OECD Health Policy Studies

Securing Medical Supply Chains in a Post-Pandemic World

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BETTER POLICIES FOR BETTER LIVES

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Foreword

Shortages of medical products in OECD countries – including essential medicines and medical devices – were common prior to COVID-19. The pandemic put immense strain on already stretched supply chains, as a result of both unprecedented levels of demand and widespread bottlenecks in supply. It has become clear that despite countries' efforts to curb medical product shortages, both routinely and in times of severe crisis, urgent action is needed.

Previous analysis identified the main reported root causes of medicine shortages across OECD countries, namely issues in manufacturing quality, and economic factors such as high pressure on prices of off-patent multi-source medicines in some contexts. The high concentration of some manufacturing steps (e.g. active pharmaceutical ingredients) in a small number of sites, often concentrated in the same geographical area, was also identified as a potential supply chain vulnerability (e.g. to natural disasters). While more robust data to understand this complex problem is needed, these reports already highlighted the need for more information on supply chains to better anticipate and potentially avert occurrences of shortages.

This report, based on further investigations on medicine and medical device supply chains, on case studies (vaccines, plasma-derived medicinal products and continuous positive airway pressure devices), and on stakeholders' consultations, aims to identify available policy options to better anticipate and reduce shortage risks, both in routine circumstances and in the context of severe crises.

Although sound evidence of the effectiveness or cost-effectiveness of policy options is not always available, the report lists several strategies to improve the security of supply of medical products. Better anticipation of risks is a key priority and depends on improvements in regulators' visibility of manufacturing and distribution supply chains. This not only requires regulatory changes to impose information sharing but also significative investments in data infrastructure and analytics. The reduction of shortage risks should also be a key priority, and this rests on a better identification of the root causes to better address them. Public policies should focus on more strategic procurement to contribute to market shaping that is more conducive of reliable supply chains. Public policies could also support the expansion and diversification of supply of medical products for products assessed as "critical" for countries. Further trade facilitations and regulatory harmonisation would ease the movements of good across countries. Beyond all these strategies, countries also need additional capabilities to prepare for severe crises.

Co-operation between countries and between the public and private sectors will be crucial to really improve the security of medical supply chains.

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The chapters were written by Valérie Paris, Suzannah Chapman, and Tom Raitzik Zonenschein of the Health Division in ELS, and Sébastien Miroudot, of the Trade Policy Division in TAD. Ruth Lopert contributed to the conceptualisation of the project and edited the final report. Paula Mendoza, Noa Triki, Lisbeth Waagstein and Marjolijn Moens of ELS, and Cemre Balaban and Alexandra Vodentzis of TAD, contributed to the research and/or drafting. Andrea Andrenelli and Charles Cadestin of TAD, also contributed to data analysis.

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The authors would also like to express their thanks to the representatives of more than 30 companies, regulatory agencies, and regional and international organisations that were interviewed or consulted in the development of the case studies or in the broader context of the project.

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Executive summary

Reliable medical supply chains are a cornerstone of resilient health systems. Supply chains, in the context of this report, refer to the flows of goods and services needed from production to distribution, and ultimately to final consumption (or use) of a medical product – medicine or medical device – by patients, health professionals or healthcare institutions. Each product supply chain is unique, as products are often made up of many different components sourced and produced across different sites and countries and involving many stakeholders. A supply chain failure occurs when supply cannot meet demand for a product marketed in a given country. Shortages of medicines were common and increasing in frequency prior to the COVID-19 pandemic, the latter generating specific challenges for a range of medical products. Medical product shortages can have major implications on health and societies – e.g. delayed treatment and diagnoses, strain on already stretched healthcare systems, increased healthcare costs, loss of productivity, to name a few. Their proliferation has drawn policy attention and prompted calls for action to strengthen medical supply chains – both routinely and in anticipation of the next health crisis.

Medical supply chains are complex and increasingly internationalised

Medical product supply chains are complex and often spread across multiple locations, in different countries, even different continents. They involve many stakeholders. While there may be similarities in the organisation of some supply chains, particularly for medicines, each product supply chain is unique. Medical device supply chains exhibit greater variability than medicines, and often use multiple suppliers of components, some of which are specific to individual devices, while other components are used to produce non-medical goods.

In the last decades, medical supply chains have become more internationalised, albeit with a degree of geographical concentration in the manufacturing of some finished pharmaceutical products and active pharmaceutical ingredients. Global trade in pharmaceuticals increased 10-fold over the past 30 years, reaching USD 900 billion in 2022, and intermediate inputs (e.g. active pharmaceutical ingredients) now account for half of the total movement of goods by value, likely much more by volume. Over the past 30 years, global trade in medical devices has increased 7-fold in value, reaching a total of USD 700 billion in 2022, of which one-third are intermediate goods, one-third are finished products, and approximately one-third are capital goods (durable equipment). The internationalisation of medical supply chains has played an important role in the development of capacities to produce more affordable medicines and medical devices, while also providing flexibility to producers and governments to source essential medical products.

Shortages of medical products were already widespread prior to the COVID-19 crisis

Shortages were already common and increasing prior to COVID-19. Across OECD countries, medicine shortages mainly affect older, off-patent medicines, and are particularly prevalent among central nervous

system, cardiovascular and anti-infective medicines. Manufacturing and quality issues are the most frequently reported reasons (50-60%) for shortages, while "commercial issues" are often cited in generic markets where competitive price pressures are intense. In the EU, 8% of shortages are reportedly due to distribution issues. Prior to the COVID-19 crisis, shortages of medical devices received less attention than medicine shortages. Nevertheless, several sources of risk to medical device supplies have been identified, including reforms to the EU medical device and in-vitro-diagnostic (IVD) regulation; competition with other sectors for raw materials and electronic components; and recently, significant inflation in the costs of inputs. Data on shortages of medical devices and IVDs and their causes are scant, however, as reporting requirements are less stringent than for medicines.

The COVID-19 pandemic imposed immense strain on already stretched supply chains both due to unprecedented levels of global demand and widespread disruptions to supply. During the initial stages of the pandemic, there were shortages of key medicines, testing reagents, and personal protective equipment. This global crisis showed that even though internationalisation and complexity cannot be considered as the root cause of shortages or disruptions in medical supply chains, they have implications for the transmission of shocks, and interdependencies among producing and consuming economies.

Policies must improve the ability to anticipate and mitigate shortage risks

The proliferation of medicine and medical device shortages has raised the need to **strengthen supply chains both routinely and in anticipation of future crises**. Until recently, initiatives to increase medical supply chain security have most commonly been implemented at country-level. In the context of global supply chains, however, national policy action is challenging and should be complemented by **international co-operation and co-ordination**, as well as **collaboration with the private sector**. Supply chains are complex adaptive systems with no single point of control, especially when they span across a large number of countries. While **evaluations of the effectiveness of different policies implemented thus far are scarce**, policy makers can consider several options.

A first action is to **improve visibility and harness information across the whole supply chain**, to **anticipate** and, where possible, **avert shortages** more readily. Today, regulators lack information on upstream supply chains to assess their vulnerability and mainly rely on manufacturers to notify shortages or potential risks of shortages. What happens in distribution chains is even less clear. As a first step, policy makers should consider how to harness information already reported to regulators by manufacturers to identify and assess points of vulnerability in manufacturing supply chains. On the distribution side, implementing track-and-trace systems building on unique identifiers already required in many countries for medicines (to fight fraud) and high-risk medical devices (for materio-vigilance and real-world performance assessment) would enable better monitoring of supply, demand, and available stocks; characterisation of the nature and scope of notified shortages in real-time; and the organisation of effective re-allocation of available stocks. For critical products **–** e.g. essential medicines with vulnerable supply chains **–** closer monitoring of volumes and flows should be established in partnership with suppliers. In general, achieving better visibility requires more routine collection of granular, real-time information on the structure, content, and status of medical supply chains. This would entail an enabling regulatory environment, as well as investments in data infrastructure and analytics **–** both by firms and governments. Better anticipation of risks also requires **information sharing** between stakeholders, which should be permitted where appropriate and necessary.

Second, policy action should focus on **addressing the root causes of shortages**, to **mitigate (or reduce exposure to) risks of shortages**. To address quality issues, public authorities need to require manufacturers to maintain quality management systems meeting the highest established standards and to monitor their implementation. For markets where excessive pressure on prices is suspected to lead to degradation of quality standards, product withdrawals and market exits, as well as concentration of supply to achieve economies of scale, some policy options may contribute to **market shaping**. *Cross-country*

pooled procurement can be useful, for example to enhance prediction of demand and to secure supply for small markets that might not be supplied otherwise. The Pan-American Health Organisation's revolving fund for the purchase of vaccines is a good example. *Strategic public procurement* approaches that consider criteria other than price alone can also relieve some pressure on prices while elevating the importance of supply security in decision making. The "most-economically advantageous tender" (MEAT) criteria for public procurement recommended by the European Commission is a potential vehicle for more strategic procurement. Procurers of medical goods could also consider the diversification of supply as a rationale for splitting awards. **Diversification of supply**, however**,** may require further action. Re-shoring and near-shoring policies are high on the policy agendas of several countries seeking to reduce dependency on highly concentrated sources of certain raw materials, active pharmaceutical ingredients and finished products. These policies can expand production capacity, reduce concentration, and help meet increasing global demand. However, careful consideration should precede their implementation as they entail substantial cost. They should only be focused on "critical products" as previously, ideally, defined at supranational level.

Third, policy action should encourage greater **agility and flexibility into the system,** to **reduce risks of potentially harmful supply disruptions**. Trade facilitation and harmonisation of regulatory requirements for marketing authorisation would ease the movement of goods across countries. Appropriate inventory strategies and co-ordinated stockpiling policies can help mitigate shortages due to spikes in demand and/or interruptions in supply chains in the short term but are of limited effectiveness in long-term disruptions. The proliferation of national stockpiling policies, however, can potentially worsen supply gaps. Regional and co-ordinated stockpiling may be an option for responding to short-term mismatches between supply and demand, by allowing swift re-allocation of stocks where they are most needed.

Beyond these, additional actions should anticipate future severe crises

Countries need additional capabilities to prepare for and mitigate risks on medical supply chains in the event of a severe crisis. Here, **international co-operation and close collaboration between the private sector and governments** are important to ensure a **cohesive, collective, and efficient response**.

Severe crises call for **better preparedness for quicker responses**. Preparedness plans, for pandemics and other shocks, should include specific measures to address medical supply chain issues that can be rapidly enacted. Stakeholders must work together to establish processes for **defining lists of critical products** specific to different emergency situations and **putting in place mechanisms to monitor international and regional flows** of these products. These lists could also be used for multi-country pooled procurement. Countries should also agree on clear mechanisms to **share critical medical products' supply and demand data**, and additional regulatory flexibilities such as rules refraining them from exacerbating supply chains issues through hoarding and export restrictions. Multilateral or regional trade agreements could – before the next crisis occurs – include provisions for co-operation in ensuring the continuity of supply of medical goods.

Severe crises also require that **mechanisms are already in place to mitigate risks of shortages**. Policy makers may need to **support expanding production capacity** in cases of surging demand and **mandate prioritisation of the medical sector** for the supply of raw materials and electronic components. Preparing and implementing necessary legislation in advance is critical to facilitating rapid responses. Regardless of the policy approach chosen, policy makers should ensure that mechanisms are in place to **facilitate worldwide access and fair allocation** of existing technologies, while supporting R&D efforts and encouraging **the transfer of technologies developed during crises** (such as new vaccines and treatments).

1 Vulnerabilities of medical supply chains

This chapter takes stock of the vulnerabilities of medicine and medical device supply chains, making a case for the importance of enhancing their resilience. First, it provides insight into the complexity and variability of the organisation of these global supply chains and presents trade statistics. It then explores the growing issue of medical product shortages, which pre-dated the COVID-19 pandemic, including potential causes of disruption. Finally, the chapter discusses additional strain that is placed on supply chains in times of severe crises.

Key findings

Medical supply chains are complex and have become increasingly internationalised over time. Supply chains, in the context of this report, refer to the flows of goods and services needed from production to distribution, and ultimately to final consumption (or use) of a medical product – medicine or medical device – by patients, health professionals or healthcare institutions.

- The production of medicines involves complex transnational supply chains, generally beginning with raw materials that are transformed into active pharmaceutical ingredients (API) at primary manufacturing sites, with secondary sites producing the finished pharmaceutical products. Global trade in pharmaceuticals has increased 10-fold over the past 30 years, and now accounts for about 4% of total trade by value. About half the movements of goods (by value) concerned intermediate inputs (such as APIs) in 2022. The share of traded intermediate inputs in the value of final pharmaceutical products peaked at 25% in 2015 and has been declining since.
- Medical device supply chains are even more varied and, and in some cases more complex, than those of medicines, with some bearing a closer resemblance to supply chains for non-medical products such as clothing or electronics. Medical devices span a huge range of products, and their supply chains are highly product-dependent, with manufacturing reliant on a large number of suppliers of individual components that may be specific to individual devices or commonly used by non-medical manufacturers. Over the past 30 years, global trade in medical devices has increased 7-fold in value, to reach a total amount of USD 700 billion in 2022, with one-third in intermediate goods, one-third in final products and about one-third in capital goods (durable equipment).

Medicine shortages were already widespread prior to the COVID-19 pandemic. Although shortage definitions and notification rules vary widely across countries and regions, multiple studies have reported steady increases in the prevalence of shortages in various contexts.

- These studies show that **shortages predominantly affect older, off-patent medicines**. However, one study looking at 20 countries in the European Economic Area (EEA), found that these medicines do not necessarily have a higher probability of being in shortage. The most commonly affected medicine types varied across countries and periods. Central nervous system, cardiovascular and anti-infectives medicines were among the most commonly affected classes, with injectables more likely to be in shortage than oral dosage forms.
- **Manufacturing and quality issues are by far the most frequently reported causes of medicines shortages** (50-60%). “Commercial reasons” are also often cited (25% in one study of 20 EEA countries). Market dynamics have been identified as an important root cause in the United States, where competitive pricing pressures on off-patent multi-source products can be very intense. For other countries, empirical evidence on root causes of shortages is lacking.
- The contribution of the nature of distribution chains in local or national shortages has not been established empirically.
- **Some medicinal products face specific challenges arising from unique features of their supply chains.** These include vaccines (which are subject to exceptionally rigorous requirements, notably with regard to quality controls and testing), plasma-derived medicines (dependent on plasma collection) and radio-pharmaceuticals (whose production costs are subsidised by manufacturing countries).

Prior to the pandemic, shortages of medical devices received less attention than shortages of medicines, likely due in part to differences in notification requirements. Experts and industry representatives have nevertheless identified several risks to the future supply of medical devices. These pertain to long-awaited reforms in medical device and in-vitro-diagnostic regulation in the European Union; competition with other larger industrial sectors for the acquisition of raw material and electronic components used as intermediate inputs; possible changes in the regulation of certain chemical substances; and, more recently, significant inflation in the costs of inputs. Data on the occurrence and evidence of the causes of shortages of medical devices and in-vitro diagnostics are, however, very scant.

The **resilience of medical product supply chains in the face of severe crises has been tested on several occasions.** For example, large surges in demand occurred with the H1N1 and COVID-19 pandemics, and in the latter, these were coupled with significant disruptions in manufacturing and trade restrictions, together exacerbating the pre-existing issues. Despite being severely stressed during these periods and facing several shortages, medical product supply chains demonstrated considerable resilience.

Chapter 1 takes stock of the vulnerabilities and particularities of medical product supply chains. Supply chains, in the context of this report, refer to the flows of goods and services needed from production to distribution, and ultimately to final consumption (or use) of a medicine or medical device – by patients, health professionals or healthcare institutions (Section 1.1). A supply chain failure is said to occur when supply is unable to meet demand for a product marketed in a given country. While shortages of medical goods were increasing in frequency prior to the pandemic of COVID-19 (Section 1.2), the crisis demonstrated the critical importance of securing supply chains of medical goods to address future severe health crises (Section 1.3).

1.1. Understanding the complexity of medical product supply chains

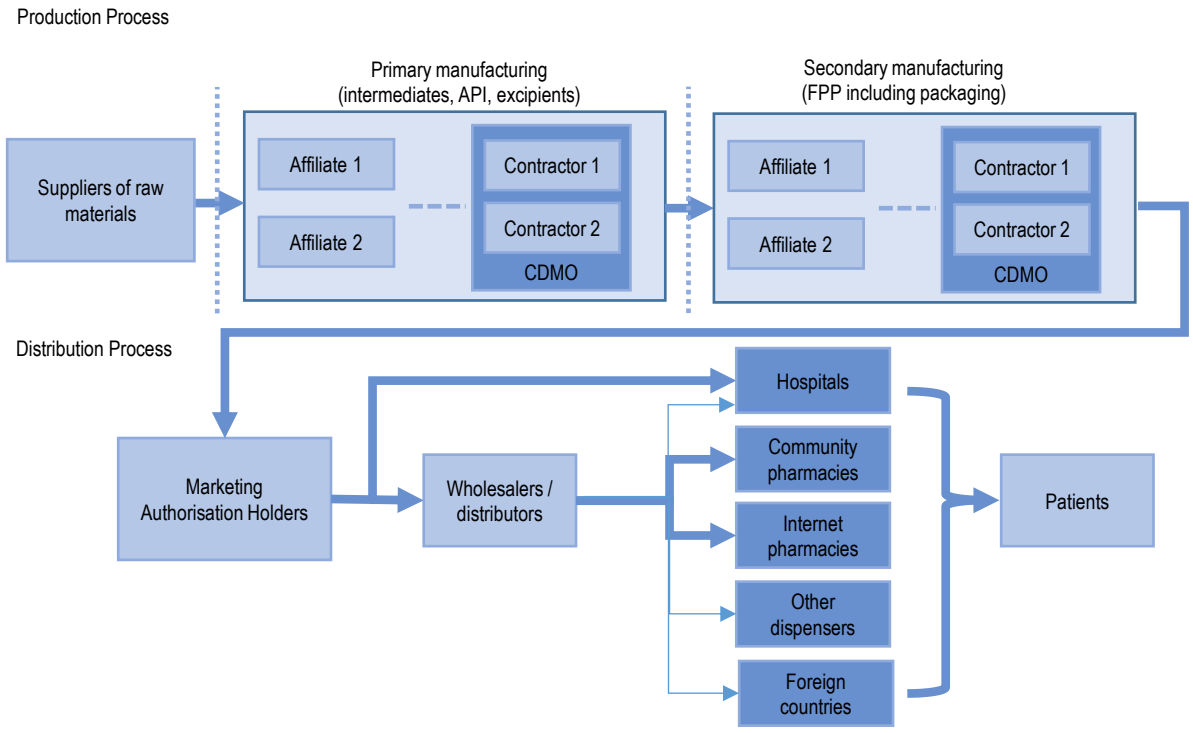
Medical product supply chains are complex and often fragmented, with many different stakeholders involved globally. The term “medical products” itself encompasses a wide variety of items and substances used in healthcare, including pharmaceuticals (i.e. medicines), vaccines, medical devices (i.e. products or equipment intended for a medical purpose), biological products, blood and tissue products, diagnostic tools and tests, personal protective equipment (PPE), and medical consumables (e.g. disposable items such as blood collection tubes, syringes) etc. Medicines may also be used in combination with medical devices, further adding to the complexity. It is important to note that regulatory oversight, manufacturing processes, and safety standards for these products can vary widely depending on their type, intended purpose, and the level of risk they pose, as well as by jurisdiction. For example, while regulatory authorities authorise medicinal products (including medicines, vaccines, plasma products, etc.) by assessing their safety, efficacy, and quality they may have different and distinct regulatory responsibilities for medical devices.[1] The sections below describe some of the specifics of supply chains of medicines (Section 1.1.1) and medical devices (Section 1.1.2) for human use.

1.1.1. Pharmaceutical supply chains are complex and internationalised

Figure 1.1 offers a basic schematic of pharmaceutical supply chains, as described by Chapman, Dedet and Lopert (2022[1]). The production of medicines involves complex transnational supply chains, with the organisation often driven by cost containment practices and the structures of production processes. They can involve multiple stakeholders across different facilities and countries. For example, small-molecule (non-biological)[2] medicine production starts with raw materials transformed into active pharmaceutical

ingredients (APIs) at primary (often specialised) sites, while secondary sites turn these APIs into finished pharmaceutical products (FPPs). Marketing authorisation holders (MAHs), i.e. the companies or legal entities with authorisation to market the products, often also use contract manufacturers. Medicines are then supplied by manufacturers to distributors (i.e. wholesalers) and to retail dispensing points, with hospitals in some places bypassing wholesalers and being supplied directly by MAHs. Disruptions in manufacturing and production processes may have a global impact on the availability of medicines, while problems in distribution processes are more likely to have localised effects (e.g. local or national).

Figure 1.1. The complexity of pharmaceutical supply chains



Note: Dotted vertical lines represent the possibility of an international border. API: active pharmaceutical ingredient; FPP: finished pharmaceutical product; CDMO: contract development and manufacturing organisation.
Source: Adapted from Chapman, S., G. Dedet and R. Lopert (2022[1]), "Shortages of medicines in OECD countries", https://doi.org/10.1787/b5d9e15d-en.

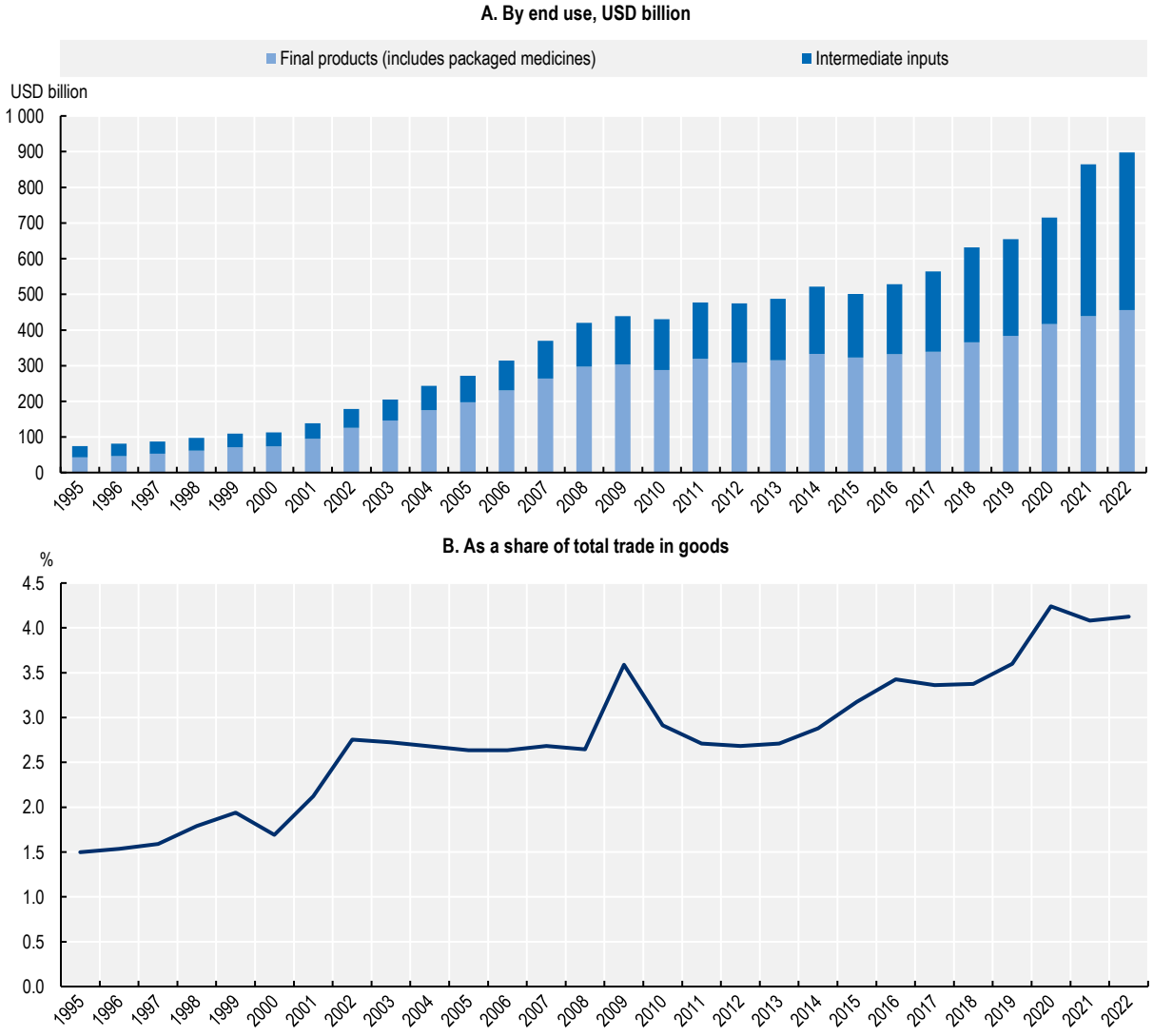
Trade in pharmaceutical products has increased, especially for intermediate products

Since 1995, there has been a remarkable increase in trade in pharmaceutical products, with a notable surge in the second half of the 2010s, and a further acceleration following the COVID-19 pandemic (Figure 1.2, Panel A). This can be attributed to several factors, including advancements in pharmaceutical research and development, and increased global demand for healthcare products. It is also explained by the expansion of global supply chains, as highlighted by the increasing share of trade in intermediate inputs (such as APIs) in Figure 1.2. In addition, the share of pharmaceutical products in total world trade by value has been steadily increasing (Figure 1.2, Panel B). This trend is indicative of the growing importance of the pharmaceutical industry in the global economy.

Higher values for trade in pharmaceutical products during the pandemic are partially explained by higher prices. However, they also illustrate how trade in pharmaceuticals outpaced the overall growth in merchandise trade in recent years, as well as the role played by trade to address pandemic-related

disruptions and shortages. While there is some granularity in trade data,[3] it remains challenging to analyse trade flows for specific products (such as face masks during COVID-19) and trade statistics do not allow for a full analysis of supply chains when not coupled with input-output data.

