari *et al.* (2019) consider training hours for skilled staff in their multi-criteria social objective function and (Kravanja & Čuček (2013) include education in their proposed social index.Issues such as discrimination and human rights are not evidently assessed in the analysed SC models.

2.4.4. Health and Safety

Working in a secure environment is a fundamental contributor for the well-being of a company's employees that has been the second most assessed indicator in SC models, after employment. Here, a distinction is made between safety and health. Safety relates to accidents and their consequences at work, thus focusing on process factors (inventory, temperature, pressure, equipment safety); if these accidents are avoided and do not happen, one can consider that the employee works in safe environment. Health (or the lack of) appears as a long-term consequence of the work an employee performs or the conditions in which he or she is exposed.

Minimization of injuries or accidents is the most common used strategy to assess safety issues in SC modelling. Bouchery *et al.*, (2012) propose a mono-criteria objective function while other authors choose to combine it with more information such as the severity of the injuries which can be categorized according to the days absent from work (Alsaffar *et al.*, 2016; Chen *et al.*, 2014; Kamyabniya & Fakhrzad, 2016). In Chen and Andresen model, injuries or illnesses that are less severe are given a low severity level, while the highest rank can even consider work-related fatalities and the severity is represented by an exponential function. The exponential function can show that the higher the class, the more unfavourable an incidence. In this way, the model can guide the decision maker to employ production methods that will decrease the danger of severe injuries or illnesses. On the other hand, minor incidences become acceptable to a certain degree, which cannot be preventable (cuts).

Multi-criteria social objective functions consider job creation alongside safety issues. Charmondusit *et al.* (2014) try to minimize the number of accidents per million hours work, per year and Arampantzi & Minis (2017) implement the same methodology but focusing on injuries or fatalities caused by transport accidents. Devika *et al.* (2014) also quantifies accidents and work damages distinguishing the ones that occur during the installation and construction of facilities from those that occur during operation (manufacturing/handling of products). Pishvaee *et al.* (2014), Sahebjamnia *et al.* (2018) and Tsao *et al.* (2018) add the number of lost days of work to other indicators to assess social impacts of their decisions.

Health is usually associated to SC chain models with chemical processes, in which the toxicity potential (by ingestion, inhalation and dermal exposure) is assessed (How & Lam, 2018). These authors develop an Inherent Safety Index which they aim to maximize considering not only process safety issues (accidents) but the chemical inherent safety related to heat of reactions, chemical interaction, flammability, explosiveness, toxic exposure and corrosiveness. Health is also used in multi-criteria

objective functions, alongside job creation; Tsao *et al.* (2018) consider the amount of hazardous by-products associated with the selection of production technology and materials in their social benefits function as well as the number of workdays lost cause by workplace hazards. Finally, Hong *et al.*, (2019) model social dimension by the medical costs incurred to remedy the negative impacts of particulate emissions of a gas to the atmosphere, devising a total medical cost measurement. These authors develop a model that minimizes the undesirable social medical costs.

2.4.5. Community Development

Creating jobs with good conditions, already tackled in this work, is not the only contributor to the development of local communities, choosing and supporting local suppliers also stimulates local economies (Arampantzi & Minis, 2017). Social responsibility is becoming more relevant leading some companies to dedicate time and resources to the development of projects that benefit society and improve life quality. Charmondusit *et al.* (2014) count the number of projects they support and the respective investment in their social performance. Darbari *et al.* (2019) include not only the number of hours their employees dedicate to community service, but also product donations to non-governmental organizations in their social impact multi-criteria objective function.

2.4.6. Social pillar assessment overview

A quantification of the number of papers reviewed that use and develop social indicators in their SC models was performed and is presented in Table 1 of Annex A and illustrated in Figure 1 and Figure 2.

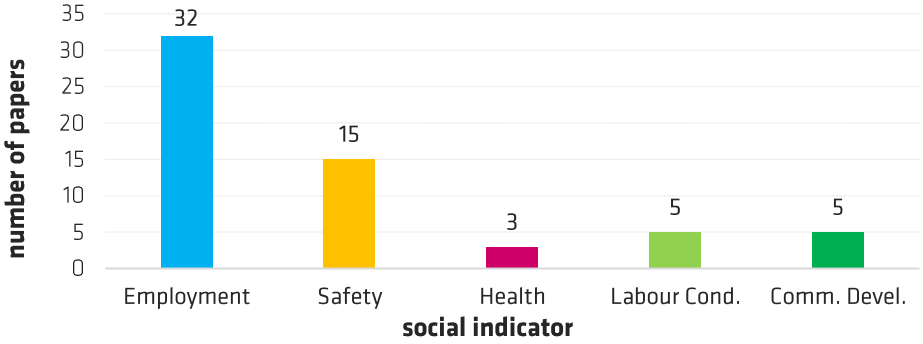

Figure 2.1. – Social indicator usage frequency in reviewed SCM optimization models.

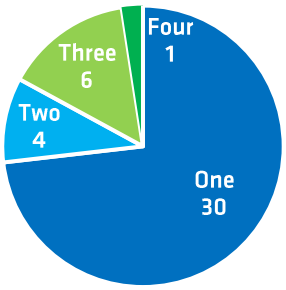

Figure 2.2. – Number of indicators used per number of papers reviewed.

In Annex A, Table 1, it is also registered the industry sector to which each model is applied. Data from case studies is usually used to validate the proposed models. The analysed models relate to a variety of different types of industries, being the bioenergy sector the most tackled (11 out of 42). Six of the studied models were generic models aiming to be applied to any industry type.

2.5. Chapter conclusions

This chapter starts with a small review of the definitions of supply chain and supply chain management, from which it can be concluded that industry started to worry about these concepts by the end of the 20th century. Supply chain has been defined with many different scopes and stakeholders, having been enlarging its coverage in business context, from the raw-material supplier to the final consumer, passing through the whole transformation and production process and logistics. Optimizing an industry supply chain as a whole and not just focusing on individual facilities or on the transportation aspects, has brought benefits and profit to companies. Inclusion of sustainability factors is becoming a priority in many supply chain optimization models, giving importance not only to environmental issues but also to the social dimension. However, social benefits and welfare were considered, for some time, as just a direct consequence of ecological or environmental improvement until, by the end of the first decade of our century, aspects as employment, labour conditions and safety started to be seen as a separate social pillar, having been given a specific objective function.

The most found indicator in SC optimization models was job creation, an indicator which creates income to communities and wealth to regions. GDP, population density and unemployment rates are employment related aspects usually taken into consideration by the analysed models. Safety and health form the second group of indicators evaluated in SC models, followed by labour conditions motivated by human rights concerns, which relate to the quality of the jobs that models aim to create. Consequently, industries and their associated supply chains can have a big impact in societies, if they are managed towards valorisation of people and maximization of their welfare, contributing to community development, the last studied aspect.

Some of the SC models reviewed are generic models aiming to be applied to any industry type, developing the most complete social objective functions found, assessing more than one of the referred indicators. There is a significant number of models designed for a specific sector, the bioenergy industry (biofuel or biomass production), presumably due to the environmental benefits of this cleaner energy and the social impact concerns of the installation of refineries, as well as the rural development where biomass is collected. Job creation was the most used social indicator in these industries as well as in the textile sector. Hydrogen related industries SC models put their focus on safety which can be easily imputed to the instability and danger associated with this gas. Summing up, SC models which are not generic tend to adjust their social objective functions to the most relevant aspect associated to their type of activities, not tackling the social dimension in its full globality and potential.

During the searching process, some articles on supplier evaluation were found, mentioning several social aspects, especially health indicators when it comes to food industry: use of genetic modified products, pesticides. However, only models that optimize the whole supply chain were analysed.

Given the wide scope of the optimization, causing reallocation of facilities, warehouses and inducing deep changes in transportation, staff, among other aspects, on the long-term, almost every studied model works at the strategic level, requiring executive management decisions.

3. The pharmaceutical sector characterization

This chapter starts with a presentation of the pharmaceutical industry, highlighting its importance. The typical pharma supply chain is analysed, as well as the challenges it faces and driving forces for future perspectives. Sustainability, particularly its social pillar, is tackled in this chapter with an overview of the social performance of leader pharma companies.

3.1. What is the pharmaceutical sector?

The pharmaceutical sector comprises several activities related to drugs used for medication (medicines) or vaccines, such as research, development and production. The pharma industry is a very *sui generis* sector because of its unusual characteristics and impact (Taylor, 2016). Although heavily based on the chemical industry, its products are classified as specialty chemicals (in contrast with bulk or fine chemicals), thus, adding complexity to the pharma industry (Marques *et al.*, 2020). These products can be highly differentiated and are usually purchased based on their function or perceived value, rather than price or chemical composition and tend to be produced in small quantities with very large margins (Smith, 2005). Due to the sophistication of pharmaceuticals and the need to find treatments to new diseases (or old ones which haven't efficient solutions yet), the pharma industry needs to invest considerably in research, which leads to intellectual property concerns. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), the cost of researching and developing a new chemical or biological entity was estimated in €1,926 million in 2014 and by the time it reaches the market, an average of 12 to 13 years have passed since the first synthesis of the new active substance (10 years of research and development: pre-clinical development + clinical trials and 2 to 3 years of administrative procedures). Furthermore, on average, one to two of 10 000 substances synthesised in laboratories successfully passes all stages of development required until it reaches the market.

3.1.1. Importance and impact

Medicines are special commodities which means that "access and affordability directly influences the lives of patients" (Ding, 2018). Along with vaccines, medicines have a direct influence on the populations' quality of life and also contribute to significant cost reductions in healthcare cost of a country, since they reduce expensive surgeries or long-term care in hospitals (Pfizer, 2018). As such, the products that result from this sector's activity are of great responsibility and impact.

EFPIA (2018) states that European citizens saw their life expectancy increased by 30 years in a century as a result of the development of pharmaceuticals. 30 years is more than a third of an 80-year-old person's life. For instance, major advancements allowed several reductions in mortality from HIV/AIDS or several cancers. High blood pressure and cardiovascular diseases, the most common according to the World Health Organization (WHO) can now be controlled with antihypertensive and cholesterol-lowering medicines. EFPIA studied the contribution of a subset of medicines with HIV and breast cancer in 2016, estimating that over 650 thousand people were treated with these medicines who are estimated

to have gained around 2 million healthy life years (average of 3 years per person), contributing to a 27 billion productivity gain for the EU economies and 13 billion health care cost savings due to avoided complications. And yet, satisfactory solutions still remain to be found and developed for a series of diseases and condition such as, for instance, Alzheimer's, Multiple Sclerosis, many cancers, and orphan diseases[1] indicating growth of this sector since more cases are diagnosed every year.

Besides social and health impact, the economic impact of this sector is also very significant. According to the Global Use of Medicines report from the IQVIA Institute for Human Data Science (IQVIA, 2019), the global market for pharmaceuticals reached $1.2 trillion in 2018, $100 billion more than 2017 and is expected to surpass $1.5 trillion in 2023. In 2018, the USA spending reached $485 billion and Europe totalized €260 billion spending on production. 80% of the world's pharma sales occur in North America, Europe and Japan. In the European Union, according to the EFPIA, pharma industry granted €105 billion of trade balance and was responsible for 765 thousand direct jobs having generated four times more employment indirectly, thus representing approximately 1,6% of total jobs. The investment in research and development of pharmaceuticals and biotechnology reached € 36 500 million in the EU, of which 100 million were figured in Portugal, ranking first on industrial sectors by overall R&D intensity (EFPIA, 2018).

3.1.2. Key types of players

The pharmaceutical sector has been divided in five groups from the point of view of manufacturing, according to Shah (2004):

- **large R&D multinationals**, which study and test new products of which few reach the market with exclusive rights (patents), having a global presence in branded products (both ethical/prescription and over-the-counter) and manufacturing sites in many locations;
- **generic manufacturers** operating in the international market, who produce out-of-patent prescription and over-the-counter products;
- **local companies** based in only one country, usually their home country, which produce both generic products and branded products under licence of contract;
- **contract manufacturers without their own portfolio of products**, however producing either active ingredients or even final products by providing outsourcing services to other companies;
- **biotechnological companies** mainly concerned with drug discovery, with less significant manufacturing capacity and in most cases start-ups.

[1] An orphan disease is defined as a condition that affects fewer than 200,000 people nationwide. This includes diseases as familiar as cystic fibrosis, Lou Gehrig's disease, and Tourette's syndrome, and as unfamiliar as Hamburger disease, Job syndrome, and acromegaly, or "gigantism." Some diseases have patient populations of fewer than a hundred. (FDA, 2012)

The first group, the research pharmaceutical companies which study and test new products of which few reach the market with exclusive rights (patents), is economically the most important one and tends to have large and complex supply chains due to its activity's global nature (Sousa *et al.*, 2011).

Generic pharmaceutical companies, which rarely have an unsuccessful product as they only produce what has already been commercialized and free of patents, are low-cost, low-margin and low-risk businesses whose competitive differentiation is then based on the cost of the products, and profitability dependent on market share. These companies contrast with research pharma companies since the latter's business model is based on innovation which is expensive, time consuming and highly risky (Taylor, 2016). Generic manufacturers supply the vast majority of medicines worldwide in terms of prescription volume, so their supply chains are mainly characterized by large portfolios of finished products and distribution chains, without the highly risky discovery research and product development activities (Marques *et al.*, 2020).

Biotechnological companies that work in the pharmaceutical sector are usually called biopharmaceutical companies (or biopharma) and have had a considerable development and presence in the market. Professional services recruitment firm Morgan McKinley define these two subsets of this sector in this way: "pharmaceutical companies produce medicines that cure or manage diseases and protect people from infection. While products can include vitamins, livestock feed supplements and animal health products, the main products of the pharmaceutical industry are drugs that treat human illness. For this, plant- and chemical-based compounds are used to produce medicines. Biopharma medicines and drug products are manufactured in living organisms like bacteria, yeast and mammalian cells. The prefix "bio" refers to how drugs are produced. Biopharma is the subset of drugs produced by biological methods." Although research is the main driving force of this group of companies, this work will focus more attention on big R&D pharmaceutical companies supply chain.

3.2. How does the pharmaceutical industry work?

Focusing on R&D pharmaceutical industry, according to Azzaro-Pantel (2018) the pharma industry goes through two phases: (1) drug development phase and the (2) marketing (production and distribution) of successful drugs.

A new product development (NPD) phase (1) can last for 15 years and encompasses four activities: discovery, pre-clinical tests, clinical trials on humans and approval and product launch. During discovery activities thousands of compounds are tested until a promising new molecule, the Active Pharmaceutical Ingredient (API), is achieved, which is then subjected to the pre-clinical tests conducted in animals to determinate toxicity and safety levels. Clinical trials are next, in humans, and are the most expensive and time-consuming step of this phase, since it requires a significant amount of drug to perform the rigorous number of tests imposed by regulatory agencies. Firstly, the new drug is tested for purposes of safety and dosage determination (phase I of the clinical trials), then tests are conducted in unhealthy humans to assess efficacy (phase II) and finally, tests are performed on a large-scale to compare results with existing treatments (phase III). Then, both product and production process must be approved by regulatory agencies: European Medicines Agency (EMA) in Europe or Food and Drug Administration

(FDA) in the USA. Lack of differentiation or unperceived therapeutic value by consumers, especially healthcare systems, can hamper market success because end-users might be more concerned with cost/benefit impact of the new drug compared to existing treatments (Marques *et al.*, 2020).

After market launch, production and distribution phase (2) starts when companies try to capture and establish a market share as large as possible, depending of course on the effectiveness of the therapy compared to other treatments, side effects that may originate and economic factors. After reaching a stable demand level, "me-too" products[2] may emerge and when patent life ends, generic manufacturers start producing bioequivalent products, at a lower price (Marques *et al.*, 2020). The pharmaceutical manufacturing process comprehends two steps: primary production and secondary production. In the first, the API is manufactured through chemical/biological processes characterized by its high product variability, batch operation, multipurpose equipment and long processing times (Sousa *et al.*, 2011). Then, the API is transformed at the secondary production stage into a product suitable for patient administration involving non-ingredients addition as well as further processing and packaging to ensure product stability and integrity.

When the product is ready, it is distributed, reaching the healthcare system and finally patients.

3.2.1. Pharma supply chain

Given the previous topic, a typical pharmaceutical supply chain, based on a traditional batch production, the operation mode most commonly established, includes (1) suppliers, (2) primary production (also called "drug substance manufacturing"), (3) secondary production (also called "drug product manufacturing"), (4) warehouses/distribution centres, (5) wholesalers, (6) healthcare providers and (7) consumers, where different stakeholders are involved. This will be analysed next.

Figure 3.1. – Typical pharmaceutical supply chain on a batch operation mode.

3.2.2. Stakeholders overview

As mentioned, pharma industry has many stakeholders from the beginning to the end of its supply chain such as suppliers, manufacturers, wholesalers, healthcare providers, regulatory agencies and, at last, patients (e.g. consumers). Suppliers are the first ones to appear, which provide raw materials for medicine production. Since industry manufacturers are very strict about ensuring the safety and quality of drugs at each level of the supply chain, suppliers tend to be fixed and regulator-certified (Benson & Prowse, 2019). Raw materials are processed by manufacturing companies, that produce high value

[2] Me-too product is a product created by a company that is similar to a competitor's product in order to prevent that competitor from maximizing its market share. Creating me-too products is considered risky because the company may lack the knowledge or expertise necessary to create a competitive product. (Farlex Financial Dictionary, 2009)

products (primary and secondary production), which are usually big companies, multinationals that ensure large-scale drug production and storage (many of which have their own warehouses and then distribute to wholesalers). The biggest pharma companies are tackled in section 3.3.

Medicines, unlike food industry for example, have a less local and decentralized supply chain, thus wholesalers and distributors play a very important role in pharma supply chain. Wholesalers are the main purchasers from manufacturers ensuring products reach a variety of locations, such as pharmacies, hospitals, clinics, and laboratories, their role being to make the process of purchasing drug products from pharmaceutical manufacturers more efficient. They enable manufacturers to ship bulk quantities of medications to a comparatively small number of distributor warehouses instead of shipping directly to thousands of pharmacies and outpatient dispensing outlets. Some wholesalers specialize in dealing with a particular range of products, such as biologics or to specific types of customers, such as nursing care facilities. Today, wholesale distributors provide a range of specialized services such as specialty drug distribution, pharmaceutical repackaging, electronic order services, drug product buy-back programs and reimbursement support, specialty pharmacy and disease management services. By combining their purchasing power, wholesalers can help smaller pharmacies better negotiate with manufacturers of generic drugs (Datex Corporation, 2019).

Healthcare providers, such as hospitals, clinics and medical practitioners, ensure that approved drugs manufactured and sold by the pharmaceutical companies are put to the right use (adequate drug and dosage), usually by means of a prescription or even administrating them themselves to patients. Certain drugs like morphine, for example, are addictive and if misused, they could turn to be dangerous and lethal therefore they need to be under control. As such, only the medical practitioner is able to administer use of such pharmaceutical drugs (Datex Corporation, 2019). On the other hand, some drugs do not require a medical prescription (over-the-counter medicines) giving the patient the autonomy to choose the brand and where to buy it, since these medicines can be sold by other retail players besides pharmacies (such as “parapharmacies” in Portugal).

3.2.3. Challenges and driving forces

The following topics present the identified challenges and driving forces of the pharma industry associated to each certain supply chain phases, as well as a global assessment of the sector.

3.2.3.1. Product development and market launch

The first challenge faced by pharmaceutical company, that bases their work on research, is the process of development of a new product itself, especially due to the inherent uncertainty and the high levels of investment required. Typically, the new product development (NDP) phase involves four activities: discovery activities, pre-clinical tests (animals), clinical trials on humans, approval and product launch as referred in the beginning of section 3.2. of this work. The average time between discovery and launch is almost 15 years and if something fails in one of these phases, the process stops, the product either being abandoned or returned to the discovery phase. 50% of the investment in this phase goes alone for the clinical trials which are the most time consuming due to the number of tests (and drug) required to complete its three regulated subphases (Marques *et al.*, 2020). The probability of a successful clinical

trial product getting approved is 11,83% according to DiMasi (2016) and the success rate of a clinical development in 2018 was 11,4% in the USA, according to IQVIA. This low probability can be attributed to the regulatory scrutiny that is becoming stricter, making quality and compliance issues more complex (Mckinsey & Company, 2013).

Marques *et al.* (2020) identified the following main challenges related to the development of a new product:

- minimization of the development time (reduction of time-to-market);
- minimization of development costs;
- maximization the product portfolio value, by guaranteeing a good balance between the number of products and their technical quality (safety, efficacy, and market differentiation).

Then, after a new **product is launched** in the market under patent protection, whose production process must be also regulated and approved by the regulatory agencies. Market success may not be guaranteed since:

- the new product might not be enough differentiated, or its therapeutic value is not perceived by end-users;
- healthcare providers are more concerned about the relation cost/benefit, sometimes preferring existing cheaper treatment solutions.

After market launch, the product enters the **growth phase** which depends on:

- the effectiveness of the therapy compared with other therapies,
- side effects that may emerge,
- economic environment.

When reaching **maturity phase**, the product may face two situations, already tackled in this work:

- appearance of “me too” products, similar drugs with a similar function, which can emerge a few years after launch and may capture some market share, creating price competition but not necessarily generating a significant downward in price;
- generic drug production when patent reached its end, bioequivalent products, resulting in a quick drop in price.

Product development and market launch faces major and important challenges, internal and external, that compromise the whole sector and its supply chain.

On an external scope, the increasingly regulatory necessities are viewed as one of the impediments to innovation in the pharma sector as it is becoming more time consuming and expensive. This is stated to be partially caused by new and more complex molecular entities which require more extend trials and more post-approval monitoring mechanisms, as well as the natural tendency to improve consumer safety, eliminating as potential adverse effects as possible. Regulatory attention includes also logistics, where temperature and humidity control in storage and transport is becoming also stricter. (Marques *et al.*, 2020). Different regulation procedures and legislation in each country (or between the biggest markets – EU, USA and Japan) also contribute to the complexity of the regulatory environment.

Internally, the high investments in R&D, the reduction of the success rates during clinical development and the recovery of investment decrease result in low levels of R&D productivity. This decrease in clinical success rate, i.e., fewer approved drugs, is the result of the longer clinical trials mentioned, complexity, stringent regulatory requirements, the urge to address ever more challenging diseases and the poor focus on target selection by the industry itself. The decline in R&D productivity is particularly problematic since it causes reduction in new approved drugs, the most important driving force of this sector owing to the inherent patents. Innovators need to guarantee a continuous flow of new products to replace older ones whose patents expire to keep being competitive. Concerning patents, another identified challenge is their decrease in effective duration associated with the delayed time-to-market period of a new drug, caused by the long development cycles and, again, increasing regulatory burden. Again, this reduces the investment recovery opportunity under market exclusivity (Marques *et al.*, 2020).

Overall, product development in the pharmaceutical industry is still highly inefficient, with very low levels of productivity, making it a fruitful area for improvement (Pammolli *et al.*, 2011; Paul *et al.*, 2010)

3.2.3.2. Production and manufacturing

As mention in the beginning of this section, the pharmaceutical drug manufacturing process comprises usually two stages primary production (API production) and secondary production (product production). The first challenge that can be identified in this process is the disjunction of these two stages, as secondary production is often physically and organizationally separated from primary production, with manufacturing sites geographically distributed to satisfy local markets which can pose communication/coordination difficulties (Sousa *et al.*, 2011). However, owing to the simplicity of the processes involved in the secondary stage, the construction of these facilities independently is easier and less time consuming (Hansen & Grunow, 2015).

The primary production is most often operated in batch mode involving chemical or biological reactions (upstream) followed by the purification and separation process (downstream). Batch processes use low volumes and offer high product variability, presenting several positive aspects such as:

- facilitated quality control;
- easy contamination remediation (by simply correcting the next batch);
- well defined steps, allowing to know intermediaries;
- lot traceability, crucial in the pharma industry;
- high flexibility;
- good capital efficiency, due to the utilization of the manufacturing resources across multiple products.

However, batch mode has several features that lead to a poor performance characterization (Marques *et al.*, 2020; Shah, 2004):

- long production cycle-times;

- having many unproductive tasks (changeover, Cleaning-in-Place (CIP), Sterilization-in-Place (SIP) necessary between batches, causing long setup times which can reach weeks and high utilization of energy and water);
- high levels of inventory needed to compensate slow responsiveness to market dynamics;
- high levels of expired final product due to the excess of inventory, especially in distributors or pharmacies;
- inefficient materials utilization due to low production yields;
- low equipment utilization.

Continuous production is currently appointed has a solution and an improvement to these limitations, not having yet been implemented massively in the pharma industry.

Secondary production gives form to the products which can be various (tablets, capsules, ointments, gels, injectables) and defines dosage. Some of these formulas require more sterilization of equipment (injectables), which is time-consuming and complex (Yabuta *et al.*, 2018).

Bioindustry faces even more challenges since biologic products have increased challenges related to temperature, pH, oxygen, nutrients and even agitation sensitivity. Moreover, gene and cell therapies, important new treatment in terms of personalized medicine based on genomic characteristics, must be produced in much smaller quantities requiring a more agile production and a change from the mass production paradigm to mass customization.

3.2.3.3. Distribution and end of the chain

Lack of agility is identified one of the major challenges of the pharma supply chain which has a contribution of this phase of the chain. Replenishment when shortage occurs, for example, is essential for the well-functioning of healthcare services and crucial when life dependent drugs are at stake. Shortages are critical because they create opportunities for counterfeiters and gray-market vendors, threatening patient safety and cutting into the revenues of legitimate companies (Mckinsey & Company, 2013).

Personalized medicines are also a considerable challenge in terms of distribution since the traditional network, where the wholesaler plays a central role, might inevitably be replaced by a more direct distribution model, ensuring more contact with the patient. Personalized characteristics and dosages need to use a better metric as well as a good system of validation and monitoring for which digitalization and communication technologies might be very helpful (Marques *et al.*, 2020)

The price of medicines is also a factor with great impact in end-users such as governments which pay a part of some medicines to the general public (with medical prescription), in developed countries. In developing countries, governments and non-governmental organizations work on the affordability and access to their very low-income populations. Thus, governments and payers make pressure on the pharma industry to drop prices, creating regulation policies on medicine prices (Marques *et al.*, 2020). Moreover, generic drugs are usually chosen by medical prescriptions, when available owing to their lower price, which is not convenient for R&D based pharma companies (IQVIA, 2019).

3.2.3.4. Global challenges

According to Mckinsey & Company (2013), pharma companies are expanding their product portfolios to meet the fast-changing markets, reflected by healthcare systems improvements, new diseases and sustainability concerns, which induces some uncertainty to the business. However, supply chain change is still a field with much room for improvement. For example, they not only state that “a typical Asian laptop manufacturer can accept an order on a Monday and deliver a pallet of freshly assembled customized computers to a European customer little more than a week later. In contrast, a typical pharmaceutical manufacturer has a lead time of about 75 days”, but also compare inventory days between pharma industry and fast-moving consumer goods (groceries), which are 2 to 4 times less, in order to learn from them.

On an internal perspective segmentation, agility and measurement are key areas to improve. Segmenting supply chains according to the characteristics of products and the requirements of the customers, developing forecasting, production and distribution strategies for each, reduces inefficiencies, high inventories and the use of expensive air transport when one product suffers shortage, in opposition to a “one-size-fits-all supply-chains” *modus operandi.* Agility allows acting fast in emergencies, for which analysing patterns in demand, improving communication and transparency between all supply-chain stakeholders, can help program manufacturing processes and distribution networks. Standardization in metrics used across countries and plants is also fundamental to improve models and cooperation. Alignment and collaboration are appointed as even more beneficial, since a global and common set of standards that support data interchange, processes and capabilities may increase efficiency and patient safety, putting obstacles to counterfeiters and improving recall processes. Overcoming cultural barriers and fomenting a team acting spirit are also contributing factors for the improvement of the efficiency of the sector.

Sustainability concerns are also challenging for companies since the processes rely on resource-intensive operations, with large amounts of water, solvents and energy spent. Increasing resource-efficiency utilization as well as reducing waste requires adjustments in the processes, sometimes expensive. Waste includes unused and expired drug products, many times related to inventory excess, recalls and the absence of collection, reintegration and disposable solutions. New concepts have been developed to turn supply chains more eco-friendly such as “reverse logistics”, “closed-loop supply chains” and “life cycle assessment”. Additionally, besides the environmental component, the social aspects are nowadays more respected due to human rights and labour condition improvement pressure by public opinion in developed countries. Integrating social concerns and metrics in the pharma supply chain (as tackled in Chapter 2 of this work), enabling an efficient interaction between industry, society and also ecosystems, can lead to an end-to-end chain redesign, but is still an aspect with much to be done. The following topic overviews the social performance of leader pharma companies in sustainability, identifying which social aspects are now being considered by this sector industries.

3.3. Who leads in sustainability?

Pharmaceutical companies recognized by the *Dow Jones Sustainability World Index* as leaders in sustainability, in 2019, were identified and analysed with emphasis on their social performance.

According to this index, for each sector, the company with the highest score is named Industry Leader and is considered the company in its sector with the highest capacity to take advantage of opportunities and manage risks arising from economic, environmental and social factors. In 2019, GlaxoSmithKline PLC was recognised as the industry leader with an 90% score[3]. Companies whose score is within 1% of the leading company score receive the Gold Class distinction, which that year only Roche achieved that distinction. All companies that receive a score within a range of 1% to 5% of the leader company score receive the Silver Class distinction which no company achieved in 2019. Companies that score within a range of 5% to 10% of the leading company score receive the Bronze Class distinction. In this class, the year under review includes only Sanofi. All companies that are not distinguished but have been included in the yearbook are listed in the Sustainability Yearbook Member. For a company to be listed in the Yearbook, it must fall within a range of 15% to 30% of the leading company's score (S&P Global, 2020). In this work, six companies in the pharmaceutical sector that achieved high scores as the most sustainable by the *Dow Jones Sustainability World Index* will be analysed on their social performance, namely the 3 distinguished as Gold and Bronze Classes, as well as 3 more that scored above 75% (AstraZeneca PLC, Daiichi Sankyo Co Ltd and Takeda Pharmaceutical Co Ltd).

3.3.1. Social performance

Chapter 2 of this work reviews the main social indicators used in supply chain optimization models, aiming to evaluate how these models quantify the social dimension of sustainability in supply chain management, dividing them in four groups: employment, labour conditions, health and safety, and community development. Here, a brief analysis of the six pharmaceutical leaders in sustainability is performed bearing the groups of indicators proposed in Chapter 2, detailed in Annex B.

3.3.1.1. GlaxoSmithKline

GSK, the leader in sustainability performance according to *Dow Jones Sustainability Index*, has 13 commitments that aim to ensure a responsible business management from which 11 are related do social aspects and people. Their priority is to make products more available and affordable, reducing prices, increasing product reach and healthcare access, especially in developing countries. To address

[3] The score is calculated from the CSA (Corporate Sustainability Assessment), S&P Global's tool to identify the companies that are best equipped to identify and respond to emerging opportunities and risks resulting from global sustainability trends. The CSA consists of an annual analysis of the sustainability performance of companies (over 4,000 companies). The annual assessment is based on an online questionnaire supported by company documentation (such as Sustainability, Health and Safety, Social, Financial or other company documentation). Other sources are media or stakeholder reports and other available public information (S&P Global, 2020).

these needs, they propose the use of science and technology to create global health (mainly through reduction of infectious diseases that affect children focusing on HIV; malaria and tuberculosis), new medical innovations (such as vaccines) and to improve health security (helping the world to prepare for future disease outbreaks with pandemic potential and tackle antimicrobial resistance). Meanwhile, they pretend to be a “modern employer” prioritizing having engaged employees, accelerate the progress on inclusion and diversity (improving gender balance aiming for over 37% female representation in senior roles and recognition in global LGBT+ indices, by 2022), as well as to be a leading company on employee health, well-being and personal development.

This company shows good results in several social indicators on the four tackled groups of this work (employment, labour conditions, health and safety of and community development). See Annex B. Employee survey engagement score (78% in 2019) stands out, supported by a 6,7% voluntary leavers turnover in a universe of 99 437 employees all over the world.

When it comes to equity in medicine access, a major concern of this work, GSK is committed to reach 800 million people by 2025, having already reached 192 million, especially children via disease eradication programs and access strategies. Furthermore, GSK already provided access to several healthcare services, via healthcare workers training, education, children care services, to almost 8 million people.

3.3.1.2. Sanofi

Sanofi’s major social sustainable commitments concern access to healthcare for the underserved communities, community development, employee health and safety and gender balance presenting results on social indicators performance (See Annex B).

Concerning better access of healthcare, Sanofi’s ambitions are to contribute to eliminating sleeping sickness by 2020 (already showing results in Congo), polio eradication by 2023 (making possible to immunize 70 million children) and reducing the burden of non-communicable diseases such as childhood cancer and diabetes in low and middle-income countries. According to WHO, in high-income countries 80% of children with cancer are cured, whereas in low and middle-income countries this number only reaches 20%. Sanofi has launched 75 projects in 48 countries to train 25 000 healthcare professionals and provide treatment to more than 85 000 children), showing good concern with community development and health improvement.

3.3.1.3. Roche

Roche has a strong variety of measures to improve access to healthcare and its affordability around the world. The company has put in place patient support programmes such as the Unmol Programme to provide cancer medicines in Pakistan (Roche covers 50% of the treatment and Pakistan government the remaining 50%) and the Genentech Patient Foundation that aims to ensure that Americans have access to its medicines irrespective of their ability to pay providing them to people who meet certain financial criteria without insurance (60 000 patients are helped annually free of charge).

Donation programmes are also included in Roche's strategy such as the European Haemophilia Consortium Partners Programme and the World Federation of Haemophilia's Humanitarian Aid Program funding treatment for 1000 people where there is no treatment available, and the Global Access Program to increase diagnostic test for infectious diseases such as AIDS, tuberculosis, hepatitis B and C and human papillomavirus.

Increasing outcome certainty for health care systems by means of equipment flexible pricing has been one of Roche's contributions to improvement of healthcare especially on immunotherapy treatments in Belgium and lung cancer treatments in China.

This company also reports on several social indicators on the four tackled groups of this work (see Annex B), standing out for its work on education programmes for disadvantage young people, community training on developing countries on solutions against climate change and catastrophes and training investment on the company's own employees.

3.3.1.4. AstraZeneca PLC

AstraZeneca's goals in what concerns access to healthcare comprise non-communicable diseases prevention and treatment, especially cancer, cardiovascular, renal, metabolic and respiratory diseases. To achieve this, besides investment, donations, training and health promotion, they work on "breaking down cultural barriers to improve treatment adherence", an interesting aspect not always tackled. AstraZeneca states to have given training to more than 81000 healthcare workers and having reached 19,8 million people through their access programmes and 9,7 million through their Patient Assistance Programmes. The company follows the UN 2030 Agenda for Sustainable Development using its Goals to define their own objectives.

On the internal scope, the company shows a significant variety of social well-being and improvement measures, mentioning ethics as a central concern in their management policies. The complete analysis can be read on Annex B, nevertheless some aspects can be highlighted such as special concern for the reduction in employee driving collisions rate in their work/home to work travels and the implementation of a healthy work environment with healthy food, tobacco cessation policies, physical fitness and workspace pressure management.

3.3.1.5. Daiichi Sankyo Co Ltd

Daiichi Sankyo Group defines oncology as a priority area to improve healthcare and makes investments in a concentrated manner for three main pillars: the ADC (antibody drug conjugate) franchise, the AML (acute myeloid leukaemia) franchise, and Breakthrough Science (creating first-in-class or best-in-class compounds with breakthrough mechanism of action or modality). The company also aims to create innovative medicines that change the treatment for rare diseases outside of the oncology field. Daiichi contributes to the Global Health Innovative Technology (GHIT) Fund since its establishments, which aims to achieve drug discovery for combating infectious diseases in developing countries.

From the internal point of view (see Annex B), this company shows specific results on employment, labour conditions and community development but not on health and safety of their employees. They

differ from the other analysed companies since they present a percentage of employees with disabilities (mental or physical), proving their inclusion concern, alongside gender balance information, although results are still far from desirable.

3.3.1.6. Takeda Pharmaceutical Co Ltd

Takeda, as the other five companies, is also committed to improve healthcare access, highlighting for their partnerships to accelerate diagnosis for children with a rare disease. Globally they provided treatments to 125 000 people, trained more than 4000 healthcare workers and screened 1,1 million patients for noncommunicable diseases (including cancer). Investment in community projects and education/training partnerships are strong action lines of Takeda Pharmaceutical. On an internal view, health and safety of their employees is a major concern, although engagement and turnover information was not found.

3.3.1.7. Overview

The presented analysis revealed that the leader pharma companies in sustainability are not far from one another in terms of challenges and goals. With facilities in several countries they try to eliminate asymmetries in human rights, inclusion and diversity in employment for which some of them present some initiatives/measures for specific countries or regions. Being pharma companies, they all state that their main goal is to improve healthcare access, medicine affordability and providing training in developing countries contributing with their knowledge and expertise. Their commitments follow the Goals of the United Nations Agenda for Sustainability Development and four of them (GSK, Sanofi, Roche and Takeda) assess their sustainability performance based. Data sources for this work are summarized in Table 3.1.

Table 3.1. – Leader pharmaceutical companies in sustainability analysis data sources.

Company	Country	Data Sources
AstraZeneca PLC	United Kingdom	- AstraZeneca Sustainability Report 2019
Daiichi Sankyo Co Ltd	Japan	- Daiichi Sankyo Group Value Report 2019
GlaxoSmithKline PLC	United Kingdom	- GlaxoSmithKline Environmental, Social and Governance Performance Report 2019
Roche	Switzerland	- Roche Annual Report 2019
Sanofi	France	- Sanofi Integrated Report 2019 - Sanofi Corporate Social Responsibility Report 2019
Takeda Pharmaceutical Co Ltd	Japan	- Takeda Sustainable Value Report 2019

3.4. What does the future reserve?

In order to achieve better healthcare and medicine access as the analysed companies desire, the sector needs to overcome its challenges and change some paradigms. Becoming more efficient and collaborative is essential to reduce costs and, consequently, make pharma products more affordable.

In the manufacturing processes, continuous operation mode is suggested as one of the enablers of production efficiency. It relies on a steady flow of material between unit operations and makes possible to have an also steady flow of final product, allowing the reduction of inventories in wholesalers. Moreover, elimination of set-up steps between operations and elimination of intermediaries handling and transfer operations contributes to the reduction of process inventory and cost reduction (Marques *et al.*, 2020). Continuous processes can be more automated lowering human error risk, less variability (compared to the batch mode), consequently improving product quality uniformization. However, continuous processes implementation requires extended knowledge of the equipment to convert each operation unit to a continuous configuration which in some cases is not easy (chromatography purification processes). Lack of initiative by companies to adopt new technologies and operation modes is notorious mostly caused by the regulatory burden and high investment needed (Settanni *et al.*, 2017). Biopharmaceutical products, such as proteins, enzymes, antibodies or genetic molecules, manufacturing is even more challenging to automate, being highly dependent on batch processes. Contamination risk of cell cultures and mutations is a major issue in biologic product handling favouring batch preference.

Biotechnology is changing the way diseases are treated, thus being one of the future trends in the pharmaceutical industry. Recombinant DNA technology opened the possibility of producing biopharmaceuticals, also called biologics, which can mimic complex body proteins, for example, which can help the treatment of diseases in entirely new ways. Understanding how to produce biologics also means that understanding of mechanisms of diseases is being achieved, resulting in the development of innovative medicines and vaccines for illnesses lacking treatments, for instance, cancers, rheumatoid arthritis, Crohn's disease, multiple sclerosis, macular degeneration, retinal vein occlusions, psoriatic skin diseases and Gaucher disease. The biologics include biosynthetic monoclonal antibodies, insulins, peptide hormones and analogues, haematopoietic and non-haematopoietic growth factors, interferons, interleukins, erythropoietins, fusion proteins, 'recombinantly produced antigens' (vaccines) which are entering the global market of pharmaceuticals and already represent one third of the actual new medical entities launched (Ghia *et al.*, 2015).

Biopharmaceuticals also play central role in the new patient-centric paradigm of therapies in which patient genomic characteristics knowledge allows the personalization of medicines matching an individual patients or small niche of patients. Personalized medicine is becoming a major trend and its rising market will have a significant impact in supply chain at an operational level, since regular changes in what to produce and when might appear, thus mass production and standardization gets replaced by customization (IQVIA, 2019; Marques *et al.*, 2020).

Regulatory agencies also encourage the development of personalized therapies, recognizing that strict regulations pose major obstacles to the advancement of this area. EMA has created a programme to optimize the development process and accelerate market launch of this time of medicines that address unmet needs for niches of patients such as rare diseases. PRIME programme, EMA offers early support with scientific advice and creates an regulatory framework which accelerates assessment at the time of application of a product marketing authorisation (EMA, 2018).

Industry 4.0 is also a trend that has started to have impact on the process industry. Its principles are a decentralized self-organizing and reconfigurable facility where equipment and materials are connected by cyber-physical systems, communicating and exchanging data, taking actions autonomously and intelligently, coordinating all operations, including of the whole supply chain. Internet-of-Things and digitalization of the various supply chain steps (using sensors in manufacturing sites, etc) are crucial steps to reach Pharma 4.0. This could be a key enabler of efficiency throughout the supply chain since it allows real-time monitoring and action if needed, improving the so mentioned agility of the chain as well as its responsiveness. Manufacturing would have a smart production line, leading the way for better customisation and personalization of drugs (for example adjusting automatically a batch quantity knowing when to produce it and where to deliver it, coordinating not just manufacturing but also distribution), eventually leading to just-in-time delivery. Quality is also improved since better monitoring with adequate responses mitigates human errors and controls environmental factors (sterility, particles, etc). Even waste can be reduced, as well as overproduction and energy consumption. Quality-by-design paradigm becomes a reality, since better understanding of the whole process, due to predictive analysis of potential failures with machine learning algorithms, includes quality concerns at the very beginning of the research & development process, instead of just being at the end as control (Ding, 2018).

Communication and democratization of information in a real-time basis (patient, product, process and supply chain data) is, alongside digitalization, fundamental to achieve an Industry 4.0 based pharmaceutical industry, leading to more flexibility, agility, responsiveness and efficiency in its supply chain, as result of its gained end-to-end visibility (Marques *et al.*, 2020).

Responsiveness, flexibility and agility alongside with preparedness are ideas included in the concept of resilience, the ability to withstand disruptions, adapt and prosper, while at the same time continues to be sustainable or moving towards sustainability (Gartner, 2020). The year 2020 is one of the best tests to the pharmaceutical capacity to be resilient after being impacted by the pandemic of COVID-19, while it tries to contribute to its “resolution” with vaccines and treatments. This topic will be addressed in the next chapter.

3.5. Chapter conclusions

This chapter seeks to overview the pharmaceutical industry sector, its challenges, driving forces, future directions with special attention to its social performance.

Pharma products are by themselves a challenge of this industry, owing to their unique characteristics, high value, vital impact on society and long and complex creation process. The development of a new product undergoes research (on an average 15 years until market launch) and strict regulatory policies.

Given this singular set of features, the pharmaceutical supply chain is complex, including a significant number of players, from the beginning of the chain (suppliers of raw materials) to the end-users (patients), whom are not yet fully connected and cooperative, causing inefficiencies and lack of affordability of pharma products. Pharma supply chain needs to become more agile, flexible, responsive and robust, *i.e.,* resilient to answer to the more and more demanding healthcare challenges. Fast-changing markets, scientific and technological breakthroughs difficult to catch up, increased societal pressures and new regulations are amongst the changes faced by this sector in particular. Regulatory burden, although strongly necessary to ensure safety and quality of the products, is contributing to a decrease in R&D productivity and, combined with the natural difficulties of the discovery process, is often seen as the most critical stage in the pharmaceutical product life-cycle, leading regulatory agencies to create new ways of accelerating drug approvals. A new concept as emerged to answer this issue, Quality-by-design, which alongside personalized medicines, biopharmaceutical products development, continuous manufacturing operation mode and industry 4.0 are some of identified future trends to achieve the mentioned improvement needs in pharma supply chain.

Societal pressure (also referred as public opinion) triggers sustainable concerns, namely social performance of big pharma companies. As such, an analysis of the six leaders in sustainability according to *Dow Jones Sustainability Index* was performed to identify best practices and what is being done by these big players in this field. The six of them revealed to be in line with the UN Agenda of Sustainability Development Goals for 2030, focusing their contribution on the improvement of healthcare access and affordability. For this, they work on several projects and partnerships with local governments and NGO's to take medicines and education to the most undeveloped areas of the world, as well as training of healthcare professionals. In addition, they present concern with the quality of their working environment, tackling several social aspects also assessed by some supply-chain optimization models. The most transversal to the six companies are: gender balance and inclusion improvement, employee engagement evaluation, accidents/injuries prevention and reduction, mental health/stress assistance and, surprisingly, driving collision reduction efforts (work and non-work related). It is already possible to notice some identical metrics and an effort to follow GRI, but there is still much work to do in the uniformization of these indicators' assessment.

Supply chains are dynamic systems, inserted in every society with its different challenges. Thus, new challenges are constantly emerging, forcing SC to respond and adapt to the new panoramas in order to stay resilient and sustainable. The next chapters analyse the impacts of the biggest pandemic of our century on the pharma supply chain and the caused new social challenges.

4. The COVID-19 effects on global supply chains

In this chapter, an analysis of the effects of disruptions in supply chains is performed, focusing of the COVID-19 pandemic repercussions. Based on both researchers and consultancy experts' studies until November 2020, recommendations are formulated on what can companies and their chains can do to be better prepared to this type of disruption, as well as how they can respond and recover.

4.1. What can disrupt a supply chain?

A considerable variety of factors can cause disturbances in a supply chain (Blos *et al.* 2015; Finch 2004), as summarized in Table 4.1. Manufacturing can be easily stopped by raw material shortages, accidents, quality issues or strikes; product distribution can suffer from several transportation issues such as delays, accidents or bad product handling; and customers can even face problems accessing some products if demand changes are sudden. In addition, natural disasters, economic crisis, terrorist attacks and poor internal and external communication can disturb the whole supply chain.

Competitive business environment, outsourcing and globalisation have enlarged several supply chains making them more complex, with several stakeholders and, consequently, added less visibility and more communication challenges. Thus, SC become more vulnerable to disruptions (Shao, 2013).

In the pharmaceutical industry, while manufacturing processes are complex, disruptions can also result from biological contaminations, regulatory actions or drug recalls due to secondary effects appearance, defective products/containers or mislabelling (Azghandi *et al.*, 2018). These disruptions can originate stock-cuts, shortages and, thus, inability to meet customer demand, in some cases, leading to increasing costs and product prices.

Table 4.1. – Supply-chain disruption main causes.

Disruption points	Causes
Supply, Manufacturing and Distribution	Raw materials/parts shortages
	Transportation delays
	Quality issues
	Operational issues
	Accidents
Organization	Ineffective communication
	Strikes
	Ineffective management strategies
External	Demand changes
	Natural disasters
	Economic crisis
	Terrorist attacks
	Wars
	Computer virus attacks

Nowadays, we are living the most serious pandemic of modern history, another major event that has joined the supply chain challenges' agenda.