Figure 1.2. World trade in pharmaceutical products (1995-2022), by value

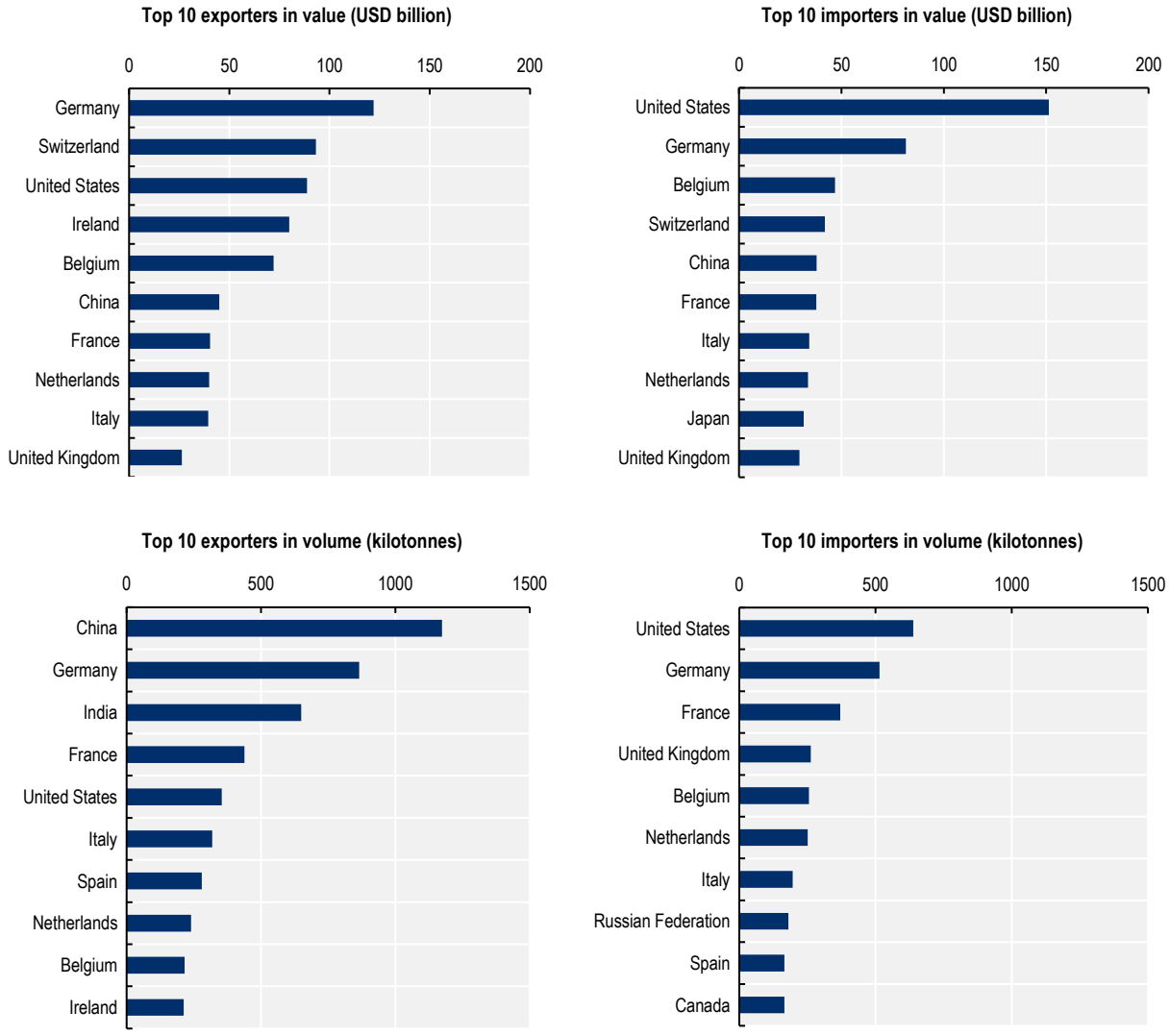


Note: Pharmaceutical products as defined by the WTO Pharma Agreement (HS Chapter 30, and headings 2936, 2937, 2939, 2941). Data prior to 2017 are based on older versions of the HS classification and may not accurately reflect the list of products.
Source: BACI (CEPII) (2023[2]), *BACI Trade data*, www.cepii.fr/CEPII/en/bdd_modele/bdd_modele_item.asp?id=37; and Drevinskas, E., E. Shing and T. Verbeet (2023[3]), *Trade in medical goods stabilises after peaking during pandemic,* www.wto.org/english/blogs_e/data_blog_e/blog_dta_23may23_e.htm.

Germany, Switzerland and the United States are the top exporters of pharmaceutical products by value, reflecting their strong positions in high-value, research-intensive pharmaceutical activities. In contrast, the People's Republic of China (hereafter "China") and India are among the top 3 exporters by volume, signifying their roles in the mass production of APIs and off-patent medicines (Figure 1.3). Germany stands out as a top exporter and importer in both volume and value, suggesting that the country plays a role upstream in pharmaceutical supply chains, while also being the largest consumer market in the European Union (EU). The United States stands as the top importer of pharmaceutical products in both volume and

value, driven by its large consumer market and high per capita healthcare spending. Belgium and Switzerland have small domestic markets but are both major exporters and importers of pharmaceutical products (by value). This is another illustration of how pharmaceutical supply chains have become global with specialised economies acting as key hubs for the transformation and distribution of pharmaceutical products.

Figure 1.3. Top exporters and importers of pharmaceutical products (2021), by value and volume



Note: Pharmaceutical products as defined by the WTO Pharma Agreement (HS Chapter 30, and headings 2936, 2937, 2939, 2941). Data prior to 2017 are based on older versions of the HS classification and may not accurately reflect the list of products.
Source: BACI (CEPII) (2023[2]), *BACI Trade data*, www.cepii.fr/CEPII/en/bdd_modele/bdd_modele_item.asp?id=37; and Drevinskas, E., E. Shing and T. Verbeet (2023[3]), *Trade in medical goods stabilises after peaking during pandemic,* www.wto.org/english/blogs_e/data_blog_e/blog_dta_23may23_e.htm.

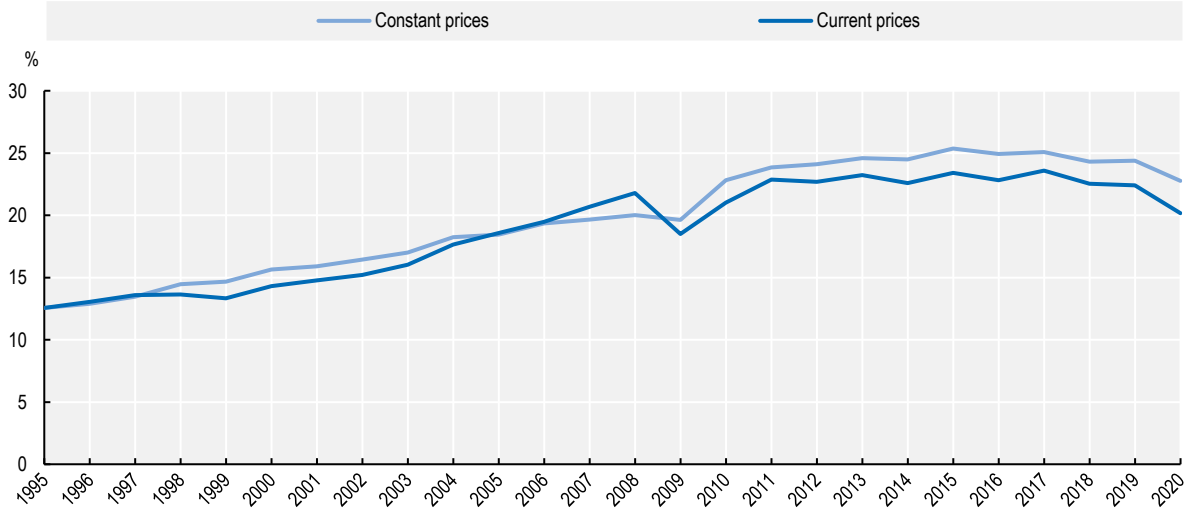
Sourcing of pharmaceutical products has become increasingly internationalised

When using input-output data (such as the OECD Inter-Country Input-Output tables), the internationalisation of pharmaceutical supply chains becomes even clearer (Figure 1.4). These data lack any granularity beyond the specification of the pharmaceutical industry (identified through ISIC code 21

corresponding to “manufacture of basic pharmaceutical products and pharmaceutical preparations”). However, the data indicate that when looking at the world output of pharmaceutical products (i.e. all intermediate and final products produced by firms belonging to the pharmaceutical industry), the share of output corresponding to all the intermediate inputs traded upstream in their supply chains (from any country and industry) steadily increased between 1995 and 2015. In 1995, there were only 12 cents of trade intermediate inputs for each 1 dollar of output in the pharmaceutical industry; in 2015, there were more than 25 cents of trade in intermediate inputs (in constant prices).

Figure 1.4. Import intensity of pharmaceutical production (1995-2020)

As a share of world gross output of pharmaceutical products (%), in value



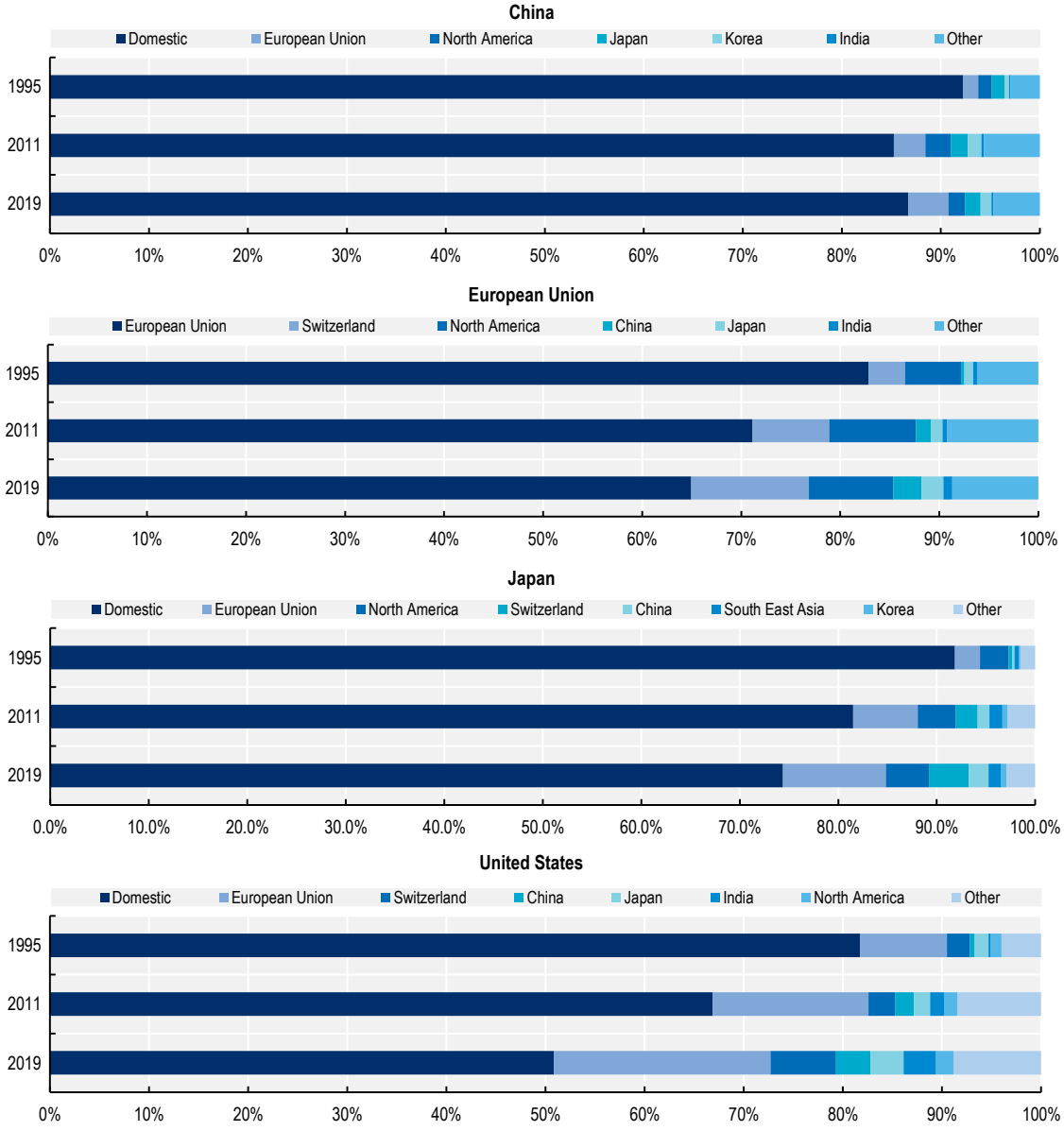
Note: The import intensity of production indicates for each dollar of final output in the pharmaceutical industry the share of value corresponding to all trade in intermediate inputs upstream in the value chain. Data for the world are estimated via an average weighted by final demand in each country and masks substantial heterogeneity across countries and products. Data in previous year’s prices.
Source: OECD (2023[4]), *OECD Inter-Country Input-Output Database*, http://oe.cd/icio.

From Figure 1.4 it can be seen that 2015 was the “peak year” in the globalisation of the pharmaceutical industry, with a trend towards more domestic supply chains in 2017-20 (i.e. a lower share of traded intermediate inputs in final output). While this trend began prior to the pandemic, 2020 should be regarded as an exceptional year in which the import intensity of production was lower due to disruptions in international trade. Trade data post 2020 indicate an important surge in trade of pharmaceutical products (Figure 1.2) that may be associated with more foreign inputs trade and higher import intensity of production. It remains to be seen whether the pandemic has also triggered a restructuring of pharmaceutical supply chains with a re-shoring of inputs manufacturing. Such a trend would take time to materialise into actual shifts in trade flows and a change in the input-output structure. Importantly, Figure 1.4 shows average figures that belie significant heterogeneity across buyers, and suppliers, as well as across products.

Some country and region-specific results are shown in Figure 1.5, highlighting not only a shift in the overall use of foreign inputs but also changes in the geographical distribution of suppliers. In the European Union, Japan and the United States, pharmaceutical products have been produced with a smaller share of domestic value-added[4] over the years (and there has been no decline in the import intensity of production for these economies). China is the only country in this sample for which pharmaceutical supply chains became more domestic between 2011 and 2019.

While as suppliers of inputs, China and India have benefited from the internationalisation of EU, Japanese and US supply chains, more foreign value added is actually coming from other OECD economies. Most of the increased foreign value-added in US and Japanese pharmaceutical supply chains is the result of growth in sourcing in the EU, and in Switzerland, while EU supply chains rely more on Switzerland and North American suppliers (i.e. Canada, Mexico and the United States). There is an increase in the value added coming from China in EU, Swiss an US supply chains, but relatively small. While these results are for all pharmaceutical products, they are not inconsistent with more product-specific assessments identifying a high level of sourcing from India and China (but concentrated in certain off-patent medicines and specific APIs). In addition, data on the origin of value-added in final consumption do not reflect the magnitude of countries' contributions to final consumption in terms of quantities.

Figure 1.5. Origin of value added in final consumption of pharmaceutical products (1995, 2011 and 2019)



Note: Based on a decomposition of final demand for products of the pharmaceutical industry (ISIC code 21 – manufacture of basic pharmaceutical products and pharmaceutical preparations) identifying the country of origin of value added.
Source: OECD (2023[4]), *OECD Inter-Country Input-Output Database*, http://oe.cd/icio.

Distribution of medicines takes variable forms across countries

Post production, the distribution of medicines follows a range of different pathways, depending on the country, the type of medicine and the final intended use (administration in inpatient care, dispensing in retail pharmacies, etc.). Medicines dispensed by retail pharmacies to patients are generally supplied by wholesalers, subject to different regional or national regulations and obligations. Adapting to market conditions, wholesalers adopt a variety of organisational structures. In the United States, there are ~33 500 wholesale distributors and third-party logistics providers (FDA, 2023[5]). Across Europe, the number of wholesalers and warehouses vary significantly. For example, in 2021, Germany counted 9 full-line wholesalers[5] with 106 warehouses, while Poland had 122 full-liner wholesalers with 190 warehouses. In Germany, 2 413 authorisations had been issued for wholesalers (including those who only distribute a sub-set of medicines) compared with 421 in Poland (GIRP, 2022[6]).[6] In some cases, however, generic manufacturers may choose to bypass wholesalers and gain direct access to pharmacy shelves by offering financial or in-kind discounts or complementary services. The effect of this high variability in wholesale activity on reliability of supply is unknown.

In the EU, medicines dispensed or administered in hospitals are mainly purchased directly from manufacturers. In 2021, manufacturers delivered 7% of their products directly to retail pharmacies and 35% to hospitals, with the remainder 58% delivered to wholesalers for distribution to retail pharmacies (52%) and hospitals (6%) (GIRP, 2022[6]).[7]

Flows and practices in the distribution chains may lead to local shortages. Within the European Economic Area (EEA), so-called “parallel-trade” is often cited as a possible cause of national shortages. This type of trade consists of purchasing medicines in a country where (often regulated) prices are low, and reselling them in a country with higher prices, without the consent of the manufacturer. The practice is consistent with the principle of free movement of goods within the EEA and enables savings in recipient countries. According to the association of companies engaged in parallel trade, Affordable Medicines Europe, parallel trade imports accounted for 2.8% of the total EU pharmaceutical market in 2020. At that time, Germany, the United Kingdom and the Netherlands were the 3 top importers, with respectively 51%, 14% and 10% of EU parallel imports by value. Denmark, the Netherlands and Sweden had the highest shares of parallel imports in their national markets, with 25%, 10% and 10% respectively. According to members’ responses to a survey by the association, 50-60% of imports in these countries originated from high-income countries. France and Germany were the largest exporters in terms of global sales (Aguiar and Ernest, 2021[7]).

Individual pharmaceutical product supply chains are unique: Some examples

While each pharmaceutical product supply chain is unique, some general insights can be gained from examining the supply chains of selected product categories. Chapter 11 of *Ready for the Next Crisis?* (OECD, 2023[8]) includes several detailed case studies:

- **Propofol** (an intravenous anaesthetic) has a complex manufacturing process, requiring the API to be part of a stable emulsion (i.e. a mixture of two non-miscible substances such as oil and water). Propofol’s API (2,6-diisopropylphenol) has a relatively diversified supply in India, Italy, Switzerland and the United States, but the overall number of suppliers remains fewer than 10. Secondary manufacturing of propofol is a controlled and sterile process that involves creation of the emulsion and preparation of the final product. It is generally outsourced to either a subsidiary of the brand manufacturer or an independent contract manufacturer. Testing and packaging generally take place in locations separate from manufacturing. There are several manufacturers of propofol, but only a limited number are authorised to sell in each market.

- **Low-molecular-weight heparins** (LMWH – a class of anticoagulants, with a case study based on the example of enoxaparin) are biologicals[2] derived from unfractionated heparin, most of which originates from porcine (pig) intestines. China plays a crucial role as a producer, supplying 60% of the crude heparin utilised in the United States for the production of heparin sodium in 2010 (US Congress, 2018[9]). After purification in a laboratory, heparin extracts are transformed into heparin sodium, with capacity in China, Singapore and the United States. Subsequently, full length heparin is converted into smaller LMWH fragments through depolymerisation, a process requiring sophisticated techniques to ensure product stability and quality. This step is conducted by the brand manufacturer or a specialised contract manufacturing firm. Exports of heparin increased significantly during the COVID-19 pandemic.
- **Macrolide antibiotics** (a class of antibiotics, using the specific example of azithromycin) require specialised production processes that are currently highly concentrated. Fermentation to produce the intermediate ingredient, erythromycin, takes place in several geographical locations in China. This technique requires clean water, a favourable environment, and adequate infrastructure. Primary manufacturing of the azithromycin API from erythromycin requires several intermediate (chemical) steps that can be split across countries and companies, although interviewees suggested that this step generally occurs in Asia. The formulation stage is more geographically diverse. However, few companies market azithromycin.

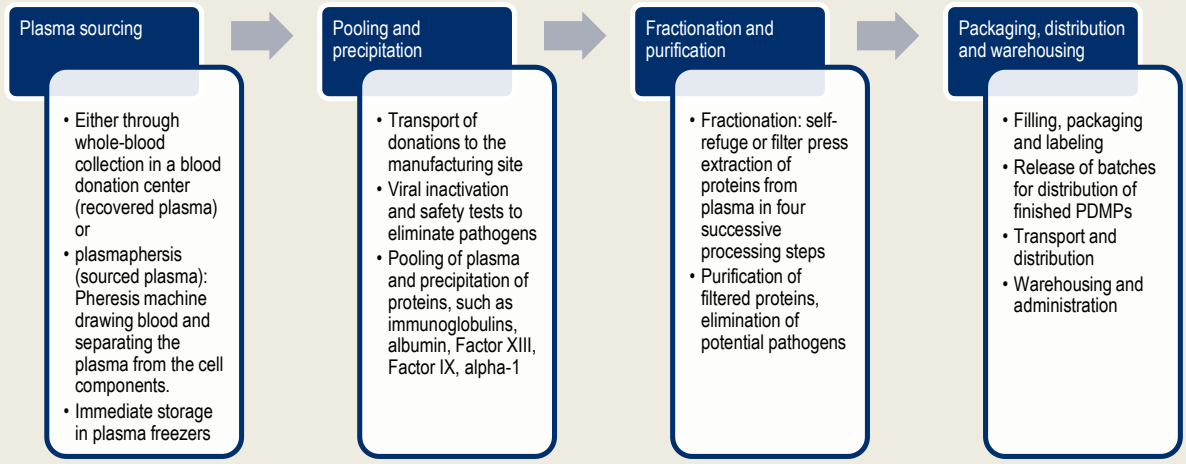
The OECD has also analysed the supply chains of plasma-derived medicines and vaccines, both of which are classified as biologics.[2] Box 1.1 and Box 1.2 outline some of the supply chain characteristics of these products.

Box 1.1. Plasma-derived medicinal product supply chains at a glance

Plasma-derived medicinal products (PDMPs) are essential for preventing and treating a range of conditions that include immune deficiencies, autoimmune and inflammatory conditions, and bleeding disorders, and they are also indicated in certain infectious diseases and critical situations such as septic shock and severe burns (Strengers, 2023[10]; Strengers, 2017[11]; Brand et al., 2021[12]; Schmidt and Refaai, 2022[13]). They are classified as biologicals, manufactured from human blood plasma through a process called fractionation. This technique involves separating, purifying, and concentrating different types of proteins found in blood plasma into therapeutic doses (see Figure 1.6). A range of PDMPs serve critical functions in healthcare, including in particular albumin (the major plasma protein responsible for regulating blood volume), coagulation factors (essential for blood clotting, used to treat genetic bleeding disorders and surgical bleeding) and immunoglobulins (essential for defence against infectious agents and the regulation of the immune system). Currently around 20 different therapeutic proteins can be purified from plasma, and PDMPs are licensed for the treatment of many diseases and disorders (Schmidt and Refaai, 2022[13]). In most jurisdictions, PDMPs are regulated as prescription medicines, subject to particularly rigorous regulation, testing, and controls. Their importance is underscored by the inclusion of several PDMPs in the World Health Organization's Model List of Essential Medicines (WHO, 2023[14]).

The PDMP manufacturing process starts with the collection of blood plasma from healthy donors, which is a resource of human origin (PPTA, 2022[15]). Plasma can be obtained either through whole blood donation (recovered plasma) or directly by apheresis (plasmapheresis or sourced plasma). Most PDMPs are primarily sourced from plasmapheresis, a method by which whole blood is collected and centrifuged, plasma separated, and red blood cells returned to the donor (Strengers, 2023[10]). Compared to whole blood donation, which only takes 10-20min, plasmapheresis is a longer and more laborious process, taking around 60-90 min, but is more efficient as it generates two to three times more plasma per donation.

Figure 1.6. Schematic of plasma manufacturing process and supply chain



Note: The stages depicted in this schematic are intended to provide a general overview of plasma production and are not comprehensive.
Source: Authors' elaboration based on Kluszczynski, T., S. Rohr and R. Ernst (2020[16]), *Key economic and value considerations for plasma-derived medicinal products (PDMPs) in Europe*.

As the sourced plasma must conform to the highest safety standards, it is subject to viral removal processes, pathogen elimination, and multiple inactivation steps. In a second step, multiple donations are pooled in large manufacturing vessels. As depicted in Figure 1.6, proteins are first precipitated from the plasma. Each plasma contains valuable proteins that are extracted, such as immunoglobulins, albumin, Factor VIII, Factor IX, alpha-1 antitrypsin, and many more (Kluszczynski, Rohr and Ernst, 2020[16]). The harvest is obtained either through self-refuge of the plasma while the proteins are in motion or through filter press extraction. This process is also described as fractionation as it separates the plasma into four successive processing steps, so-called fractions, where different protein types are obtained for the final product (Strengers, 2023[10]). In the case of immunoglobulins, the plasma pool has to be large and geographically diverse, containing at least a thousand donations that in some jurisdictions may be sourced from all over the world (Kluszczynski, Rohr and Ernst, 2020[16]). Geographic diversity is important to ensure that the final product contains a wide spectrum of antibodies to fight against various pathogens. The filtered proteins are then purified, and potential pathogens eliminated before they are filled, packed and batches of finished PDMPs released for distribution.

The demand for PDMPs, such as intravenous immunoglobulins (IVIg), which are polyvalent and without an alternative or recombinant version, is growing at a rate of 6-8% per year globally, likely due to expanded access to medical care, the development of new products and advanced diagnostics (Schmidt and Refaai, 2022[13]; Strengers, 2023[10])[1]. Immunoglobulins are essential in the body's immune defence against foreign agents such as viruses and bacteria. Furthermore, the increasing number of patients with immunodeficiencies caused by oncology treatments and the growth in off-label use of IVIg are contributing to the increasing demand (correspondence with experts, 2023; (Schmidt and Refaai, 2022[13])).