4.2. Pandemics and epidemics

History reports several health incidents accounting for high damage of human and material capital, suffering and deaths, such as the plague in medieval Europe or the Spanish-Influenza pandemic in the beginning of the 20th century (Dasaklis *et al.*, 2012). Our century has, on its second decade, registered six public health emergencies of international concerns, according to the World Health Organization (WHO), the H1N1 (influenza A) in 2009, polio in 2014, Ebola (out broke in West Africa in 2014), Zika (2016), Ebola again (Democratic Republic of Congo in 2019) and COVID-19 (2020).

The definition of an epidemic, one type of "emergency" as stated by the WHO is "the occurrence in a community or region of cases of an illness, specific health-related behaviour, or other health-related events clearly in excess of normal expectancy. The community or region and the period in which the cases occur are specified precisely. The number of cases indicating the presence of an epidemic varies according to the agent, size, and type of population exposed, previous experience or lack of exposure to the disease, and time and place of occurrence."

WHO does not offer a formal definition for pandemic, but according to the Oxford Dictionary of Epidemiology (Last, 2001) it is referred as "an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people" thus, with greater impact. Pandemics are not just a public health concern since they can trigger socio-economic and political crises in infected countries.

Epidemics are also related to the aftermath of natural disasters, with respiratory infections, measles, malaria and diarrhoea being the most common diseases (Watson, Gayer, & Connolly, 2007). Climate change is also suggested as a catalyst to accelerate epidemic incidents and the re-emerging of some diseases such as yellow fever, dengue and cholera as Dasaklis *et al.* (2012) identified in some studies. These authors also briefly note that bioterrorist attacks can originate epidemic outbreaks as seen in the anthrax attacks in the USA in 2001. They also point that intensified urbanization and rapid population growth can be contributing factors to aggravation of this public health problems and even state, in that year, that "a possible outbreak combined with changes in demographic conditions like population distribution, size and density could potentially lead to a pandemic of unprecedented proportion where available capacities and resources could be strained to their limits". Unfortunately, this unprecedented proportion pandemic arrived 6 years later by the name of COVID-19.

4.2.1. The COVID-19 pandemic

COVID-19 stands for **CO**rona **VI**rus **D**isease occurred in the year 20**19,** and is already considered as the most crucial global health calamity of the century and the greatest challenge humankind faced since the 2nd World War (Chakraborty & Maity, 2020). By November 2020, it had infected more than 50 million people in 216 countries presenting a death toll of 1 265 thousand deaths (Worldometer, 2020).

The COVID-19 disease is caused by SARS-CoV-2, a virus with a single strand of RNA of the coronavirus family, first identified in Wuhan, in China (Huang *et al*., 2020). This virus seriously affects the respiratory system causing cough, shortness of breath, sore throat, loss of taste or smell as well as headache, nausea, vomiting and fever, leading to pneumonia or septic shock (Jantien Backer, 2020; Sauer, 2020). With an incubation period of 14 days, and many asymptomatic individuals, the virus travelled the world reaching more than 200 countries between January and March 2020.

China and Europe applied confinement measures of social distancing, declaring the State of Emergency, in order to reduce transmission of the disease, resulting in the closing of several economic establishments for two or three months and even layoff. Lockdown forced the suspension of flights (42% in Europe according to (EUROCONTROL, 2020), railway services, buses, trucks with only exceptions to essential goods. Commercial, educational, cultural and spiritual institutions have also stopped their activity as well as tourism, raising unemployment and increasing prices. Some products ran out of stock in supermarkets as a result of a panic effect (toilet paper, soap or hand sanitizer, for example) combined with replenishment constraints due to the production interruption of many goods.

4.2.2. COVID-19 effects on businesses and supply chains

Restrictions on movement and muted demand, due to COVID-19, created uncertainty throughout the global economy bringing new challenges to the supply chain management.

Lockdown policies prevented people from working in order to ensure social distancing, thus interfering with manufacturing operations and transit routes (PwC, 2020). Consequently, disruption on production lines caused supply shocks in some sectors and goods. Moreover, the centralization of global supply chains in China (the first country to be affected by the disease), especially in terms of parts and components manufacturing, compromised the supply chain downstream making retailers, who relied on inputs from these factories, not being able to acquire enough products to sell, and second manufacturers, not being able to acquire their raw materials (Zhu *et al.*, 2020).

Then, panic buying fearing food and essential goods shortages during this period caused an increased demand variability and in some case shocks. Variability is particularly difficult to handle by small business, since they have weaker structures and less versatility to maintain an acceptable level of product supply during demand shocks (Parsons 2020).

Alongside supply and demand shocks, the pandemic also contributed to an increasing of the bullwhip effect on supply chains. The variation of a demand signal is distorted from the consumer until the chain upstream, increasing like a whip trajectory. As explained by Steifert & Markoff (2020), downstream players artificially inflate their supply requirements demanding a larger amount of a scare resource when they preview a supply shortage, calling it “shortage gaming”. This can lead to stockpiling, the accumulation of exaggerated quantities of inventory and ultimately, waste.

Cost increasing is also an effect, especially on transportation since commercial flight connections have been severely reduced, resulting in higher air freight costs. Alternative travel modes had to be found to transport air cargo borne by these flights, facing transit restrictions and closed borders. In cases where

borders remain opened, safety measures such as custom procedures and approvals cause delays and costs for the suppliers (Shira, 2020).

With the reopening of commerce after the March-June lockdown, extra safety and health measures were introduced such as reduced people density in establishments, available disinfectant dispensers, higher cleaning frequency, protective masks and gloves and single-use equipment introduction, increasing costs for all supply chain stakeholders, also supported by the consumers. The pandemic effects on a global supply chain are summed up in Figure 4.1.

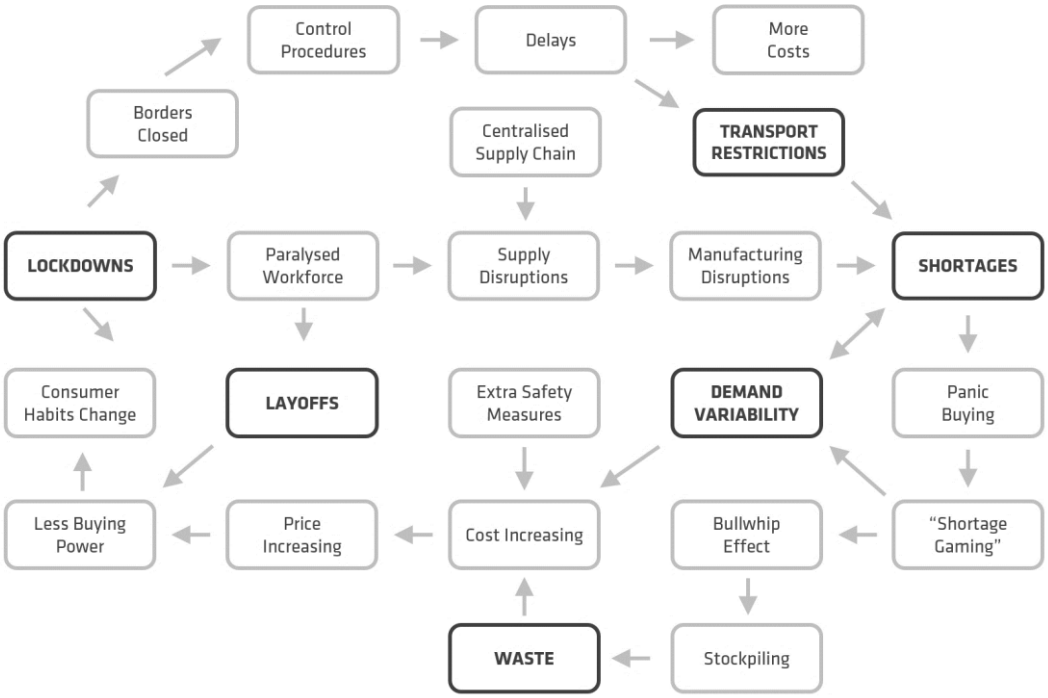

Figure 4.1. – Effects relationship of the COVID-19 pandemic on a global supply chain.

4.3. How can a supply chain cope with a pandemic?

Supply chain management related to the pandemic is a topic not often mentioned on our current social media but has recently gathered the concern of both academics and business players. Although companies' annual reports are not yet produced and the mid and long-term effects of the pandemic are not yet fully known, there are already several studies performed by researchers or consulting organizations that provide some conclusions and recommendations.

4.3.1. Literature material collection

4.3.1.1. Academic Data Sources

A brief literature review was performed, once again, in the *Web of Science* database, with the final set of papers collected in November 2020. Only papers in English were chosen, considering only articles and reviews. Table 4.2 summarises the keywords selected for the search, as well as the results obtained for each individual search.

Table 4.2. – Search results on the relation between the pandemic and supply chains in the *Web of Science* database, in November 2020.

		Keywords	Results obtained
supply chain	**AND**	pandemic OR epidemic	391
		(pandemic OR epidemic) **AND** (pharmaceutical OR pharma)	19
		(pandemic OR epidemic) **AND** resilience	41
		(pandemic OR epidemic) **AND** (pharmaceutical OR pharma) **AND** resilience	6

These publications were subject to a content analysis, being excluded if they did not satisfy all the following criteria:

4. The paper is written in English and was published in a peer-reviewed journal;
5. The paper tackles the effects of an epidemic or a pandemic on supply chains globally or associated to the pharmaceutical sector;
6. The paper assesses actions or strategies concerning the resilience of supply chains in an epidemic or a pandemic situation.

Some of the documents were excluded because they were not openly accessible. The material collection performed was not exhaustive as other databases were not included. Thus, it is possible that relevant papers were not considered. A final set of 10 papers was analysed.

A small analysis was performed to assess the interest in this topic over time. Since there has been other epidemic episodes in history besides COVID-19, it was expected to notice an increase in paper publication around those periods, especially in 2009/2010 – the outbreak of influenza A (H1N1). However, the publication numbers grew timidly until the current pandemic, in 2020, evidencing its unprecedent proportion.

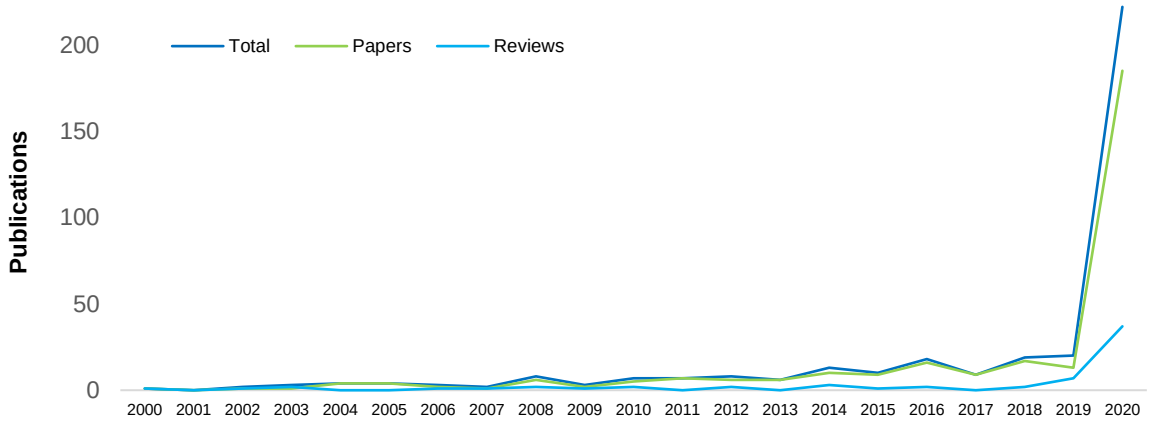

Figure 4.2. – Paper and review publication growth in the *Web of Science* database, since 2000.

4.3.1.2. Industrial Data Sources

On the industrial sector, mainly the consultancy companies have been publishing on the theme and redirected their efforts to the understanding of the situation and how would it impact the economy, businesses and their supply chains. The following are the analysed reports, webpages or experts' articles:

- Accenture (2020). *Supply Chain Disruption & How to Respond*.
- Gartner (2020). *Weathering the Storm : Supply Chain Resilience in an Age of Disruption Supply Chains in an Age of Disruption*.
- Larson (2020). *The effects of COVID-19 on global supply chains: short term pain but potential long term benefits*. SGSME.SG.
- Lund, & Barribal (2020). *COVID-19 and Supply Chain Recovery: planning for the future.*
- Mckinsey & Company. (2016). *Supply Chain 4.0 – the next-generation digital supply chain.*
- Mckinsey & Company. (2020). *COVID-19: Briefing materials | Global health and crisis response*.
- Parsons (2020). *How coronavirus will affect the global supply chain.* Johns Hopkins University.
- Sandahl, J. (2020). *Dual sourcing: The pros and cons of 'backing up' supply chains.*
- Sheffi, Y. (2020, May 27). *Who Gets What When Supply Chains Are Disrupted?*
- Steifert *et al*. (2020). *How supply chains are adapting to the COVID-19 lockdowns*

4.3.2. Resilience and agility

Until the COVID-19 pandemic, supply chain players were mainly focused on its efficiency, tending to implement lean methodologies and inventory minimization (Gartner 2020). Literature review suggests that influenza is the most visible epidemic outbreak (before COVID-19) having canalized supply chain management research to optimization of resources allocation and distribution of medical goods, *i.e.*, efficiency (Queiroz *et al.*, 2020).

Globalized supply chains, despite their dimension, are not infallible. COVID-19 highlighted several weaknesses of supply chains such as poor visibility across the chain, heavy outsourcing or centralized and dependent production. As Lund & Barribal (2020), from McKinsey & Company, state in an interview, even before COVID-19, companies should expect a disruption in their production lines of 1 to 2 months, every 3 to 4 years. Although knowing this risk and their weaknesses, businesses did not prioritize investment on the preparedness of their supply chains, going for just-in-time systems in contrast with a just-in-case perspective (Gartner 2020).

Increasing resilience is now starting to become one of the key priorities to ensure the viability of supply chains. According to Ivanov (2020), a viable supply chain is "dynamically adaptable and structurally changeable value-adding network, able to react agilely to positive changes, be resilient to absorb negative events and recover after the disruptions, and survive at the times of long-term, global disruptions by adjusting capacities utilizations and their allocations to demands in response to internal and external changes in line with the sustainable developments to secure the provision of society and markets with goods and services in long-term perspective", which means that a viable supply chain has

to be resilient, agile and sustainable. Resilience has been associated to the “ability of an organization to absorb and adapt in a changing environment to enable it to deliver its objectives, to survive and prosper” (Gartner 2020), thus “the capacity to withstand disruptive events and recover to a robust state of operations and normal performance” (Ivanov 2020). These authors report that tolerance for uncertainty, and the ability to make choices that put key objectives at risk in order to adapt to the current situation, are important elements to consider when trying to make their organization more agile.

Some studies propose resilience actions to act or be prepared to a pandemic situation. Queiroz *et al.* (2020) suggest to look upon these actions in four categories: systems (structures, resources, capacities), process (production, distribution, transportation, resources allocation), control (inventory, sourcing, manufacturing control) and recovery. Rapaccini *et al.*, (2020) suggest a crisis management model with four stages: calamity, quick and dirty, restart and adapt to normal, tackled in sections 4.3.4 and 4.3.5, of this work. Mckinsey & Company (2020) propose the fundamentals of “the right organization for the next normal”. Thus, based on these perspectives and the literature material collected, some recommendations are systematized in this work divided by what supply chains can do before (prevention), during (control) and after (recovery) a pandemic like COVID-19.

4.3.3. Prevention recommendations

The aim of epidemic and pandemic preparedness is to maintain a certain level of available resources so as to reduce morbidity and mortality when an epidemic outbreak occurs, thus ensuring the continuous supply of goods (Dasaklis *et al.* 2012). Most of the actions or changes concern what can be done before a disruption, identifying vulnerabilities on what companies control on the chain (Lund & Barribal, 2020).

Here, the following recommendations are tackled:

- Safety stock existence
- Sourcing diversification
- Decentralization of manufacturing capacity
- Localizing/Regionalizing supply chains
- Improving visibility
- Vertical integration
- Digitalization
- Product design simplification

4.3.3.1. Safety / buffer stock

Firstly, it is unanimous that stocking some extra quantities of a product, especially pharmaceuticals, can make a big difference if production is disrupted and a prompt response is needed. Risk mitigation inventory allows the SC to meet customer demand in case of a supply chain disruption. It is a “just-in-case” perspective, contrasting with the lean based just-in-time operation. Just-in-time pretends to eliminate non-valuable added activities, reduce costs and improve operational performance, in which reduction of inventory is included. Lean global supply chains are now main contributors within the supply shortages during this pandemic (Azghandi *et al.* 2018).

However, a balance between these two operation strategies must be found since investing in buffer inventory must consider the companies' market position and profitability (keeping inventory has costs), the nature of the products (to know how to storage and conserve it) and regulatory influences (important in the pharma industry) (Queiroz *et al.* 2020).

4.3.3.2. Diversification and dual sourcing

Many companies are dependent on just one supplier for raw materials or parts, risking disrupting their production lines if that supplier fails them. Dual sourcing and supplier diversification increase possibilities and reduces this risk creating redundancy (Fonseca & Azevedo, 2020; Zhu *et al*., 2020).

In addition, dual sourcing allows a company to keep up if an increase in orders occurs (due to demand shocks, for examples), since the manufacturer can switch to another supplier for a certain period of time, instead of expecting a single supplier to ramp up production (Sandahl, 2020).

4.3.3.3. Decentralization of manufacturing capacity

In their globalization processes, supply chains have become dependent on low-cost locations such as Asia, where wages are low and industrialization is growing fast, particularly China. In the same way of dual sourcing, manufacturing capacity depending just on one company is risky, so redundancy is important. Besides, China is nowadays "the world's factory", so if some instability is felt in this country, it can affect the rest of the chain. This instability can be political which, in some countries, can cause variability in wages, laws, energy costs, among other factors, increasing uncertainty. The United Sates are pushing for a deallocation of their supply chains closer to home, many CEO's have asked to search for sources fully independent from China and even Chinese companies such as Samsung and Honda are expanding beyond just China in order to mitigate risks (Mckinsey & Company 2020; Zhu *et al.*, 2020).

4.3.3.4. Localizing/Regionalizing Supply Chains

Apart from decentralization of the manufacturing capacity that, as mentioned, avoids dependency on one manufacturer or one country (commonly China), localizing supply chains can add even more advantages. There are already companies considering bringing manufacturing in-house (for example to the home country) or closer to home (for example, to the European Union, in the case of an European country), in which laws and regulations are easily understood and complied (Zhu *et al*., 2020).

Consequently, less intermediaries would be needed due to the proximity of manufacturers and consumers, accelerating business processes and making it easier to adapt distribution and logistics processes, since the network is smaller and easier to control (Larson, 2020). Regionalizing of trade between neighbour countries is growing, according to Sarah Lund and Ed Barribal (2020). Closer suppliers allow a better collaboration with manufactures which helps to capture shifts in demand (information from manufacturers to suppliers) and adapt production due to raw materials provision fluctuations (suppliers information to manufacturers).

Furthermore, localizing supply chains, allows a better understanding of regional preferences (consumers tastes and options), facilitating demand preview. Regionalizing supply chains enable better

customization of products and services, thus achieving better levels of consumer satisfaction (Gartner, 2020; Larson, 2020).

Finally, reducing transportation distances immediately contributes to a more environmentally friendly supply chain, reducing costs and stimulating local employment, thus increasing its sustainability. Larson (2020) also points that consumers are progressively more mindful of the products' origins and their environmental and ethical concerns related to their manufacturing. Therefore, a local choice for production provides more transparency (tackled on the next topic) and, thus, easier for consumers to know these products' important aspects.

Governments play an important role in this change, since they can motivate local production by supporting the return of manufacturers especially in the case of medical equipment (protection equipment and generic drugs). Trading blocs such as the EU can also impose export restrictions on global manufacturing and importation policies, as well as regulate information that companies have to provide to consumers (Gartner, 2020).

4.3.3.5. Improving supply chain visibility

The more comprehension and knowledge of the whole supply chain the better, since preparation and adequate risk mitigation measures can be easily set.

Knowing who a manufacturer buys from, who their suppliers buy from and what they buy (that does not reach the manufacturer) helps understanding the origin and vulnerabilities of that supply line. Geographical information of suppliers and immediate suppliers, etc, provides information about the political surroundings of those suppliers, allowing a better prevision of prices variation or even disruptions. In addition, visibility brings transparency, more and more scrutinized due to environmental and human rights (labour) public awareness (Lund & Barribal, 2020; Zhu *et al*., 2020).

4.3.3.6. Vertical integration

One of the most effective ways of gaining more visibility throughout the chain to the manufacturers/distributers is to own suppliers and their intermediaries. Assuming control of the upstream players, integrating them, allows to seize autonomy over costs and quality (Zhu *et al*., 2020).

Having more control over the whole network can also facilitate redesigning of the chain (or some parts) when needed and improve communication and cooperation between the chain different stakeholders, since they stop viewing each other as independent companies and even competitors.

4.3.3.7. Digitalization

Improving visibility across the chain can be strongly driven by the digitalization of processes since it can facilitate the interplay between supply chain players by sharing information. Data analysis, for instance, can play a decisive role in understanding tendencies and real time evolution of orders, helping predicting demand and, consequently, monitoring the supply-chain performance. Creating a system aiming to process big data, premises data and information share, thus promoting transparency within the chain, which can then be transposed to the consumer (Lund & Barribal, 2020).

Digitalization can make the supply chain faster, more flexible, accurate and more efficient, according to Mckinsey & Company (2016), which can be understood by the better adaptation capacity due to the improved information fluxes, avoiding disruptions and, consequently, price variations. Lund & Barribal (2020) also mention that logistic operations can also be turned more efficient and even more automatized, based on “sensing and responding” quick procedures.

Industry 4.0 contributes to this digitalization implementation as it gathers the concepts of *internet of things* which provides connection between equipment, workers and management systems, internet of services and smart factories, claimed to be more robust and closer to the optimization of value chains, saving energy, reducing overproduction and reducing costs. A good communication strategy with efficient technological tools is basically the key to improvement the overall supply-chain operation (Ding, 2018).

According to Queiroz *et al.* (2020) review, firms that are successful in digital manufacturing networks seem to be better positioned in crisis times and in the coordination of future recovery processes.

Digital tools at disposable of consumers also enable products to efficiently reach customers, and ensure continuity of business operation in the case of lockdowns and physical stores closing. Mckinsey & Company (2020) observed, in a survey applied in April 2020, that consumers – business-to-consumers (B2C) - accelerated the adoption of digital channels in baking, grocery, apparel and travel sectors, grocery registering the most first time users (31% of the respondents). Similarly, business-to-business (B2B) decision makers have also declared that they believe digital sales interactions will be two times more important than tradition interactions in 2020.

4.3.3.8. Simplification of product design

Redesigning processes and products in order to make them simpler is briefly pointed by Lund & Barribal (2020), since complexity of products might introduce extra complexity to their manufacturing process and, thus, more vulnerabilities.

4.3.4. Response recommendations

When a disruption of great proportion like the COVID-19 pandemic occurs, serious challenges occur, with great social impact. So, businesses must react, control damages and plan their response. Italy was the first European country to feel the impact of the pandemic, having set in motion severe confinement measures, since February 2020. A survey-based study to companies in Italy, by Rapaccini *et al.* (2020) published in May, proposed a crisis management model to the situation which comprises four phases:

1. **Calamity** | Gaining knowledge (Days)
2. **Quick and dirty** | Adopting protocols (Weeks)
3. **Restart** | Reorganize the business (Months)
4. **Adapt to the next normal** | Understand the changes (Years)

The actions proposed in the first two phases are assessed in this subsection, since they give guidelines for the immediate period after the pandemic arrives while phases 3 and 4 are tackled in subsection 4.3.5. Recovery recommendations, of this work.

Obrenovic *et al.* (2020) discussed, in July 2020, the effectiveness and sustainability in operations and productivity during a pandemic, proposing some resilience actions based on these principles: **assess, identify, define and deploy**.

To respond to both the immediate impacts of the pandemic and prepare for what comes next, Accenture (2020) proposes a cyclic approach comprising **mobilization, sensing, analysis, configuration**, and **operation** to optimize results and mitigate risks.

These three approaches have in common three principles: mobilizing, gaining knowledge and then act, after an epidemic outbreak. Bearing them in mind, the present work proposes the following set of response recommendations:

- **Activating task forces**
- **Assessing the situation**
    - Gathering information on the phenomena
    - Identifying scenarios and available resources
    - Inform employees and business players
- **Response actions**
    - Adopting health and safety protocols
    - Defining a response strategy
    - Implementing the defined measures

Recommendations on social issues, for example related to the SC workforce, are tackled in Chapter 6.

4.3.4.1. Activating task forces

Rapaccini *et al.* (2020) study identified that all firms established task forces and crisis units to manage the emergency, with no operational responsibilities, completely focused in gathering information, coordinating decisions, transferring knowledge.

CEOs shall gather elements from every department or function of the organization and experts in relevant areas (consultancy companies if external help is needed) to come up with contingency plans as well as their operational response. Enhance flexibility and innovation are driving forces for a company to prosper, to which out-of-the-box thinking is essential to stimulate brainstorming, necessary to enhance products, reroute sources, find new streamlines. As different people, with different backgrounds and areas of expertise, interact and cooperate, coordinating and adapting their daily (our hourly) activities, cross-unit leadership emerges as well as new leaders that step out of rigid structures. New and unexpected business models might even be implemented (Obrenovic *et al*., 2020). Networked organizations are more resilient since they have a faster diffusion of novel ideas and solutions and shared norms and values eases cooperation between employees (Rapaccini *et al*., 2020).

4.3.4.2. Assessing the situation

Crisis tasks forces shall, firstly, understand what is happening in detail, gathering information such as necessities and risks. Firms shall become aware of the situation in other countries, sectors and business and study their limitations as soon as possible in order to evaluate which resources, technologies and

experience can then be deployed after an epidemic outbreak in their communities, especially if it might lead to lockdowns. A close relationship with universities can provide helpful information regarding the pandemic and disseminate it (Rapaccini *et al*., 2020).

Then, making employees and business players aware of what is happening and what the business response is going to be, keeping them updated, maintains trustworthy relationships across the chain, especially with consumers, mitigating abrupt consuming habit shifts.

Digitalized businesses improve their probabilities to strive from the pandemic. Monitoring social media, user demand, website visits, can help identifying demand indicators and consequent rapid adjustments and timely responses (Obrenovic *et al*., 2020).

With the acquired information, it is advisable to evaluate scenarios, run simulations to predict when and where excesses and shortages are likely to occur, and facilitate the response planning (Accenture, 2020).

4.3.4.3. Defining and implementing a response strategy

Literature suggests a vast set of actions taken by companies during the first COVID-19 lockdown months, to make the most of their resources and technologies, respecting and adopting health protocols, ensuring the employees safety. Defining the strategy according to the collected or the ongoing acquired information shall be as quick as possible as well as implementing it, sending quality information to the employees and players of the supply chain.

After evaluating demand fluctuations and the possible scenarios, defining priorities can be immediate actions to manage shortfalls due to the lockdown, such as prioritizing micro-segments and some products or even favouring the most important customers (Accenture, 2020; Sheffi, 2020). However, treating everyone equally is also suggested in Sheffi's (2020) article (the social concerns related to the supply chain performance during a pandemic are tackled in Chapter 5 of this work). After prioritizing which products to produce, parts shortages can be temporarily solutioned by cannibalization of other products, meaning that viable parts of other products are reallocated to the manufacturing of the products desired.

Sheffi's article also proposes the alteration of the product itself, reformulating it under a certain quality standard, however lower, in order to avoid rising prices (for example, when a chemical company dilutes some substance in manufacturing or even the product itself). Nevertheless, this can be risky if the alteration is well noticed by the consumers and causes regular consumers to choose alternatives.

Rapaccini *et al.*, (2020) study suggests some actions related to customer and support services that have also suffered disruptions, such as product swap in case of impossibility of repairment or part cannibalization. Moreover, if a technician cannot be sent to a certain region or country, another one from a branch of the same company in a still not locked down zone can be a solution.

Online shopping and take-away selling modalities are widely chosen options to overcome the consumer impossibility to buy at closed shops. Digital tools play, once again, an essential role in the survival of businesses and the continuity of the supply line, having been highly accelerated and empowered.

Sustaining labour force, in the best way possible, ensuring health safety protocols, is also fundamental to maintain constant operations. Workforce issues during the pandemic are tackled in Chapter 5.

After a few months of a new reality, in this case a pandemic, mid-term planning must be done, in order to prepare for a repetition of the event (for example, a second peak of coronavirus cases, that arrived in Europe in November 2020).

4.3.5. Recovery recommendations

By the time of this work, the pandemic was at its second wave peak, so the recovery actions recommended here are based on the first pandemic wave aftermath studies.

Rapaccini *et al.* (2020) study, published in May, proposed a crisis management model to the situation which comprises four phases, as mentioned before, from which the last two are tackled here. Once the information is gathered and a response plan has been set motion and time has passed since the pandemic outbreak, a restart phase is proposed, with a time horizon of months, during which the business should be reorganized to resume activity as normal as possible. Safety measures to ensure the reopening of facilities and both guarantee social distancing and protection of workers are necessary, such as population density reduction indoors, rearranging layouts and common areas, allocate work to employees in shifts and, in some cases, open on extraordinary periods. The introduction of temperature control and regular, or serological, testing is also among the health risk mitigating actions, as well as providing necessary protective equipment (masks, sanitizer and, if needed, gloves and proper suits). Selection of which products (and their portions) must be manufactured once again, adjusting to the new necessities, figuring out what portion of demand has been lost or what has just been delayed. Having figured out the demand peaks dimension and the consumers behaviour during the epidemic outbreak, preparations for a second wave or a similar situation shall be done. Detailed documentation of the response actions taken, and its careful analysis, might help on this preparation. So, in this work, it is recommended not to dissolve the activated task forces immediately.

Then, adaptation to the next normal (fourth phase of Rapaccini's study) is necessary, understanding the changes to the business due to cultural, economic and societal effects. Companies need to be ready to evolve and adapt and society must be openminded to accept new business models and practices. Once more, flexibility and redundancy emerge as major topics to be on the agenda. To achieve them, the study suggests five actions, that meet the prevention recommendations previously tackled in this work:

- review the logistics, moving from globalization to regionalization, putting stock closer to consumers;
- reorganize the workplace to accommodate remote working regimes and potentiate a cultural change in the way people approach their work;
- digitalize customer services and support, as well as trying to overcome barriers and scepticism with digital technologies, since it allows the adoption of easier communication flows and faster monitoring and control tools, promoting better data analysis and according response actions;
- improve investment resilience and agility and, consequently, rethink prices/competitiveness of businesses, finding ways to compensate possible increases due to that investment, for example opting for repairing services, moving away from single service/low cost manufacturers;

- develop risk management capabilities, and if these capabilities are mastered and reliable, new insurance opportunities can be added, with the creation of full-risk solutions including fees/rents in contractual agreements, safeguarding activity continuity in critical disruptions such as a pandemic.

4.3.6. Recommendations overview

Following the previous sections review, a set of overall recommendations to improve the supply chain performance during a pandemic situation like COVID-19 is proposed in Table 4.3.

Table 4.3. – Recommendations overview on how to act on the supply-chain during a pandemic.

Stage	Recommendation
PREVENTION	▶ Safety stock existence ▶ Redundancy: diversification and dual sourcing ▶ Decentralization of the manufacturing capacity ▶ Regionalization of suppliers and manufacturing ▶ Improving visibility across the chain ▶ Vertical integration in the chain ▶ Digitalization of processes, equipment, and information flows ▶ Product design simplification
RESPONSE	**Mobilize |** *Who is going to deal with this?* ▶ Activate a task force **Assess the situation |** *What is happening?* (Days) ▶ Gather information on the phenomena ▶ Identify scenarios and available resources ▶ Inform employees and business players **Action Plan |** *What to do?* (Weeks) ▶ Adopt health and safety protocols ▶ Define a response strategy ▶ Implement the defined measures
RECOVERY	**Restart** (Months) ▶ Apply safety measures and reorganize workplaces ▶ Prepare for a close repetition of the event and register what has been done during the outbreak ▶ Do not dissolve task forces immediately **Adapt to the new normal** (Years) ▶ Digitalize customer services adapted to the new reality ▶ Improve resilience and agility, revisiting prevention recommendations ▶ Develop risk management capabilities

These recommendations are the base for the framework in Chapter 6, focused on SC social performance.

4.4. Chapter conclusions

Supply chains are, as known, essential dynamic systems that guarantee that all we need is available for our daily routines and necessities. Having so many connections and players increases its complexity and, therefore, its vulnerability. There are several possible causes to disrupt the good performance of supply chains, that can lead to either shortages, product alterations, or waste. COVID-19 pandemic was certainly one of the most unprecedent episodes due to its global effect comparable, by some authors, only to a world war.

In this chapter, an analysis of what can be done to better prepare companies and their chains to situations like this, as well as how can they respond and recover, was performed. Recommendations were then formulated according to what both researchers and consultancy experts have stated during 2020, divided in prevention, response and recovery.

Prevention actions are the most significant focus of this work since risk mitigation plays an important role and prepares contingency plans to set in motions as soon as the problem arrives. Resilience, agility, redundancy and digitalization are, perhaps, the most found words in literature as well as regionalization. In a world progressively more globalized with suppliers in one continent, manufacturers in another and constantly increasing consumers all over the world, reflection on this way of producing goods and trading has risen to the table, with this pandemic. Dependency on Asia, especially China, is being questioned and localizing processes, suppliers and distribution has been already pointed as beneficial to local communities, safer access to products and even better adaptation to their preferences and cultures.

Response actions corroborate that traditional models of management and business endanger flexibility and, thus, efficiency of supply chains during disruption events like COVID-19 lockdowns. Networked companies, less rigid hierarchies potentiate new ways of leading better adapted to cope with the velocity of changes.

Recovery actions are still difficult to tackle with rigour and certainty since, by the time of this study, a second wave of the pandemic is enduring in Europe and vaccines are not still being administrated. However, studies indicate to a re-evaluation of business structures and strategies based on actions already stated as prevention recommendations, granting a cyclic paradigm to a pandemic handling process like COVID-19.

Preparing the supply chain for disruptions, especially the pharmaceutical, cannot be done without bearing in mind social impacts and challenges, which is the topic developed in the next chapters, especially Chapter 6.

5. The pharmaceutical sector and the COVID-19 pandemic

The pharma industry has been affected by this pandemic, as many other sectors, having encountered many of the challenges faced by global supply chains, tackled in the previous topics. Being intensively related to healthcare services, this sector is of significant importance in this crisis, not only because a disruption in its supply chain can have serious consequences but also because the most decisive solution to this pandemic is to immunize people, achieved by the developing and producing a vaccine. In this chapter, a review on the impacts of the pandemic is again performed, in this case, focused on the pharma supply chain, emphasizing the new vaccines' development and supply process.

5.1. Impact of COVID-19 on the pharma supply chain and response actions

As mentioned in subsection 4.2.2. of this work, COVID-19 pandemic had several impacts due to the consequent lockdown and global restrictions imposed. Ayati *et al.* (2020) assessed the pharmaceutical market crisis during the first semester of 2020 looking to both their country (Iran) and the world's biggest economic blocks (the USA and the EU), identifying short-term and long-term implications. Demand changes, supply shortages, panic buying and stocking, regulation changes and communication shift to remote interactions and R&D process changes are pointed as short-term impacts while on the long-term approval delays, moving towards self-sufficiency, industry growth slow-down consumption trend changes emerge as probable issues. Each of these aspects is tackled in the following topics.

5.1.1. Demand changes and shortages

Firstly, the increased hospitalization due to COVID-19, especially in Intensive Care Units (ICU), has risen medical equipment demand, namely ventilators, as well as related medicines. Anti-COVID-19 potential drugs such as hydroxychloroquine and chloroquine were included in the FDA shortage list in February 2020, as well as typical prescribed medicines to patients with critical respiratory conditions such as pneumonia: antibiotics (azithromycin), cardiac failure therapies (dobutamine and dopamine), sedatives/painkillers (midazolam, fentanyl, propofol or dexmedetomidine) and anticoagulant (heparin) and lung airways opening medications (fluticasone and albuterol) (Ayati *et al*., 2020; FDA, 2020). Azithromycin and antivirals like ribavirin orders have tripled and fentanyl, midazolam and propofol have increased by 100%, 70% and 60% respectively (Cundell *et al.* 2020).

Simultaneously, lockdown restrictions (border closings and air cargo suspensions), as mention in the previous subsections of this work, disrupted production or delayed distribution causing shortages in basic non-COVID-19-related medicines used for hospital treatment of other diseases such as antibiotics and anaesthetics, as well as pharmacy/open access drugs. Then, panic buying, stockpiling and falsely increased orders ("shortage gaming") took over, creating generalized unpredictability in demand. An estimated overall 8,9% induced demand increase was verified in global pharma market, especially chronic disorders therapeutics (19,8% growth in cardiac therapy drugs and 18,2% in anti-diabetic drugs, in March 2020). In the USA, from 13th to the 21st of March 2020, asthma medications rose by 65% and type 2 diabetes medications increased by 25% (Ayati *et al*., 2020).

To respond to this shortages and demand shocks, regulatory adjustments play a decisive role as they can impose restrictions on exportations of pharmaceuticals and request pharma companies and wholesalers not to supply medicines beyond the usual demand (measure enforced by the German Federal Institute for Drugs and Medical Devices in March, for instance). Similarly, restricting the retail dispensing of essential medicines to a 30-day emergency supply, including for cash-paying customers, is appointed by Alexander & Qato (2020) as a strategy to reduce the probability of demand surges and drug shortages. Lengthening the expiration dates within safety standards to mitigate critical drug shortages was allowed by the FDA in February 2020, as well as flexibilizing importation processes to those seeking to take protective equipment into the USA, providing instructions to manufacturers on how to inform the USA Customs and Border Protection with specific advice on expedite regulatory clearance. Also, FDA allowed the emergency use of converted equipment (modified anaesthesia gas machines positive and pressure breathing devices) as ventilators.

Companies of other sectors started producing medical and protective equipment, thus helping to fill in the sudden demand of ventilators or masks. For example, Dyson (vacuum cleaner producer) designed a new ventilator in 10 days and received an order for ten thousand units from the UK government, while similarly General Motors made a partnership with Ventec Life Systems and Ford with GE Healthcare to produce ventilators (Benchoff, 2020). In Portugal, in April 2020, 30 companies in the textile sector had already started producing and estimated 1 million face masks a week with reusable fabric, according to the EU health and safety requirements, some exporting 90% to other EU countries (Pinto Miguel 2020).

Operational adjustments such as alterations in manufacturing schedules and additional shifts creation can contribute to ensuring essential drug products are not in short supply (Cundell *et al*. 2020).

To overcome transportation limitations, in order to expedite required goods and while reducing face-to-face contact, emergency licenses for medical equipment supplies issuing has been accelerated by sending them to online communication systems, receiving approval within one business day (Ayati *et al*., 2020), once more corroborating the facilitating role of digital communication.

5.1.2. Active Pharmaceutical Ingredients (API) dependency and manufacturing issues

As understood in the previous global supply chain disruption assessment, manufacturing facilities are concentrated in Asia and the pharma industry, namely generic drugs, is no exception, especially labour-intensive batch processes (Houlton 2020). China and India are now the biggest suppliers of raw-materials and the biggest producers of APIs supplying an estimated 80% of the chemicals used to make drugs sold in Europe. The majority of China's production plants is located in the eastern part of the country and is responsible for the production of small molecules, while the south focuses on biologics, where the Hubei province is located (with more than 40 FDA/EMA approved sites), the epicentre of the COVID-19 outbreak. Production was, then, reduced, leading to an export temporary restriction of 26 products (Alvaro *et al.*, 2020).

Apart from APIs, excipients are also an important part of the process. They are inactive substances that serve as vehicles (bulk capsules, tablets or other semi-finished forms), in which drugs are formulated. These are usually manufactured closer to their ultimate end market, although it is not uncommon for the

USA and the EU to import bulk products and even fully finished or packaged. Packaging and labelling are necessary for the distribution of drugs, which rely on components like resin-based bottles and films, stainless steel needles, cartons and other materials, all required to safely contain, transport and administer medicines. These components supply lines also suffer from national lockdowns (Jung, 2020).

Decentralization of manufacturing sites and redundancy creation aiming to achieve self-sufficiency of generic drugs on a long-term is being studied by the USA to reshoring the pharmaceutical supply chain. Gurvich & Hussain (2020) identify four steps to be taken to achieve this. Firstly, "new prior" knowledge is needed, conjugating existing prior knowledge from when the original drug was approved with the new technologies and methodologies, identifying gaps, to stimulate efficient development and manufacturing of generic drug products. Secondly, advanced and innovative manufacturing tools, such as continuous manufacturing processes (tackled in Chapter 3 of this work) is claimed to offset the costs of low-waged labour in developing countries, where cost savings due to cheap labour often translate into poor product quality. Moreover, a highly skilled and highly productive workforce can operate advanced manufacturing lines. Then, to acquire advanced knowledge and innovative methodologies, engaging with the academic and engineering community is fundamental or even creating new focused technological training/educational centres, specifically focused on the design and development of materials, products and continuous manufacturing processes. Finally, creating a drug quality index to enable people to access and appreciate information about their medicines, can facilitate acceptance of these new home-produced generics by the general public, reinforcing confidence.

Once self-sufficiency is achieved, regulatory intervention can, once more, have an important contribution since APIs may be temporarily restricted for domestic consumption, like the India Government issued this year to ensure its internal supply ability (Ayati *et al*., 2020).

5.1.3. Research and development issues

On the short-term, it is difficult for researchers to keep up with the immediate on-going evolution of an outbreak of a new virus pandemic. As seen in this work, a new product development involves discovery activities, pre-clinical tests, clinical trials, approval and product launch and the average time between discovery and launch is almost 15 years, the process stopping if something fails in one of these phases.

The academic community all over the world put their immediate efforts in finding adequate medicines to treat the infected people and off-label drugs started to be administrated in hospitals. Off-label drugs are medication for COVID-19 not yet regulated that physicians use when the condition is serious and there is evidence of potential benefit, not existing approved therapy, with the consent of patients. FDA, in February 2020, created a new policy for certain laboratories that develop and begin to use validated COVID-19 diagnostics before the FDA has completed reviewing their request (Cundell *et al*., 2020).

Conducting biomedical research on off-label medications needs considering ethical and scientific principles, guidelines and approval even in disasters such as this pandemic (Shojaei & Salari, 2020). The authors observed, however, lack of information towards patients, administrating these off-label medications with a treatment-investigation perspective, leading to the results publishing as a research article, calling this pseudo-research. Ethical issues are naturally raised and from the research point of

view, since there is no proposal, the sample size is limited, the validity of the method is under question and the results are of little value. Also, the researcher is the main healthcare provider, possibly being biased because he/she would like to obtain positive results.

COVID-19 redirected lots of time and investment spending for the development of medicines or vaccines, as well as laboratories' resources towards testing, for example in universities putting other projects in standby. In the University of Lisbon, five faculties (FCUL, IST, FFUL, ISA, FMUL/IMM) started performing tests in April creating tasks forces with their biosciences and chemical researchers and lab technicians, also implementing an internal staff and student testing programme (600 daily tests) in October 2020 (FCUL, 2020; FFUL, 2020; IST, 2020; Público, 2020a).

Redirecting science attention from other research projects as well as the regulatory institutions attention to COVID-19, caused delays in approvals for non-COVID related pharmaceuticals, due to several month of application review postponements and clinical trials delays (Ayati *et al*., 2020).

5.1.4. Market trends changes

The pandemic caused an overall economical slow-down for many countries and the pharma industry, although being crucial in this crisis a previously less sensitive to slowing economic growth, is not expected to strive unaffected.

A growth slow-down is predicted due to the entry of newer medications stimulated by a spiked research effort and priority change, possibly obsoleting some existing ones (Ayati *et al*., 2020). New technologies may shift the overall pharma industry such as, for instance, mRNA technology that has rapidly been developed, since many of the COVID-19 vaccine candidates are mRNA-based. Pharma industry may look for new ways to increase repurpose and increase existing capacity to accommodate more advanced processes. Adoption of continuous manufacturing will also change the configuration of manufacturing processes, since it requires less space, less upfront investment and creates flexibility in potentially enabling more local production (Mckinsey & Company, 2020b).

Market evolution will be also influenced by the referred reshoring of the pharma industry since it will require infrastructure rebuild investment and it will not be an overnight process. Badrot (2020) predicts a 10-year long journey to re-emerge the USA, European and Japanese finance and infrastructure capacity to bring back pharma manufacturing and face the political challenges since these types of facilities are often "misunderstood and unwelcomed by residents". Once again, government intervention can be decisive to accelerate this process if the right incentives and given to pharma companies.

Technology advancement is not only expected to change the pharma industry economic performance but also interactions and consumption habits, based on digital tools, with positive impacts. During the pandemic, pharmacies (and supermarkets) were the few establishments that remained opened, as they do not offer home-delivery services. In the USA, only 10% of retail prescriptions were mail-ordered in 2018, confirming that the increasing in online ordering systems is necessary (Alexander & Qato, 2020).

Social behaviour changes and trends, for example, tele-health, as well as their impact in the pharma supply chain will be tackled in Chapter 6 of this work.

5.1.5. Pharma supply chain pain-points and response actions overview

Following the previous topics review, the identified pain-points of the pharmaceutical supply chain during the COVID-19 pandemic and proposed response actions are summarised in Table 5.1.

Table 5.1. – Pharma supply chain pain-points and response actions, during a pandemic situation like COVID-19.

Type	Pain points	Actions
Research and development	▶ Sudden new disease appearance ▶ New product development long duration ▶ Non-COVID-19 related research projects delayed ▶ Non-COVID-19 related research projects investment redirected ▶ Universities laboratory facilities conversion into Testing Centres	▶ Fast-track regulatory approvals ▶ Building a partnership network between public-private and public-public institutions ▶ Science investment raise
Suppliers and Manufacturing	▶ Centralized raw-materials suppliers in Asia ▶ Centralized production in Asia (APIs and excipients) ▶ Movement restrictions of raw-materials, APIs, excipients, packaging materials drugs due to lockdowns ▶ Labour task forces stopped due to social distancing	▶ Raw-materials suppliers redundancy ▶ Online systems and data exchange to improve transparency ▶ Reshoring manufacturing facilities ▶ Invest in innovative processes to balance higher labour costs (USA/EU/Japan) ▶ Involve universities and create new educational programmes ▶ Schedule adjustments and additional shifts creation to ensure production
Distribution	▶ Movement restrictions of finished drugs due to lockdowns ▶ Limited transparency on stock levels and demand ▶ Imprecise product information in warehouses ▶ Unsuitable warehouses for life sciences products ▶ Lack of expertise to handling products ▶ Frequent import regulation changes and country variations	▶ Flexibilizing importation processes ▶ Emergency transportation licenses issuing ▶ Online systems and data exchange to improve visibility ▶ Workers training ▶ Defining common customs policies (example: EU)
Healthcare Providers and Consumers	▶ Increase demand of respiratory conditions medication ▶ Panic buying (in pharmacies) ▶ Falsely induced demand (hospitals) ▶ Lack of confidence in new pharmaceuticals ▶ Interaction limitations between healthcare providers and patients	▶ Lengthening expiration dates ▶ Government regulation on ordering quantity by consumer/hospital ▶ Government temporary restriction on exportations ▶ Drug quality index creation for generics ▶ Digitalization of ordering processes and health services

5.2. The pharma industry solutions for the pandemic and their challenges

Developing effective treatments and vaccines is, naturally, the most important contribution of the pharma industry to deal with this pandemic. Until the beginning of December, EMA had 2 authorized drugs, 4 vaccines undergoing evaluation and 71 other medications (both antivirals and vaccines) in research and development stage which have already received some advice from the agency (EMA, 2020).