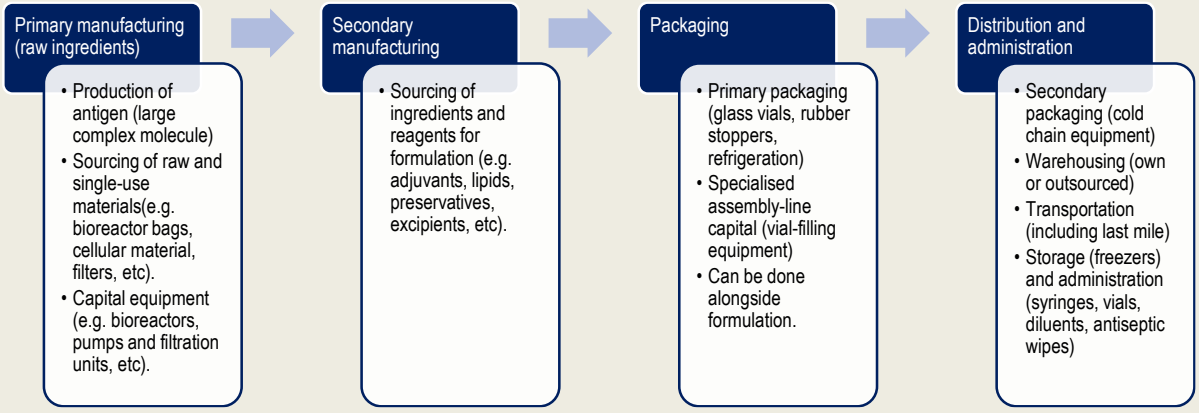
Despite decades of effective therapeutic use, these treatments still face serious patient access challenges due to an uneven plasma donation landscape across countries, lengthy manufacturing processes taking up to 7-12 months under strict safety procedures, and complex regulatory frameworks that impede the collection and manufacturing of plasma (Kluszczynski, Rohr and Ernst, 2020[16]). The key challenges appear upstream in the value chain, beginning with the collection of the raw material, i.e. plasma, which can only be sourced from eligible and healthy human donors.

1. Latest research demonstrates that consumption in Europe alone is projected to increase by one-third from 50.5 tonnes in 2017 to 67.5 tonnes in 2025 (Marketing Research Bureau, 2023[17]). The plasma collected in this region meets 63% of the demand and the rest is mainly supplied by the United States (Kluszczynski, Rohr and Ernst, 2020[16]).
Source: Authors as cited and from consultations with experts in 2023.

Box 1.2. Vaccine supply chains at a glance

Vaccines are biological medicines intended to stimulate immunity to a particular infectious disease or pathogen and may be deployed as part of population-based immunisation strategies as well as in response to seasonal and emergency outbreaks. Although the precise stages and inputs needed for the production of a given vaccine vary depending on the technology platform (e.g. inactivated vaccine, live attenuated vaccine, viral vector-based, recombinant protein, messenger ribonucleic acids (mRNA) etc.), vaccine supply chains can be broadly described as in Figure 1.7.

Figure 1.7. Schematic of vaccine manufacturing process and supply chain



Note: The stages depicted in this schematic intend to provide a general overview of vaccine production and are not comprehensive.
Source: Author's own elaboration based on OECD (2021[18]), *Using trade to fight COVID-19: Manufacturing and distributing vaccines*, https://doi.org/10.1787/dc0d37fc-en; Bown, C. and T. Bollyky (2021[19]), "How COVID-19 vaccine supply chains emerged in the midst of a pandemic", https://doi.org/10.1111/TWEC.13183; OECD (2023[8]), *Ready for the Next Crisis? Investing in Health System Resilience*, https://doi.org/10.1787/1e53cf80-en.

Primary manufacturing consists of the initial production steps to create the vaccine's active ingredient i.e. the antigen, which is responsible for inducing an immune response. The process and type of production facility needed for this vary according to the type of vaccine being produced. Typically, it includes culturing and propagating the target organism (e.g. virus or bacteria) in bioreactors, inactivating or attenuating the pathogen, and purifying the antigenic components – to create what is often known as "bulk antigen" or "bulk vaccine".

Secondary manufacturing involves the formulation of the vaccine, by combining the vaccine's active ingredient with all other components and mixing them uniformly in a single vessel. Here, stabilisers, adjuvants, and preservatives may be added. Additional ingredients in the production or packaging of a vaccine may require separate mini supply chains.

For packaging, vaccine formulations are transferred to a separate facility in order to "fill" (squirt doses into vials) and "finish" (cap the vials with stoppers and then label and package) the vaccine. This requires specialised assembly-line capital equipment, in addition to inputs such as glass vials and stoppers. In some cases, the formulation and fill and finish take place in the same facility. Stringent quality controls are taken at this stage.

Finally, vaccines doses must be transported at appropriate temperatures, and delivered while maintaining the cold chain. The cold chain is interconnected with refrigeration equipment; while most vaccines can be kept between 2°C and 8°C, some require temperatures as low as -20°C or -70°C.

The three main manufacturing stages described above can take place in different factory buildings, as well as across several countries. Each step also involves rigorous quality controls and testing, which represent up to 70% of the manufacturing time (Vaccines Europe, 2020[20]). On average, the entire manufacturing process is long and can take up to two years, with differences according to the technology platform.

According to the World Health Organization's 2022 Global Vaccine Market Report, the vaccine supply base is highly concentrated geographically and at firm level (WHO, 2023[21]). In 2019, an estimated 76% of vaccine production took place in Europe, followed by North America (13%), Asia (8%) and the rest of the world (3%) (Vaccines Europe, 2019[22]). In 2021, excluding COVID-19 vaccines, 10 manufacturers alone provided 71% of vaccine doses globally. When looking at individual vaccines, often only two or three suppliers provide more than 80% of supply (WHO, 2023[21]).

The geographical concentration of the manufacturing base underscores the role of trade. As of 2019, vaccines were imported by 209 economies and exported by 90 economies. Cao, Du and Xia (2023[23]) found that vaccine trade links remain highly concentrated within developed countries in Europe and the United States, a pattern largely in line with the WHO's assessment (WHO, 2023[21]). In 2021, the EU was the largest exporter of vaccines, with Belgium as the top exporter by both value and volume, accounting for 16% of global volume exports, followed by the United States (14%) and China (12%)[1]. Export volume rankings differ from value rankings, revealing heterogeneity in unit prices across suppliers. In relative terms, imports are less concentrated in both value and volume, although the top 20 importers represent 52% of global import volumes (72% in value)[1].

As mentioned above, production of vaccines relies on several ingredients. For example, the manufacture of pertussis-containing pentavalent vaccine requires approximately 160 different ingredients. Using 2017-19 UN COMEXT trade data for 20 vaccine ingredients and items needed to distribute vaccines, Evenett et al. (2021[24]) found that the EU was a net importer of only three vaccine ingredients and distribution items. China and the United States were identified as key non-EU sources of vaccine inputs, followed by Switzerland and Japan (Evenett et al., 2021[24]).

1. OECD calculations using trade data from the BACI database, 2023.
Source: Authors as cited and from consultations with experts in 2023.

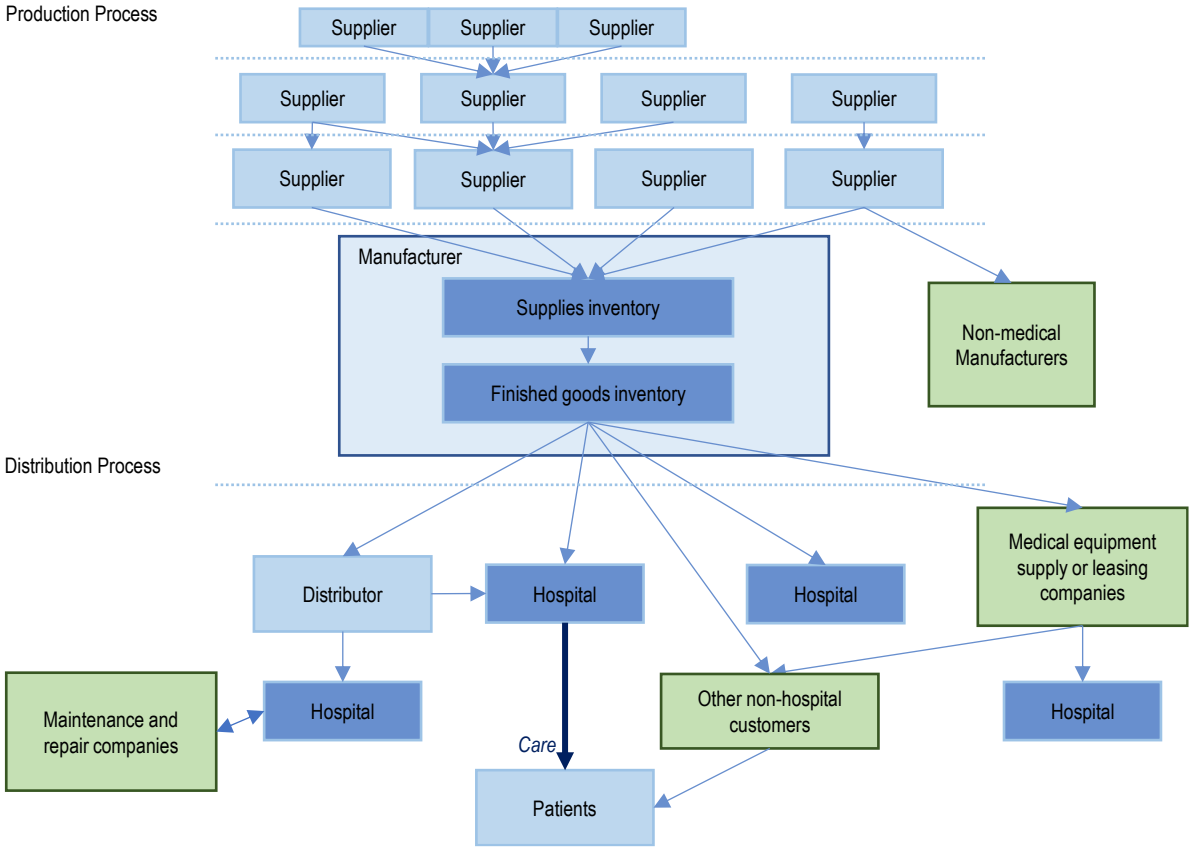
1.1.2. Medical device supply chains exhibit even more variability

Medical device supply chains exhibit even more variability, and in some cases more complexity, than pharmaceuticals, with some bearing a closer resemblance to supply chains for non-medical products such as clothing or electronics. According to the WHO (2023[25]), medical devices "include all the health technologies (except for vaccines and medicines) required for prevention, diagnosis, treatment, monitoring, and palliation"; countries also have their own definitions. Such broad definitions mean that medical devices cover a huge range of goods, from simple tongue depressors to complex ventilators with many associated parts (e.g. semi-conductors, other bespoke consumables). Medical device manufacturing is highly product-dependent, and a linear process flow is not adequate to capture their complexity. Like medicines, there may be multiple steps in several countries, however, some components of medical devices (e.g. chips) may be produced for both health and non-healthcare markets (OECD, 2023[8]). The perceived simplicity of a product may belie complexity in its supply chain.

Figure 1.8 depicts a basic schematic of a supply chain for a medical device, based on Chen et al.'s (2021[26]) analysis in a 2021 report prepared for the United States Government. Manufacturers source individual components or devices from the suppliers who produce them, who in turn source individual components or parts (raw materials) to make certain components from other suppliers, and so on. The number of suppliers can be vast, and suppliers also provide many of these same components to non-

medical manufacturers (e.g. for electronics). However, there are instances in which components (e.g. a pressure regulator) are specific to a particular medical device (e.g. a ventilator), and there may be limited sources for these components. Once the manufacturer assembles the final product, it may require sterilisation (often by a contract steriliser, which is another type of supplier), before being ready to be sold to customers. Customers vary according to the type of device, but can include hospitals, physician practices, pharmacies (where patients may purchase the product directly), other medical supply stores, or even consumers in other non-health industries such as mining and construction. Hospitals typically purchase either from distributors (i.e. wholesalers) or directly from manufacturers. In some countries, group purchasing organisations (GPOs) may play a role in the movement of goods from manufacturers to hospitals and be involved in the purchasing process. Some medical devices also require maintenance and repair through various types of contracts; this involves additional components, services and providers.

Figure 1.8. The complexity of medical device supply chains

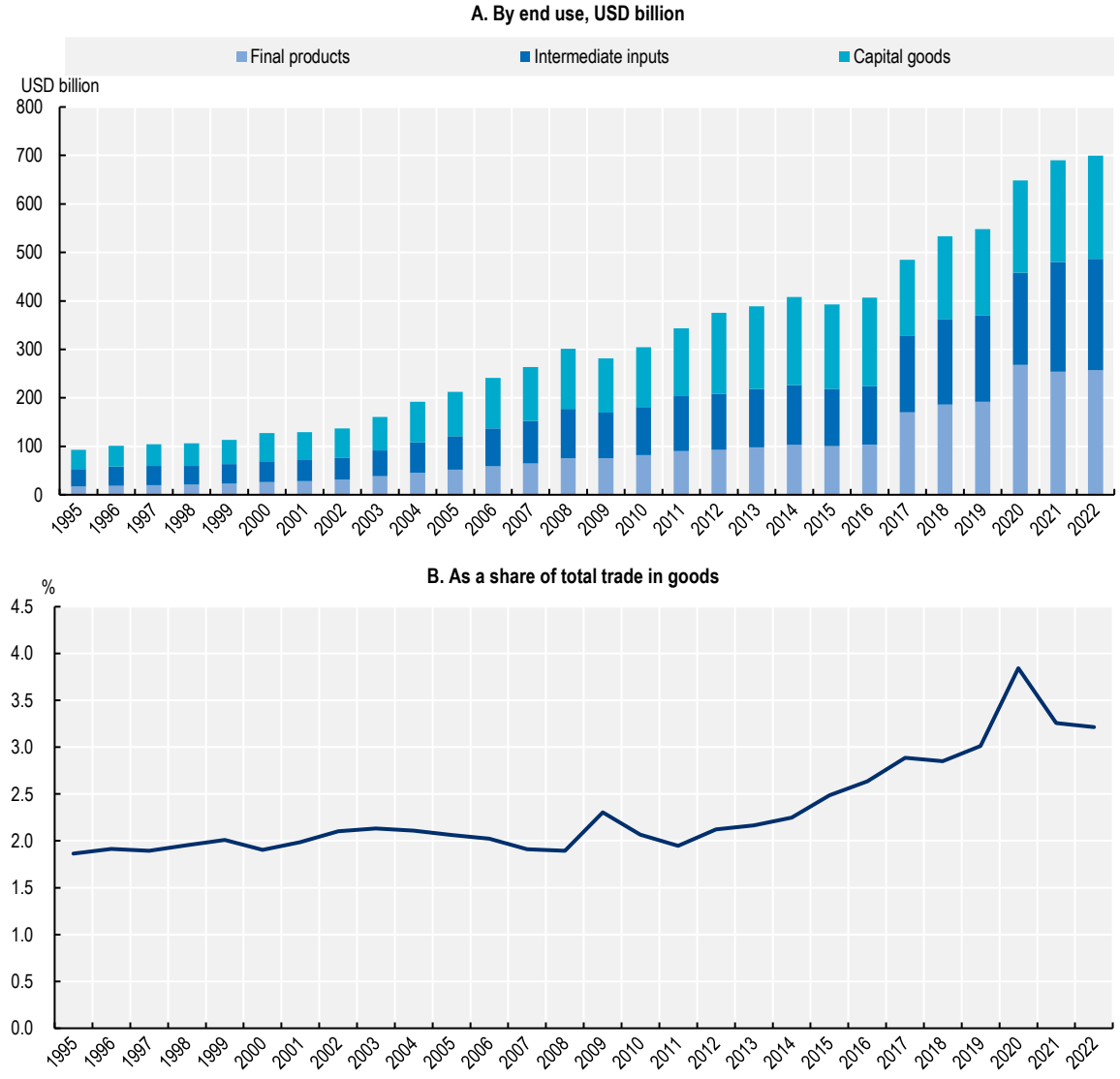


Note: Solid blue arrows depict flow of goods; dotted blue lines represent the possibility of an international border; green boxes depict examples of particularities to some medical device supply chains. This schematic is not intended to be exhaustive.
Source: Adapted from Chen, P. et al. (2021[26]), *Medical Device Supply Chains: An Overview and Description of Challenges During the COVID-19 Pandemic*, https://aspe.hhs.gov/reports/medical-device-supply-chains.

Trade in medical devices has also been on the rise, with increasing diversity of leading exporters and importers

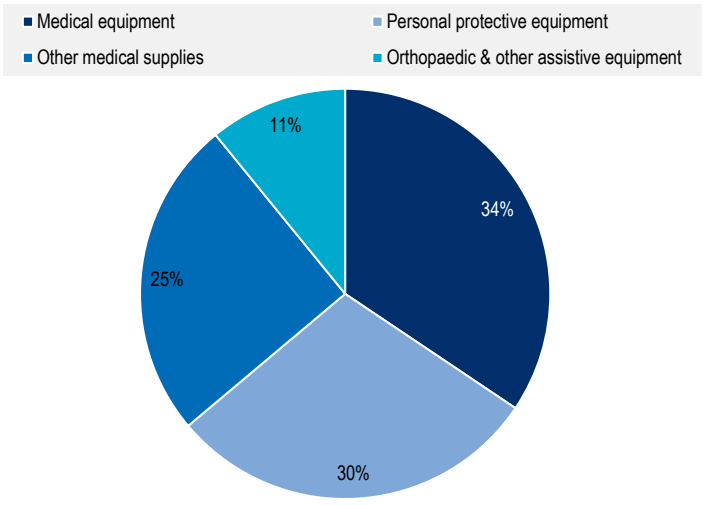
Trade statistics for medical devices (as defined by the WTO in its work on the identification of medical products in trade statistics) suggest trends similar to those of pharmaceutical products, with increasing trade flows and an internationalisation of supply chains (Figure 1.9). Medical devices also include capital goods, i.e. machines and devices that are used repeatedly to provide health services or used to manufacture other medical goods. Trade in medical equipment accounts for the largest share of trade in medical devices by value (34% in 2022) followed by personal protective equipment (30%) and other medical supplies (25%), with the smallest share observed for orthopaedic and other assistive equipment (11%) (Figure 1.10).

Figure 1.9. World trade in medical devices (1995-2022), by value



Note: Based on WTO list of medical equipment and machines (majority of products in HS90), orthopaedic devices, personal protective equipment and other medical supplies. Data prior to 2017 are based on older versions of the HS classification and may not accurately reflect the list of products.
Source: BACI (CEPII) (2023[2]), *BACI Trade data*, www.cepii.fr/CEPII/en/bdd_modele/bdd_modele_item.asp?id=37; and Drevinskas, E., E. Shing and T. Verbeet (2023[3]), *Trade in medical goods stabilises after peaking during pandemic*, www.wto.org/english/blogs_e/data_blog_e/blog_dta_23may23_e.htm.

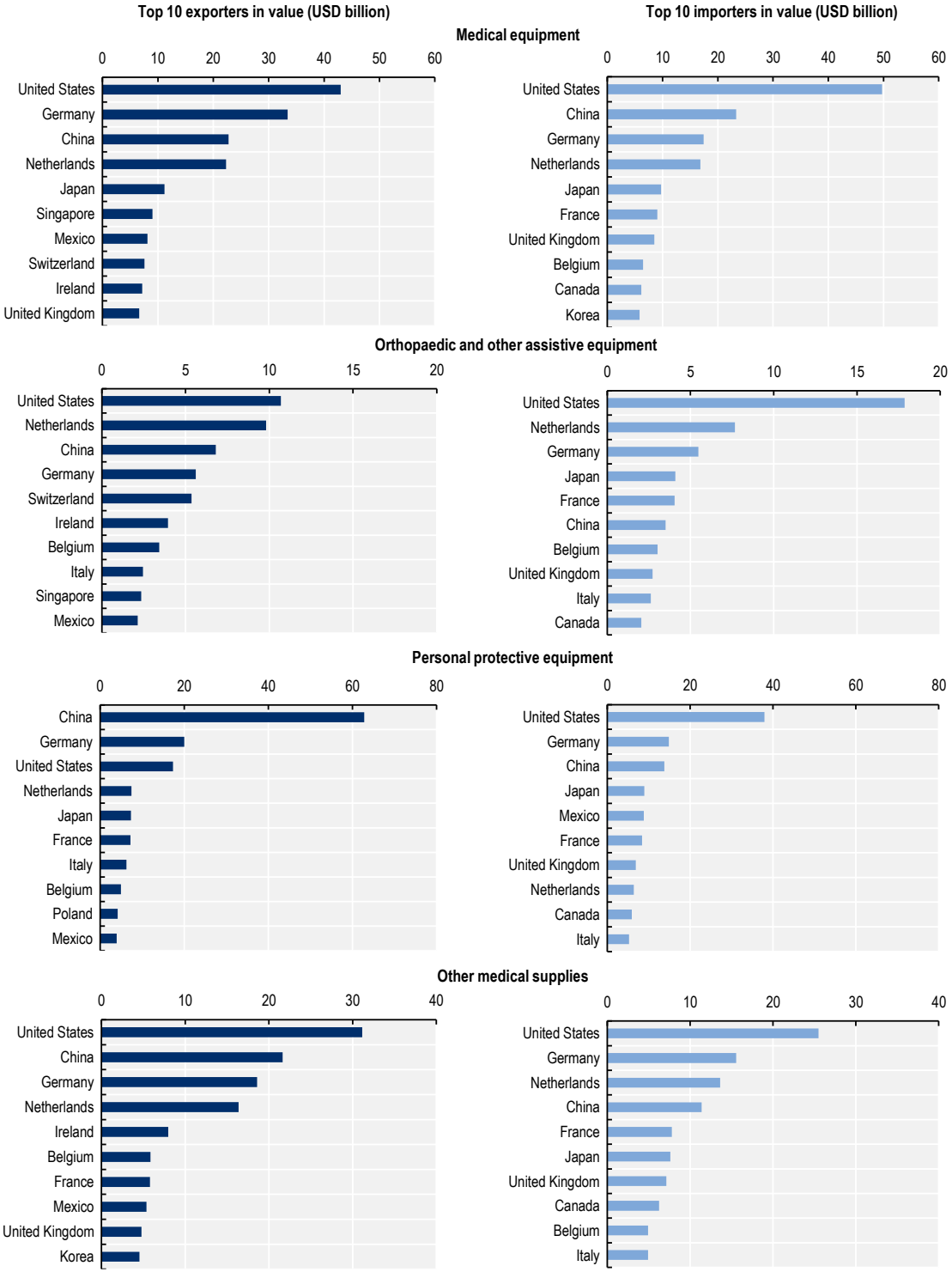
Figure 1.10. Composition of world trade in medical devices (2022), by value



Note: Medical equipment = Medical equipment and machines (majority of products in HS Chapter 90) including magnetic resonance imaging apparatus, X-ray tubes and operating tables; Orthopaedic and other assistive equipment = items such as wheelchairs, spectacles, hearing aids and artificial teeth; Personal protective equipment = Equipment and single-use items, such as gloves and face masks (excluding protective garments, as HS classifications largely overlap with products for non-medical use); other medical supplies = Hospital and laboratory inputs and consumables, such as syringes.
Source: Drevinskas, E., E. Shing and T. Verbeet (2023[3]), *Trade in medical goods stabilises after peaking during pandemic,* www.wto.org/english/blogs_e/data_blog_e/blog_dta_23may23_e.htm.

The heterogeneity of medical devices traded and the variability of their supply chains lead to an even more geographically diverse array of leading exporters and importers than for medicines (Figure 1.11). The United States is the leading importer of all types of medical devices by value due to its large market and high level of health spending. With the exception of personal protective equipment, the United States is also the top exporter of medical devices. However, some Asian economies are specialised in the production of medical devices. China is the leading exporter of personal protective equipment and among the top three exporters in other categories of medical devices. Singapore is also among the leading exporters of medical and orthopaedic equipment.

Figure 1.11. Top exporters and importers of medical devices (2022), USD billion



Note: Medical equipment = Medical equipment and machines (majority of products in HS Chapter 90) including magnetic resonance imaging apparatus, X-ray tubes and operating tables; Orthopaedic and other assistive equipment = items such as wheelchairs, spectacles, hearing aids and artificial teeth; Personal protective equipment = Equipment and single-use items, such as gloves and face masks (excluding protective garments, as HS classifications largely overlap with products for non-medical use); other medical supplies = Hospital and laboratory inputs and consumables, such as syringes.

Source: Drevinskas, E., E. Shing and T. Verbeet (2023[3]), *Trade in medical goods stabilises after peaking during pandemic,* www.wto.org/english/blogs_e/data_blog_e/blog_dta_23may23_e.htm.