5.2.1. Treatments

EMA's authorised medicines are remdesivir, an antiviral, and dexamethasone, a corticosteroid.

Dexamethasone is used for its anti-inflammatory and immunosuppressant effects and has been tested in hospitalized patients with COVID-19 in the UK's national clinical trial showing a mortality reduction by about one third, and for patients requiring only oxygen, mortality was cut by about one fifth (WHO, 2020a). This drug is not new, so good news come with this medicine since it already has a robust supply chain, has been on the market for nearly 60 years and, at this point, is already a generic. Generic drugs are not stuck with patents, meaning they are easier to produce freely across the world, ensuring redundancy and preventing shortages (Foley, 2020).

The same, however, cannot be said of remdesivir, since it is under research, proven to be a broad-spectrum antiviral agent with *in vitro* activity against multiple RNA viruses, including Ebola. It shows RNA polymerase inhibitory activity against SARS-CoV-1 and the Middle East respiratory syndrome (MERS-CoV) having also the ability to inhibit SARS-CoV-2 *in vitro*, still lacking approval for clinical use. (Beigel *et al*., 2020; Marto & Monteiro, 2020). The production is challenging since it is a long linear chemical synthesis process whose scale-up process can take up to 9 months to complete. Firstly, procurement of raw materials is a significant part of the process since chemicals are sourced from several different countries, including the USA, Canada, Japan, China and the EU (namely Portugal), and are not typically stocked in large quantities. Production of raw materials and conversation into API takes 150 days because raw materials must be processed into multiple intermediaries, one step at a time, each taking almost a week. Additional 28 days are required to manufacture the final product. Being an intravenous treatment, it has to be produced in sterile conditions, which limit the number of organizations capable of manufacturing it (Gilead, 2020). To supplement the worldwide demand, Gilead is considering granting licenses to manufacturers in several countries, such as India, in order to supply the developing parts of the world (Stat News, 2020). Until October 2020, Gilead had already shipped more than 20 thousand doses to the EU, which could treat around 3400 patients (FiercePharma, 2020).

5.2.2. Vaccines

Immunization is, definitely, the most effective way of fighting an infectious disease, since vaccines stimulate our natural defences systems to build protection, creating memory in our immune system, before an infection. Twenty life-threatening diseases are currently prevented with vaccines, saving 2-3 million deaths per year from infections like influenza, tetanus and diphtheria, for instance (WHO, 2020b).

5.2.2.1. Development overview

Developing a vaccine starts at the laboratory with the study of potential agents that will have effect on the target disease, considering its pharmaceutical quality. Then, non-clinical trials are performed to assess the immune response triggered of the discovered agent both *in vitro* and *in vivo* (animals), *i.e.*, if it works to prevent the infection. Clinical trials start afterwards, in humans, comprehending three phases (EMA, 2020):

- **Phase I**: Human pharmacology studies (20 to 100 healthy volunteers), to confirm if the medicine has the expected behaviour based on the previous laboratory tests.
- **Phase II**: Therapeutic exploratory studies (several hundred volunteers, split into different age groups), to identify the best dose needed and shown side effects.
- **Phase III:** Clinical efficacy and safety studies (thousands of volunteers) to verify how efficacious the vaccine is, comparing with the placebo treatment as well as the uncommon side effects.

Once these stages are completed, regulatory institutions can decide on the approval of the vaccine, which then goes for manufacturing (to which a production scaled-up process has to be developed). Figure 5.1., elaborated by EMA, synthesises all these phases (EMA, 2020).

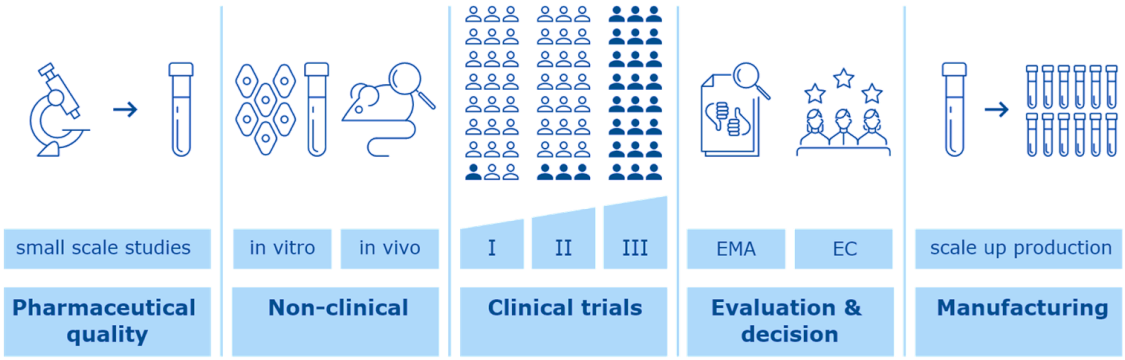

Figure 5.1. – EMA's overview of the typical development stages of a vaccine.

Due to the unprecedent gravity of this pandemic, full attention was put to the research, development and testing of viable vaccines to start administrating as soon as possible. Combined phases of trials, meaning that two stages take place simultaneously, were performed in order to accelerate the process, as EMA explains in Figures 5.2. and 5.3.

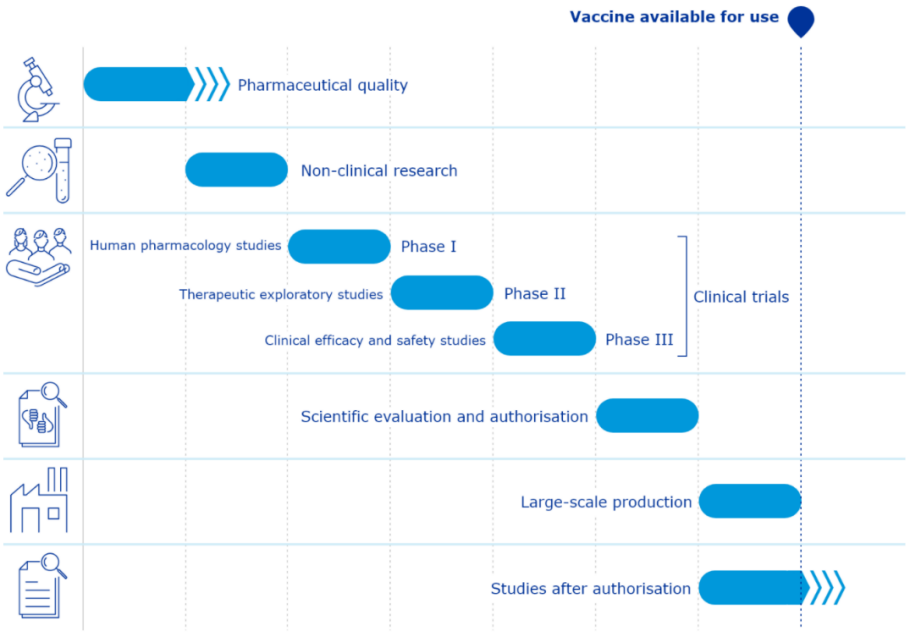

Figure 5.2. – Indicative timelines for standard vaccines (EMA, 2020).

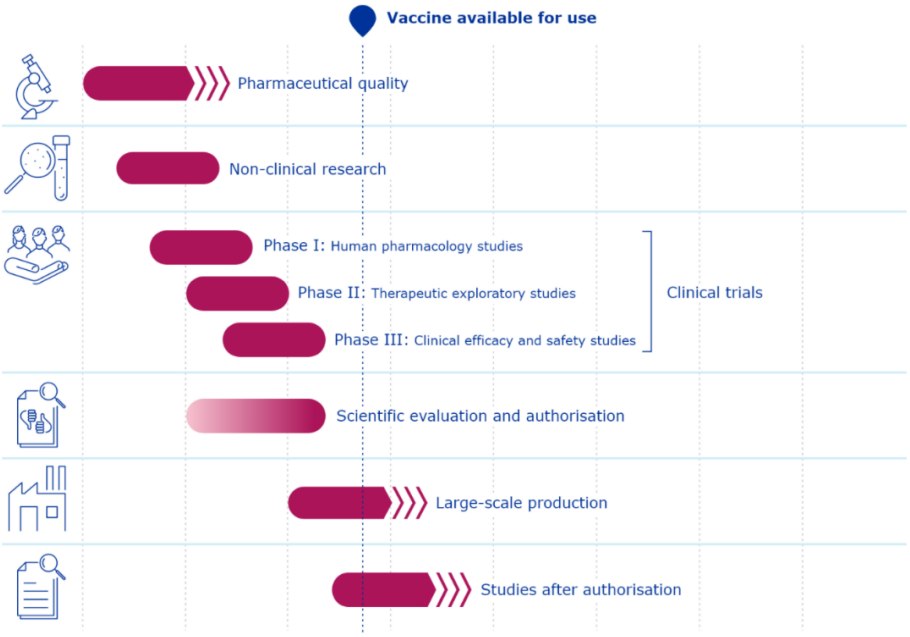

Figure 5.3. – Indicative timelines for the COVID-19 vaccines (EMA, 2020).

Fast track development was performed, using existing vaccines' knowledge and early scientific advice from regulators (already identified in Chapter 3, prior to this pandemic, as a pharma development enabler), free of charge, featuring no pre-specified submissions deadlines, reduced review time from 70 days to 20 days and flexibility on the type/extent of documentation.

Given that vaccine development has taken, historically 10 to 15 years, having one being administrated in one year since early research stage is unprecedent (IFPMA, 2019).

5.2.2.2. Types of vaccines proposed

There are, currently, four categories of vaccines in phases I to III of clinical trials, according to GAVI (2020):

- **Whole virus vaccines**: created from inactivated (can't replicate), destroyed by heat, chemicals or radiation or attenuated coronaviruses (weakened but still able to replicate).
- **Protein-based vaccines**: which contain fragments of proteins (or whole proteins), including Virus Like Particles (VLP).
- **Genetic material vaccines**: containing either RNA or DNA that instruct cells to produce the antigen and then trigger the immune response.
- **Viral vector vaccines**: also containing genetic material to trigger an immune response that is carried by a different virus (mainly adenovirus), mimicking a natural viral infection.

Each one of these types of vaccines have pros and cons. While whole attenuated virus vaccines can trigger a strong immune response, since they provide a very realistic infection scenario, they have a risk of triggering the disease and are not suited for immunosuppressed people. On the other hand, protein-based vaccines and viral vectors are very safe since it is not the virus that is entering the system, however, might need adjuvants to boost the immune response. Viral vectors are difficult to manufacture and protein vaccines take longer to develop since the best antigen combination must be found. Genetic

vaccines (RNA-based) have a strong immune response and are easily manufactured however have never been licensed to humans and require freezing costly storage conditions (GAVI, 2020). GAVI's review on the advantages and disadvantages of the four types of vaccines is presented in Table 5.2.

Table 5.2. – Advantages and disadvantages of the four categories of vaccines against COVID-19 (GAVI, 2020).

Type	Advantages	Disadvantages
Whole Virus	*Attenuated Virus Vaccines* ▶ Well-established technology ▶ Strong immune response ▶ Immune response involves B cells and T cells ▶ Relatively simple to manufacture *Inactivated Virus Vaccines* ▶ Well-established technology ▶ Suitable for people with compromised immune systems ▶ No live components, so no risk of triggering the disease ▶ Relatively simple to manufacture ▶ Relatively stable	*Attenuated vaccines* ▶ Unsuitable for people with compromised immune systems ▶ May trigger disease in very rare cases ▶ Relatively temperature sensitive, careful storage necessary *Inactivated Virus Vaccines* ▶ Booster shots may be required
Protein-based	▶ Well-established technology ▶ Suitable for people with compromised immune systems ▶ No live components, so no risk of triggering the disease ▶ Relatively stable	▶ Relatively complex to manufacture ▶ Adjuvants and booster shots may be required ▶ Determining the best antigen combinations takes time
Genetic (DNA/RNA)	▶ Immune response involves B cells and T cells ▶ No live components, so no risk of triggering the disease ▶ Relatively simple to manufacture	▶ Never licensed in humans ▶ Booster shots may be required ▶ RNA vaccines require ultra-cold storage
Viral Vectors	▶ Well-established technology ▶ Strong immune response ▶ Immune response involves B cells and T cells	▶ Previous exposure to the vector could reduce effectiveness ▶ Relatively complex to manufacture

Currently, there are more than 50 vaccine candidates already in clinical trials stage of development from which 27 have reached or passed Phase 2 of the clinical trials: 5 whole-virus-based, 9 protein-based, 9 genetic-based and 4 viral vector based (The New York Times, 2020). Information of the leading vaccines including origin, efficacy, and storage conditions is detailed in Table 1 of Annex C. EMA's 4 under evaluation in the beginning of December were developed by Pfizer (RNA based), Moderna (RNA based), AstraZeneca (viral vector) and Johnson & Johnson (viral vector) (Table 5.3).

Table 5.3. – EMA's authorised vaccines, on December 12th.

Name	Developer	Country	Efficacy	Dose	Storage
BNT162b2	Pfizer + Biontech	USA + Germany	95%	2 doses 3 weeks apart	-70ºC
mRNA-1273	Moderna	USA	94,5%	2 doses 4 weeks apart	-20ºC
AZD1222	Univ. Oxford + AstraZeneca	UK	90%	2 doses 4 weeks apart	4ºC
Ad26.COV2.S	Johnson & Johnson	USA	*unknown*	1 dose	4ºC

5.2.2.3. Estimated production

Pfizer and BioNTech declared to produce 50 million doses until the end of 2020 and 1,3 billion doses in 2021, while Moderna guarantees 20 million doses in 2020 and 1 billion doses in 2021 (RTP, 2020).

In September 2020, DHL elaborated a report based on expert interviews from DHL and Mckinsey, noting the announced production capacities for each group of vaccines for 2021, summarized in Table 5.4.

Table 5.4. – Announced production capacities for 2021 (DHL Research and Innovation, 2020).

Type	**Production** (million doses)
Protein subunit	2 000
VLPs	100
Inactivated virus	200 – 220
DNA	1
Viral vectors	4 000
RNA	3 300
Total	9 600

In 2021, is it predicted almost 9,6 billion doses, which can vaccinate around 4,8 billion people (rough approximation), considering that several of the proposed vaccines must be taken in 2 doses, thus, not enough to vaccinate the world's population (7,8 billion) next year.

5.2.2.4. Distribution

Required storage temperature is the main challenge in what concerns distribution of COVID-19 vaccines, especially the RNA based ones. Pfizer's vaccine demands the coolest conditions, enduring in -70ºC for 6 months, and 5 days after is transferred to a refrigerator, the most common equipment in hospitals and health facilities, at usually 2ºC to 8ºC. Moderna's vaccine holds up to 6 months at -20ºC and 30 days in a refrigerator, and AstraZeneca's vaccine can endure in a refrigerator for up to 6 months (Aliakbarian, 2020).

Logistics requirements turn the quick vaccine supply chain challenging, since cooling equipment is needed in intercontinental distribution, warehouses, downstream distribution and use points. Air freight is likely to be the main transportation mode due to the urgency of the pandemic, with estimated 15 thousand flights, in 200 thousand pallet shippers to ensure global coverage (DHL Research and Innovation, 2020). Lockdowns have grounded fleets and downsized airline networks so government intervention might help to recover capacity and bring back workers.

Dry ice (frozen CO_2) has already been proposed as a solution to maintain low temperatures such as -78ºC and is being incorporated in cooler boxes to transport these vaccines. Dry ice supply is not expected to be a bottleneck for vaccine distribution, although, packaging equipment needs and maximum-allowed quantities of dry ice on airplanes might complicate this process. Dry ice is carbon dioxide that sublimes at room temperature, displacing breathable oxygen in the cabin, however, due to the emergency, the USA Federal Aviation Administration has allowed United Airlines to carry five times more dry ice than the allowed quantity to accommodate 1 million doses in a Boeing 777 (Schaper, 2020). Ensuring constant temperature management to avoid product damage is more complex for a set of boxes than for a single pallet shipper, and physical handling of the ultra-deep-frozen shipments needs adequate equipment (gloves) to avoid injury. Thus, information and training has to be provided to the network's workers (DHL Research and Innovation, 2020).

Distribution network design depends on temperature requirements, transport volumes and distances, warehouses capacity, costs and packaging equipment availability. DHL defines three possible archetypes of end-to-end logistics solutions for COVID-19 vaccine distribution:

- **Direct shipment**: through which vaccines go directly from fill-finish point to the final destination, by the fastest and most direct way via air or truck.
- **Local cross-docking**: carrying the vaccine to the destination country, where it is labelled, cross-docked and transported, via truck, to end destinations.
- **Local warehousing**: using warehouses to store vaccines in pallets which then are distributed for last mile delivery, in small parcels, according to each region needs.

Direct shipment is the fastest option and might be suitable for the initial global distribution, enabling quick access to the vaccine to more affected regions (big metropolitan areas), as well as areas near the manufacturing point. This can be an option for RNA vaccines such as Pfizer's or Moderna's, since it reduces time from manufacturing to administration, dispensing new costly cooling equipment installation. Local cross-docking minimizes cross-borders shipping costs since the product enters the country through one way and is internally distributed. This can be viable in small countries like Portugal but difficult at the EU scale. Local warehousing is a promising option for vaccines that do not require stringent temperature requirements such as AstraZeneca's vaccine, also permitting to create some safety stock.

Pfizer's conservation cool box is equipped with GPS-enabled thermal sensors controlled by a control tower to track the location and temperature of each vaccine shipment, allowing Pfizer to act before unwanted deviations occur and monitor the integrity of their product (Pfizer, 2020), an example of a digital communication tool to provide data and improve visibility and transparency along the chain.

Cold-chain logistic equipment is already proving to be scarce in developing countries which are also in warm-regions of the globe: Africa, South America and some countries in Asia. Dry-ice appears as a solution, although its production is centralized in developed countries, which can pose a challenge if refilling is required after 3-5 days (DHL Research and Innovation, 2020).

Sustainability along the chain must not be neglected, especially when choosing packaging materials (reusable), transportation modes and reverse logistics to collect waste. Innovative packaging, recycling opportunities and waste management shall be considered whether return logistics are not possible in all regions. A good research opportunity emerges for environmentally friendly solutions in a global crisis scenario argued to be the biggest mobilizing occurrence since WWII.

A phased vaccination plan is then required, to define priority groups and ensure that the most vulnerable have access to a vaccine. Confidence in the vaccine is also indispensable for the success of a population immunization process where government, media and community involvement are decisive. These topics are tackled in Chapter 6.

5.3. Chapter conclusions

In this chapter, the impacts of the COVID-19 pandemic assessment are particularized for the pharmaceutical sector and supply chain. Drug shortages and the dependency of major economies such as the USA and the EU on Asia for the production of APIs are two major tackled aspects, as well as actions taken or recommended to counteract these challenges. Reshoring manufacturing capacity, regaining knowledge, and using off-label medicines (such as remdesivir) during the outbreak are suggested measures. In addition, reacting to a pandemic, for the pharma industry, is not an easy and fast task since new medicines need to be developed, to which research is a critical and slow step.

An overview on the pharma contributions for this pandemic is done, in this chapter, focusing on the vaccines' development process and its challenges. Research and regulatory approval were the first critical aspects of this process and then ensuring manufacturing and distribution capacity on an unprecedent scale. Four types of vaccines are in development, from which one of them has never been licenced in humans but has been the first to have completed phase 3 of the clinical trials successfully (RNA vaccine from Pfizer/BioNTech). Scale-up and production started before the approval of the new medicine, due to the overall pressure and regulatory agencies collaboration and accelerated advisory. Distribution of the developing vaccines faces harsh and different cold temperature requirements and infrastructure mobilization, for which different strategies are being developed to ensure that the biggest logistics challenge, as many already refer to, is successful.

The social implications of the pandemic in global and pharma supply chains are tackled in the next chapter.

6. Social concerns in the pharma supply chain in a pandemic

This chapter starts with a review on the social challenges faced by the pharmaceutical supply chain, during the outbreak of the COVID-19 pandemic. Then, a set of GRI standards disclosures is selected to be prioritized in the 2020 companies' sustainability reports, with four additional suggested disclosures. Finally, the concept of social resilience is defined based on four pillars leading to a proposed framework aiming to help pharma supply chain stakeholders improving and ensuring its good social performance.

6.1. Social challenges during the pandemic

Lockdowns, postponements and social distance challenged the economic activity, imposing constraints on industries and their supply chains, with several social impacts. From a pharmaceutical organization/supply chain internal angle, literature highlights social concerns related to the workforce such as remote working, unemployment and layoff, training and support, as well as management practices. Additionally, but from an external point of view, aspects such as healthcare system (costumers) interaction with manufacturers/wholesalers, consumers interaction with healthcare system and, particularly concerning the vaccine, confidence and public perception are discussed. Equity in access to pharmaceuticals is an essential aspect to which governmental influence can be the main contributor.

6.1.1. Organizational and management issues

Creating the right organizational and management environmental is fundamental for a good and rapid response when a disruption occurs, with minimized social impact. An adaptable and flexible management culture, in which hierarchies are less rigid, enables the launch of new temporary cross-functional teams fit to tackle complex situations and propose new solutions (Mckinsey & Company, 2020a). Sharing leadership, delegating activities and certain jurisdictions to specific members of an organization, when managers don't possess the expertise, might be necessary for crisis taskforce teams to succeed (Obrenovic *et al*., 2020).

Also, new leaders are able to emerge when a new and unknown situation occurs, which are team members not appointed or elected, who step up as leaders over time due to their group interactions (Gerpott *et al*., 2019). According to Obrenovic *et al*. (2020), emergent leaders are characterized as "highly trained and skilled individuals with the capacity and competency to take on different responsibilities, assignments, and initiatives, able to cope with stressful situations and react rapidly by combining all the relevant information from all the organizational key nodes and transforming them into the most optimal actions." As such, they are the perfect individuals to cope with a disruptive situation such as pandemic.

A certain level of informality is common in these leaders, allowing them to engage their organization, looking for team brainstorming, exchange of perspectives and enabling a more effective communication (Obrenovic *et al*., 2020).

Reducing two to four layers of hierarchy is advised to easier communication within the organization, while authorization and approval chain of command gets also simplified, fastening decision making. Eliminating some of the usual internal reports and long meetings can also save time to use in urgent work, particularly important in crisis management (Mckinsey & Company, 2020a).

Having a well-prepared workforce requires investment in training and educational programmes, which empower workers to assume positions they don't usually have in disruption situations. Furthermore, demand labour is shifting, new skills are needed especially related to new digital and technological knowledge (Mckinsey & Company, 2020a; Obrenovic *et al*., 2020)

6.1.2. Workforce alterations

Social distancing and lockdowns pushed a significant part of companies' workforces' home, implementing remote work routines. According to Mckinsey & Company (2020), work from home increased 50% from April to May 2020, in the USA, and most companies achieved a successful transition. A pandemic prior inquiry, performed by Buffer (2020) on 3500 remote workers in various sectors around the world, shows an impressive overall satisfaction with this work regime whether it is a considerable amount of time, but not all of the time working remotely. They highlight the ability to have a flexible schedule and workplace and avoiding commuting as its main benefits (details in Table 6.1.).