Individual medical device supply chains are unique: Some examples

As already mentioned, the term “medical devices” encompasses a broad range of products and product types, each with a unique supply chain. To illustrate these differences, some examples are described below:

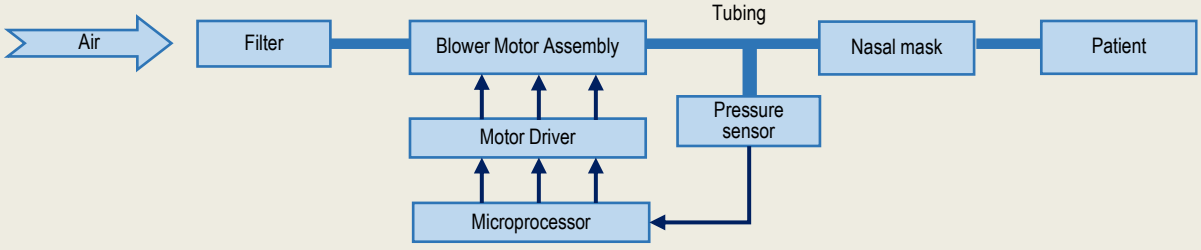
- **Ventilators** are a form of durable equipment, although their use involves various disposable items (Chen et al., 2021[26]). They consist of durable machinery responsible for air pressurisation, valves to manage pressure regulation, and electronics that monitor and control the delivery. Plastic tubes connecting the patient to the ventilator are disposable components. Ventilator supply chains involve medical equipment companies, maintenance repair companies, and repair service contractors. While supply chains of the disposable components are fairly simple, ventilators can consist of more than 1 500 parts, involving many different suppliers. Some individual components may be common to other types of devices manufactured by companies in both the health and non-health sectors, while others may be specific to a particular application or care setting. While consumables, such as disposable ventilator circuits, are often sold through distributors, ventilators are sold directly to hospitals or healthcare organisations or leased through medical equipment companies (Chen et al., 2021[26]).
- **Facemasks**, a form of disposable personal protective equipment (PPE), are generally made from nonwoven fabric made of synthetic fibres (primarily polypropylene, a polymer derived from oil) that are melted (or “melt-blown”) to create a filtration system that can trap small particles (Chen et al., 2021[26]; OECD, 2020[27]). They are an example of a device supply chain that includes both non-medical manufacturers and non-hospital end users. Facemask production is a relatively complex process with different types of inputs and assembly of various parts, requiring specialised machinery. They generally consist of three layers of different materials, in addition to nose strips made from metal, and ties or loops that need to be manufactured separately. Masks then need to be sterilised prior to testing and packaging. While the manufacture of polypropylene non-woven fabric is widespread, as the input is used by non-medical manufacturers (e.g. as crop cover, for air filters, diapers, personal care products etc.), the melt-blown process is concentrated among a limited number of companies. The primary constraint in facemask production has been linked to a shortage of propylene non-woven fabric, the key input. Before the COVID-19 pandemic, China was the main producer of masks, accounting for around half of global production (OECD, 2020[27]). The sourcing of facemasks has since become diversified with additional suppliers emerging in other countries (OECD, 2022[28]).
- **Testing supplies and equipment** are the components required to conduct clinical laboratory testing for disease diagnosis, screening, and surveillance. Required components depend on the specific type of test, each with its own manufacturing processes. As an example, COVID-19 tests (including polymerase chain reaction – PCR – and antigen tests) are composed of various components, nearly all of which can be used for other types of tests. The supplies and equipment include nasal swabs, blood collection kits, chemical laboratory reagents, transport media (i.e. packaging that aids transfer to laboratories without contamination), testing machinery, and simple plastic consumables such as micropipettes, among others (Chen et al., 2021[26]; OECD, 2020[27]). Consumable testing components such as the pipettes, swabs, reagents etc., have similar supply chains to that shown in Figure 1.8, and are typically sold through distributors. However, testing machinery, such as PCR machines, have more complex supply chains that involve laboratory equipment leasing companies, third party maintenance companies, and service maintenance contracts (Chen et al., 2021[26]).

To inform this report, the OECD also analysed the supply chain of continuous positive airway pressure (CPAP) devices more closely, described in Box 1.3.

Box 1.3. Continuous positive airway pressure (CPAP) device supply chain at a glance

Continuous Positive Airway Pressure (CPAP) ventilation is an important therapeutic modality in respiratory medicine. CPAP machines provide non-invasive positive pressure ventilation to patients through a tight-fitting nasal mask, face (oro-nasal) mask or helmet to improve oxygenation and reduce the work of breathing (see Figure 1.12 for the device setup). They are generally used to treat obstructive sleep apnoea, although they can also be used as respiratory support in certain medical conditions including COVID-19. While CPAP devices assist in keeping airways open via a constant flow of air, they differ from the traditional invasive mechanical "ventilators" in critical care that can take over the entire breathing process to provide respiratory support to intubated patients who cannot breathe on their own. Many ventilators can support multiple methods (or modes) of ventilation[1], including CPAP; however, this is part of the broader functionality of the ventilator itself, and is not a standalone CPAP device.

Figure 1.12. Block diagram of the CPAP device setup, showing the different components



Source: Reproduced from Chen, Z., Z. Hu and H. Dai (2012[29]), *Control system design for a Continuous Positive Airway Pressure ventilator,* https://doi.org/10.1186/1475-925x-11-5 (CC BY 2.0).

While Bilevel Positive Airway Pressure (BiPAP) offers dual pressure levels catering to inhalation and exhalation, and invasive ventilators cater to more acute patients, CPAP remains a critical component in this spectrum, ideal for conditions such as COVID-19. CPAP devices were included in the WHO priority list of medical devices in the COVID-19 response (WHO, 2020[30]). Their fundamental role in enhancing oxygenation, coupled with the potential ability to avert the need for invasive intubation and ventilation, underscores their value, especially when planning for future respiratory health crises.

CPAP devices have long and complex global supply chains. The most important components of a CPAP device are the electronic board and the blower. The electronic board or printed circuit board (PCB) is responsible for controlling the functionality of the device and the communication chips necessary for running the board, from regulating airflow to adjusting pressure settings based on the user's needs. The PCB's design and manufacturing require precision engineering, often involving advanced electronic manufacturing services from different parts of the world. The communication chips, integral to the PCB, enable the board's functionalities. These chips ensure that different parts of the CPAP machine communicate effectively with each other. They also allow for data logging and, in some modern devices, enable remote monitoring of patient usage and device functioning through wireless connectivity. The blower or turbine is another crucial component, responsible for generating a consistent and controlled flow of air. The quality and reliability of the blower are vital for the effectiveness of CPAP therapy, as it needs to maintain a steady air pressure regardless of external factors like voltage fluctuations or varying breathing patterns of the patient. Apart from these main components, there are various other elements often built into a CPAP device, depending on its functionality and purpose. These elements include different kinds of gas supply systems, oxygen blender, separate oxygen and air flowmeters, tubing systems, humidifier, bacterial and viral filter, a mask, as well as various other plastics.

1. Other modes of ventilation (i.e. methods of inspiratory support) supported by ventilators include Pressure Control, Volume Control, Pressure Regulated Volume Control, Pressure Support, and BiPAP (Bilevel Positive Airway Pressure) which is another form of non-invasive ventilation.
Source: Authors as cited and based on consultations with experts in 2023.

1.2. Growing issue of medical product shortages pre-dated the COVID-19 crisis

A shortage occurs when demand for an approved medical product exceeds its supply, making it inaccessible to patients in need. Shortages may be local, national, or global; they may last a few days, months or even years. Not every reported shortage will impact patients, but a shortage can become a public health issue if no appropriate alternative exists. Even when alternatives are available, shortages may incur costs to health systems, because of the time spent by health professionals to adapt treatments and source alternatives. Furthermore, shortages of different types of medical products (e.g. diagnostics) may interfere with the appropriate use of others (e.g. certain medicines). Country definitions of shortages vary widely (see Box 1.4 for an example).

Medical product shortages can have multiple causes. They may arise because of a sudden, unanticipated surge in demand, for example during exceptional outbreaks of seasonal infections. Most often, they occur due to disruptions in the supply chain although disruptions do not necessarily result in shortages if appropriately managed. Shortages may also be due to market exit from the manufacturer.

While COVID-19 highlighted vulnerabilities in supply chains, shortages of medical products had become increasingly common in a number of countries prior to the pandemic. The following text summarises available information on shortages of different types of medical products and highlights some of the related causes. It does not address COVID-19 specific shortages, which are discussed in Section 1.3 of this chapter.

Box 1.4. Medicine shortage definitions vary from country to country

Formal definitions of "medicine shortages" vary widely, and these have been discussed extensively elsewhere in the literature (e.g. (World Health Assembly, 2017[31]; WHO, 2017[32]; Acosta et al., 2019[33]; Troein et al., 2020[34]). In general, OECD countries consider a medicine shortage to exist when supply is insufficient to meet demand at national level, and may include both temporary and permanent discontinuations (i.e. withdrawal from the market). Some countries also include a minimum duration of supply disruption in their shortage definitions.

For the purposes of this report, a "medicine shortage" is referred to as "any supply disruption or sudden change in the supply-demand equilibrium of a marketed pharmaceutical product that leads to an actual or anticipated lack of stock on the shelf for patients", as per the definition used by (Chapman, Dedet and Lopert, 2022[1]). These include both temporary and permanent supply discontinuations; the latter sometimes referred to as "availability issues". This definition does not include situations of "non-availability" or "unavailability", where a product has not been marketed in a particular jurisdiction.

As medicine shortage definitions vary widely from country to country, so do reporting methods and requirements and, as a consequence, so does the content of national shortage notification databases. For example, some notification databases capture temporary supply disruptions at pharmacy or wholesaler level, while others only include notifications from marketing authorisation holders of shortages resulting from upstream factors for those medicines deemed most critical to the country's health system. This lack of harmonisation renders cross country comparisons of shortage notification data particularly challenging.

The "non-availability" of a medicine, which is not considered as a shortage in this report, may nevertheless be matter of significant concern for public health. For example, a number of countries report the absence of paediatric formulations for tuberculosis treatment in their domestic markets (WHO, 2023[35]). While products exist globally, they are not approved for sale in these countries and must be imported from others. In Europe, for example, the relatively low prevalence of tuberculosis means that some manufacturers consider the market too small to launch their products. Low prices and high regulatory standards discourage some companies from producing, registering, and supplying their products in these markets, preferring instead to focus on markets with higher disease burden and potentially greater returns (Chorba, 2023[36]; Edwards et al., 2023[37]).

1.2.1. Shortages of pharmaceuticals have gained increasing attention in recent years

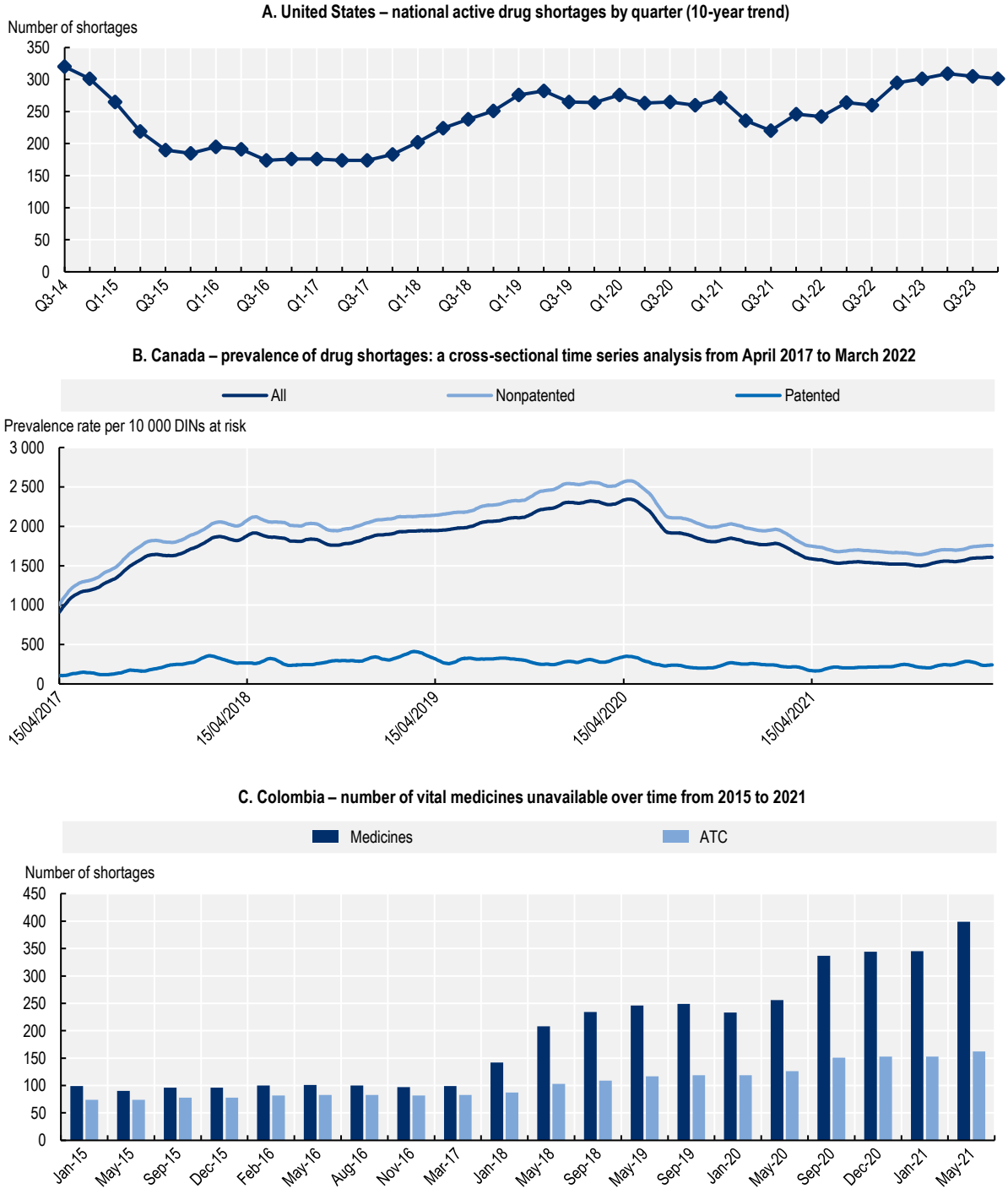
Previous OECD work published in 2022 found that, in a sample of 14 OECD countries, the number of shortage notifications increased by 60% over the period 2017 to 2019 (Chapman, Dedet and Lopert, 2022[1]). Differing stakeholder perceptions and a lack of a standardised definition of a shortage, however, make their quantification challenging. Studies have examined medicine shortages at international, hospital, and community pharmacy levels. A 2020 analysis across 11 EU countries revealed that cardiovascular medicines were most severely affected by active shortages between January and August 2019, accounting for 27% of shortages, followed by nervous system medicines at 25% (Troein et al., 2020[34]). Shortages affected a diverse range of products and manufacturers in different countries (ibid.). Hospital pharmacists reported increasing problems with shortages, with antimicrobials consistently the most frequently affected, followed by oncology medicines and anaesthetic agents. Community pharmacies also faced shortages across all medicine classes, with cardiovascular medicines being the most severely affected. Overall, shortages primarily involved older, off-patent medicines, with injectables and generics featuring prominently (Chapman, Dedet and Lopert, 2022[1]).

These findings are generally consistent with a 2022 study analysing the situation in 20 EEA countries between 2008 and 2020 (Jongh et al., 2021[38]). Over the entire period and for the full sample, the medicine classes featuring most prominently in shortage notifications were central nervous system (22% of notified shortages), cardiovascular system (14%), general anti-infectives (12%), alimentary tract and metabolism (10%) and antineoplastic and immunomodulating agents (7%). These shortages impacted both retail and hospital pharmacies. Nearly half (45%) of all reported shortages affected tablets, and around a quarter (23%) injectables or infusions. However, the latter had a higher probability of being in shortage (+32% vs. +26% for tablets). One-third of medicines reported in shortage are listed in the World Health Organization Model List of Essential Medicines (WHO EML). Although 97% of medicines in shortage were off-patent and rather old products, statistical analysis shows that patent status and time since launch were not significantly associated with the probability of being in shortage. Around 76% of all shortages involved multisource products for which alternatives existed, while the product in shortage likely represented the only available version for the remaining 24%. The duration of shortages was highly variable from 1 day to 13.5 years, and the average duration across all notifications was 137 days. Two-third of all notifications were resolved within the first three months. Longer durations were reported for shortages arising from commercial reasons.[8]

The total number of shortages across the 20 EEA countries increased rapidly over the whole period, but this partly reflected an increase in the number of countries reporting shortages. The average number of notified shortages per country grew more modestly. The number of notified shortages in 2019 varied widely, from 13 in Greece to more than 6 500 in Portugal, partly reflecting differences in notification systems and their date of implementation (e.g. Greece had just implemented a notification requirement in 2019) (Jongh et al., 2021[38]). A more recent analysis of shortage notifications in eight EU countries (Belgium,[9] Croatia, Finland, Germany, Norway, the Slovak Republic, Slovenia and Sweden) between January 2020 and November 2022 counted 17 250 temporary drug shortage notifications, with the highest numbers observed in Finland, Sweden and Norway. For the same period, 1 737 notifications for permanent drug product withdrawals were counted in Slovenia, the Slovak Republic and Belgium (Ravela, Airaksinen and Lyles, 2023[39]).

Recent statistics for North American countries show varying trends across countries (Figure 1.13). Although the quarterly number of active shortages in the United States had been steadily increasing from 2017 to 2019, it stabilised during the pandemic, decreased slightly in 2021 and began increasing again in 2022 (ASHP, 2023[40]).[10] In Canada, the prevalence rate of shortages was increasing until spring 2020; it then declined during the pandemic, before seeing a slight increase in 2022 (Lau et al., 2022[41]). In Colombia, shortages increased steadily prior to May 2021 (Sabogal De La Pava and Tucker, 2022[42]).

Figure 1.13. Recent trends in national shortages of medicines in 3 countries



Notes: For the United States: Points indicate active shortages at the conclusion of each quarter. The underlying data are from the American Society of Health-System Pharmacists (ASHP) Drug Shortages website; ASHP commonly lists more shortages than US FDA as it includes shortages that do not meet criteria defined by US FDA (see end note 10). For Canada: DIN Drug Identification Number. For Colombia: ATC Anatomical Therapeutic Chemical classification.

Source: For the United States: Reproduced from ASHP (2023[40]), *Drug shortages statistics*, www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics?loginreturnUrl=SSOCheckOnly; For Canada: Reproduced and adapted from Lau, B. et al. (2022[41]), "COVID-19 and the prevalence of drug shortages in Canada: a cross-sectional time-series analysis from April 2017 to April 2022", https://doi.org/10.1503/cmaj.212070; For Colombia: Reproduced from Sabogal De La Pava, M. and E. Tucker (2022[42]), *Drug shortages in low- and middle-income countries: Colombia as a case study,* https://doi.org/10.1186/s40545-022-00439-7 (CC BY 4.0).

Antimicrobials are among the most frequently reported shortages (Chapman, Dedet and Lopert, 2022[1]; Jongh et al., 2021[38]; Beraud, 2021[43]; EMA, 2023[44]). In particular, the 2022 winter season saw a spike in shortages of essential antibiotics in many countries (EMA, 2023[44]). As described in Section 1.1.1, previous OECD analyses highlighted the significant complexity of the manufacturing process for azithromycin (an example of a macrolide antibiotic), with a high concentration of API production in certain countries, albeit with manufacturing sites in different geographic locations (OECD, 2023[8]). Due to pressure on prices and low profitability of generic antibiotic production, there are few competitors at the different stages of the supply chain. A disruption at any stage can result in a shortage. Antimicrobial shortages are a worrying trend, particularly in the face of the wider threat of antimicrobial resistance (OECD, 2023[45]).

Root causes of medicines shortages are multifactorial, but difficult to identify

In many countries, shortage notifications made to regulatory agencies by manufacturers include information on their causes, often selected from a pre-defined list of potential causes. These lists may differ across jurisdictions.

Shortages of medicines during routine circumstances tend to be attributed primarily to one of two main causes. Around 60% of manufacturer reported shortages are attributed to manufacturing and quality issues (FDA, 2019[46]; Benhabib et al., 2020[47]), such as production defects, input shortages, inventory management problems, temporary or permanent production suspensions due to technical problems or non-compliance with manufacturing standards, and site closures or relocations. The other reason often cited is market dynamics, where poor profitability and a lack of economic incentives make the production of older off-patent products in particular unattractive. Competitive public and private procurement processes often drive prices down to near the marginal cost of production, discouraging suppliers from maintaining surplus stock or investing in capacity and quality improvement. Finally, co-ordination failures in transportation and delivery systems, including cyberattacks, can disrupt supply chains even when supply and demand are balanced (Chapman, Dedet and Lopert, 2022[1]; FDA, 2019[46]).

In the 2022 study on shortages in 20 EEA countries, available information on causes of nearly 7 000 shortages was reclassified into 7 categories (Jongh et al., 2021[38]). Between 2015 and 2020, 51% of shortages were due to quality and manufacturing issues, 25% to commercial reasons[8], 9% to unexpected increases in demand, 8% to distribution issues, 4% to regulatory issues, 1% to unforeseen major events or natural disasters, and 1% to other issues. Over the period, however, the relative proportions of commercial and distribution issues varied inversely, suggesting a degree of overlap. Looking more closely at notifications in Portugal and Ireland, the study identified two major causes: changes in manufacturing site and increased demand in another country. Commercial reasons were further analysed, using stakeholder interviews: tendering practices, penalties for late delivery, and poor profitability were mentioned as influencing shortages in individual countries, but their respective contributions could not be estimated (ibid.).

More generally, empirical analyses of root causes are sparse. A 2021 systematic review identified only three studies (de Vries et al., 2021[48]). Among them, Yurokoglu, Liebman and Ridley (2017[49]) estimated the impact of a 2005 reduction in US Medicare reimbursement rates on shortages of injectable medicines, which had dramatically increased in the 2000s. Looking at a sample of 308 injectable medicines over 12 years, the authors estimated that a 50% cut in reimbursement rates had led to a reduction in manufacturers' prices and increased the average duration of shortages by about 2 weeks (from an average duration of 59 weeks for the whole sample and the whole period). Since then, Frank, McGuire and Nason (2021[50]) presented empirical evidence on the link between generic prices, market entry/exit and shortages in the US market. Looking at markets for a large -albeit not representative- sample of 89 molecules-forms that lost patent protection between 2010 and 2013, the study showed very different patterns for oral and injectable markets, and for small and large markets in the 4 years following patent loss. For oral forms (66 molecule-form "markets"), larger markets saw robust competition with multiple manufacturers and prices

declining, while smaller markets attracted fewer manufacturers and saw prices increase. Shortages were reported in one-third of these 66 "markets" and were more frequent in large markets (about 50%) than in smaller ones. Product recalls grew sharply in number over the period and affected larger markets (60% of recalls up to 2017) more than smaller ones. For injectable forms, markets are generally smaller, have fewer entrants and exhibit a significant degree of price volatility. Shortages were observed in 16 of 23 of these "molecule-form markets" over the period, but were more frequent in smaller and medium sized markets (80%) than in larger ones (50%). Recall rates grew after 10 quarters to reach 65% (ibid.).

In a study of the US market, the IQVIA Institute examined market concentration (measured using the Herfindahl-Hirschman Index – HHI[11]) for medicines in shortage. Multi-source medicines in highly-concentrated markets (HHI 2 501-9 999) accounted for 68% of shortages; single-source medicines 27%, and multi-source medicines in moderately concentrated markets (HHI 1 500-2 500) another 19% (IQVIA, 2023[51]). However, information on market concentration for medicines that are not in shortage is not presented in the report. The report also shows that the proportion of medicines in shortages increases when the price "per extended unit"[12] decreases.

Only very limited information is available on (local) shortages due to misallocation in the distribution chain. A single study reports that in Italy, some cases of local shortages due to maldistribution were investigated and found to be the result from illegal behaviour by retail pharmacies (Di Giorgio et al., 2019[52]).

Example: Vaccines

Shortages of several key vaccines have occurred in recent years in OECD countries. However, published reports often group vaccines with antimicrobials, limiting insights about vaccine-specific shortages. Nevertheless, there are some examples. In Europe, Filia et al. (2022[53]) found a total of 115 vaccine shortages/stock-outs reported in 19 of 21 European countries surveyed between 2016 and 2019, with a median stockout duration of 5 months (ranging from less than 1 month to 39 months). The most commonly affected vaccines were Dipetheria-Tetanus (DT)- and Td-containing combination vaccines,[13] hepatitis B, hepatitis A, and Bacillus Calmette-Guérin (BCG). Around 30% of shortage/stockout events for which information was available led to temporary changes in countries' national immunisation programmes (e.g. alternative schedules, changes to the timing of doses or boosters, prioritisation of vulnerable groups) (ibid.). In the community pharmacy setting in Europe, 55% of responding countries reported vaccines to be in short supply in 2022, up from 44% in 2021, but well below the 88% reported in 2020 (PGEU, 2022[54]). The number of vaccine shortages reported by hospital pharmacists in the EU has been declining, with only 15% of survey participants reporting them as an issue in 2023 compared to 43% in 2018 (Miljković et al., 2019[55]; EAHP, 2023[56]). In the United States, a 2017 study found that there were 59 reported shortages of vaccine and immune globulin products in the period between 2001 and 2015, with half of these shortages involving paediatric vaccines (Ziesenitz et al., 2017[57]). They also found that the median number of new shortages reported annually to be 3, and a median shortage duration of 16.8 months (ibid.). In Australia, several "high" and "critical" impact shortages of different vaccines of variable duration were reported by manufacturers between 2014 and 2023, based on national medicine shortage data.[14]

The fluctuations in national vaccine shortages over time may reflect so called "global shortages or disruptions" of specific vaccines. For example, 2015 saw a shortage of pertussis-containing combination vaccines as a result of reduction in pertussis antigen production capacity (ECDC, 2016[58]). Fourteen EU Member States reported shortages of DT- containing vaccines in the period 2016-19; which were mainly attributed to interruptions in production and supply (Jongh et al., 2021[38]; Filia et al., 2022[53]). Another example saw reported shortages of hepatitis A vaccine in several European countries (e.g. Austria, Denmark, Italy, Portugal, Spain and Sweden) as well as in the United States, linked to a spike in demand arising from an outbreak of hepatitis A, compounded by existing production issues (ECDC, 2017[59]; WHO, 2017[60]). Similarly, the BCG vaccine has been in shortage across multiple countries since 2012, also due to manufacturing quality problems and high demand (Filia et al., 2022[53]).