However, challenges have been faced and it is already realized that a completely remote work regime may not to be a long-term solution, since there are some obstacles of communication. Some processes are not designed for virtual modes such as recruiting, welcoming new employees and the office/company own culture gets faded. Informal and organic interactions, that promote teambuilding and empathy are much more difficult, since non-verbal and emotional cues are harder to read when virtual. Consequently, managers find difficult to know what their teams are doing or feeling in a virtual basis, although they may be successful leaders in person. The Buffer (2020) study, also shows struggles faced by remote workers stating that, besides the communication challenges, psychological well-being can be affected, mentioning loneliness, inability to unplug and motivation issues (Table 6.1.).

Table 6.1. – Benefits and struggles of remote work, reported by 3 500 workers inquired by Buffer in February 2020, from more than 16 countries and 14 different industry sectors.

Benefits	Struggles
• Ability to have a flexible schedule • Flexibility to work from anywhere (coffee shops, coworking spaces, libraries, etc), especially from home • Not having to commute • Ability to spend time with family	• Collaboration and communication • Loneliness • Not being able to unplug • Distractions at home • Being in a different time zone than teammates • Staying motivated • Taking vacation time • Finding reliable Wi-Fi

Hybrid solutions (remote and in person) seem to be the common option within organizations, so re-evaluating the workforce operation is expected to be a key focus for most industries, where

pharmaceutical operations will be no exception. Changes in design and operating models can result in a redistribution of talent as well as reskilling, with the adoption of digital and analytics tools and automation. Pharmaceutical-operations organizations may need workers that can programme, operate, and interpret data (Mckinsey & Company, 2020b). Laboratory positions, related to research and development, are the most difficult ones to transition to remote work, so it is expected to continue in person work, while human resources, finance, marketing and supporting staff shall continue with home working periods.

On the medium/long-term, although layoffs were applied during the first months of the pandemic, an employee increase in the pharma sector might be expected since healthcare demand is increasing (Nair, 2020), as well as delocalization of the workforce if North American and European pharmaceuticals choose to reshore their manufacturing capacity.

6.1.3. Industry – healthcare system interactions

Contact restrictions posed challenges to the interactions between the upstream of the supply chain (manufacturers and wholesalers), the customers (hospitals, health care practitioners and pharmacies) and, ultimately, the consumers (patients).

When a new medicine is launched, companies need to address health practitioners in order to provide information on the innovative aspects or effects of their new products, as well as advantages over existing therapies. This pandemic delayed several non-urgent treatments and redirected a significant number of health practitioners to COVID-19 patients care, causing an accumulation of work. Physicians have scarce spare time and are, thus, less receptive to new products launch, conference attending and face-to-face engagement. Although it has not had a significant effect on new active substance launches in the first half of 2020, it is expected to have impact, so pharma companies should adjust healthcare practitioner (HCP) engagement teams to be more customer centric, as well as providing remote digital communication tools for HCP and real-time data access (IQVIA, 2020). Long-term economic crisis is expected to influence healthcare budgets, thus, requiring more product evidence and pharma services for HCPs.

6.1.4. Healthcare system / pharmacies – patient interactions

Patients had also less contact with healthcare providers as a result of appointment postponements during lockdowns. A survey mentioned in an IQVIA webinar in Germany, France, Italy, Spain and the UK to physicians of 5 medical specialities, showed that around 30% of patients did not receive treatment they should have, due to no show or delays. Accumulation of patients after a lockdown period result not only from reduced visits but also from diagnosis or treatment initiation delays, which can worsen the patient's condition and disturb chronic diseases therapeutics. In addition, low patient awareness on unreported conditions (diabetes, chronic kidney disease) and low involvement in treatment decision process intensify with the current pandemic. IQVIA's webinar proposes patient support programmes, by pharma companies, to free physicians of some medicine related advice.

Tele-health surges to counteract the inability to have medical appointments, however it does not solve every problem, since it doesn't allow physicians to examine patients and is critical with less digital users, such as elder people.

Pharmacies can play an important role since they can be the local support for these patients, particularly in rural areas, ensuring some assistance, since they were (alongside supermarkets) the only exceptions to lockdowns' policies (McKesson, 2020). Aside from physicians, changes in pharmacists practises due to the pandemic have been identified, to guarantee and support patients care, especially in vulnerable populations, such as patient counselling, as well as becoming a hub of information on COVID-19 and other conditions (Hayden & Parkin, 2020). In some countries, pharmacists can prescribe medication (UK), perform treatments and administrate vaccines.

However, time spent at pharmacy encounters got shortened and opening hours got reduced, pushing information to be provided via written documentation (ex: flyers, treatment guides) and causing lack of privacy, due to impossibility to use consultation rooms, as appointed by patients in a study in The Netherlands' pharmacies (Koster *et al.,* 2020).

Online communication tools and monitoring technology are once more crucial to improve tele-health appointments and follow-up, as well as remote delivery when it comes to pharmacy ordinary orderings, contributing to unnecessary physical interactions' reduction.

6.1.5. Medicines access equity

Equity is, perhaps, one of the most complex social challenges faced, since companies are not the only players that influence the equitable access of products, particularly medicines. Political decisions have great impact in this issue, especially in times of emergency and crisis, as witnessed during COVID-19.

When it comes to medicine shortages, different attitudes can be seen as Sheffi (2020) points: favouring order shipping according to the importance of each customer, treat everyone equally or taking care of the vulnerable. Treating everyone equally is an option that can be honourable but easily gambled, since customers might inflate orders. Thus, some companies have allocated products based on pre-disruption historical order volumes, as well as fixed-volume orderings (commonly seen in the end of supply chain, limiting shoppers in supermarkets to maximum fixed amount of some products per bill).

Helping the most vulnerable is considered especially when quantities required to ensure a customer survival are not large and there is great dependence from that customer on a supplier/manufacturer. For example, Verifone, a credit card processing equipment producer, wasn't a large customer for the electric motors but heavily dependent on these motors. The company got hardly hit by Thailand floods in 2011, so suppliers fulfilled its orders. During COVID-19, some retailers devised special ways to help vulnerable customers, for example, creating early morning shopping hours for elderly people to get to restocked shelves first (Sheffi, 2020).

6.1.5.1. COVID-19 vaccine global access

COVID-19 vaccines pose new challenges since it is the first vaccination mobilization of this dimension in the world. As the most expected effective way of dealing with this pandemic, governments are unlocking funds to buy vaccines for their populations so there has been already some discussion about the disparity of vaccine ordering between western developed countries and African, south American and Asian countries. On the 23rd November 2020, there had already been ordered enough vaccines for the whole population, however some countries such as Canada (601%), Australia (267%), the UK (290%) or the USA (168%) and the EU (160%) bought more than the required doses to vaccinate 100% of their populations, expecting to order additional doses (Público, 2020b) (Figure 6.1.).

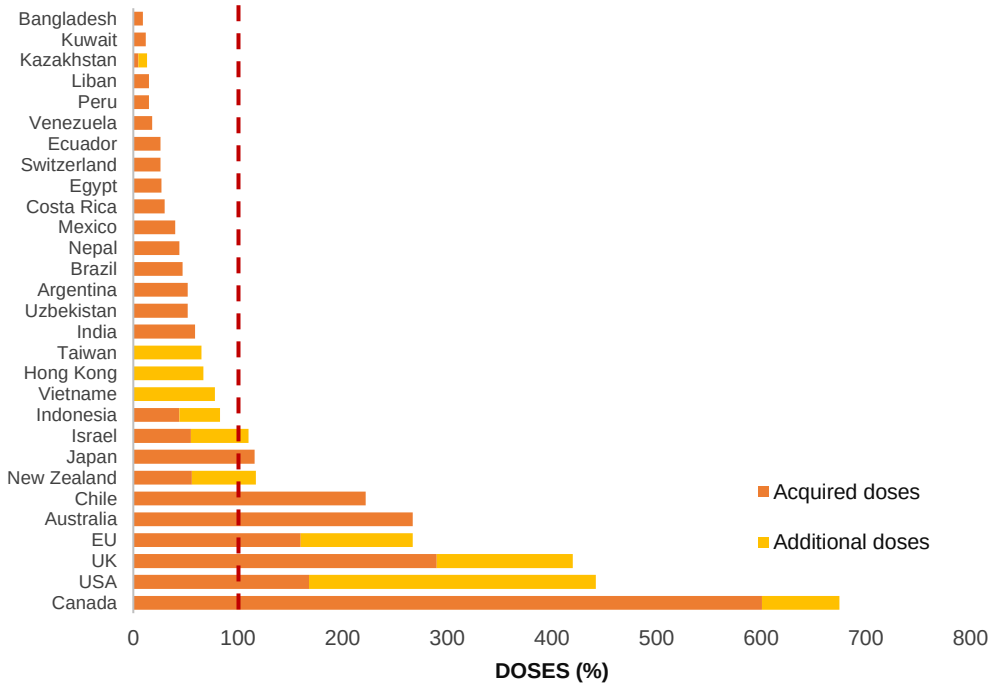

Figure 6.1. – Population vaccination capacity in terms of ordered doses, already acquired (orange) and predicted additional doses (yellow), according to an analysis performed by Público, last updated on the 23rd November 2020.

To vaccinate Africa, 1500 million doses would be needed, a number very close to what the EU has already bought, although its population rounds the 450 million, less than half African's inhabitants. It is clear that richest countries/economic blocs will have greater and faster access to the COVID-19 vaccines due to the agreements and purchases they have been doing with pharma companies.

However, in the EU, six contracts have been approved (AstraZeneca, BioNTech/Pfizer, Johnson & Johnson, Sanofi, CureVac and Moderna) by the European Commission, alongside a vaccination strategy based on equal access to all member-states (proportionally to their population) with a simultaneous quick-off (European Commission, 2020a). The European Parliament has also stated that a global approach is needed, rejecting "vaccine nationalism" as the virus does not respect borders and claiming that the "EU has a leading role to play in facilitating equal access to vaccines across the world" (European Parliament, 2020). The Commission has, jointly with the WHO and the French Government, founded COVAX, an initiative to accelerate vaccine development and promote equitable access, led by

WHO and GAVI, integrated in the “Access to COVID-19 Tools Accelerator” collaboration. COVAX ensures vaccines for at least 20% of all countries’ populations and delivery as soon as they are available. The EU has already contributed with 400 million euros to the COVAX Facility, an insurance mechanism to reduce risk for manufacturers that are investing without assured demand, and for countries, concerned about not being able to provide a viable vaccine, planning to have delivered two billion doses by the end of 2021 (European Commission, 2020b).

Criticism emerges when the powerful countries such as the USA and Russia haven’t contributed to the COVAX yet and when key contributors such as the EU have done huge bilateral deals with pharmaceutical companies: “money can't buy vaccines that have already been sold” (CNN, 2020) and “lots of verbal support but so far limited concrete financial commitments” (Torreele, 2020).

Vaccines are being developed by pharma companies, some in collaboration with universities or research laboratories, which means intellectual property is also an inevitable topic when vaccines get the needed approval and have to be produced. Since the beginning of COVID-19 pandemic, influential world leaders such as the UN Secretary-General António Guterres and the European Commission President Ursula von der Leyen alongside politicians and academics all over the world have argued that the pandemic’s exceptional context and impact gives grounds for considering the COVID-19 vaccines the ‘people’s vaccines’, or ‘global public goods’, or ‘global health commons’, although, not yet followed with consequent actions (Torreele, 2020).

India and South Africa have means and capacity to produce vaccines and other medicines, having presented a proposal to the World Trade Organization for the suspension of intellectual property rights in order to enable faster access to the vaccines worldwide. This proposal got the support of Mozambique and Pakistan and was discussed already in two meetings (10th and 17th December) but decisions were delayed, following on the opposition of richest countries (Público, 2020b; The East African, 2020).

6.1.5.2. COVID-19 vaccination in Portugal

On a national dimension, a quick assessment to the Portuguese vaccination strategy (information available in December 2021) is performed here to overview the access equity in an EU country. Vaccination will start in all EU countries between 27th and 29th of December, following the approval of the first vaccine (BioNTech/Pfizer) by EMA and the Commission on the 21st of December, and Portugal will receive 22 million doses, enough to immunize the whole population, during 2021 (Público, 2020c).

Portugal’s vaccination plan comprises 3 phases (DGS, 2020a):

- Phase 1 (950 thousand people): Healthcare practitioners, residents in homecare institutions, people with more than 50 years old with serious chronic diseases (cardiac failure, coronary disease, kidney chronic disease and respiratory diseases) and military/security forces.
- Phase 2 (2 700 thousand people): people with more than 65 years old (with or without chronic diseases) and people between 50 and 64 years old with the remaining chronic diseases).
- Phase 3 (6 900 thousand people): rest of the Portuguese population.

The first doses will be administrated in the biggest hospital groups (Centro Hospitalar Lisboa Norte, in Lisbon and Centro Hospitalar de São João, in Porto) due to logistics issues "we are going to receive two boxes with a total of 9750 doses so we have to limit the number of hospitals in the beginning") and, thus, Phase 1 starts, expecting to be complete in April 2021 (Público, 2020c).

Vaccination in the first phase is expected to be done at the institutions were people work and receive care such as homecare residents, hospitals, military and police forces facilities. Then, primary healthcare units (*Centros de Saúde)* will be used as they are for the national vaccine plan, where in some less populated locations, people might be reallocated to another unit to minimize vaccine traveling. Phases 2 and 3 operational issues are not yet defined. Security mechanisms will be despatched to storage facilities, transportation operations and geo-tracking devices may be used if necessary. Monitoring systems (stock management, vaccination appointments) will be used and cybersecurity protocols will be implemented to the related databases (DGS, 2020b).

After identification of the priority groups, the National Health Service (*Serviço Nacional de Saúde)* is sending an SMS to ask whether the person wishes to be vaccinated or not, since vaccination is not mandatory in Portugal. Vaccines will be free for every citizen, and people who have already been infected will also be vaccinated (DGS, 2020a).

Meanwhile, training will be given to the supply chain workforce that will handle the vaccines, via webinars, and information on the efficacy and importance of the vaccine will be also given to health care practitioners so they can sensitize their patients. Communication content will be elaborated to be distributed in the SNS facilities and social media (DGS, 2020b).

Promoting vaccination will be of paramount importance since there is a generalized scepticism over these vaccines mainly caused by their record development time. Generating confidence in the vaccine will be the key to the adherence of the population to the vaccination call, since it is optional, for which science communication can complement the already planned communication strategy. Effective science communication[4] actions can play a crucial role, for explaining how the vaccines work, their development process, trial results and safety aspects, improves transparency, combats the so called "fake news", and informs in a supported and educational way, helping populations to make a conscious decision.

[4] science communication aims to enhance public scientific awareness, understanding, literacy, opinions, and culture. "It empowers the public to attain an interest in science, a confidence to talk about it, and a willingness to engage with science," providing "skills, media, activities, and dialogue to enable the general public, mediators, and science practitioners to interact with each other more effectively", according to Burns *et al.* (2003).

6.2. Social evaluation of the supply chain performance in a pandemic

Following the social issues identified, derived from the challenges posed by the COVID-19 pandemic, evaluating the supply chain stakeholders' sustainability performance in 2020 must take into account new aspects, especially social aspects.

Companies, regardless of their sector, have new social concerns to deal with what should be reflected in their annual reports, such as the analysed ones in Chapter 3 of this work for the pharmaceutical industry. Many companies' reports follow the GRI norms that aim to standardize the reporting process, helping to create key performance indicators (KPI), thus facilitating the sustainability evaluation (Global Reporting Initiative, 2020).

6.2.1. GRI social standards selection

Here, the latest GRI standards (updated in 2016 and reviewed in 2020) are used to propose the essential aspects that companies should prioritize in their reports, this year, to evaluate how they have responded to the new social challenges posed by the pandemic.

The social aspects identified, throughout section 6.1., are grouped according to the indicator groups established in Chapters 2 and 3 of this work (employment, labour conditions, health and safety, and community development). with a match to the GRI standard disclosure that reports them (Table 6.2.).

Employment

Jobs, as already mentioned before, are a crucial part of social well-being which are put at risk whenever an economic crisis emerges or, in the case of this pandemic, the shutdown of facilities during lockdowns, that took months and led to contract endings.

- **Disclosure 401-1** ("New employee hires and employee turnover*"),* helps understanding the total number and rate of employee hires and dismissals during the reporting period, by region, gender and age.

Employee turnover can result from various motives, such as the employee's own decision, negligence or inability to perform the job, or massive dismissals. As guidance notes, it is advisable to differentiate the dismissals causes in the reports to better assess the impact of the pandemic on jobs.

Several companies opted for lay-offs in order not to lose their workforce, just suspending their activity. The 401 GRI Standard that reports on Employment does not explicitly disclose the number of employees that got on lay-off, so it is proposed to add this information to the 401-1 disclosure.

Labour conditions

As recommended in Chapter 4, as the pandemic outbreaks, taskforce teams should be formed to plan the response and immediate actions, for which a flexible and adaptable management environment is essential for an agile response, in which new leaders should have the space to emerge if they have the best skills to deal with the posed crisis. Workforce training turns to be particularly important since the

best prepared workforces are usually the better trained and updated. Then, accurate and on-time information must be deployed for every employee. Thus, to assess the success of the response to these challenges, the following disclosures are highlighted:

- **Disclosure 404-1** ("Average hours of training per year per employee") and **Disclosure 404-2** ("Programs for upgrading employee skills and transition assistance"), help to understand how companies have been providing training to their workforce, reskilling it, so important to increase their adaptability and preparedness to unexpected crisis.
- **Disclosure 402-1** ("Minimum notice periods regarding operational changes") provides information on the communication efficacy between management and labour, essential to promote trust and transparency and to maintain the whole workforce well informed, involved, thus, committed to overcome the crisis situation.
- **Disclosure 103-3** ("Evaluation of the management approach") is recommended to use to understand how flexible and adaptable the management approaches were, and which mechanisms and adjustments were taken during the pandemic, noting if changes in leadership were performed.

Changes in work practices and regimes, due to pandemic imposed restrictions (remote work), must be monitored to assess how employees are reacting to them, so they can be adjusted to reach the workforce well-being and, at the same time, its productivity. There has not been found a GRI social standard disclosure explicitly reporting on these aspects, so this work proposed one in the next section.

Health and safety

Reporting on the safety and health of workers along the pharma supply chain is fundamental in a pandemic crisis. Healthcare systems and programmes are paramount to provide care for the COVID-19 infected workers, as well as to promote a good mental health, weakened by the working environmental changes that were faced (remote working, layoffs). The next three disclosures are highlighted:

- **Disclosure 403-2** ("Hazard evaluation, risk assessment and incident investigation") can report on the work-related hazards and assess risks on a routine/non-routine basis. The risk to become infected by COVID-19 became a regular worrying aspect of every stakeholder of the pharma supply chain, especially for the workers that have regular and direct contact with the healthcare system or even patients.
- **Disclosure 403-6** ("Promotion of worker health") gives information on the healthcare services that the company provides (or facilitates access to) as, for example, protective equipment and incentives to the participation in voluntary programmes to address and improve health risks non-work related (in which COVID-19 regular testing programmes can be included).
- **Disclosure 403-8** ("Workers covered by an occupational health and safety management system"), considered crucial this year, especially regarding mental health risk due to the changes in the work regime (remote), workspace, operations and overall anxiety posed by the uncertainty of the pandemic.

Community development

Engaging the community is part of the social responsibility duties of a supply chain, for which good and close communication strategies, aligned with governmental guidance, can make a difference in a crisis management.

- **Disclosure 413-1** ("Operations with local community engagement, impact assessments and development programs") helps to understand what has been done by the supply chain different stakeholders in terms of programmes, initiatives and campaign, and their results, regarding for example, COVID-19 prevention (mask use, regular hand sanitizing, etc), social isolation attenuation (senior populations), vaccine information campaigns and promotion.

Improving transparency along the chain helps companies to gain more control on the supply chain and, from another point of view, making more information about products available to the consumers is beneficial, since they can know how, where and by whom products are produced/transported, thus being able to choose quality, which in the case of pharmaceuticals is critical for their health.

- **Disclosure 417-1** ("Requirements for product and service information and labelling") requires reporting on the available information in product labels such as sourcing, content and its environmental/social impact, safe use and disposal impacts.

Assessing product access equity has turned to be a critical aspect when it comes to vaccine and medicine distribution, by pharma companies, for which there hasn't been found a GRI social standard or disclosure recommending the reporting on this matter. A proposal is, then, presented in the next section.

Also, the crisis caused by the pandemic led some businesses from other sectors to adapt and reshape their product portfolio in order to continue operating, stay sustainable and create value according to communities' needs, helping indirectly the pharma sector, such as protective equipment production by textile companies or hand sanitizer by several industries related to chemical products, cosmetics or even beverages. A proposal for a reporting disclosure on this matter is presented in the next section.

Governmental action is crucial in crisis times, to implement new rules (or restrictions when necessary, such as the emergency state lockdowns and sanitary measures), but also to financially aid businesses. Local, national and international measures have been put into motion (for example, the European Commission recovery plan), however, these actions can benefit from the collaboration and engagement of different business sector, where the pharmaceutical plays an important role, contributing not only with treatments but also with knowledge and science. Furthermore, pharma companies can benefit from collaboration with other public institutions such as universities to gain more knowledge and coordinate efforts, an aspect also not found in the GRI standards.

Table 6.2. – Key social aspects proposed for the evaluation of the industry performance on the new social challenges posed by the pandemic, identified throughout section 6.1. of this work, supported by the reviews in Chapters 4 and 5. The correspondent GRI standard disclosure is included or indication whether the social concern is not yet explicitly included in the GRI standards.

	Priority social aspects	GRI standard	Proposed GRI standard
Employ-ment	Dismissals (turnover)	401-1	-
	Layoffs	-	additional information to 401-1
Labour conditions	Remote working assessment	-	new disclosure to 402
	Work operations alterations communication	402-1	-
	Training (new skills needed to face the crisis)	404-1, 404-2	-
	Flexible and adaptable management teams	103-3	-
Health and Security	Workspace health safety measures	403-6	-
	Protective equipment providing	403-2	-
	Health assistance programmes	403-8, 403-6	-
	Mental health support	403-6	-
Community Development	Product access equity (population access)	-	new disclosure to 413
	Portfolio reshaping to respond to the community's needs	-	new disclosure to 413
	Solidarity initiatives, communication campaigns	413-1	-
	Government/public institutions collaboration and dialogue	-	new disclosure to 419
	Transparency improvement	417-1	-

6.2.2. GRI additional social standards proposed

After selecting the GRI standards that address the key social aspects highlighted in this work, recommended to be included in the 2020 annual sustainability reports, four new disclosures are proposed now to report on the non-assessed aspects by the GRI standards.

▶ Disclosure: New work practices assessment

This disclosure is proposed to be integrated in GRI Standard 402 Labor/Management Relations and is based on the identified challenges regarding workforce alterations analysed in subsection 6.1.2.

Reporting requirements:

The reporting organization shall report the following information:

a. Changes in the work daily basis due to management indication, referring:
   i. new routine schedule;
   ii. new workplace;
   iii. motives for this change.
b. Number of workers affected by the changes.
c. Evaluation of the employees' satisfaction with the new work regime assessing:
   i. personal impact on the employee well-being;
   ii. collaboration with other employees;
   iii. individual productivity change.
d. Management evaluation on team/departments productivity evolution.