Causes of vaccine shortages are likely multifactorial. It is important to consider, however, that vaccines are different to other medicines, with lengthy production processes involving highly specialised facilities and equipment, and with additional quality controls and testing to ensure the safety and quality of these products that are administered to otherwise "healthy" populations. According to Filia et al. (2022[53]), the two most commonly reported causes of stockouts/shortages in 19 European countries surveyed between 2016 and 2019 were interruptions in production and/or supply due to quality issues or other reasons (n = 39; 33.9%) and global shortages (n = 35; 30.4%),[15]with higher-than-expected demand due to changes to vaccine schedules or targeted groups (7.0%), inaccurate forecasts (4.3%) or an outbreak/other reasons (4.3%) (Filia et al., 2022[53]). Other factors (13.9%) included delayed delivery, lack of suppliers, and issues at procurement level (e.g. delays, legislation, absence of reimbursement) (ibid.) In the United States, manufacturing problems were cited as the primary cause of vaccine shortages between 2001 and 2015 (50% of cases), followed by issues with supply and demand (7%) (Ziesenitz et al., 2017[57]). Reported reasons for shortages of vaccines in Australia between 2014 and 2023 included manufacturing issues (measles/mumps/rubella vaccine), seasonal stock depletion (influenza), and unexpected increases in consumer demand (e.g. rabies, hepatitis A, hepatitis B, and cholera vaccines), among others (TGA, 2023[61]).[14]

The challenges in vaccine supply chains stem from a range of issues linked to complexities of the manufacturing and quality control processes, regulatory factors, and uncertain demand. From the industry perspective, Vaccines Europe,[16] an organisation representing 14 vaccine companies operating in Europe, identified several root causes of vaccine shortages in that region through consultations with experts from the four member companies with the largest portfolio of EU-marketed vaccines (GlaxoSmithKline, Merck Sharpe & Dohme, Pfizer, Sanofi Pasteur) (Pasté et al., 2022[62]). Industry experts highlighted the complexity of vaccine manufacturing, which involves intricate processes with necessary stringent quality controls, leading to lengthy production timelines that require contracts (with suppliers and health authorities) to be arranged well in advance. Complicating matters are unpredictable timelines due to independent lot releases by national control laboratories. Regulatory factors add further complexity, necessitating frequent post-approval changes to be submitted by manufacturers (e.g. due to improvements in facilities, equipment or processes; quality control; changes in suppliers etc), sometimes requiring submissions to over 100 regulatory agencies globally for a single change (ibid.). Nevertheless, these stringent requirements are necessary to ensure safety and effectiveness of vaccines, as well as compliance with good manufacturing practices.

Industry experts further highlighted that the diversity in vaccine presentations, and packaging and labelling requirements across countries results in the need to manufacture and distribute vaccines in smaller volumes, posing challenges for efficiency in production and inability to redistribute in the event of supply disruptions. Unpredictability in global demand, challenges in anticipating changes in vaccine recommendations, and difficulty in gaining accurate demand forecasts from health authorities were also cited by industry experts (e.g. due to development of national immunisation programmes, changes to existing guidelines, disease outbreaks etc). In addition, suboptimal vaccine budgets and procurement practices that do not take into account long lead times were mentioned (Pasté et al., 2022[62]). Other analyses cite similar vulnerabilities in vaccine supply chains, while also highlighting the added challenge of concentrated production with few global suppliers (Jongh et al., 2021[38]; WHO, 2023[21]).

Example: Radiopharmaceuticals

Since 2009, the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR), established by the Nuclear Energy Agency, has been working on addressing shortages in the supply of certain radio-isotopes. In the case of Technetium-99m, used in 85% of nuclear medicine diagnostic scans performed worldwide – around 30 million patient examinations every year –, ageing production facilities and low prices have contributed to inadequate production capacity, making the supply of Tc-99m unreliable. The current structure of the supply chain leaves some participants unable to increase the prices of their services to the levels needed to cover all fixed and variable costs of the required production capacity (OECD/NEA, 2019[63]).

Example: Plasma-derived medicinal products

In recent years, PDMP shortages have affected many regions across the world, particularly shortages of intravenous immunoglobulins (IVIg) for which there is no alternative broad-spectrum antibody. Following the onset of the COVID-19 pandemic, blood product donations decreased due to social restrictions and health concerns and are only rebounding slowly (Covington, Voma and Stowell, 2022[64]). For example, one study reported that several OECD countries (the United Kingdom, France, Greece, Latvia, Lithuania and Portugal) have experienced shortages of intravenous and subcutaneous IVIg as a result of insufficient supply and market withdrawals over recent years (Strengers, 2023[10]). Even countries with significant sources of commercial plasma such as Germany, Czechia, Hungary and the United States have experienced shortages of IVIg. Another study focusing on the possible impact of COVID-19 on plasma supply in the United States, reported a sharp drop in donations that is only rebounding slowly to pre-pandemic levels (Covington, Voma and Stowell, 2022[64]).

The global supply of plasma is dominated by the collection of source plasma in the United States, which not only caters for the domestic market but is also exported (Strengers, 2023[10]). Pre-pandemic data show that 67% of source plasma originated from the United States, whereas Asia-Pacific accounted for only 18%, and Europe 14% (Strengers, 2023[10]). In Europe, the majority of source plasma originates from four countries only. These are Austria, Czechia, Germany, Hungary. While on average, 14 litres are collected annually per 1 000 inhabitants in Europe, the United States collects roughly 113 litres per 1 000 inhabitants (Kluszczynski, Rohr and Ernst, 2020[16]).

Reasons for shortages are likely to be two-fold: increasing numbers of patients eligible to be treated with plasma-derived therapies, and uncertainty in the supply of the raw material (i.e. plasma from human donors). The latter depends on eligibility requirements, the allowed frequency of donation, and different donation compensation policies in each jurisdiction. The COVID-19 pandemic also impacted the volume of blood and plasma collected. Since it can take up to a year for plasma to be processed, the effect of a downturn in donations may remain unnoticed for a long period of time and will not be experienced as acutely as that of whole blood or red cells. In addition, disruptions in source plasma may not be readily perceived by transfusion services, which primarily focus on the collection of red cells and platelets (Covington, Voma and Stowell, 2022[64]).

PDMP manufacturing is challenging as it is affected by variations in the volume of donations, complex regulations, strict safety procedures to ensure purity and eliminate potential viruses and bacterial contamination, as well as lengthy manufacturing processes that can take 7-12 months (Hess, 2010[65]). The most difficult challenge is in the collection of raw material, i.e. plasma, which can only be sourced from human donors. Finding potential donors is the first and most relevant hurdle to mitigate supply shortages. Beyond eligibility requirements, varying donation frequency and compensation schemes, donations are highly vulnerable to the effects of bad weather, health crises, geopolitical tensions, that can discourage even willing donors.

Demand for PDMPs is expected to increase at an annual rate of 6-7% (PPTA, 2022[15]). Recent research suggests that consumption in Europe alone is projected to increase by one-third, from 50.5 tonnes in 2017 to 67.5 tonnes in 2025 (Marketing Research Bureau, 2023[17]). The availability of plasma has become even more relevant than in recent years as research and diagnostics have evolved (Marketing Research Bureau, 2023[17]). According to data from the International Patient Organisation for Primary Immunodeficiencies (IPOPI), there are many patients who have not yet been diagnosed with diseases that require PDMP treatment (Strengers, 2023[10]).

1.2.2. Vulnerabilities in medical device supply chains have received less attention

Before the COVID-19 pandemic, vulnerabilities in medical device supply chains received less attention than medicine shortages. This may be due in part to differences in notification requirements of potential shortages. In the United States, for example, notifications of potential shortages are required of medicine manufacturers at all times, but of medical device manufacturers only when there is a public health emergency.[17] The FDA only reported five shortages of medical devices annually between 2010 and 2019, but this increased fourfold in the first half of 2020. Pre-pandemic, 60% of shortages were reported to stem from regulatory and enforcement actions related to product quality and manufacturing. Other triggering events were natural disasters, discontinuations and economic factors (Beleche et al., 2022[66]).

In Europe, the 2023 version of the European Association of Hospital Pharmacists' Shortage Survey (2023[56]) included data on medical devices for the first time. Although these data cannot be considered representative, they provide some insights into shortages of medical devices in hospitals. According to 61% (n=765) of hospital pharmacists, medical device shortages caused issues for patients, with more than a third reporting that the shortages occurred one to three times for the same device, with another third reporting that they experienced the issue more than 10 times for the same device. Pharmacists most commonly reported supply chain problems as the reason for shortages (53%, n=658), followed by a shortage or discontinuation of a component, part or accessory of the device (48%, n=603).

Shortages affecting in-vitro diagnostics (IVD) also occurred episodically (see Box 1.5).

Box 1.5. Shortages affecting in-vitro diagnostics

In 2021, the United Kingdom experienced a shortage of blood specimen collection tubes as a key supplier announced global supply chain issues (Rimmer, 2021[67]). According to the company, shortages were caused by the COVID-19 pandemic. Manufacturers struggled to meet the high, changing, and unpredictable demand; this was aggravated by delivery delays due to global transportation issues, limited availability of, and access to raw materials, and delays due to UK border checks. In addition to this, the equipment used by the UK National Health Service (NHS) to run various diagnostic tests was set up to use tubes from a particular manufacturer. Using alternative collection tubes was possible but required prior validation of the substitutability to ensure test validity (Tsang, Absar and Gingrich, 2021[68]; Gosselin et al., 2021[69]).

A few months later, the US FDA (CDC, 2022[70]) and the Canadian Government (Government of Canada, 2022[71]) updated their respective device shortage lists to include all blood specimen collection tubes. Early in 2022, in the United States, this had a major impact on the availability of testing for sexually transmissible diseases, specifically syphilis and HIV (Raiken, 2022[72]). The company only managed to recover 97% of former supply levels by April 2023 (BD, 2023[73]).

In response to the shortages, UK NHS authorities published guidelines restricting the use of blood tests to avoid disruptions to urgent care. A clinical reference group, with advice from professional bodies covering a wide spectrum of clinical specialties, recommended actions for medical directors, nursing directors, general practitioners (GPs), pathology laboratories and all clinical staff including stock check, ordering and double tube practices; minimum re-test intervals; and usage of Point of Care haemoglobin devices (NHS, 2021[74]; The Royal College of Pathologists, 2021[75]). Physicians were told to suspend non-essential blood tests (e.g. genomic tests for cancer diagnoses). Acute and mental health trusts were required to reduce their demand by a minimum of 25% during the shortage period. Guidelines included examples of clinically urgent testing, such as a test that could potentially avert a hospital admission or onward referral; or tests for patients with suspected sepsis or conditions with a risk of death or disability (NHS, 2021[76]). The guidance also warned against stockpiling of test tubes and urged

GP practices to order supplies from NHS Supply Chain rather than trying to buy the equipment directly from manufacturers (Osborne, 2021[77]). Alternative products were being sought in co-ordination with the Pathology Incident Director and NHS Supply Chain, and all laboratories that were switching to these supplies received samples for testing and validation (ibid.).

Similarly, the FDA recommended healthcare providers, laboratory directors, phlebotomists, and other personnel to consider conservation strategies to minimise blood collection tube use and maintain quality and safe patient care for those for whom testing was medically necessary (CDC, 2022[70]).

In England and Wales, a private supplier of IVD tests – offered an alternative supply for patients outside the NHS system (i.e. without public funding), for both home tests and tests performed in clinics. For home test samples, the company used microtainer test tubes, which utilise smaller blood samples obtained via finger prick (Better2Know, 2021[78]).

Causes of medical device shortages or risk of shortages

In published reports and interviews, stakeholders cite the following issues as likely to affect medical device supply in the future:

- Competition with other industrial sectors for the acquisition of raw material and critical components has been mentioned both in case studies and stakeholder interviews. This is of particular concern where there are supply disruptions of key source materials that are not (easily) substitutable and are required for the production of critical or lifesaving devices.
- New regulations on market access applicable in the European Union (see Box 1.6). Changes in the regulatory environment in the EU and the application of more stringent criteria and processes are expected to result in bottlenecks in the evaluation process, and in the market exit of small companies marketing older products, as well as a reduction in the range of devices manufactured by others. Several deadline extensions have provided more time for manufacturers and assessment bodies to prepare for the transition but the long term impacts of the regulatory reforms on the number of products and suppliers are difficult to predict.
- Proposed changes in the regulation of chemical substances in manufacturing (Regulation on the registration, evaluation, authorisation, and restriction of chemicals – REACH). At the EU level, a proposal to restrict the use of around 10 000 per- and polyfluoroalkyl substances (PFASs) was submitted in January 2023. This proposal is intended to reduce the use of these chemical substances, which are very persistent in the environment and have negative effects on human health, and whose use is increasingly prevalent in manufactured goods (ECHA, 2023[79]). Some of these substances are used in medicines and medical devices. The European Chemical Agency, supported by specific scientific committees, produced a report addressing the risks of PFASs to the environment and human health and provided an assessment of the effectiveness, practicability, monitorability and socio-economic impacts of restriction of the use of PFAS under the REACH Regulation (ECHA, 2022[80]). According to this report, the medical device sector is one of the most relevant sectors in terms of emissions of PFAS in the use phase (i.e. excluding waste). The report analysed several sub-categories of medical devices, such as implantable devices, tubes and catheters, and diagnostic laboratory testing, to determine whether alternative devices were available, as well as the consequences of restricting PFAS use (ibid., pp. 99-102). For the three categories mentioned above, the potential for device substitution is low, and the unavailability of these devices would have a negative impact on human health. The reform proposal aims to exclude these devices from the restrictions on PFAS use. By contrast, use of PFAS in medical device packaging would be prohibited unless “vital for the functionality and safety” of the medical devices when no alternative method is available. The proposal envisages a derogation of the application of PFAS use restriction for a period of several years (to be determined), to account for the time to invest in R&D to find other solutions (ibid. pp. 127-131).

- Vertical integration in the laboratory sector, limiting the substitutability of components/reagents for IVDs. For example, during the pandemic, a specific type of blood specimen collection tubes went into shortage. Because some machines were calibrated specifically for the use of these tubes, there was no possibility of rapidly substituting other collection tubes without compromising the validity of tests (Rimmer, 2021[67]).
- Experts and manufacturers mentioned a very high inflation in energy and transportation costs recently, as well as increased costs of raw materials, as an additional risk to supply, especially where price regulation prevents companies from passing on increased costs to consumers (interviews with stakeholders in 2023; (Snitem, 2022[81]).
- Natural disasters were also mentioned as events potentially triggering supply shortages (Beleche et al., 2022[66]).

Approaches to averting and managing risks of medical device shortages are different to those of medicines, reflecting the number and extreme heterogeneity of medical devices, as well as differences in regulatory frameworks (including notification requirements). However, as for medicines, a key difficulty is in identifying when a lack of supply of a certain medical device creates a risk to health. Many devices have close substitutes; for example, medical devices approved by the US Food and Drug Administration (FDA) via the 510(K) process[18] – claiming substantial equivalence to a legally marketed device – account for about 90% of FDA approvals (Medical Device Network, 2022[82]). In 2022, in France, 80% of new medical devices assessed by the health technology assessment body had no added value over existing comparators for the same therapeutic indication, which indicates that alternative therapeutics exist – even if they are not strictly equivalent (Haute Autorité de Santé, 2022[83]).

Box 1.6. The new EU regulation for medical devices

In 2021, the medical device market in Europe was valued at EUR 150 billion, and represented 27.3% of the global market. The overwhelming majority (95%) of the 34 000 companies acting in this sector in Europe are small and medium-size enterprises (SMEs) (MedTech Europe, 2016[84]). However, a small number of large players account for significant market share.

The EU is currently transitioning from its previous legislative framework for the regulation of medical devices and in-vitro diagnostics. Since 1993, this framework set regulatory requirements for authorisation of products in the EU market, as well as rules governing their quality, categorisation, and post-market surveillance, among other topics. Approved in 2017, the Medical Device Regulation (MDR, EU reg. nº 2017/745) and In Vitro Diagnostic Medical Devices Regulation (IVDR, EU reg. nº 2017/746) aim to strengthen the regulation, and address quality and safety concerns. A transition period, which benefited from several extensions, is planned to last until May 2028, when all current and new medical devices will have to be approved under the new regulations.

The EU is undergoing consequential changes in its framework for regulating medical devices and in-vitro diagnostics

In general, MDR and IVDR will require more stringent assessments to allow for product commercialisation and utilisation in the EU. New rules can be summarised as follows:

- A wider range of products is defined as medical devices, and a larger proportion is classified as “high risk”. Some goods previously considered merely consumer products, such as aesthetic devices and software, are now recognised as medical devices, thus requiring more rigorous registration processes and quality oversight. In parallel, a much larger number of devices and IVDs are now categorised as high-risk, which entails more lengthy and demanding registration processes and post-market surveillance. For example, 80% of IVDs will have to undergo

assessment by a Notified Body (NB), the vast majority of them for the first time (European Commission, 2021[85]).

- The designation of national third-party assessment bodies for medical devices (i.e. Notified Bodies – NB) now involves a more rigorous certification process. Under EU legislation, the assessment of medical devices and IVDs for registration in the EU is conducted by notified bodies. These third-party private entities must be re-certified under the new regulation and required to undergo several evaluation processes that involves national regulatory agencies and the European Medicines Agency (EMA).
- Stronger requirements for post-market surveillance. All manufacturers will be required to present a quality management system (QMS), which describes a detailed plan to comply with MDR quality and safety requirements in accordance with the risk classification. Apart from class I devices (i.e. the lowest risk class), all medical devices are also required to present periodic safety update reports (PSURs).
- The introduction of Unique Device Identifiers (UDI). Each new medical device will be required to have a UDI tag that allows manufacturers, users, and regulators to identify each device individually. The UDI will contain technical and regulatory information about the device and will allow regulators to track products for safety and quality monitoring. All this information will be made publicly available through a centrally managed *European database on medical devices* (Eudamed), currently being implemented progressively.

Given the more stringent assessment and quality assurance measures, manufacturers and other healthcare professionals have raised concerns about the operational difficulties and costs of adaptation to the new rules. Shatrov and Blankart (2022[86]) predict that "generic" versions of medical devices will be withdrawn from the market and that compliance with the MDR will be challenging for SMEs. The paediatric medical devices sector has been particularly vocal about the increased costs of bringing and maintaining products in the market and the associated risks for supply chains (European Academy of Paediatrics, 2023[87]).

Bottlenecks in Notified Bodies' designations and increased workloads may stress the EU medical devices registration system

The transition process to the new requirements by NBs has faced some challenges and caused delays in the registration of devices. Of the 56 NBs that functioned under the previous directives, 39 have now been successfully re-certified (European Commission, 2023[88]). However, the first certification of a NB under MDR took over two years to be completed.

The current pace of submissions and certifications delivered by notified bodies is still very low relative to demands for re-certification of all existing medical devices, and submissions for new devices. By June 2023, 13 177 applications had been filed, but only 3 899 certifications had been issued. New registrations are also taking considerable time, with 71% of certificates taking longer than 13 months to be delivered by NBs (European Commission, 2023[89]).

In addition to increased workloads, more stringent and demanding assessment for medical device registration may also increase the time and resources NBs need to complete their assessments.

1.3. The case of health crises: Severe health crises, epidemics, and pandemics

An important finding from the risk management literature is that risk management approaches used for disruptions observed in "normal times" differ from those needed in extreme "black swan" events such as the COVID-19 pandemic (Sodhi and Tang, 2021[90]). Using the example of health crises, Sodhi and Tang (2021[91]) distinguish significant outbreaks of seasonal influenza, occurring every two or three years, where demand for medical products and equipment may double, from epidemics and minor pandemics, that occur every 10 years, where demand increases three or four times, and severe (global) pandemics where demand can increase more than 10-fold (as with COVID-19).

Using examples of recent crises (e.g. H1N1, COVID-19, international conflict), the following text summarises available information on shortages of different types of medical products and outlines some of the associated causes.

1.3.1. H1N1 (swine flu) pandemic

The H1N1 (swine flu) pandemic from 2009 and 2010 was a major health crisis that exposed vulnerabilities in the supply of medical products essential to containing the virus. In contrast with COVID-19, the 2009 pandemic presented different challenges in managing resources to respond to the crisis. Manufacturing capacity was considerably less affected by public health measures intended to contain the spread of the H1N1 virus with, for example, lockdowns only rarely imposed in very specific cases. Because of the nature of the H1N1 virus and its similarities with seasonal influenza, an effective vaccine was made available five months after the WHO declared the health crisis a pandemic.

Nevertheless, a strong and rapid increase in demand for medical countermeasures presented challenges for manufacturers, while a lack of preparedness measures resulted in shortages of some essential medical products. Although masks were not required for the general population, studies found a substantial uptake in utilisation of facial protective equipment. A study by Murray et al. (2010[92]) found that mask and N95 respirator utilisation in three healthcare facilities in the Vancouver area (Canada) were double that of previous flu seasons. The United States Centers for Disease Control and Prevention (CDC) guidance from July 2010 recognised that multiple healthcare facilities had reported shortages of PPE, leading the agency to issue recommendations on how to reduce health workforce exposure in order to reduce utilisation of such products (CDC, 2010[93])

Concerns around the availability of essential pharmaceuticals – such as antivirals – and influenza vaccines led some OECD countries to stockpile and purchase large quantities of some products in advance. Despite anticipated planning for influenza pandemic scenarios, health authorities in the United States did not anticipate the possibility of a shortage of vaccines. Reduced capacity in vaccine manufacturing led to considerably slower immunisation of target groups during the first two months of the vaccination campaign, followed by declining public willingness to be vaccinated due to waning incidence of H1N1 and reduced media attention. This resulted in a surplus of unused vaccines. Only 90 million of the 162 million doses produced for the general public were finally used (Institute of Medicine (US) Forum on Medical and Public Health Preparedness for Catastrophic Events, 2010[94]).

On the other hand, advance purchases in high-income countries restricted access to vaccines for developing countries (Fidler, 2010[95]). Similarly, concerns about the availability of antiviral supplies – in particular, oseltamivir (Tamiflu®) – had led multiple countries to stockpile large quantities of the medicine. By 2007, France, Austria and Ireland possessed stockholdings of the antiviral sufficient for more than 40% of their populations, and 95 other governments had also guaranteed their own supplies (Elbe, Roemer-Mahler and Long, 2014[96]). EMA had prepared to extend the shelf life cycle of Tamiflu® capsules by two additional years if needed, but severe shortage situations were not reported in the EU (EMA, 2009[97]). In the United States, stockpiling efforts by state and national authorities helped avoid a national shortage of adult antivirals. However, the unexpectedly higher incidence of influenza infection in children resulted in reports of shortages of paediatric Tamiflu® capsules during the autumn of 2009 (US Government Accountability Office, 2011[98]).

1.3.2. COVID-19 pandemic

The COVID-19 pandemic is one of the most significant health crises in the last century, causing millions of deaths worldwide, and widespread disruptions to societies and economies. In the initial stages of the COVID-19 pandemic, severe disruptions in supply and shortages of key medicines, testing reagents, and PPE occurred due both to spikes in demand and bottlenecks in supply. While these may be viewed as examples of supply chain failures, medical supply chains actually showed considerable resilience in the face of extreme stress.

Medical devices saw the most critical spike in demand during the first stages of the response to COVID-19

According to the 2022 OECD country survey on the Resilience of Health Systems, seven in every ten responding countries reported facing problems with the supply of essential medical devices prior to January 2022 (OECD, 2023[8]). Problems in supply of PPE was the most frequently reported issue during the pandemic, resolved at the time of the survey for 88% of respondents but still an issue for one country. Testing materials and ventilators were the second and third types of items with reported shortage issues (83% and 68% of respondents, respectively). In general, countries that reported issues for one device throughout the pandemic also reported it for other categories of products, while some countries did not report any shortage (OECD, 2023[8]).

International trade figures for face masks illustrate the steep surge in demand (see also Section 1.1.2 for a description of the facemask supply chain). Imports of face masks to the United States from March to May 2020 increased 15-fold in value, from USD 240 million to USD 3.7 billion (OECD, 2022[28]). Similar steep increases in imports of masks were recorded in other major OECD economies, such as Japan, the European Union and Canada. The first surge in demand from March 2020 was met mainly with supplies originating from China, which accounted for 94% of imports to the United States in July 2020. While aggregate demand for masks remained high throughout the pandemic, disaggregated trade data by different mask types (e.g. N95, FFP2) revealed variable supply chains according to the type of mask. By August 2021, the share of disposable face masks imported from China to the United States had dropped to around 60%, with increased supplies from Mexico, Korea and Viet Nam (OECD, 2022[28]).

The concentration of production of essential medical devices in only a handful of countries and locations led to considerable shocks when global demand rapidly increased. A lack of a co-ordinated response among manufacturers and suppliers upstream from different countries can potentially increase the number and duration of shortages. In late January 2020, several weeks before the wider, international disruption of global value chains, China had already begun imposing restrictions to contain the spread of Sars-CoV-2. The measures included the closure of several manufacturing plants in the country, resulting in a shortage of inputs for manufacturing plants and finished products in other economies. Surgical masks and disposable respirators are two examples of products that faced an intense shortage after a surge in demand and the closure of factories in China. In the subsequent months, as Chinese manufacturers re-opened, the disruptions in manufacturing impacted Europe and North America, where COVID-19 became a major health risk, resulting in a continuous bottleneck in production (Baldwin and Freeman, 2020[99]; OECD, 2020[100]). In March 2020, WHO was also warning countries about severe disruptions in the global supply of PPE caused by a surge in demand and misuse of available stocks. Its estimates at the time indicated that manufacturers would have to increase production by 40% to meet demand (WHO, 2020[101]).

The COVID-19 pandemic also generated a different set of demands from healthcare services, which resulted in a need for medical device manufacturers to adapt rapidly. With most hospital beds reserved for COVID-19 patients, and the cancellation of non-urgent and elective procedures, demand for certain products fell sharply, while essential products like PPE and ventilators were in very high demand (see Box 1.7 for the example of CPAP, a device normally used in sleep apnoea that was used to assist breathing

in COVID-19 patients). At the same time, a widespread and sharp increase in costs for different inputs and logistics services during the pandemic strongly impacted some manufacturers' capacity to supply the market and sustain their operations. In France, manufacturers surveyed by their trade associations estimated that the prices of commodities such as plastic materials and rare minerals saw a 40 to 90% and a 40 to 370% increase, respectively, from 2020 to 2021 (Snitem, 2022[81]). According to the same source, electronic components such as semiconductors, which are used in a variety of medical devices, also went into shortage globally, resulting in a 4-fold increase in costs. About 50% of respondents reported a suspension in production for 2 weeks to a month after the outbreak, and 90% reported increases in costs. Delivery times were also deeply affected, in some cases taking three times longer than pre-pandemic timeframes (Snitem, 2022[81]).