Guidance

The evaluation proposed can be done via inquiries to every employee and a summary of the main conclusions can be presented in the report. Data can be presented by department, team, office or type of task.

Indicators suggested:

- number of employees in the new working regime (ex: remote work) and respective percentage within the total workforce
- number of hours of remote work vs number of hours worked in person, by employee (average or detailed by department/team)
- percentage of workers that claim to be satisfied with the new working practices.

Background

Management changes, new strategies, innovation, portfolio changes or even crisis situations can trigger changes in the way the workforce is organized and operates. COVID-19 pandemic caused lockdowns and movement restrictions opening the way for a generalized adoption of remote work regimes, which has benefits and negative consequences. Analysing employee engagement and feedback about the new context can reveal the need to make adjustments to improve the workforce well-being as well as the overall productivity.

▶ Disclosure: Product access equity

This disclosure is proposed to be integrated in GRI Standard 415 Public Policy and is based on the identified challenges regarding medicines access equity analysed in subsection 6.1.5. of this work.

Reporting requirements:

The reporting organization shall report the following information:

a. Purpose and impact of the products/services involved
b. Society dependency on those products/services
c. Strategies and policies to ensure equitable access to those products/services

Guidance

An organization can report on this topic using its products showing demand data, competitors' environment, infrastructure and equivalent products existence. In addition, governmental agreements or internal distribution/stocking management decisions that promote equitable access can be described.

Indicators suggested:

- number of products considered to be unique, *i.e.*, with no equivalent on the market (ex: vaccines)

- percentage of satisfied ordering demand, by region/country (to assess this, demand points can be created based on the population (most vulnerable, elderly or the whole population), presenting data on the supply performance of those points – satisfied or not satisfied demand. An similar approach is based on the (Cardoso *et al.*, 2016) approach of equitable long-care network optimization, considering geographical and socioeconomic equity).

Background

Different industry sectors have different impacts on society due to their unique products/services, added value, competitor's existence and products/services use. Water and electricity are essential goods, just like food, but the water supply chain infrastructure is far more complex than, for example, a fruit brand. A consumer has several options to get food, while water is, usually, run by one regional company, posing special social responsibilities to that company. Pharmaceuticals (excluding generics) are another sector that has unique products with high added value (ex: vaccines), whose access is in the hands of companies and governments, not the consumers.

▶ Disclosure: Collaboration with public institutions in crisis situations

This disclosure is proposed to be integrated in GRI Standard 415 Public Policy and is based on the identified challenges analysed in sections 5.1. and subsection 6.1.5 of this work.

Reporting requirements:

The reporting organization shall report the following information:

a. Contribution to national/international governmental crisis task forces
    i. Expertise allocation - number of allocated employees
    ii. Financial/products aid - donations
b. Collaboration to legislative processes
c. Collaboration with scientific institutions (universities, laboratories, observatories)

Guidance

An organization can mention which taskforces have contributed and why, showing the outcomes of that contribution (to the community and to the organization). It is advisable to report on this alongside Disclosure 415-1 ("Political contributions") since this disclosure helps to identify lobbyist activity.

Indicators suggested:

- number of employees allocated to collaborative taskforces,
- number of committees/taskforce teams the organization participated,
- number of governmental decisions (laws, regulations, guidance documents) for which the organization contributed,
- number of educational protocols and/or number of projects (with universities),
- number of university's students/researchers working on the organizations' projects
- donations/financial help (patronage/sponsorship) for educational/research projects/institutions.

Background

Reducing the gap between governmental decision making and the several supply chain stakeholders during a crisis situation can provide expertise that governments do not have. Also, creating good communication channels with governmental institutions via closer collaborations, can contribute to a faster response by the supply chain once legislation/regulation is passed. It is, however, important to note that private intervention on public institutions must be regulated and supervised to prevent lobbyist abuses. On the educational field, partnerships between industry stakeholders and universities on research projects encloses academics, that provide new knowledge, and companies, that have the means to develop technology.

▶ Disclosure: Product/services portfolio adjustments to community's needs

This disclosure is proposed to be integrated in GRI Standard 413 Local Communities and is based on the identified challenges illustrated in subsection 5.1.1. of this work.

Reporting requirements:

The reporting organization shall report the following information:

a. New products/services aiming to respond to the communities needs
    i. Causes for this response
    ii. Impact in the community
b. Investment mobilized and financial impact

Guidance

This indicator is particularly important during crisis periods.

Indicators suggested:

- number of new products/services provided apart from the organization's usual portfolio,
- investment mobilized to the organization's adaptation to provide those products/services,
- demand evolution for those products/services and the achieved capacity (%) to satisfy it.

Background

Organizations show great social performance and resilience when they adapt their portfolio to the current necessities of their customers, since they make the effort to adjust their facilities and operations and still create value in the community. The textile conversion to mask production and universities/alcoholic beverages to hand sanitizer production, during COVID-19 pandemic outbreak, are examples of what can be expected to be reported with this disclosure.

6.2.3. Comparison to the pre-pandemic reported aspects

A brief analysis is done here to assess if the social aspects valued by the six most sustainable companies in 2019 (Annex B) overlap the new social priorities after the pandemic outbreak.

Employment and training concerns were already an important aspect reported with use of disclosure 401-1 and disclosures 404-1 and 404-2, respectively. Health promotion and assistance programmes are also common priorities both before and after the pandemic outbreak, reported with disclosures 403-6 and 403-8, to which 403-2 is added regarding protective equipment and measures required to protect the workforce from the virus. Although fatalities, injuries and illnesses work related or non-related are not selected as priority aspects to tackle in this crisis situation (with disclosures 403-9 and 403-10), it is recommended that companies do not stop doing it, to which additional information of numbers of fatalities/illnesses related to COVID-19 can be added.

Disclosure 413-1 is also a common topic to both reports in 2019 and selected key aspects to report in 2020, since it regards the community engagement, essential in crisis times to help protecting the most vulnerable and counterbalance life quality that has eventually been lost. Product access equity strategies and product portfolio adjustments are the new suggestions in a crisis scenario, to reinforce local community protection.

In 2019, companies reported on the employee satisfaction and engagements to which this work proposes to bear also in mind the communication and feedback practises, deployed by management teams, on changes and operational adjustments that impact employees (disclosure 403-2).

Finally, topics such as gender balance, employee diversity and human rights control and awareness, although are not defined as key priorities during a pandemic crisis, are not to be forgotten and continuously improved, especially once the crisis panorama starts improving itself.

6.3. Social resilience framework for pharma supply chains

This work was elaborated during the first 10 months of the COVID-19 pandemic, focusing on its social impacts in the pharmaceutical supply chain. The review on the challenges it faced pointed to the need of ensuring resilience so it can respond to the needs of its end-stakeholders: patients, thus, everyone that needs healthcare. Healthcare services and medicines, in contrast with several other services and products, neither come as optional to those who need them, nor vary according to the preference of the customer as food or clothes, for example. This is a sector in which the social pillar of sustainability plays a rare central role.

Combining the great importance the social performance has in the pharma supply chain with the experts' strongly stated need for resilience on global supply chains, a framework to help prepare, improve and assess the pharma supply chain's performance in crisis situations is proposed here, pillared on the proposed concept of social resilience.

Based on the UN Sustainability Development Goals (mentioned in Chapter 1) and the social issues observed during the reviews performed throughout this work, before (Chapters 2 and 3) and after (Chapters 4, 5 and 6) the pandemic outbreak, it was commonly identified that the principal of **Equity** is underlined any social concept defined. In addition, four pillars are considered essential to ensure social resilience on the pharma supply chain (Figure 6.2.):

- **Access:** the possibility to provide access, in an equitable way, to everyone that needs healthcare services, treatments or vaccines, regardless of their geographical location or their socioeconomic condition – focus on patients.
- **Stability:** the ability to ensure continuous and stable production of the needed medicines, with a steady distribution flux, without disruptions for the supply chain workers (ex: dismissals) - focus on workforce.
- **Support:** caring for the surrounding communities' development and well-being as well as the supply chain workforce, providing solidarity initiatives, training, information, and assistance programmes - focus on communities and workforce.
- **Quality:** the capacity to ensure that the provided health services and produced medicines meet the quality and regulatory requirements, ensuring good labour conditions for these services/products providers: the supply chain workforce - focus workforce and patients.

Figure 6.2. – Proposed social resilience pillars to assess and improve the pharma supply chain performance.

Following the assessment on the pharma supply chain challenges during the COVID-19 pandemic, presented in Chapters 4 and 5 of this work, three major problems were identified:

- the risk of medicine supply disruptions, causing shortages in hospitals, pharmacies and households (***Shortages***);
- the inefficient performance of the chain, following the changes that the pandemic brought, reducing the value produced by the pharma supply chain: adequate/quality products, delivered on time, satisfying demand (***Inefficiency/Lack of value***);
- the inexistence of proper medicines to treat and prevent the new disease (drugs and vaccines) (***No treatment available*)**;

A set of measures, based on the recommendations made on the previous chapters, is compiled on the proposed framework (Figure 6.3.) to promote pharma social resilience, each action associated to one of the defined four pillars (Figure 6.2.).

The proposed actions are organized according to the mentioned three identified problems (medicine shortages, inefficiency/lack of value and no treatment available) divided by major players that are responsible for operating them (the pharma supply chain stakeholders or the governments/regulatory authorities). Moreover, the suggested measures are distributed according to the used stages for the recommendations proposed in section 4.3.6, (prevention, response and recovery) to increase the supply chain's resilience before and after a pandemic outbreak.

Prevention actions

From the three problems identified, shortage assessment is the one that permits the most actions before the pandemic outbreak, since prevention is the best way to avoid them. As seen in Chapters 4 and 5, maintaining safety amounts of medicines in storage enables the healthcare system and wholesalers to buffer supply/manufacturing disruptions, ensuring continuous access to drugs for a certain period. This safety stock must consider expiration dates and be dynamically managed to prevent stockpiling.

Supply disruptions can be prevented by ensuring that manufacturing facilities are not dependent on just one supplier, meaning that the supply chain has redundancy. Decentralization of the Asian manufacturing facilities prevents dependency of one country/region/manufacturer that can be affected by political instability, a natural disaster or the beginning of a pandemic as seen with COVID-19. Access and Stability are the assessed social resilience pillars here, as patients continue to receive medicines, while productivity instability and consequent loss of jobs are avoided. Following decentralization, regionalization reduces intermediaries and improves customer and patient support due to their increased closeness of the pharma companies/distributors (Support pillar assessed). An overall better control of the supply chain is essential to improve the preparedness against shortages, which can be achieved with better visibility along the chain, meaning that the raw-materials'/product's origins, their production conditions, and their supply vulnerabilities are known. Transparency gets improved, not only for the inner supply chain stakeholders, but also for consumers, that can push for more quality standards and make choices when equivalent medicines are available (generics) (Quality pillar assessed). These measures result from the challenges detailed in section 4.3.3. and are, essentially, on the hands of the supply chain stakeholders, mainly pharma companies that detain manufacturing facilities.

Inefficiencies in both the supply chain operations and delivery of products, with the necessary value to the communities they supply, can be primarily improved with a skilled workforce and management teams, aware of the present challenges and well prepared to be adaptable and fast. Workers training elevates the work quality and productivity, at the same time maintaining employees working on the pharma supply chain, since knowledge is essential. This provides job and productivity stability if efficient and flexible management strategies are implemented across the SC stakeholders (see sections 2.4.3. and 6.1.1.). Common policies across the pharma sector and across countries put everyone working in the same way, following the same quality product and service standards, human rights standards, as well as equitable distribution strategies (as exemplified by the EU's Vaccination Strategy, described in section 6.1.5.1), thus contributing to the four social resilience proposed pillars: Quality, Support, Access and Stability. Policies are, essentially, on the governments' hands (national or supranational), as well as regulatory agencies such as EMA and FDA.

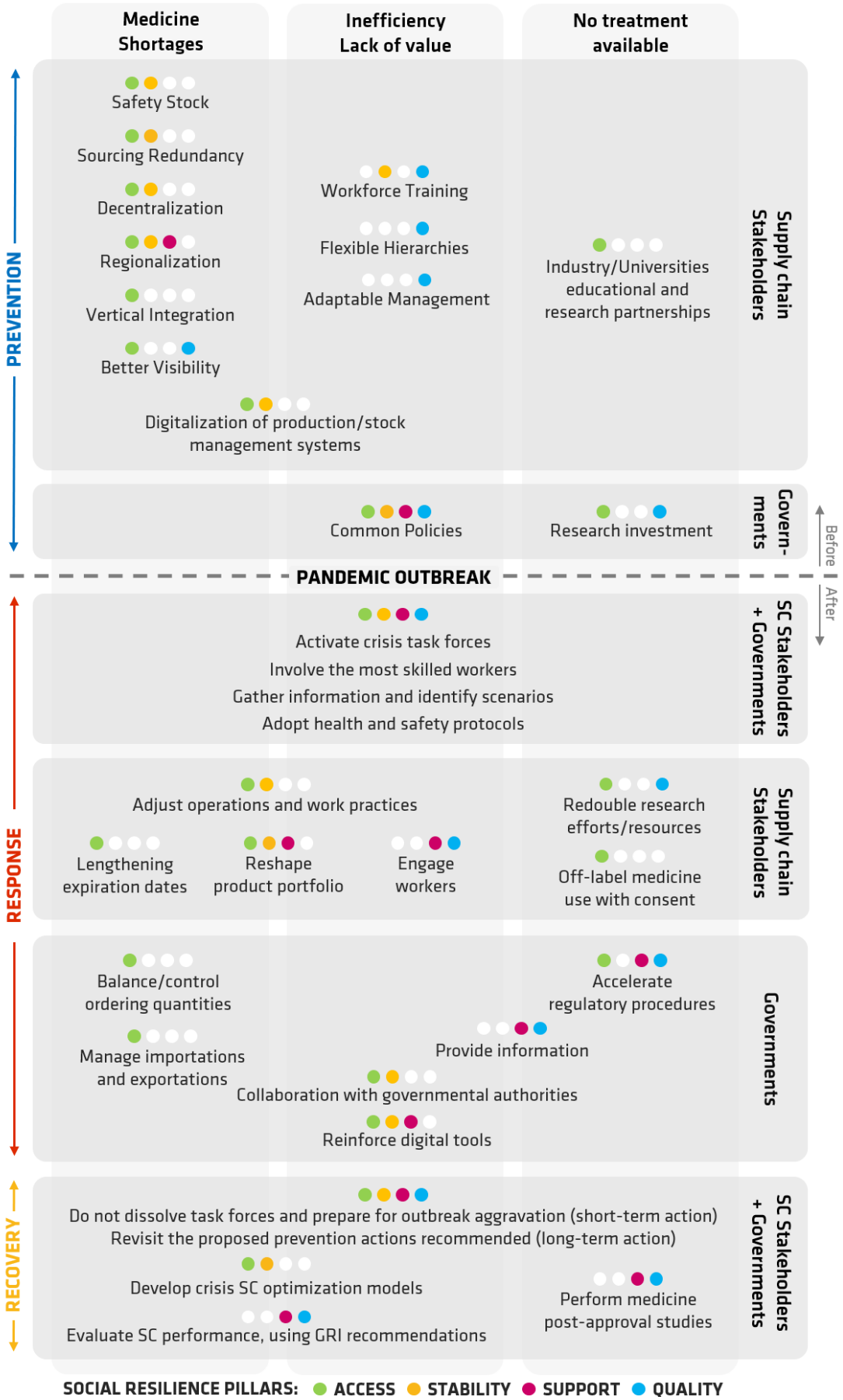

Figure 6.3. – Proposed framework to prepare the pharma supply chain to a pandemic crisis like the COVID-19 and improve its social resilience.

Digitalization is one of the most recommended actions observed across the literature reviewed in the previous chapters, both before and after the pandemic outbreak, being associated with the improvement of Access and Stability. Interconnected production and stock management systems help to monitor demand and inventory in real time, as well as manufacturing capacity, helping to predict some shortage situations in advance and anticipate adjustments needed. Industry 4.0, for example, tackled in section 3.4., is a trend that seeks to automatize and digitalize industries.

The inexistence of treatment is inevitable when a new and unknown disease appears. Investing in science infrastructures and qualified personnel is the best way to ensure that once a new infectious virus or bacteria is discovered, suitable treatment medicines and vaccines start to be developed. Partnerships between industry stakeholders and universities via educational programmes or research projects encloses academics that provide new knowledge and companies' developed technology. Governments must create mechanisms to allow these partnerships to occur since universities are generally public institutions.

Response actions

A set of four actions is suggested to be taken immediately after the pandemic outbreak, starting with the formation of a task force to assess the situation, identify scenarios and plan the response. It is advisable to be composed of management members and workers with the most adequate skills for this situation (for which the mentioned workforce training is essential). Internal teams are crucial but also wider taskforces, involving various SC stakeholders and also governments are important to a more cohesive response. It is here that new leaders may emerge, more suited to manage future crisis situations if hierarchies are flexible and management teams are adaptable, two prevention actions. Planning the response to avoid shortages, lack of inefficiency and bring value to the pharma supply chain leads to Access and Stability, accompanied by the implementation of health and safety protocols to ensure the products' and work environment's Quality and the reinforcement of assistance programmes (Support). These four measures are in line with the response recommendations proposed in section 4.3.6..

To answer medicine shortages after the outbreak, expiration dates can be lengthened within certain limits; order quantities can be controlled to ensure equitable distribution of medicines; and exportations temporary restrictions can be imposed to satisfy internal demand; emergency measures that must be taken by governments and pharma stakeholders to guarantee access, as seen in section's 5.1. review.

Adjusting operations and work practices to produce the new products or the same ones in new working conditions (remote work, shifts, reorganized workspace) is also of paramount importance to ensure the efficient delivery of products and stability, both on productivity and jobs (minimizing dismissals due to lockdown working restrictions) (Access and Stability). Collecting feedback on these alterations assessing the well-being and engagement of the workforce, correcting what is needed, is also important to ensure health and psychological stability of employees and their motivation, consequently affecting productivity positively (details on section 6.1.2.). Engaging employees is in line with the suggestion of the new GRI disclosure (*new work practices assessment*), in section 6.2.2., to evaluate the companies' performance on these matters.

Reshaping product portfolio to adapt to the new challenges posed by the pandemic proved to be crucial in both ways: providing valuable and needed products to the communities (Access) and ensuring the survival of business and, thus, jobs (Support and Stability) (examples in section 5.1.1.).

Regarding the inexistence of available treatment, it is the proposed research and development partnerships that have the floor in this immediate stage after the outbreak. Relations and work collaborations are already established making it easier to just start working on the new challenge, redirecting resources and efforts. Furthermore, while laboratories are still conducting trials, industry can design the manufacturing processes (scale-up), with simultaneous involvement and advisory of regulatory institutions to ensure fast approval of new medicines (as seen with the COVID-19 vaccines), illustrated in section 5.2.2.1. Research and development provide the needed treatment (Access) as well as faster regulatory procedures, that also ensure quality of medicines (Quality) and provide information to the healthcare system and patients (Support). Until an effective treatment is developed, off-label medicines might be used with patient consent to, meanwhile, try to provide a treatment (Access), as stated in section 5.1.3.

Digitalization is once again part of the solution as it was proven when online communication systems ensured continuity in orderings, healthcare services (the ones that could be done at distance) and assist the supply chain workforce remote work. It was also responsible for information providence and maintained proximity between all the supply chain stakeholders, thus, assuming a Support role.

Finally, collaboration between governments and the pharma supply chain stakeholders is, as already referred, essential to overcome bureaucracy and define a cohesive strategy.

Recovery actions

Once the outbreak has passed and the situation is getting back to normal, meaning stabilizing, there is a “new normal” as mentioned in section 4.3.5.. The first proposed recovery measure is to not dissolve the created crisis taskforces as new peaks of the pandemic might arise or an overall situation aggravation with new unforeseen occurrences. Furthermore, when an outbreak occurs a considerable amount of resources is allocated to respond to the situation (e.g. vaccine production effort), which pose as excess when the situation stabilized. This excess must be used efficiently and with innovation, for example to develop products/provide services to vulnerable communities (developing countries). In addition, environmental solutions to remediate waste caused by single-use protective equipment (e.g. masks and gloves) must be found, with the help/coordination of these crisis taskforces.

On the long-term, the prevention measures are advised to be reviewed to improve what can still be improved, regarding the resilience of the supply chain, essential to ensure Access and Stability, maintaining the good practices identified after the outbreak, namely: the operational and work adjustments; health measures; information providing actions; new tele-healthcare practices; new leaders and management strategies; and workforce engagement, thus promoting Quality and Support, completing the four proposed social resilience pillars.

Research must not rest, intensifying post-approval studies on the new medicines, especially the new vaccines, as new strains of the virus might appear, and new side effects of the drug might be identified.

Consequently, new action must be taken accordingly and guidance provided to healthcare practitioners. This measure intends to ensure both Quality and Support pillars.

Regular evaluation of the supply chain performance is advised, as pharma companies already do in their annual sustainability reports (see section 3.3.), now mentioning how they coped with and recovered from the outbreak, using GRI standards, namely the new disclosures proposed in section 6.2.2.

Following the evaluation performed, this work suggests the development of pharma supply chain quantitative optimization tools, focused on crisis situations, to improve resilience more accurately and systematically. The social objective functions shall respect criteria based on key performance indicators, based on the selection of GRI standards as, for example, the proposed ones for the new disclosures (section 6.2.2.), to be quantified when minimizing social impact or maximizing social benefit.

6.4. Chapter conclusions

The COVID-19 pandemic had many impacts on global supply chains, especially social impacts. In this chapter, a review on the social challenges faced by the pharmaceutical supply chain during the pandemic outbreak is performed. Adaptable and flexible management structures, new working modes assessment, workforce engagement, interactions between the pharma supply chain stakeholders and the equitable access of medicines are the highlighted topics.

Then, to assess these challenges and evaluate the pharma stakeholders' performance in 2020, a set of GRI disclosures is selected to be prioritized in their sustainability reports, with four additional suggested disclosures. It was identified that there are several new aspects to be tackled in 2020, not usually valued. For each new disclosure quantitative indicators to be used in decision making tools are suggested.

Finally, to ensure the good social performance of the pharmaceutical supply chain stakeholders in crisis situations, a framework is proposed, after defining the concept of social resilience, based on four pillars (Access, Stability, Support and Quality), with suggested actions to be taken before and after an epidemic outbreak such as the COVID-19 one. New optimization models intended for crisis situations, namely pandemics, are identified as necessary to be formulated, with a significant social component.

7. Conclusion

In 2015, the United Nations 17 Sustainable Development Goals of the 2030 Agenda for Sustainable Development were established aiming to perceive equity and an overall improvement of life quality for everyone. Social challenges, naturally, arise when trying to achieve these goals, some of them, related to supply chains performance, in particular, the pharmaceutical one.

Sustainability has gained more importance in nowadays political agendas, mainly fostered by the environmental challenges our societies face. However, the absence of the social pillar is still felt in supply chain decision-making tools such as optimization models, when compared to the other two (economic and environmental). In Chapter 2 review on the social indicators identified in forty models, job creation and dismissals are the most found ones, in some cases related to the regional GDP, population density or unemployment rate, forming the first group of indicators defined: employment. Safety and health form the second group of indicators analysed, followed by labour conditions motivated by human rights concerns, which relate to the quality of the jobs that models aim to create. People's valorisation and maximization of their welfare contributes to community development, the last studied aspect.