COVID-19 tests – including PCR and antigen tests – were developed and approved for use within the early months of the pandemic, with demand steadily increasing over time. COVID-19 diagnostic testing was one of the critical components in containing and mitigating the impact of the virus. The tests and associated equipment consist of various components with different manufacturing processes (see Section 1.1.2). Despite a ramping up of production of the components and a substantial increase in trade flows (Amirian, 2022[102]), the supply of tests did not match the demand (Behnam et al., 2020[103]), sometimes the result of supply chain issues (Griffin, 2020[104]). The testing supply chain experienced issues in ascertainment, production, and distribution of almost all component parts. Early 2021 data indicated that clinical laboratories in the United States were operating at 40% of their normal capacity, with key supply shortages of test kits and consumables as well supplies for non-COVID-19 tests (Congressional Research Service, 2021[105]). Demand for rapid antigen tests was high in early 2021, with shortages seen in the United States (CDC, 2021[106]) and increasing difficulty in obtaining the tests in Europe (Ding, 2022[107]). The reasons for shortages of already approved tests throughout pandemic included lack of raw materials and inputs including chemical reagents, RNA extraction kits, foam swabs etc, issues with logistics and distribution, as well as incorrect demand assessments.

Box 1.7. Challenges to CPAP supply chains during COVID-19

The production of Continuous Positive Airway Pressure (CPAP) devices is complex, relying on multiple global supply chains and a variety of regulatory frameworks (see Box 1.3 above). These features, together with an increased demand, led to bottlenecks in the supply of CPAP devices during the COVID-19 pandemic. In the United States, shortages of CPAP also occurred due to a recall due to potential health risks (FDA, 2021[108]).

At the crux of the CPAP device production challenge during COVID-19 was the heavy reliance on component manufacturers based in affected countries in East Asia. Most interior components of these devices are sourced from this region. In interviews, manufacturers indicated that a significant proportion of communication chips and chip boards were manufactured in Wuhan, China. Such a degree of dependency renders the entire supply chain vulnerable to disruptions, as was evident during the pandemic.

Another striking bottleneck was in raw materials essential for microprocessors. Expert interviews revealed that the majority of microprocessor raw materials originate from a single factory in Chinese Taipei. This degree of centralisation anywhere in the world poses significant risks, as any disruption, be it political, environmental, or economic, can halt production globally.

Overlapping regulations across jurisdictions add to the complexities faced by CPAP device manufacturers, as reported in expert interviews. Ongoing discussions by the US FDA, the UK regulatory agency, and their European and Asian counterparts, on harmonising regulatory frameworks have yet to yield comprehensive results. The recent transition from the Medical Device Directive (MDD) to the Medical

Device Regulation (MDR) raised the bar in the European market, with potential consequences expected to include exit from the market by some manufacturers. In such circumstances, navigating regulatory frameworks becomes an added overhead, sometimes overshadowing core production challenges.

During unprecedented health crises, such as the recent pandemic, the specifications and requirements for CPAP devices may differ from the norm. The intrinsic design and function of CPAP devices, and indeed of many medical devices, are optimised for specific sets of conditions and use-cases. For example, most CPAP machines designed by prominent manufacturers are not optimised for oxygen conservation, given that oxygen supply is not usually a limiting factor in developed countries. However, during health emergencies, oxygen conservation can become pivotal. This calls for rapid design alterations to cater to the emergent demand – a challenge that not all manufacturers may be sufficiently agile to accommodate.

Source: Based on consultations with experts in 2023.

Pharmaceuticals showed relatively greater resilience, although shortages occurred

Pharmaceutical supply chains showed relatively greater resilience in the face of such tremendous stress. Nevertheless, demand increased significantly for essential medicines used in acute care settings, such as anaesthetics, creating disruptions in supply and local shortages (Choo and Rajkumar, 2020[109]; Dey et al., 2021[110]; Gereffi, Pananond and Pedersen, 2022[111]). The OECD analysis in Chapter 11 of *Ready for the Next Crisis?* (OECD, 2023[8]) discusses the situation for propofol and azithromycin:

- **Propofol** (an intravenous anaesthetic) supply chains were placed under pressure during the early stages of the pandemic, exacerbating existing shortages of anaesthetics. Several countries reported shortages, resulting in the need to request special importations from companies without domestic marketing authorisations. In the United States, many propofol shortages were reported in the American Society of Health-System Pharmacists' shortage database[10], citing issues due to increased demand and shipping delays.
- **Azithromycin** (a macrolide antibiotic) manufacturers coped relatively well with increased demand during the pandemic, but depleted most of their inventories, leading to longer lead times (from 45-90 days to 6 months). Export restrictions, such as bans or licensing requirements, were imposed on antibiotics, particularly azithromycin, aiming to prioritise domestic markets and prevent exports to other countries. These limitations, even with exceptions for export-specific medicines, caused delays and extra expenses for exporters resulting from approval procedures and border controls, thereby worsening shortages. Moreover, certain markets (e.g. Canada), faced greater challenges due to export bans and logistics issues, stemming from a lack of local production capacity.

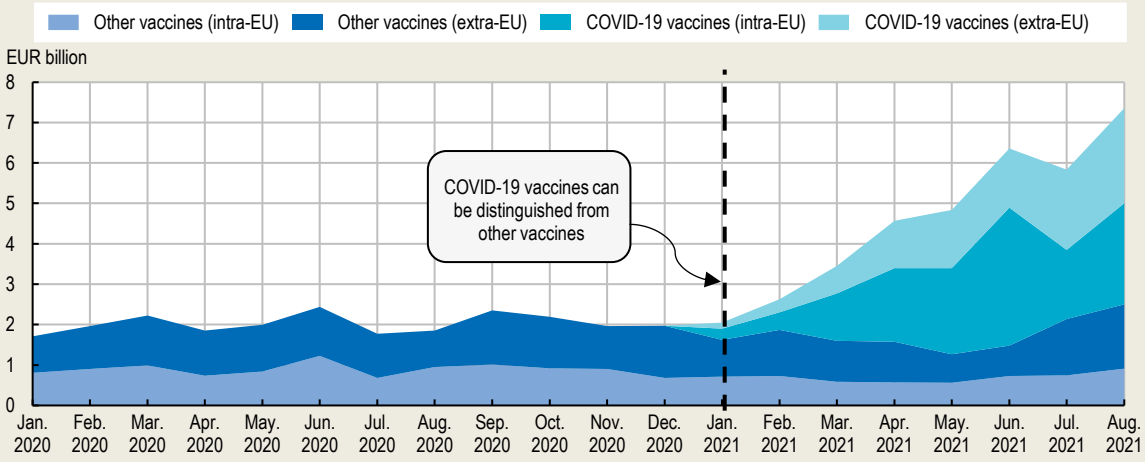
New COVID-19 vaccines were developed with exceptional speed over the course of the pandemic. While the topic of access and availability of these new vaccines is out of scope of this report, Box 1.8 explores some challenges in general vaccine supply chains during COVID-19.

Box 1.8. Challenges to vaccine supply chains during COVID-19

The World Health Organization's 2022 Global Vaccine Market Report indicates that there is no evidence that the global patterns of reported non-COVID-19 vaccine stockouts (i.e. lack of stock of a particular vaccine for a duration of at least one month) caused by quality issues were altered by the COVID-19 pandemic, based on data from 2019, 2020 and 2021 (WHO, 2023[21]). However, a 2021 report by UNICEF highlighted issues with the manufacturers of certain non-COVID-19 vaccines that UNICEF procures for non-OECD countries, citing competition with COVID-19 vaccines for production and resource allocation (UNICEF Supply Division, 2021[112]). Other issues include difficulties in obtaining raw materials and consumables such as filters, vials and syringes, as well as limitations in skilled workforce and transport.

In the European Union, exports of COVID-19 vaccines appeared to temporarily displace those of non-COVID-19 vaccines, leading to reduced exports of these other vaccines in the first half of 2021. However, exports were back up to pre-COVID-19 levels by mid-2021 – Figure 1.14 (OECD, 2022[28]).

Figure 1.14. Exports of vaccines (COVID-19 and non-COVID-19) from the EU, 2020-21



Note: The vertical line indicates the adoption of a separate nomenclature for COVID-19 vaccines.
Source: Reproduced from OECD (2022[28]), "Global supply chains at work: A tale of three products to fight COVID-19", https://doi.org/10.1787/07647bc5-en.

1.3.3. Impact of conflicts and geopolitical tensions on medical supply chains in OECD countries

Regional conflicts can impact global supply chains. The closure of manufacturing plants, disruptions to trade routes, and diversion of the workforce are some of the direct consequences from wars that can affect the availability of essential products. For example, Russia's war of aggression against Ukraine has caused severe disruptions in the global supply of products such as agricultural fertilisers or some critical raw materials for industrial production and the green transition (OECD, 2022[113]). Early analysis of suppliers' vulnerability highlighted the risk of inflationary pressures and high oil prices affecting energy costs for manufacturers in many countries. Increase in costs and reduced availability of essential raw materials that had a considerable share of supplies coming from Ukraine and Russia could particularly affect the manufacturing of semiconductors, an important component in some medical devices. For instance, 90%

of the highly purified, semiconductor-grade neon chip production used by the United States originates from Ukraine (Athanasia and Arcuri, 2022[114]).

Medical supply chains, however, have suffered less direct impacts from this conflict. The pharmaceutical sector is one of the less impacted when running simulations of trade disruptions on output, including within Ukraine and Russia (Arriola et al., 2023[115]). Nevertheless, there is a relative dependence of Russia on imported pharmaceutical products. Supply chain data also highlight impacts in the pharmaceutical sector of other countries, such as Latvia, through trade linkages.

At the same time, wide-ranging and increasing sanctions against Russia are generating repeated shocks for pharmaceutical manufacturers – particularly those with plants or providers in that country. Although some exceptions have been put in place to facilitate the supply of medical products, obtaining licenses can be a cumbersome process, with different rules applying to each item, often causing delays and increased costs for firms. Disruptions to transportation routes and the risks of crossing conflict zones further add to the difficulties of maintaining the continuity of supply chains that involve Ukraine and Russia (Fassion, 2022[116]).

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Notes

[1] For example, see the European Medicines Agency's responsibilities by type of medical device at the following link: www.ema.europa.eu/en/human-regulatory/overview/medical-devices (last accessed 21 November 2023).

[2] Biologicals are medicines manufactured in, or sourced from, living systems such as microorganisms, or plant or animal cells. Most biologicals are very large, complex molecules or mixtures of molecules. For more details, see www.who.int/health-topics/biologicals (last accessed 7 August 2023).

[3] With the Harmonised System (HS), a standardised classification of 5 000 products at the six-digit level developed by the World Customs Organization.

[4] In this chart, the European Union is regarded as a single economy, with "domestic" value-added including intra-EU transactions.

[5] Wholesaler activity consists of the purchase, warehousing, storage, order preparation and delivery of medicines. Pharmaceutical full-line wholesalers carry and distribute the complete assortment of products in range and depth within the framework set by the authorities and the market to meet the needs of those with whom they have normal business relations.

[6] Information provided by GIRP, the European Healthcare Distribution Association, via personal correspondence in 2023.

[7] Market value, at ex-factory prices. See https://girp.eu/sites/default/files/2022-06/GIRP%20Annual%20Report%202021-2022.pdf.

[8] Commercial reasons were defined in the report as "company-driven decisions linked to business aspects such as pricing negotiations; discontinuation; change in reimbursement status; low sales (i.e. low number of patients); business strategies prioritising other markets" (Jongh et al., 2021[38]).

[9] For Belgium, the observation period was July 2022–November 2022.

[10] These data are from the American Society of Health-System Pharmacists (ASPH) Drug Shortages website and include shortages that do not meet the criteria defined by the US FDA. For example, FDA only lists shortages on its website once it is confirmed that overall market demand is not met by the manufacturers, while the ASHP lists those in shortage even if full market demand is met. ASHP therefore commonly lists more shortages than FDA. Explanations of these differences are available at www.ashp.org/drug-shortages/current-shortages/fda-and-ashp-shortage-parameters?loginreturnUrl=SSOCheckOnly, last accessed 29 January 2024.

[11] The is calculated as the sum of the squares or market shares of each supplier ($HHI=s_1^2 + s_2^2 + s_3^2 + \ldots + s_n^2$, where s_i represents the market share (%) of supplier i). It can range from close to 0 to 10 000, where the latest represents a single supplier.

[12] An extended unit is defined as a millilitre for some injections, and as a pill for oral solids (see Definitions for more details).

[13] DT-containing vaccines protect against diptheria (D) and tetanus (T). dT-containing vaccines have a reduced dose of dipetheria.

[14] Based on archived data downloaded from Australia's medicines shortages register on 19 November 2023 (TGA, 2023[61]). For more information see www.tga.gov.au/safety/shortages.

[15] "Global shortages" were reported by 13 countries, and reported for BCG vaccine, DT-containing vaccines, hepatitis A, adult hepatitis B, and rabies vaccines.

[16] Vaccine's Europe is a specialised group within the European Federation of Pharmaceutical Industries and Associations (EFPIA).

[17] For example, see the requirements for notifying the FDA about medical device shortages at the following link: www.fda.gov/medical-devices/medical-device-safety/medical-device-supply-chain-and-shortages#authority (last accessed 18 January 2024).

[18] A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent, to a legally marketed device (Section 513(i)(1)(A) FD&C Act).

2 Policies for enhancing supply chain security routinely

This chapter reviews the landscape of policies that could be implemented routinely, as a foundation, to enhance medical product supply chain security. First, it examines initiatives aimed at improving the ability to anticipate or avert risks of shortages, such as enhancing visibility across the whole supply chain. It then looks into policies that aim to mitigate or reduce exposure to these risks, including addressing the root causes of shortages and encouraging flexibility and agility into the system.

Key findings

Shortages of medical goods were common and increasing in frequency prior to the COVID-19 pandemic, with issues of manufacturing, quality and market dynamics key contributors to supply disruptions. However, the pandemic significantly magnified pre-existing issues, with unprecedented spikes in demand and bottlenecks in supply exacerbating shortages of essential products.

Companies are responsible for and have an interest in ensuring the reliable supply of their products, and, in most cases, they deliver. The proliferation of shortages, however, has drawn policy attention and prompted calls for action. Policies are needed to enhance the resilience of medical supply chains and ensure continuity of supply, both routinely and in times of severe crisis (see Figure 2.1 for an analytical framework). This chapter focuses on the former, while the latter are discussed in Chapter 3.

Policies to enhance medical supply chain security routinely involve 1) better identification, anticipation and aversion of risks, and 2) mitigation of risks of shortages. In general, promoting the long-term resilience of medical supply chains would benefit from **collaborative approaches** that balance measures best undertaken by the **private sector** with those more appropriately managed by **governments** or **supranationally**.

Anticipating risks

- Policy makers would benefit from **improved visibility of supply chains to more readily anticipate and, where possible, avert shortages**. As a first step, they could **harness the information already required by regulatory agencies to identify and evaluate points of vulnerability** in supply chains. Regulatory agencies collect information on manufacturing sites potentially involved in supply chains but do not routinely draw on it to analyse risks to supply or evaluate in real-time the impact of a natural disaster, for example. Second, policy makers need **better visibility of flows in distribution chains**. Although unique identifiers are being implemented for medicines (to fight fraud) and for medical devices (for materio-vigilance and assessment of performance in real world conditions), these systems do not generally allow tracking of the flows of medical products in the distribution chain, albeit with some exceptions (e.g. medicines in Türkiye). Tracking would enable better prediction of supply, demand, and available stocks; characterisation of the nature and scope of notified shortages in real-time (local, national or global) and organisation of effective (re)allocation of available stocks.
- Policy makers could also consider implementing **closer monitoring of volumes and flows of "critical products" –** products identified as both "clinically essential" and having a vulnerable supply chain (according to criteria to be defined). Such a monitoring mechanism would need to be established in partnership with the suppliers of these products.
- Gathering granular, real-time, information on supply chains and investing in data analytics are key to anticipating and preventing shortages.
- Better anticipation of risks also depends on information sharing among stakeholders. Regulatory authorities should be authorised to share supply chain information with other government agencies and other countries, where appropriate.

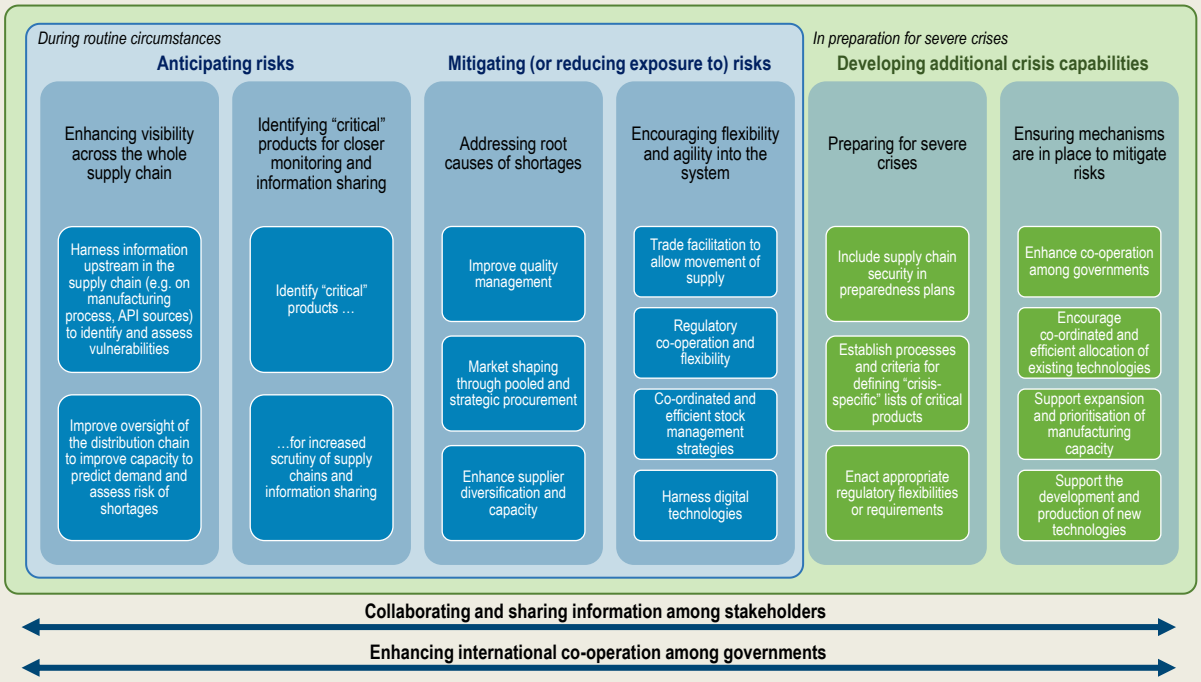
Mitigating (or reducing exposure to) risks

- The most effective way to reduce exposure to shortage risks is to **address the root causes,** as identified in former studies, i.e. quality failures, the most frequently reported reason for shortages, pressure on prices in off-patent markets and, to a lesser extent, reducing vulnerabilities arising from excessive concentration of sources of supply**.**

- **Improvements in quality management** are critical. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), recently published guidelines that aim to improve manufacturers' quality risk management programmes, and seven regulatory agencies have already implemented them. Public authorities need to require manufacturers to maintain management systems meeting the highest established standards and to monitor their implementation.
- In off-patent markets, excessive pressure on prices is suspected to lead to degradation of quality standards, product withdrawals and market exits, as well as concentration of supply to achieve economies of scale. Further empirical analyses are needed, at local or regional level, to confirm these trends in different contexts. Some policy options, however, may facilitate **market shaping**. *Cross-country pooled procurement* can be useful, for example to enhance prediction of demand and to secure supply for small markets that might not be supplied otherwise. The Pan-American Health Organisation's revolving fund for the purchase of vaccines is a good example. *Strategic public procurement* approaches that consider criteria other than price alone, such as supply chain security, can also relieve some pressure on prices while elevating the importance of supply security in decision making. The "most economically advantageous tender" (MEAT) criteria for public procurement recommended by the European Commission is a potential vehicle for more strategic procurement. Procurers of medical goods could also consider the diversification of supply as a rationale for splitting awards.
- **Diversification of supply** may require further action beyond improving procurement methods. Re-shoring and near-shoring policies are high on the policy agendas of several countries seeking to reduce dependency on highly concentrated sources, certain raw materials, active pharmaceutical ingredients (APIs) and finished products. These policies can expand production capacity, reduce concentration, and help meet increasing global demand. However, careful consideration should precede their implementation as they entail substantial cost. They should be focused on "critical products" as previously, ideally, defined at supranational level.

- Encouraging **agility and flexibility** into the system can also help to reduce risks of potentially harmful supply disruptions.
  - **Trade facilitation** and **harmonisation of regulatory requirements** for marketing authorisation can ease movements of medical goods. As an example, e-leaflets, in particular for hospital-administered products, can facilitate re-allocation of products across countries with different languages and labelling requirements.
  - **Appropriate inventory strategies and co-ordinated stockpiling policies** can help mitigate shortages due to spikes in demand and/or interruptions in supply chains in the short term, but are of limited effectiveness in long-term disruptions. Countries have adopted a variety of strategies for stockpiling, with differences in the range of products, and in stock management and financing mechanisms. The proliferation of national stockpiling policies, however, can potentially worsen supply gaps. Regional and co-ordinated stockpiling may be an option for responding to short-term mismatches between supply and demand, by allowing swift re-allocation of stocks where they are most needed.
  - **Digital technologies**, such as big data analytics and artificial intelligence, could be harnessed by all stakeholders to gain a better understanding of and improve predictions of supply and demand, as well as of the movement of goods.

Figure 2.1. Analytical framing of policies to improve medical supply chain security



Note: API active pharmaceutical ingredient. "Routine circumstances" refers to routine or "business as usual" situations in which minor or major supply disruptions occur absent a major crisis. Severe crises refer to major events (e.g. pandemic, other type(s) of major events or health threats).

Chapter 2 presents a range of policy options that could be implemented routinely to enhance the resilience of medical product supply chains. The overall objective is to improve the ability to anticipate and assess the risks of shortages (Section 2.1) but also to mitigate or reduce exposure to these risks (Section 2.2) by addressing the root causes of shortages and encouraging flexibility and agility into the system. In recent years, the issues of supply chain security and resilience have been high on the agenda of policy makers, particularly in light of the COVID-19 pandemic. Many different initiatives spanning a range of policy areas have been developed, or are currently being discussed at national, regional, and international levels. Annex A presents some examples of these initiatives, although it should not be considered as an exhaustive list. As an example, in October 2023, the European Commission published a communication on "*Addressing medicine shortages in the EU*" (European Commission, 2023[1]). This wide-ranging document covers many different topics, including the strengthened mandate of the European Medicines Agency (EMA), the expansion of the Commission's Health Emergency Preparedness and Response Authority (HERA), the Union Civil Protection Mechanism and the proposed reform of the European Union (EU) Pharmaceutical legislation. The communication sets out steps for mitigating shortages of critical products in the short and medium term, as well as more structural mid and long-term measures (ibid.). Other international efforts are ongoing in this space, particularly in the context of severe crises. These are discussed further in Chapter 3. Addressing rapid responses to shortages at the point of care, while important to mitigate the direct impact of shortages on patients, is out of scope of this particular report.

2.1. Anticipating (or averting) risks of shortages

Anticipating the risks of supply chain disruptions relies mainly on effective oversight (i.e. visibility) of the whole supply chain. Ensuring the reliability of manufacturing supply chains is generally the responsibility of the marketing authorisation holder (MAH). Companies have an interest in sustaining supply and matching demand for their products. Until recently, public authorities had focused their attention on the quality of the manufacturing process, as part of their mandate to ensure access to safe and quality-assured products. The multiplication of shortages, however, has pushed many of them to act and no longer rely only on companies to ensure security of supply. This section examines regulatory agencies' oversight on supply chains visibility and their ability to help prevent shortages, and suggests new approaches for more effective risk anticipation and prevention.

2.1.1. Enhancing visibility and harnessing information across the whole supply chain

Enhancing visibility and monitoring of the stages, participants, flows and stocks in supply chains are critical not only to preventing or anticipating disruptions, but also to mitigating their effects when they occur. The COVID-19 pandemic brought this issue to the forefront of health authorities' attention, with many countries struggling to assess vulnerabilities in the supply of essential medical goods during the dramatic first months of the crisis, while also facing challenges in forecasting demand. Shortage management in non-crisis situations can also be severely hampered by a lack of visibility. Without accurate data from both supply and demand sides, it is very challenging to assess the nature, extent, and severity of a "shortage" (local, national or global, due to bottleneck in manufacturing and or distribution, etc.) or to identify how best to mitigate its impact.

Enhanced visibility across the whole supply chain would require data from several stakeholders, including MAHs, distributors, hospitals, and pharmacies, as well as some sophisticated digital IT infrastructure to gather and analyse them. Some of these data would be considered commercially sensitive, thus it is important to consider for whom improved visibility is essential, for what purpose, and for which products, as well as whether requirements for data collection can be harmonised. However, before attempting to embark on the establishment of a global system, it is important to clarify the nature and the extent of the data that are currently available and how they are used, and what supplementary data should be collected. As a first step towards improving visibility, the following sections describe the nature of the information currently available on manufacturing processes (i.e. sourcing of raw materials, primary manufacturing of active ingredients, secondary manufacturing of finished products) and on the flows of goods within distribution chains (e.g. through distributors, to hospitals and pharmacies).

Harnessing available information on manufacturing processes to assess vulnerabilities in supply chains

As part of this study, the OECD conducted a survey of regulators' visibility of medicine and medical device supply chains, receiving responses from 24 countries and the European regulatory agency (European Medicines Agency – EMA).[1] Information presented in the following paragraphs reflects insights drawn from responses to this survey (summarised in Table 2.1) and additional desk research.

Medicines

Regulatory agencies already collect information on manufacturing sites involved in the production of medicines approved for sale in their respective jurisdictions (see Table 2.1). Companies are required to declare all sites potentially involved in the production of the final product and these sites, wherever they are located, may be subject to quality inspections. In some jurisdictions, for example the United States, the regulatory agency is not allowed to publicly disclose this information. The New Zealand regulatory agency MedSafe, by contrast, makes this information available to the general public on its website.

However, regulatory agencies do not generally use this information to assess vulnerabilities in supply chains. The information is not always structured in a way that would enable them to address questions such as whether any part of the manufacturing of a particular product is concentrated in a single site or which products in a domestic market might be affected by a natural disaster in any part of the world.

Requesting information on volumes produced in each site involved in the manufacture of a product for a specific market would be a step further. Companies generally regard this information as confidential and sensitive, making them hesitant to share it. In addition, when a company relies on several suppliers and serves several markets, it may apply some flexibility and adjust sourcing to fluctuations in domestic markets. Providing information to regulators in real-time would not only require goodwill but also a powerful digitalised and interoperable system. From policy makers' point of view, however, only centralised information on volumes produced by individual sites would address questions such as: do all generics of active substance X have the same and unique active pharmaceutical ingredient (API) source?

According to OECD's 2023 survey on supply chain visibility, some regulators already request information on volumes sold in their domestic markets. Since 2020 and the adoption of the Coronavirus Aid, Relief, and Economic Security (CARES) Act in the United States, all US Food and Drug Administration (FDA) registered establishments are required to report annually the monthly quantities of each listed drug that they produce. They must also disclose their suppliers of components, but are not required to share information on the quantities provided by each of them (US Congress, 2020[2]; HHS, 2022[3]).

In some jurisdictions, MAHs are required to submit information on volumes only in certain circumstances. For example, EU regulation that expanded the mandate and responsibilities of EMA (EU Regulation 2022/123) requests MAHs to submit data on demand and supply volumes to EMA only during public health emergencies or major events, and for those medicines included in lists of critical medicines, to monitor and mitigate/prevent shortages (European Council and Parliament, 2022[4]). The EMA has no mandate to request volume data from industry at national level. Individual countries may, however, impose different rules. In Germany, in case of critical shortages, when requested, MAHs are required to submit data on production, sales, and demand to the national competent authorities. They are also required to submit this information every two months for certain "high risk" medicinal products. Data on the available stocks of medicinal products can also be obtained at wholesaler level, as well as from hospitals and hospital pharmacies. In Spain, this information is also collected in specific circumstances, for critical shortages, or every three months for medicines susceptible to shortages.

In other OECD countries that responded to the survey, regulatory authorities do not have access to this information. In Korea, for example, company data on volumes are considered trade secrets that can only be accessed through a legal procedure to obtain disclosure.

Table 2.1. Regulatory authorities' visibility of supply chains of medicines and medical devices

Based on responses to the 2023 OECD country survey on supply chain visibility

		EU/EEA countries															Non-EU/EEA countries									
		EMA	BEL	BGR	CZE	DNK	EST	FIN	DEU	LTU	LUX	NLD	NOR	POL	ESP	SWE	AUS	CAN	CRI	ISR	JPN	KOR	MEX	TUR	CHE	USA
Medicines	RA requires information on production sites	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√		√	√	√	√	√	√	√	√	√
	Changes in suppliers must be notified to the RA	√	√	√	√	√	X		√	√	√	√	√	√	√	√		√	√	√	√	√	√[1]	√	√	√[1]
	RA requires information on production volumes	√[2]	√	X	X	X	√[3]	X	√[4]	X	X	√[3]	X	X	√[5]	√[6]	√	X	X	X	X	√	X	√	X	√[7]
	Changes in production volumes must be notified to the RA	√[8]	√				√		√[5]			√			√	√[5]	√[9]	X				√		X		X
	RA can share data on sites and/or volumes to third parties to address shortages	√	X	√	√[10]	√	X	X	√	√	X	X	X		√	√	X	√[11]	X	√	X	√	X	√		X
	RA conducts site inspections for GMP	X	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
	RA is part of an international co-operation network for mutual recognition of site inspections	√		√	√	√	√	√	√	√	√	√	√		√	√	√	√	X	√	√	√	√	√	√	√
	The country implemented a full national track-and-trace system	X		√[12]		X	√	X				X	√					X	X	X	X	√	X	√	X	√
	The country implemented an end-to-end national track-and-trace system	X	√[13]		√	X		X	√	√[14]	√	X			√	√		X	X	X	X		X		X	
Medical Devices	RA/NB requires information on component manufacturers and production sites [15]	√	X	X		X	X	X	√	√	X	√	X		√	√	X		√		√	√	√	X	√	
	RA can share information on component manufacturers and production sites to address shortages	√						X	X	X		X			√	√	√[16]		X		X	X	X		X	
	Quality inspections performed for sites involved in production		√	X	√	√	√	√	√	X	√	√	√		√	√	√		X		√	√	√	X	√	
	The country implemented a UDI system	√	√	X	X	√	√	√	√	X	√	√	√		√	√	X		X	X	√	√	X	√	√	

Notes: The authors have exceptionally revised country response to reflect more detailed descriptions and ensure consistency.
EU European Union; EEA European Economic Area; EMA European Medicines Agency; RA Regulatory Authority; GMP Good Manufacturing Practices; NB Notified Body; UDI Unique Device Identification.
√ indicates that the answer was "Yes" in dark cells, or "Yes, partly" in lighter cells. X indicates that the answer was "No". Empty cells mean that the country did not answer.

1. Only for major changes.
2. Only in case of severe crisis or major event and for critical medicines listed for the crisis (e.g. COVID-19, mPox).
3. Batch size range must be provided for products and related substances (at the time of application for marketing authorisation for the Netherlands).
4. Information on production provided on RA's request in case of critical shortage. For some high-risk products, data must be provided every 2 months.
5. Only in some circumstances (shortages or crisis).
6. Upon request.
7. Every registered company must report annually the amount of listed drugs that are manufactured, prepared, propagated, compounded, or processed for commercial distribution.
8. Changes in batch size only.
9. Marketing authorisation holders have to report any breach in Minimum Stockpiling requirement.
10. Only information on manufacturing sites.
11. Shared within a specific stakeholders' groups to prevent shortages.
12. Wholesalers and retailers (including hospital pharmacies in medical institutions) are obliged to submit data daily, at the end of the day. Marketing authorisation holders submit data weekly.
13. Limited to prescription medicines.
14. Wholesalers must report information monthly.
15. For all EU countries, information on sites involved in the production of medical devices and in-vitro diagnostics is required for all sites covered by the Quality Management System (QMS) of the manufacturer. The QMS differs across risk classes. The information is held by Notified bodies in charge of certification. Regulatory agencies do not have direct access to this information. The EUDAMED database, in development, will include information on sites involved in the manufacturing of the final product.
16. Only with marketing authorisation holder permission or for safety reasons.

Source: OECD survey on regulatory visibility of medicine and medical device supply chains, 2023.

Another important feature of the system is the ability of regulatory agencies to share information about production sites and/or volumes with third parties for the purpose of addressing shortages. In the EU, according to Heads of Medicines Agencies (HMA)/EMA Guidance on the identification of commercially confidential information, information on production sites cannot be shared with third parties, unless authorised by MAHs, except information already made public lawfully (e.g. for biologicals) (HMA/EMA, 2012[5]). A general exception is permission to share confidential information (such as production sites) with other EU/EEA national competent authorities on a case-by-case basis. Permission to share information with other government agencies varies across countries; Lithuania may share information on volumes with the public, while Spain and Sweden may share information with their respective health ministries.

As regulator visibility of upstream supply chain information from which to assess supply vulnerability is generally poor, regulators mainly rely on notifications of shortages (or risks of shortages) by manufacturers. However, definitions, reporting methods, and requirements for shortage notifications, vary widely by country (see Box 1.4 in Chapter 1 and (Chapman, Dedet and Lopert, 2022[6]).

In some cases, regulators have discretionary powers to impose fines for non-reporting, on a case-by-case basis. Half of the 24 countries surveyed by Vogler and Fisher (2020[7]) indicated that fines may be applied to MAHs that do not comply with shortage reporting requirements. For example, the French agency for the safety of medicines and health products (ANSM) has the power to impose sanctions where companies fail to notify current or potential future shortages. Fines can be levied for amounts as high as 30% of the firm's revenue from the product in shortage, determined according to a set of criteria that take into account the gravity and duration of the shortage, the degree of co-operation by the supplier in addressing the issue, and whether the supplier has repeatedly failed to fulfil its supply obligations (ANSM, 2022[8]). Since the release of the 2020 study, several countries have introduced legislation allowing regulators to sanction non-compliance with shortage reporting. In Sweden, new regulations came into force in July 2023 that impose fines ranging from EUR 2 200 to as much as EUR 8.7 million (Kleja, 2023[9]). By contrast, in the United States, the FDA does not have the authority to apply financial sanctions to manufacturers that do not comply with notification requirements.

Medical devices

According to the 2023 OECD survey, regulators have even less visibility of this information for medical device supply chains. Only a minority of countries indicated that regulatory authorities or notified bodies (for EU countries) collect information on all manufacturing sites involved in the production of medical devices and their main components (see Table 2.1), and this mainly applies to high-risk devices.

Improving knowledge of distribution chains to enhance supply-demand forecasting

Tracking the movement of medical goods in the distribution part of the supply chain offers an opportunity to improve the security of supply in several ways. In the event of local or regional shortages, knowing where existing stocks are being held within the distribution network may help, allowing stakeholders to co-operate to move stocks where they are most needed.[2] This information could also be used to better predict changes in demand. For example, Snowdon and Forest (2021[10]) mention the case of Alberta, Canada, where a highly digitised supply chain infrastructure capable of tracking the location and utilisation of every product across the entire health system, enabled leaders to source personal protective equipment (PPE) in December 2019, well in advance of nearly every other jurisdiction. This degree of visibility requires the use of unique identifiers (UIs) to follow products to the last part of the supply chain. UIs are being implemented for medicines and medical devices in some parts of the world, for different reasons. Until now, they have not been used to prevent or address shortages.

Medicines

The progressive introduction of UIs for medicines began with the main objective of fighting falsification, fraud and counterfeiting. In theory, UIs allow the implementation of full track-and-trace systems in which participants in the supply chain can authenticate products and transmit digital data to a central management system that stores relevant information (e.g. expiry dates, recalls, falsification alerts) (Kootstra and Kleinhout-Vliek, 2021[11]). Current systems, however, are generally not capable of this.

For the time being, two types of track-and-trace systems exist:

- In the "Point-of-dispense check" or "end-to-end" system, finished products are only scanned at the beginning and end of the distribution process of the supply chain (i.e. point of dispensing or administration). The main purpose is to protect patients by verifying the authenticity of a product by validating them at the dispensing points with a code designated in the manufacturing process (WHO, 2021[12]). This does not require scanning of products at every stage of the supply chain or at different transaction points (e.g. between wholesalers and distributors). Many European countries have implemented these systems, which are less costly to manage than full track-and-trace systems. Since February 2019, all prescription medicines, unless explicitly exempt, have been required to comply with safety measures specified in the Delegated Regulation (EU) 2016/161, which mandates the assignment of a unique identifier in packages. The European Medicines Verification System (EMVS) was created for this purpose. Packages are only scanned at the production and dispensing stages of the supply chain, and in many cases, only where there are concerns about falsification. As a result, unique identifiers cannot be used to track medicines throughout the supply chain in order to anticipate and mitigate risks of shortages. Moreover, the data centralised in the EMVS may only be accessed by regulatory authorities on request, for the purposes of investigating potential incidents of falsification, reimbursement or pharmacoepidemiology and pharmacovigilance (European Commission, 2016[13]). At the time of writing, the system had been implemented in all EU/EEA countries except Greece and Italy, which have their own serialisation systems. The deadline for these countries to comply with the EU regulation is February 2025. However, even with full participation, the EMVS cannot readily be used as a full track-and-trace system, which would require legal and technical adaptation.[3] In the interim, the European Federation of Pharmaceutical Industries and Associations (EFPIA) has suggested that the information collected through the current systems, used with complementary data sources, could nonetheless be used to providing additional intelligence in monitoring shortages (Bouvy and Rotaru, 2021[14])
- A "full" track-and-trace system follows products throughout the entire distribution chain, through a scan validation at every transfer of ownership, beginning with release from the manufacturer. It allows for real-time tracking and stock management along each stage of the distribution chain, thus facilitating timely detection and prevention of shortages, targeted recalls, and reduction of fraud, theft, and medication errors (Parmaksiz, Pisani and Kok, 2020[15]). Only a few countries that responded to the OECD survey reported having such a system (Bulgaria, Estonia, Norway, Korea, Türkiye and the United States). The Turkish and the US systems are described in Box 2.1. These systems have not been used so far to anticipate or avert shortages.

Box 2.1. Full track-and-trace systems for medicines

Ilaç Takip Sistemi (ITS), the Turkish track-and-trace system for essential medicines

ITS, the full track-and-trace system, was introduced in Türkiye in two phases. The first phase began as a pilot in 2010 with a point-of-dispense check system managed using software developed by the Ministry of Health. The system was originally implemented to fight reimbursement fraud. The second phase was launched in 2012, this time by a private company, and for the first time encompassing all actors within the regulated supply chain. The company and the Ministry of Health are jointly responsible for the maintenance and development of the platform. The data are pooled in a centralised database managed by the ministry, which provides the authorities with visibility of the supply chains of relevant products.

The system is based on cross-checking movements of products between each participant in the supply chain. A central database stores all information, and a cross-checking system compares sales and purchasing notifications at every step. Sales are disabled when notifications cannot be matched. A notification of provision is required for reimbursement by national health insurance (NHI).

The industry bears the costs of compliance with the regulation, investing in adding the track-and-trace system to their production and distribution flows. The obligation to comply with established rules to trigger reimbursement by NHI was a strong incentive, since 95% of the Turkish population are covered by NHI.

Since ITS registers purchases and sales throughout the entire supply chain up to dispensing, it allows health authorities to monitor stocks of medicines, and gives manufacturers, wholesalers, and pharmacies control over and visibility of inventories (Parmaksiz, Pisani and Kok, 2020[15]). However, the Ministry of Health recognises that the system is largely reactive, and that the data produced by ITS could be used more effectively to help avert shortages and stock-outs. For this reason, the government is looking to implement a proactive alert system that provides a notification when a particular product's supply falls below a specified threshold (ibid.).

Track-and-trace system for medicines in the United States

In the United States, the Drug Supply Chain Security Act, enacted in November 2013, defined a procedure to implement an interoperable, electronic tracing of medicinal products to identify and trace certain prescription drugs as they are distributed. The system is intended to identify and remove potentially dangerous medicines from the supply chain and requires manufacturers, re-packagers, wholesale distributors, and dispensers to comply with standards for package-level tracing of medicines and data exchange of product tracing between participants in the supply chain (FDA, 2023[16]). Operators were initially expected to comply with this regulation by sharing information electronically or on paper. The implementation of an "all electronic" system was expected by November 2023. The FDA recently published guidance for suppliers to support this implementation (2023[17]), and operators were given one additional year in which to implement it (FDA, 2023[18]). For the time being, the regulation stipulates that regulatory authorities may only ask trading partners to share product tracing information in the event of a recall, or for the purposes of investigating a suspect or illegitimate product.

In March 2021, the World Health Organization (WHO) published a policy paper on the traceability of finished medicinal products from manufacture (i.e. lot/batch release) to the point of dispensing (i.e. pharmacies) or administration (e.g. hospitals) (WHO, 2021[12]). The paper outlines some of the main features of existing traceability systems that are designed to be used to identify falsified and substandard products and offers guidance for developing regulation on the topic. The findings were developed in consultation with regulators from WHO Member States, as well as in collaboration with the International

Coalition of Medicines Regulatory Authorities (ICMRA) and the European Directorate for the Quality of Medicines and HealthCare (EDQM). The paper emphasises, *inter alia*, the importance of establishing an appropriate governance process, identifying costs and benefits of different approaches, and using global standards to maximise international interoperability. While not the intended purpose of most existing traceability systems, the paper also recognises their potential use in maintaining efficient stock management at different levels, and in identifying shortages and monitoring the reasons behind them.

In August 2021, ICMRA published a technical document with recommendations for interoperability of track-and-trace systems at global level that would enable different systems to exchange and use relevant information on medicines and their supply chains to advance various public health goals. The document recognises the potential benefits of traceability systems for supply chain management and mitigation of medicine shortages (ICMRA, 2021[19]).

In the absence of performant track-and-trace systems, initiatives relying on information from the distribution chain have helped to identify and address shortage issues, albeit on a more "reactive" basis (see Box 2.2). Furthermore, increasing the predictability of demand through better forecasting, where possible, and surveillance systems, as well as ensuring appropriateness of prescribing according to clinical guidelines, would help to anticipate and prevent shortage issues. In the vaccine space, for example, vaccine manufacturers have emphasised the importance and value of early collaboration between decision-makers and manufacturers in anticipating changes in demand (e.g. the introduction of a new vaccine to a national immunisation programme) in order to plan for adjustments to supply or increased production capacity (Jongh et al., 2021[20]). In other cases, inappropriate prescribing has resulted in shortages of some products (e.g. azithromycin during COVID-19). More recently, several agencies have called for appropriate use of a GLP-1 analogue that has been extensively promoted in social media and is being prescribed widely and inappropriately off-label for weight loss while at the same time being in short supply for authorised use in diabetes (Brafman, 2023[21]; TGA, 2023[22]).

Box 2.2. When distribution information assists the management of shortages

In Spain, **the Centre for Information on the Supply of Medicines (CISMED)** is a pharmacy-based system which automatically detects supply issues affecting patients. The information provided by pharmacies can be used by health authorities to visualise and respond to shortages in supply on a regional or national level. From November 2019, Digital Health Europe, with funding from the European Commission, has launched a cross-border mechanism for information sharing on medicine supply chains between Spain, France, Italy and Portugal. Analyses of standardised shortages data provided by pharmacies has enabled the identification of similarities in trends in stockouts among the participating countries, such as increasing shortages of neurological medicines between 2019 and 2020 (Consejo General de Colegios Oficiales de Farmacéuticos, 2023[23]). The collaboration between pharmacy associations has illustrated how countries can work together to exchange valuable information on medicine shortages, and suggests that co-operation like this could be implemented at the European level (Digital Health Europe, 2023[24]). Learnings from this initiative could also help inform the implementation of the European Shortages Monitoring Platform.

In France, two systems have been implemented. In **TRACStock,** manufacturers feed stock level data into the system, which is managed by a third-party to ensure the appropriate utilisation of any sensitive or confidential information. Developed by the association representing the pharmaceutical industry (LEEM) TRACKStock can detect possible disruptions in advance and indicate alternative therapeutics for medicines in shortage, if any. While this tool is industry-led, the French agency for the safety of medicines and health products, ANSM, has full access. Another system, **DP-Ruptures,** was developed by the French Chamber of Pharmacists. It tracks pharmacies' shipping requests and automatically

notifies the MAH if a delivery is taking longer than 72 hours. The MAH can then inform pharmacists of any recurring issues in supply, the measures being taken to resolve the issue, and possible alternative medicines that could be substituted for the one in shortage. When more than 5% of pharmacies using DP-Ruptures report late deliveries of supplies, the shortage is included in a list and ANSM is notified (Ordre National des Pharmaciens, 2022[25]). Apart from keeping retailers better informed about disruptions in supply, MAHs can also benefit from greater transparency in the logistic systems delivering their medicines, which can aid the assessment of stock and production levels.

Medical devices

The progressive implementation of Unique Device Identifiers (UDIs) in the medical device sector has a different history and very different objectives: it was designed to improve materio-vigilance and to collect data to build real-world evidence on the performance of medical devices. The UDI system for medical devices, promoted by the International Medical Devices Regulators Forum (IMDRF) in a 2013 guidance document, provides a globally harmonised system for identification and coding of medical devices (WHO, 2021[12]; IMDRF, 2013[26]; IMDRF, 2019[27]). It is composed of two parts: the device identifier UDI-DI, which identifies a manufacturer's product and package configuration; and the production identifier UDI-PI, which identifies the unit of device production. While the system was intended to provide globally accepted identification of medical devices, it also supports inventory management, pre- and post-market surveillance, vigilance, and reimbursement (WHO, 2021[12]).

The implementation of UDI systems began with high-risk medical devices, such as implantables. In Europe, EU regulations have required UDIs for some medical devices since May 2021 and for in-vitro diagnostics (IVDs) since May 2022.[4] The data are kept in an electronic "UDI database", part of the European Database on Medical Devices (EUDAMED), which is not yet fully operational. Manufacturers are responsible for the placement of the UDI in the labelling and packaging of the device, as well as the registration of the UDI in the EUDAMED database before the device is placed on the market (European Commission, 2020[28]). Outside the EU, Japan, Korea, Türkiye and Switzerland report having systems in place (see Table 2.1). To date, however, UDI information systems have not been used to track movements of goods in health systems or predict demand for specific devices.

In the United States, with the Unique Device Identification System Rule enforced in 2013, the FDA established a system to identify medical devices from manufacturing through distribution to patients. The system requires labelers (e.g. manufacturers) to include a UDI on labels and packages and to submit information on their devices to the Global Unique Device Identification Database (GUDID), available to the public. The GUDID only includes information on the labeler and the version or model of the device (FDA, 2023[16]; FDA, 2013[29]). The UDI system in the United States is in its final phase of implementation, and when fully deployed is expected to improve patient safety and post-market surveillance.

In Australia, the Therapeutic Goods Administration (TGA) launched three consultation processes (in 2019, 2020 and 2022) for the implementation of a UDI system. The system aims to strengthen patient safety by allowing tracking and tracing of medical devices, including patient use. However, the system has not yet been implemented (Department of Health and Aged Care, 2023[30])

Canada is currently assessing the feasibility of introducing a UDI system. In June 2021, Health Canada opened a public consultation to gather feedback on a proposal for the implementation of a UDI on devices and packaging, and the submission of the information to a database open to the public (Health Canada, 2021[31]).

Gathering real-time, granular information on supply chains and investing in data analytics are key to anticipating and averting shortages

Real-time information about medical devices and medicines can help issues to be anticipated and addressed quickly. Interest in greater supply chain visibility at different points in the supply chain and the use of real-time information has been highlighted by various stakeholders, for example by respondents to a recent public online consultation by Health Canada's Drug Shortages Task Force (Health Canada, 2023[32]) (Annex A). Greater confidence in predicting the required supply may provide some lead time for manufacturers to buffer capacity (Chen et al., 2021[33]). Reporting platforms could also be improved through the development of new information systems, using data analytics to detect shortages in advance based upon real-time variations in supply and demand. Some countries already have such stock monitoring systems in place. Caution, however, must be made that any forecasts consider the possibility of stockpiling at any level (e.g. including at institutional level, in pharmacies and hospitals). Technologies such as smart labelling may also help to improve the transparency and traceability in medicine and medical device supply chains. Diprivan® (a brand of propofol), for example, is one of the first medications to benefit from a radio-frequency identification system (Fresenius Kabi, 2020[34]). So called "smart labels" may also help hospitals with inventory management and allow manufacturers to anticipate changes in demand.

In addition, various supply chain technologies (including digital technologies relying on predictive analytics, artificial intelligence and blockchain) are available to monitor supply chains and anticipate risks (Ye et al., 2022[35]). For example, encrypted blockchain technology can help build trust along the value chain, while also facilitating the exchange of information and collaborative relationships (Hosseini Bamakan, Ghasemzadeh Moghaddam and Dehghan Manshadi, 2021[36]). Governments can assist by ensuring that regulatory environments are favourable to the deployment of digital technologies, and by addressing issues such as governance, data ownership, privacy and security in data transmission, that are particularly important in the context of health systems (see Section 2.2.2 on harnessing digital technologies).

2.1.2. Identifying "critical" products for closer monitoring and increased information sharing

Given the vast array of medical products – particularly medical devices – available in the market, supply chain resilience efforts are best directed towards those products deemed "critical" by national (or regional) authorities. The definition of "critical" varies from country to country, in part depending on disease burden and the availability of alternatives, and may change with the advent of a major issue of public health concern. The terms "critical" and "essential" are being used with variable meanings. Different lists are being developed at national and supranational levels: lists of medical products deemed important for inclusion in the range of benefits covered by health systems; those that are deemed "essential" to always have in adequate quantities; and those that are deemed to be "critical" in the event of a major crisis. The last group is discussed in more detail in Chapter 3.

The subsections below outline examples of countries' efforts to identify "critical" medical products for their national markets for objectives relating to supply chain security. While a "common language" is still missing, to improve supply chain security for these products it is pertinent to consider mechanisms for increasing visibility and information sharing, beyond those already described in Section 2.1.1. For example, sharing information on supply and demand volumes between relevant stakeholders would help in both anticipating risks and mitigating the impact of any supply disruptions on patients. In other cases, these lists may be used to guide stockpiling or re-shoring efforts.

Medicines

Most OECD countries already have lists of medicines deemed important for their populations and covered by health insurance or national schemes. Not all of these medicines would be considered "essential", according to the WHO definition. Since 2007, WHO has established and regularly updates a Model List of Essential Medicines (WHO EML), which as of the year 2023 includes 643 medicines (and 143 therapeutic alternatives) (WHO, 2023[37]). The list is intended as a guide for countries in the development and updating of their national essential medicine lists. The inclusion of medicines in the WHO EML considers disease burden and public health relevance, safety and efficacy, and comparative cost-effectiveness. In OECD countries, the range of medicines covered is usually wider than the EML.

Several OECD countries have developed lists of critical medicines, although with different objectives and criteria for inclusion or exclusion. In 2021, Germany, the Slovak Republic and Spain had compiled their own national lists of critical medicines and medicines at high risk of shortage, and at least eight other European countries were considering doing so (Jongh et al., 2021[20]). Since then, several other countries have created lists, including Denmark and France. Some examples are included below:

- Germany's list was developed by a multi-stakeholder advisory board at the Federal Institute for Drugs and Medical Devices, with representation from patients, doctors, pharmacists, and industry, and focuses on prescription medicines that are relevant for the entire population (Bundesamt für Justiz, 2022[38]; BfArM, 2023[39]). For the ~400-500 medicines on the list, specific actions may be taken to avert or mitigate supply shortages. For example, stockpiling may be requested in the case of medicines containing a "supply critical active substance". Electronic information on available stocks, API production and manufacturing sites, sales volumes etc., may be requested from manufacturers, wholesalers, and pharmacies.
- Portugal has identified a list of ~250 "essential medicines of critical nature" for which specific measures may be applied (regulatory, economic, or other) in order to ensure access in the Portuguese market (Diário da República, 2023[40]; Infarmed, 2023[41]). The criteria include that a medicine must be considered an essential medicinal product; have a data protection period that is still valid; have a history of shortages; have identified vulnerabilities in the manufacturing and distribution chain (from raw material to final product) etc.
- Spain's national list of strategic medicines, developed by the Spanish Agency of Medicines and Medical Products, AEMPS, contains medicines that requires specific actions to ensure their availability (AEMPS, 2023[42]). The selection methodology takes into consideration two complementary criteria – the clinical importance of the medicines, and the availability of adequate alternatives – including only those medicines for which there are only one or two authorised medicines available with the same active(s) substance(s), strength, and dosage form. For each of the criteria, one of three risk levels (low, medium and high) is assigned to the product of interest.
- France developed a list of essential medicines, published in June 2023, to serve as the basis of a roadmap for managing shortages (Ministère de la Santé et de la Prévention, 2023[43]; Ministère de la Santé et de la Prévention, 2023[44]). Based on the work of several learned societies, the list of nearly 450 medicines includes those based on criticality of need and therapeutic area (e.g. infectious diseases, anaesthesia, intensive care etc). The overall criticality of the medicine is determined by simultaneously considering (1) the required frequency of dosing (e.g. once a day, once a week) and (2) the significance of a disruption in supply (e.g. no alternative, and life-threatening if not available, significant impact, limited consequence of a delay, etc). The final list also includes 50 medicines for which production should be relocated or reinforced (see Box 2.4) (Ministère de l'Économie, 2023[45]).