After characterizing the pharmaceutical sector and its driving forces, these four social indicators groups were used in Chapter 3 to analyse the social performance of six pharmaceutical leaders according to the *Dow Jones Sustainability Index* - AstraZeneca, Daiichi Sankyo, GlaxoSmithKline, Roche, Sanofi and Takeda - based on their 2019 sustainability reports. The most common social issues reported were: employee turnover, gender balance and inclusion improvement, employee engagement evaluation, accidents/injuries prevention and reduction, mental health/stress assistance and, surprisingly, driving collision reduction efforts (work and non-work related), revealing special concern for their workforces well-being. Four of these companies use the GRI Standards guidance to elaborate their reports, but there is still much work to do in the uniformization of these indicators' assessment.

Disruptions like the COVID-19 pandemic highlighted the vulnerabilities of this sectors' supply chain and its consequences to healthcare systems. The existent social concerns are tested while new challenges emerge, emphasizing the need to turn supply chains more agile and prepared, *i.e.*, more resilient.

The analysis showed in Chapters 4 and 5, first on global supply chains and then particularized to the pharma sector, pointed out the need to create supplying redundancy, maintaining safety stock, decentralize manufacturing capacity regionalizing suppliers and manufacturers while improving the overall visibility across the chain. Reshoring API's production facilities on western regions (Europe and North America) is strongly advised by several experts with a simultaneous regain of knowledge and investment in innovation and research infrastructures. Investment in research is corroborated by the probability of new diseases to emerge and its rapid propagation in a globalized society as ours.

On the social domain assessed in Chapter 6, the pandemic brought workforce alterations, such as remote work, layoffs and even dismissals due to the lockdowns, and an overall change in interactions between the supply chain players. It also confirmed the benefits of adaptable and flexible management strategies with less rigid hierarchies to better respond to crisis situations.

The pharmaceutical sector faced all these challenges while continued working on the perhaps most significant contribution to the improvement of the pandemic situation: the development of treatments and vaccines. The challenges associated to the research process, manufacturing capacity and distribution highlighted the big logistics requirements and the medicine equitable access social concern, reaching the difference still felt between the richest regions of the globe and the poorest. Resilient supply chains are the most capable to answer this call so, in the last chapter of this work, a set of recommendations is given to improve the pharmaceutical supply chain performance, especially from the social pillar point of view.

Firstly, awareness must be created as well as understanding on each SC stakeholders' social performance, so a set of ten GRI Standards disclosures is selected to be used in crisis periods reports. Four new disclosures are also created for the new social challenges not fully reflected by the existent GRI Standards. Reporting in employment continues to be an essential issue, with even more relevance after the pandemic outbreak, with special notes on dismissals or layoffs caused by the pandemic. Employee engagement must be intensified to evaluate the impacts of new work regimes. Health assumes a central role, adding the need to reinforce reporting on assistance programmes, injuries/illnesses rate by the pandemic and safety measures implemented. Community engagement is not forgotten, as pharma stakeholders can make the difference on governmental action, assistance services, information providing, and satisfy the population's product needs.

Then, alongside these four disclosures, quantitative indicators are suggested to help reporting subjective aspects and to simplify their inclusion in decision-making quantitative tools, contributing to the increase of the social pillar component in optimization objective functions.

Afterwards, the concept of social resilience was proposed pillared on four features: Access, Stability, Support and Quality, based on the identified pharma supply chain challenges and social issues. Finally, to provide guidance on how to prepare to and act during a pandemic like COVID-19, a framework was designed with recommendation measures that intend to address three main problems: shortages, no treatment available and inefficiency/lack of value in the chain, leading to an improvement of its social resilience. Divided in prevention, response and recovery actions, collaboration, workforce valorisation (training and engagement), research investment and digitalization are perhaps the most transversal recommendations identified.

7.1. Limitations and Future Work

This work's limitations are predominantly lack of validation of the reviews on the pharmaceutical characterization since no inquiries were made to pharma companies, namely the six analysed ones. Interviews with management teams and surveys to these (and other) companies' workforces would help supporting the perceived challenges and respective recommendations proposed. It would also bring to this work what are the current recovery plans on the short and long terms. Likewise, surveys to both pharmacies, healthcare practitioners and patients would provide more information on the interaction changes and obstacles their daily activities faced. Direct contact with governmental institutions (e.g.: the Portuguese Health Ministry, DGS and the European Commission) to better understand the response

strategies, what worked and what did not was so successful, would provide more information to include in the framework regarding the governments' actions. Lastly, the last month of this work posed some challenges to the information gathering regarding the vaccination developments because there were daily updates and announcements every day.

The analysis performed in this dissertation leaves space for further investigation, firstly on the recovery process that is expected to take place in the next years, that will allow to add new measures to the framework. An analysis to the 2020 sustainability reports of the same six pharma companies would allow a comparison to be made to see if and how companies reported on new social aspects – which indicators were used and what they have in common with the proposed ones in section 6.2.2. of this work.

As indicated in the framework, developing quantitative decision-making tools to improve resilience in crisis situations, accurately and with more use of social indicators is a path that should be followed. In addition, more quantitative indicators can be developed for the more subjective already existent GRI disclosures, as this work only suggests quantitative indicators for the new proposed disclosures.

Finally, performing this kind of study in other sectors than the pharmaceutical might be useful, as similar social challenges may probably be found. The respective, already tackled, solutions might be transposed from one to another, thus enhancing social resilience in several different supply chains, contributing to several UN Sustainable Development Goals achievement, in the next decade.

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Annex A

Table A.1. – Literature review on social indicators and quantifiers, industry sectors and decision levels of supply chain optimization models.

PAPER				INDICATOR					QUANTIFIER	SECTOR	DECISION LEVEL		
#	Authors	Title	Year	Employ-ment	Safety	Health	Labour Cond.	Comm. Devel.			Strat.	Tactic	Oper.
1	Ahmed, W. Sarkar, Biswajit	Management of next-generation energy using a triple bottom line approach under a supply chain framework	2019	x					new jobs created	Bioenergy (Biofuel)	x		
2	Alsaffar, Ahmed J. Raoufi, Kamyar Kim, Kyoung-Yun Okudan Kremer, E. Haapala, Karl R.	Simultaneous Consideration of Unit Manufacturing Processes and Supply Chain Activities for Reduction of Product Environmental and Social Impacts	2016		x				non-fatal injuries and illnesses and days away from work	Bicycle pedal components	x		
3	Arampantzi, Christina Minis, Ioannis	A new model for designing sustainable supply chain networks and its application to a global manufacturer	2017	x	x		x	x	employee-periods metric to count: new jobs created (local, non-local and sub-contracted to install and operate) dismissals idle work fatalities and injuries	Refrigerators	x		
4	Bouchery, Yann Ghaffari, Asma Jemai, Zied Dallery, Yves	Including sustainability criteria into inventory models	2012		x				injury rate	Generic model			x
5	Boukherroub, Tasseda Ruiz, Angel Guinet, Alain Fondrevelle, Julien	An integrated approach for sustainable supply chain planning	2015	x			x		transfer of employees and lay-offs travel time spent from home production site	Lumber industry		x	

6	Cambero, Claudia Sowlati, Taraneh	Incorporating social benefits in multi-objective optimization of forest-based bioenergy and biofuel supply chains	2016	x					new jobs created	Bioenergy and Biofuel	x		
7	Charmondusit, K. Phatarachaisakul, S. Prasertpong, P.	The quantitative eco-efficiency measurement for small and medium enterprise: A case study of wooden toy industry	2014	x	x			x	new jobs created (local and non-local) accident rate number of corporate social responsibility products and investment	Wooden Toy Industry	x		
8	Chazara, Philippe Negny, Stéphane Montastruc, Ludovic	Quantitative method to assess the number of jobs created by production systems: Application to multi-criteria decision analysis for sustainable biomass supply chain	2017	x					new jobs created (direct, indirect and induced)	Bioenergy Biomass Industry	x		
9	Chen, Zhixiang Andresen, Svenja	A Multiobjective Optimization Model of Production-Sourcing for Sustainable Supply Chain with Consideration of Social, Environmental, and Economic Factors	2014		x				accidents and illnesses per working hours severity of the accidents classified by period of absence from work	Steel Production	x		
10	Coelho, Karen R. Cherri, Adriana C. Baptista, Edméa C. Chiappetta J., Charbel J. Soler, Edilaine M.	Sustainable operations: The cutting stock problem with usable leftovers from a sustainable perspective	2017	x					The model does not have quantifiers since it addresses the social issue as a consequence of the improvement in environmental performance and the economic performance that creates jobs and salaries.	Generic model			x
11	Darbari, Jyoti Dhingra Kannan, Devika Agarwal, Vernika Jha, P. C.	Fuzzy criteria programming approach for optimising the TBL performance of closed loop supply chain network design problem	2019	x			x	x	new jobs created training hours community service hours donations to NGOs	Transports	x		

12	Dayhim, Muhammad Jafari, Mohsen A. Mazurek, Monica	Planning sustainable hydrogen supply chain infrastructure with uncertain demand	2014		x				safety risk index based on the number of fatalities calculated along with number of injuries and property damage/loss, multiplied by their frequency	Hydrogen Industry	x		
13	Devika, K. Jafarian, A. Nourbakhsh, V.	Designing a sustainable closed-loop supply chain network based on triple bottom line approach: A comparison of metaheuristics hybridization techniques	2014	x	x				new jobs created (fixed and variable) work damages (during the establishment of facilities or during the manufacturing and handling of products)	Glass Production	x		
14	Gao, Cong Qu, Daogang Yang, Yang	Optimal Design of Bioenergy Supply Chains Considering Social Benefits: A Case Study in Northeast China	2019	x					weighted sum of wages of new jobs created	Bioenergy	x		
15	Günther, H. O. Kannegiesser, M. Autenrieb, N.	The role of electric vehicles for supply chain sustainability in the automotive industry	2015	x					number of dismissals	Automotive Industry	x		
16	Habib, Muhammad S. Sarkar, Biswajit Tayyab, Muhammad Saleem, Muhammad W. Hussain, Amjad Ullah, Mehran Omair, Muhammad Iqbal, Muhammad W.	Large-scale disaster waste management under uncertain environment	2019	x					new jobs created	Natural Disasters Waste		x	
17	Hahn, Gerd J. Brandenburg, Marcus	A sustainable aggregate production planning model for the chemical process industry	2018				x		overtime hours worked	Chemical Industry		x	

18	Heidari, Razieh Yazdanparast, Reza Jabbarzadeh, Armin	Sustainable design of a municipal solid waste management system considering waste separators: A real-world application	2019	x					new jobs created	Solid Waste Management	x		
19	Hong, Jiangtao Alzaman, Chaher Diabat, Ali Bulgak, Akif	Sustainability dimensions and PM 2.5 in supply chain logistics	2019			x			undesirable medical costs	Generic model	x		
20	How, Bing shen Lam, Hon Loong	Sustainability evaluation for biomass supply chain synthesis: Novel principal component analysis (PCA) aided optimisation approach	2018	x	x	x			new jobs created (direct, indirect and induced) safety index based on chemical inherent factors, process factors and transportation factors (impact speed and the risk of pedestrian fatality is used to measure the road safety)	Biomass Synthesis	x		
21	Jafari, Hamid Reza Seifbarghy, Mehdi Omidvari, Manouchehr	Sustainable supply chain design with water environmental impacts and justice-oriented employment considerations: A case study in textile industry	2017	x					new jobs created	Textile Industry	x		
22	Jiang, Xianglan Xu, Jiuping Luo, Jiarong Zhao, Fei	Network design towards sustainability of Chinese Baijiu Industry from a cupply chain Perspective	2018	x					social welfare coefficient based on new jobs created and GDP per capita	Alcoholic beverage	x		
23	Jin, Enze Sutherland, John W.	An integrated sustainability model for a bioenergy system: Forest residues for electricity generation	2018	x					new jobs created	Biomass Synthesis (Energy)	x		

24	Kamyabniya, Afshin Fakhrzad, Mohammad	Sustainability in supply chain with focus on efficiency, safety, and industrial emission factors	2016		x				number of injuries and severity	Steel Production	x		
25	Kannegiesser, M. Günther, H. O. Autenrieb, N.	The time-to-sustainability optimization strategy for sustainable supply network design	2015	x					number of dismissals	Automotive Industry	x		
26	Kim, Jiyong Lee, Younghee Moon, Il	An index-based risk assessment model for hydrogen infrastructure	2011		x				safety index based on processes and technologies used	Hydrogen Infrastructures	x		
27	Kravanja, Zdravko Čuček, Lidija	Multi-objective optimisation for generating sustainable solutions considering total effects on the environment	2013	x	x		x		social index based on quality of life, housing, ecology, employment, human rights, poverty, education, health and safety	Bioenergy (Biogas)	x		
28	Kristianto, Yohanes Zhu, Liandong	Techno-economic optimization of ethanol synthesis from rice-straw supply chains	2017	x					The model addresses the social issue as a consequence of its optimization, not including the social issues from the beginning, calculating new jobs created (direct, indirect and induced).	Bioenergy (Bioethanol Synthesis)	x		
29	Martínez-Guido, Sergio I. Betzabe González-Campos, J. Ponce-Ortega, José María Nápoles-Rivera, Fabricio El-Halwagi, Mahmoud M.	Optimal reconfiguration of a sugar cane industry to yield an integrated biorefinery	2016	x					new jobs created	Sugar cane industry	x		

30	Meyer, Regina Campanella, Sandra Corsano, Gabriela Montagna, Jorge M.	Optimal design of a forest supply chain in Argentina considering economic and social aspects	2019	x					Dimensionless indicator that considers job creation, regional unemployment and lower economically active population. The higher its value, the better the social performance of the site.	Forest Industry	x		
31	Miret, Carlos Chazara, Philippe Montastruc, Ludovic Negny, Stéphane Domenech, Serge	Design of bioethanol green supply chain: Comparison between first and second generation biomass concerning economic, environmental and social criteria	2016	x					new jobs created	Bioenergy Bioethanol Synthesis (Energy)	x		
32	Mota, Bruna Carvalho, Ana Gomes, Maria Isabel Barbosa-Póvoa, Ana Paula	Design and Planning of Sustainable Supply Chains	2015	x					new jobs created	Food Retail	x		
	Mota, Bruna Carvalho, Ana Gomes, Maria Isabel Barbosa-Póvoa, Ana Paula	Sustainable supply chains: An integrated modelling approach under uncertainty	2018	x					new jobs created considering GDP	Electronic compo-nents	x	x	
33	Pedram, Ali Pedram, Payam Yusoff, Nukman Bin Sorooshian, Shahryar	Development of closed-loop supply chain network in terms of corporate social responsibility	2017	x					new jobs created	Generic model	x		
34	Pishvaee, M. S. Razmi, J. Torabi, S. A.	An accelerated Benders decomposition algorithm for sustainable supply chain network design under uncertainty: A case study of medical needle and syringe supply chain	2014	x	x			x	new jobs created number of lost days caused from work damages	Medical Material	x		

35	Sahebjamnia, Navid Fathollahi-Fard, Amir Mohammad Hajiaghaei-Keshteli, Mostafa	Sustainable tire closed-loop supply chain network design: Hybrid metaheuristic algorithms for large-scale networks	2018	x	x				new jobs created (fixed and variable) lost days due to injuries	Generic model	x		
36	Santibañez-Aguilar, José Ezequiel González-Campos, J. Betzabe Ponce-Ortega, José María Serna-González, Medardo El-Halwagi, Mahmoud M.	Optimal planning and site selection for distributed multiproduct biorefineries involving economic, environmental and social objectives	2014	x					new jobs created	Bio-refineries		x	
37	Santibañez-Aguilar, José Ezequiel Martinez-Gomez, Juan Ponce-Ortega, José María Nápoles-Rivera, Fabricio Serna-González, Medardo González-Campos, Janett Betzabe El-Halwagi, Mahmoud M.	Optimal planning for the reuse of municipal solid waste considering economic, environmental, and safety objectives	2015		x				intoxication risk based on number and probability of fatalities	Solid Waste Management		x	
38	Tsao, Yu Chung Thanh, Vo Van Lu, Jye Chyi Yu, Vincent	Designing sustainable supply chain networks under uncertain environments: Fuzzy multi-objective programming	2018	x	x	x			new jobs created amount of hazardous by-products number of workdays lost due to workplace hazards	Generic model	x		
39	You, Fengi Tao, Ling Graziano, Diane J. Snyder, Seth W.	Optimal Design of Sustainable Cellulosic Biofuel Supply Chains: Multiobjective Optimization Coupled with Life Cycle Assessment and Input–Output Analysis	2012	x					new jobs created (direct, indirect and induced)	Bioenergy (Biofuel)	x	x	

40	Zhalechian, M. Tavakkoli-Moghaddam, R. Zahiri, B. Mohammadi, M.	Sustainable design of a closed-loop location-routing-inventory supply chain network under mixed uncertainty	2016	x				x	new jobs created regional economic development (unemployment rate)	LCD and LED TV production	x		

Annex B

Table B.1 – Social performance overview of the six pharmaceutical leaders in sustainability according to the *Dow Jones Sustainability Index*, based on this companies' annual reports or corporate sustainability reports.

SOCIAL PERFORMANCE DATA		COMPANIES					
		GSK	Sanofi	Roche	AstraZeneca	Daiichi	Takeda
UN Sustainability Development Goals agenda		Yes	Yes	Yes	Yes	Yes	Yes
Global Reporting Initiative (GRI) based sustainability evaluation		Yes	Yes	Yes	No	No	Yes
Social indicators with specific data results on annual reports	**Employment**						
	Turnover - total (%)	✓	✓			✓	
	Turnover - voluntary (%)	✓	✓		✓		
	Gender balance - total (% of women)	✓	✓		✓	✓	✓
	Gender balance - senior employees (% of women)	✓	✓	✓	✓	✓	
	Employees with disabilities (physical and mental) (number or %)		✓	1		✓	
	Labour Conditions						
	Satisfaction assessment (by surveys) (%)			✓	✓		
	Engagement assessment (by surveys) (%)	✓	✓	✓	✓		
	Overall Training (various set of skills related to their tasks or other skills) (number of training initiatives / number of employees receiving training)	✓	✓	1	✓	✓	1
	Leader training (number of initiatives)	✓	1	✓	1		
	Gender balance training (women coaching to prepare/encourage for senior roles) (number of actions)	✓	✓				
	Promotions/Internal transfers (number)		✓				
	Human rights control (evaluation or surveys) (number)	✓	✓		✓		
	Human rights awareness (training and campaigns) (number)		1	✓	✓		✓
	Inclusion Measures (Disabled/LGBT+/Women in Senior Roles)	✓	✓	✓	✓		✓

SOCIAL PERFORMANCE DATA		COMPANIES					
		GSK	Sanofi	Roche	AstraZeneca	Daiichi	Takeda
Social indicators with specific data results on annual reports	**Health and Security**						
	Fatalities (number)	✓	✓				
	Incidents/Accidents/injury - total (number or frequency rate)	✓ (with illness)	✓	✓	✓		✓
	Incidents/Accidents/injury - with lost of time (number or frequency rate)	✓ (with illness)	✓		1		
	Lost of time due to accidents/injury (usually by 100 000 hours of work)	✓ (with illness)		✓			✓
	Occupational Illness - total (number or frequency rate)	✓ (with injury)	✓	✓			
	Occupational illness - with lost of time (number or frequency rate)	✓ (with injury)					
	Lost of time due to occupational illness (usually by 100 000 hours of work)	✓ (with injury)					
	Mental Health (strategies / conversations / support)	✓	✓	✓	✓		
	Health assistance programmes for employees	✓	✓		✓		
	Driving collision accidents reduction efforts	✓	✓	✓	✓		
	Healthy work environment policies (healthy food, tobacco cessation, physical fitness, workplace pressure management)		✓		✓		
	Community Development						
	community investment - total (donations, programmes, contributions) (€, $, £ or number of initiatives)	✓		✓	✓	✓	✓
	improving healthcare access programmes and partnerships	✓	✓	✓	✓	✓	✓
	community training - healthcare providers	✓	✓	✓			✓
	community training - education partnerships (schools / academic)		✓	✓	✓		✓
	employment programmes in deprived areas		✓				

[1] No quantitative data presented but with evidence of initiatives/actions/programmes

Annex C

Table C.1 – Vaccines in development data, approved or in phases 2 and/or 3, on December 12th according to review by The New York Times (2020).

Type	Name	Developer	Country	Efficacy	Dose	Storage	Stage
Whole Virus	BBIBP-CorV	Sinopharm	China	86%	2 doses 3 weeks apart	*unknown*	Phase 3 Approved in UAE
	CoronaVac	Sinovac	China	*unknown*	2 doses 2 weeks apart	4ºC	Phase 3
	Covaxin	Bharat Biotech + ICMR	India	*unknown*	2 doses 3 weeks apart	room temp.	Phase 3
	unknown	Chinese Academy of Medical Sciences	China	*unknown*	*unknown*	*unknown*	Phase 3
	unknown	Chumakov Center	Russia	*unknown*	*unknown*	*unknown*	Phase 1 + 2
Protein-based	NVX-CoV2373	Novavax	USA	*unknown*	2 doses 3 weeks apart	4ºC	Phase 3
	CoVLP	Medicago + GSK	Canada + UK	*unknown*	2 doses 3 weeks apart	4ºC	Phase 2 + 3
	ZF2001	ZFSW + Chinese Ac. Med. Scs.	China	*unknown*	3 doses 4 weeks apart	*unknown*	Phase 3
	unknown	West China Hospital Sichuan Un.	China	*unknown*	*unknown*	*unknown*	Phase 2
	unknown	Finlay Vaccine Inst.	Cuba	*unknown*	*unknown*	*unknown*	Phase 1 + 2
	unknown	Bektop	Russia	*unknown*	*unknown*	*unknown*	Phase 1 + 2 Early use: Russia
	unknown	Sanofi + GSK	USA + UK	*unknown*	*unknown*	*unknown*	Phase 1 + 2
	unknown	Spybiotech	UK	*unknown*	*unknown*	*unknown*	Phase 1 + 2
	unknown	Baylor College of Medicine	USA	*unknown*	*unknown*	*unknown*	Phase 1 + 2
Genetic (DNA/RNA)	BNT162b2	Pfizer + Biontech	USA + Germany	95%	2 doses 3 weeks apart	-70ºC	Phase 3 Approved: Canada
	mRNA-1273	Moderna	USA	94,5%	2 doses 4 weeks apart	-20ºC	Phase 3
	AG0302-COVID19	AnGes + Osaka Univ. + Takara Bio	Japan	*unknown*	2 doses 2 weeks apart	room temp.	Phase 2 + 3
	unknown	Zydus Cadila	India	*unknown*	*unknown*	*unknown*	Phase 3
	INO-4800	Inovio	USA	*unknown*	*unknown*	room temp.	Phase 2
	CVnCoV	CureVac	Germany	*unknown*	2 doses 4 weeks apart	2 – 8ºC	Phase 2
	unknown	Imperial College	UK	*unknown*	*unknown*	*unknown*	Phase 1 + 2

Type	Name	Developer	Country	Efficacy	Dose	Storage	Stage
	unknown	Arcturus + Duke-NUS	USA + Singapore	*unknown*	*unknown*	*unknown*	Phase 1 + 2
	HGC019	Gennova Biopharma + HDT Bio	India + USA	*unknown*	*unknown*	*unknown*	Phase 1 + 2
Viral Vectors	Ad5-nCoV	CanSinoBio	China	*unknown*	1 dose	4ºC	Phase 3 In use: China
	Sputnik 5	Gamaleya Research Inst.	Russia	92%	2 doses 3 weeks apart	-18ºC	Phase 3 In use: Russia
	Ad26.COV2.S	Johnson & Johnson	USA	*unknown*	1 dose	4ºC	Phase 3
	AZD1222	Univ. Oxford + AstraZeneca	UK	90%	2 doses 4 weeks apart	4ºC	Phase 2 + 3