The United States has taken a slightly different approach, and following Executive Order 13 944 in August 2020, established a "list of essential medicines, medical countermeasures and critical inputs that are medically necessary to have available at all times in an amount adequate to serve patient needs and

in the appropriate dosage forms" (FDA, 2022[46]; FDA, 2020[47]). This list, developed by the US FDA in consultation with federal partners, also aims to ensure protection against emergency events such as infectious diseases, chemical, biological, radiological, and nuclear threats. It includes ~230 products in the drug category and ~100 devices. There are specific criteria for inclusion of medicines in the list, which preference products used in the treatment of severe acute conditions and those that can be used for the widest public health impact (see Box 2.3) (FDA, 2020[48]).

Building on these efforts, and in response to an Executive Order in February 2021 (The White House, 2021[49]), a prioritised list of essential medicines was developed for an initial analysis of supply chains in the United States (ASPR/ARMI/NextFAB, 2022[50]). Through comprehensive consultations with clinical stakeholders, the original FDA Essential Medicines List was narrowed to 86 medicines considered to be the most critical in acute care (e.g. life-saving, stabilising patients in hospital for discharge, emergency surgery). Some categories of medicines on the original list were excluded because of the specificity of their supply chains (e.g. blood and plasma products). The next steps will involve identifying specific supply chain and manufacturing vulnerabilities for the most critical of these medicines, to tailor any possible solutions.

Although the creation of national "critical" medicines lists has escalated since COVID-19, the idea of assigning "criticality" of medicines in shortage management is not new. In their analysis of shortage notification databases, Chapman, Dedet and Lopert (2022[6]) found that several countries (e.g. Australia, France, Switzerland and the United States) only report or publish data on shortages affecting a subset of medicines deemed to be critical or essential to their respective health systems. In Ireland, stakeholders agreed on a gradation of "low" and "medium or high" to describe the potential impact of a shortage, based on the existence of therapeutic alternatives and the likely effects on patient health (HPRA, 2023[51]).

More broadly, the European Medicines Agency published the *Union list of critical medicines* in December 2023. The first version contains 268 listed products (EMA, 2023[52]). The work on the list was initiated under the Structured Dialogue on the Security of Medicines Supply and the 2022 Staff Working Document (Directorate-General for Health and Food Safety, 2022[53]), and progressed under the planned guidance of the Joint Heads of Medicines Agencies (HMA)/European Medicines Agency (EMA) Task Force on the Availability of Authorised Medicines for Human and Veterinary Use (TF AAM) (EMA, 2023[54]; EMA, 2022[55]). The list includes medicines that are considered the most critical for EU/EEA health systems and need to be available at all times (i.e. not just during crises). It identifies those with a significant public health impact for which measures should be taken to strengthen security of supply. For these critical medicines, supply chain vulnerabilities will be assessed, EMA will be able to make recommendations on appropriate security of supply measures, and the Commission will be able to introduce measures to strengthen these. According to the EMA, the "criticality" of medicines is initially based on two criteria: (1) therapeutic indication and (2) availability of alternatives, with low, medium and high-risk levels assigned to each criterion. For example, medicines for acute life-threatening conditions are classified as high risk under criterion (1) while medicines without available alternatives are classified as high risk under criterion (2). The resulting risk matrix determines the categorisation of medicines as either "critical medicines", "medicines at risk" or "other". After assigning a risk category, an analysis of supply chain vulnerabilities is performed for "medicines at risk" to determine whether they should be upgraded to "critical medicines" (Directorate-General for Health and Food Safety, 2022[53]). Further details of the methodology for assessing supply chain vulnerabilities are not yet available. However, as an indication, in a report commissioned by the European Commission to analyse causes of medicine shortages and policy options, the supply chain of the product Epipen® (auto-injectors of adrenaline) was assessed as "vulnerable" because the product was in a dominant position in the market and the manufacturing capacity was highly concentrated (Jongh et al., 2021[20]). The analysis being carried out by the EMA will also draw from the Critical Medicines Alliance, a multi-stakeholder policy dialogue launched by the Belgium presidency of the Council of the EU in January 2024. The alliance will focus on a first subset of medicines from the Union critical medicine list and seek expert advice on the most appropriate tools and actions to address the most pressing issues. The alliance is planned to last for an initial five year period, with a first meeting scheduled for April 2024 (European Commission, 2024[56]) (see Annex A).

Beyond the preparation of this *Union list of critical medicines*, EMA is also in charge of developing specific lists in response to emergencies (see Chapter 3).

Box 2.3. Criteria for inclusion in the United States' list of essential medicines, medical countermeasures, and related critical inputs

Selection of essential medicines

- Approved medicines considered necessary to address immediately life-threatening medical conditions in acute care settings, and that are used to stabilise patients with these conditions to facilitate hospital discharge;
- Medicines for longer-term chronic management are excluded;
- Selection of the medicines, including dosage form and presentation, is based on those that can be used for the widest populations encountered (e.g. if multiple medicines or medicine classes treat the same condition, the product that can treat the widest population is included; if more than one medicine class is identified, there is a preference for the option with a better safety profile; consideration for the inclusion of more than one medicine in a class in certain circumstances).

Selection of medicines included as medical countermeasures

- Based on the definition of "Medical Countermeasures" included in the Executive Order 13 944, the selection included "qualified countermeasures" (all approved products in the Strategic National Stockpile), "qualified pandemic or epidemic products" (approved vaccines and antiviral medicines to treat influenza), and "security countermeasures" (approved products associated with prevention, mitigation or treatment of chemical, biological, and radiological/nuclear threats);
- Selection was informed by available lists of medical countermeasures by FDA and other agencies;
- Limited to medicines approved or legally marketed in the United States.

For each medicine or medical countermeasure, the list further identifies related critical inputs, i.e.:

- All active pharmaceutical ingredients (APIs);
- All active ingredients or starting materials for biological or natural source products; and
- Other ingredients or constituents that possess unique attributes essential for the use of the product.

Source: FDA (2022[46]), Executive Order 13944 List of Essential Medicines, Medical Countermeasures, and Critical Inputs, www.fda.gov/about-fda/reports/executive-order-13944-list-essential-medicines-medical-countermeasures-and-critical-inputs.

Medical Devices

Progress on the creation of national lists of critical medical devices is less advanced. WHO has developed several lists of priority medical devices (WHO, 2023[57]) In 2021, it introduced a list of over 500 priority medical devices essential for managing cardiovascular diseases and diabetes across all healthcare levels (WHO, 2021[58]), including in emergency situations such as cardiac arrest and stroke. This list offers clinical guidelines for specific conditions and associated interventions, encompassing surgical instruments, PPE, and diagnostic tools. Under the Priority Medical Device Project, WHO is continually updating lists for the management of high-burden diseases such as cancer and COVID-19, as well as for specific populations

such as older adults, pregnant women, and neonates. The selection process involves reviewing clinical guidelines, determining the devices necessary for each care level, and consulting with a multidisciplinary group of experts. These lists support countries in developing or revising their national essential or priority lists to advance universal health coverage.

In the United States, critical device medical countermeasures are included in the list already described above (FDA, 2022[46]). The device medical countermeasures list includes products such as diagnostic testing kits and supplies for rapid test development, PPE, vital sign monitoring devices, vaccine delivery devices, and devices to manage acute conditions such as ventilators. Devices are included if it is medically necessary to always have an adequate available supply and they cannot be substituted with another device on the list. Critical inputs (i.e. components) of these devices are also included if they are essential for the use/manufacture of a device, reasonable substitutes are not easily available, and substitutions would require reassessment of device safety and performance. Critical inputs are also listed if they are a component common across multiple devices of a specific type.

Following a consultation with the private sector, the French agency for the safety of medicines and health products, ANSM, resolved to rely on companies to self-assess the risk that a shortage of an "indispensable" medical devices or IVDs would lead to a "critical situation", i.e. a critical impact on patient health. The assessment considers the critical role of the medical device or IVD (e.g. no alternative or market share > 50%, and severe disease) as well as possible mitigation measures involving all actors (company, purchasers, healthcare institutions). If there is a significant risk of shortage, the information should be circulated as rapidly as possible to allow all stakeholders to contribute to mitigation efforts (ANSM, 2021[59]). Since 2021, the ANSM publishes a list of medical devices and IVDs at risk of, or in shortage, with reasons. (ANSM, 2023[60]). The system was originally established on a voluntary basis, but since 2023, companies have been required to declare any risk of disruption, and may face financial sanctions if they fail to do so. At least one company was fined for not having reported issues in its supply chain that led to a shortage of tests for Down Syndrome.

2.2. Mitigating (or reducing exposure to) risks of shortages

Mitigating the risks of supply chain disruptions involves addressing the underlying causes of shortages (Section 2.2.1), while also encouraging flexibility and agility into the system (Section 2.2.2).

2.2.1. Addressing root causes of shortages

Quality issues and pressure on prices are most frequently cited as the root causes of shortages, particularly for medicines, and to a lesser extent, vulnerabilities arising from excessive concentration of manufacturing capacity (see Chapter 1). The sections below describe some policy options aimed at addressing these root causes, from improving quality management, to market shaping, as well as strategies to diversify supply.

Encouraging improvements in quality management

Companies selling medical products are responsible for quality management in their supply chains, in accordance with standards set by regulators. Requirements for marketing authorisation are already stringent in most OECD countries, encompassing quality management standards for companies and inspections by regulatory authorities. For example, in guidance published in February 2023, the European Medicines Agency outlined manufacturers' role in optimising quality management systems in the context of strengthening the reliability and resilience of supply (see Annex Table 2.A.1). Quality breaches nevertheless happen, potentially leading to shortages. An important issue for regulators is to ensure that this strict regulation is adhered to in the context of complex supply chains. In that respect, co-operation between regulatory agencies is being explored by several of the stringent regulators. For example, since

2011 an international active pharmaceutical ingredient inspection programme has enabled participating authorities to share information on good manufacturing practice (GMP) inspections related to API / active substance manufacturers, as well as planning and organising joint inspections. The programme currently includes 12 participating authorities, several European institutions, as well as those from Australia, Canada, Japan, the United Kingdom, the United States, and the World Health Organization (EMA, 2018[61]).

In January 2023, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)[5] adopted a revised version of its Q9 guideline that aims to improve current quality risk management programmes. The guidance invokes more objective risk assessments, which have the potential to reduce quality defects and, as a consequence, drug shortages. ICH guidelines are not binding, but many companies and national and supra-national regulatory agencies choose to follow their recommendations. At the time of writing, the new ICH Q9 guideline has been implemented by several regulatory agencies, including those in the European Union, Japan, the United Kingdom, the United States and Switzerland, and is currently being implemented in Canada and Korea (ICH, 2023[62]).

The International Medical Device Regulators Forum (IMDRF) is a voluntary group of medical device regulators worldwide that aims to accelerate international medical device regulatory convergence in several areas. Established in 2011, it builds on foundational work of the Global Harmonization Task Force on Medical Devices. OECD countries/regions that are current members of the IMDRF include Australia, Canada, the European Union, Japan, Korea, the United Kingdom and the United States. Individual working groups also draw upon expertise from various stakeholders such as healthcare professionals, patients, the industry, and academia. The improvement and alignment of quality management systems and risk management procedures are the focus of an ongoing working group of the IMDRF (IMDRF, 2023[63]).

Market shaping through pooled and strategic procurement

Pressure on prices, especially in off-patent markets, is often cited as an important issue affecting the reliability of supply. Low prices and limited profitability are thought to affect the ability to maintain high-quality supply chains, in some cases, leading to the exit of some players and market concentration, further adding to the vulnerability of supply. Empirical evidence is available mainly for the US generic market, which is quite specific. Vertically integrated joint ventures between large wholesale drug distributors and major retail drugstore chains have emerged, and in 2021 the three largest joint ventures were estimated to account for as much as 90% of all US generic drug purchases (FDA, 2019[64]).

In OECD countries, pharmaceutical markets are generally subject to a mix of price regulation and competition. Price regulation generally applies to “reimbursed” medicines sold by retail pharmacies, and often takes the form of a list of maximum reimbursement prices. Actual prices may be lower than these maximum prices, especially for off-patent products. Medicines purchased by hospitals are generally not subject to price regulation, with multi-source products often procured through tendering.

Multiple public and private actors purchase medical products at different levels within healthcare systems. While some countries have national procurement bodies that provide a range of medicines and medical devices to their healthcare systems (e.g. Denmark), most countries take a more decentralised approach, with pharmacies and hospitals purchasing products directly. The ways in which these systems are structured can be important in influencing how markets function and, consequently, on the availability of essential medical products. Procurement practices have the potential to create incentives for manufacturers to remain in the market, continue supply, and even develop buffer capacity. By adapting the duration, conditions and award criteria of public procurement contracts, governments can influence how medical supply chains work.

Collective cross-country purchasing of medical products (also known as joint procurement) is one of the key policies that countries can consider implementing to ensure market access and continuity of supply. Although generally regarded as a strategy to obtain lower prices for medical goods through purchasing

higher volumes of products, pooled procurement can also enhance the availability of medicines and improve access to high-quality products, especially in smaller markets (Parmaksiz et al., 2022[65]). Huff-Rousselle (2012[66]) also mentions more rationalised choice processes through better-informed selection and standardisation, as well as less corruption, as additional advantages of implementing joint procurement.

Current cross-country pooled procurement initiatives vary in terms of the range of products covered, governance strategies and main objectives. Since 1977, the Pan American Health Organization (PAHO) has implemented a revolving fund for the collective purchasing of vaccines and immunisation supplies, for 41 countries in Latin America and the Caribbean region. The Fund is responsible for conducting multiple steps in the tendering process, from supporting and collecting countries' demand forecasts, to preparing tenders, awarding bidders, and distributing supplies. More recently, the Nordic countries (Norway, Sweden, Denmark, Iceland and Finland) have also implemented a pooled procurement scheme, the Nordic Pharmaceutical Forum (NPF), which aims to increase their leverage in procuring older medicines, such as paracetamol and ampicillin.

As ensuring security of supply is not generally regarded as one of the main objectives of pooled procurement, these initiatives have not been assessed against this criterion (Parmaksiz et al., 2022[65]; Vogler, Salcher-Konrad and Habimana, 2022[67]). Nevertheless, they may improve the availability of medicines in countries not considered attractive for companies because of the size of the markets. This is particularly relevant for Iceland (Nordic Pharmaceutical Forum, 2023[68]) and several of the smaller Latin American countries.

Pooled procurement can also enhance the predictability and reliability of demand, which can facilitate better planning of production and supply, and may also reduce production shortfalls (DeRoeck et al., 2006[69]). Technical assistance with demand forecasting provided by PAHO is considered a key aspect of the Revolving Fund's effectiveness. In contrast, other pooled procurement initiatives have been less successful due to a lack of co-ordinated net demand measurements. This was the case with some of the EU Joint Procurement Agreements (JPA) for medical equipment implemented during the COVID-19 pandemic, where national demand for equipment was duplicated through multiple procurement channels (local, national, and European) (MedTech Europe, 2021[70]). Thus in order for pooled procurement to be an effective tool for ensuring the accessibility and continuous supply of medical products, it is important that participating countries demonstrate a commitment to securing a share of supplies from the pooled mechanism. However, there is no evidence that pooled procurement reduces stock-outs of medicines *per se* (Parmaksiz et al., 2022[65]; Seidman and Atun, 2017[71]). PAHO's revolving fund has already experienced vaccine shortages, particularly for products originating from sole suppliers. A 2006 study found that half the countries utilising the fund had reported delays in deliveries from PAHO (DeRoeck et al., 2006[69]).

One important factor that can undermine the ability of pooled procurement to improve security of supply is tenders awarded based solely on price. Strong pressure on bidders can push prices to non- or only marginally profitable levels, leading to the market exit of generics companies and fewer suppliers. To address this issue, procurement processes that capture multiple policy objectives in the award criteria can influence market practices and potentially improve supply security. EU Directive 2014/24, which regulates public procurement, requires public contracts to be awarded based on the *most economically advantageous tender* (MEAT) criteria, which can include environmental, quality, social and security of supply factors. Even though the directive has led to an increase in security of supply as an award criterion, the use of MEAT approaches only accounts for 24% of public procurement contracts for medicines in the EU, the European Free Trade Area (EFTA) and the United Kingdom (Vogler, Salcher-Konrad and Habimana, 2022[67]).

In designing its tender bidding procedures, the NPF has adopted several criteria that go beyond price alone. Supply chain security can account for 15 to 20% of bid scores, while price accounts for 25 to 55%,

depending on the product and other included criteria (Sverrisson, 2023[72]). As one of the main goals of the procurement scheme, ensuring timely availability of supply is a top priority in tender contracts. In parallel with implementing the MEAT criteria, NPF tenders also apply other strategies to enhance supply security, such as longer contract periods (3 years being the norm) and awarding tenders to multiple winners. Although the impact of MEAT and other policies have not been evaluated explicitly, supply data for medicines procured by the NPF from the Norwegian Medical Products Agency indicate that availability for products procured this way has remained stable, even during the pandemic (Sverrisson, 2023[72]). According to a study on public procurement practices for medicines in the EU, EFTA and the United Kingdom, 10 out of 27 responding countries indicated that security of supply was a criterion applied when evaluating at least some tenders (see Table 2.2) (Vogler, Salcher-Konrad and Habimana, 2022[67]).

Experts have also raised the potential advantages of contracting multiple suppliers for the same product, to secure supply if one or more suppliers fail. Several purchasers have adopted this strategy, including pooled procurement mechanisms such as PAHO's revolving fund and UNICEF's vaccine procurement. However, while pre-arranged, multi-source contracts can improve continuity in supply, they cannot be effective in all circumstances, in particular if all contracted suppliers rely on a single API contractor who fails to supply. Dube et al. (2022[73]) found the literature on whether single or multi sourcing is more effective in improving supply resilience of ventilators inconclusive, with trade-offs applicable to both strategies – single sourcing may enable the establishment of a collaborative relationship with a supplier, while having multiple sources facilitates responsiveness to disruptions. Wiedmer et al. (2021[74]) noted that multi-sourcing can actually worsen the impact of a shock when it occurs, but facilitate faster recovery of volumes afterwards. The authors suggest that sourcing from multiple suppliers tends to aggravate disruptions during a crisis, as buyers have to contact and co-ordinate with multiple suppliers dealing with their own disruptions. However, greater volumes can then be sourced from these multiple suppliers in the recovery phase. A recent IQVIA analysis of medicine shortages in the United States showed that multi-source generic molecules are more likely to be in shortage (9% of multi-source generics) than single-source molecules (7% of single-source generics) (IQVIA, 2023[75]). The report concluded that market predictability for single-source suppliers may allow them to manage stocks more effectively and mitigate the impact of market volatility (ibid.). In EU countries, utilisation of multi-award winner contracts for the supply of medicines through public procurement has generally been adopted, but often limited to certain products, where shortages are more frequent or have more severe impact (see Table 2.2).

Public procurement-based policies may follow a "stick or carrot" approach in their relations with suppliers. In one scenario, procurement contracts may offer financial incentives (e.g. higher prices) to companies that accept additional requirements (e.g. increased supply reliability, stockholding requirements etc.). On the other hand, purchasers may apply harsh penalties for poor compliance with contractual obligations. In some cases, a mix of both "stick" and "carrot" approaches may coexist. A review of policies for addressing shortages in 24 countries undertaken in 2020 found that only 6 responding countries relied on sanctions in cases of non-supply by manufacturers, and the level of enforceability of penalties was reported to be generally low (Vogler and Fischer, 2020[7]).

Table 2.2. Procurement practices and supply chain security

2022 Review of EU, EFTA countries and the United Kingdom

Country	Use of multi-award procedures	Use of the MEAT criteria in tenders	Use of security of supply as a criterion	Use of local production as a criterion
Austria	Yes (mainly for products where shortages have a severe impact)	Yes	No	No
Belgium	Yes (when supply for a product is less certain)	Yes	Yes	No
Bulgaria	Yes[1]	No	No (criteria was suspended by court due to discriminatory use)	No
Croatia	N/A	Yes[1]	N/A	N/A
Cyprus	Yes	No	No	No
Denmark	Yes[1]	Yes[1]	Yes	No
Estonia	Yes[1]	Yes[1]	No (no criteria was able to be operationalised)	No
Finland	Yes[1]	Yes	No	No
France	Yes (restricted to antithrombotics; immunoglobulins; considered hard to set up)	Yes	Yes (measured in logistic consideration: level of stock for MITM)	No (under consideration)
Greece	N/A	Yes	N/A	Yes (together with other criteria)
Hungary	Yes[1] (only one procedure)	No	No	No
Iceland	Yes[1] (when there are competing treatments)	Yes[1]	Yes (2 months security stock, penalties may apply)	No
Ireland	Yes (mostly for hepatitis C)	Yes	Yes (3-12% weight, amount in stocks and details about manufacturing sites)	No
Italy	Yes (for biosimilars)	N/A	N/A	N/A
Latvia	Yes[1]	Yes	Yes (requirement to have a bank guarantee for supply security)	No
Lithuania	No	Yes[1] (for vaccines)	No	No
Luxembourg	N/A	Yes	Yes	Yes
Malta	Yes	No (since 2016)	No (applied indirectly as condition for tenders)	No
Norway	Yes[1] (for one specific medicine with supply security concern)	No	Yes	No
Poland	N/A	N/A	No	No
Portugal	Yes (promoting “two-winner approach” in open tenders and framework agreements)	Yes (rarely)	No	No
Romania	N/A	Yes	N/A	No
Slovenia	Yes (mainly for biosimilars)	No	No	No
Spain	Yes (at regional level)	Yes	Yes (as a possibility)	N/A
Sweden	Yes[1]	N/A	Yes	N/A
Switzerland	Yes	No	Yes	No
United Kingdom	Yes[1]	Yes	N/A	N/A

Notes: MEAT most economically advantageous tender; PPM public procurement of medicine; MITM medications of high therapeutic interest (French acronym). Countries with no available information are not included in the list.

1. For centralised procurement procedures (at national or regional level).

Source: Adapted from Vogler, S, M. Salcher-Konrad and K. Habimana (2022[67]), *Study on best practices in the public procurement of medicines,* https://op.europa.eu/en/publication-detail/-/publication/ca856a7f-7c37-11ed-9887-01aa75ed71a1/language-en.

Not-for-profit manufacturing as a response to low profitability

In 2018, in order to tackle problems in the US generic markets, three philanthropic organisations partnered with seven US health systems, whose hospitals were exposed to shortages, to establish a novel, not-for-profit manufacturing company – Civica Rx. At the end of 2019, more than 50 additional health systems had joined the initiative, covering more than 1 500 hospitals. Civica Rx functions as a "healthcare utility (HCU)", with the objective of maximising access to medicines rather than maximising profits. Health systems conclude 5-year contracts for pre-specified volumes, typically 50% of the health system's projected demand for a drug (referred to as the minimum viable volume or MVV), at a transparent, prespecified price. A recent study looking at the effectiveness of the system in preventing shortages found that for 20 products procured by one health system, Civica Rx supplied 96% of its guaranteed volumes (55 orders) while wholesalers had a significantly lower fulfilment rate of 86% (302 orders). In addition, the health system received 43% more product than the contracted MVV between 2020 and 2022, the period in which COVID-19 created a major increase in demand for some of these products (Dredge and Scholtes, 2023[76]). More research, however, would be needed to confirm the interest of this approach.

Re-shoring and near-shoring as options to diversify supply

Several countries have implemented policies to incentivise domestic or regional (re)-location of the production of pharmaceutical products and/or APIs (see Box 2.4). After examining the motivations of firms to re-configure their supply chains and the pros and cons of re-shoring/near-shoring, this section looks at OECD countries' initiatives in this area.

Companies' motivations to re-configure their supply chains:

In the last two decades, medical supply chains have become more internationalised, albeit with a degree of geographical concentration in the manufacturing of finished pharmaceutical products (FPPs) and APIs. In some supply chains, the existence of only a small number of geographically concentrated API producers is seen as high risk, as it can worsen the effects where natural disasters and public emergencies are localised (Baraldi, Ciabuschi and Fratocchi, 2023[77]).

Even before the COVID-19 pandemic, risks and uncertainties in supply were among factors leading pharmaceutical companies to "bring production back home" (re-shoring) or relocate it to a less distant country (near-shoring). However, this process often involves the insourcing and re-shoring of core products and activities while still relying on offshore outsourcing or offshore insourcing for others (Huq, Pawar and Rogers, 2016[78]). Since the pandemic, there have been examples of European firms expanding their facilities in Europe, including Roche, and GlaxoSmithKline in the United Kingdom, Ipsen in France, Allergan in Ireland, and Lundbeck in Italy (Somoza Medina, 2022[79]). For Roche (a Swiss firm) and Lundbeck (a Danish firm), these are examples of near-shoring.

Motivations for re-shoring include better control on product quality, greater environmental sustainability, production closer to consumers, and restoration of brand value (Barbieri et al., 2020[80]). Interviews with re-shoring firms in the United Kingdom conducted by Theyel, Hofmann and Gregory (2018[81]) suggest that some may have overestimated the benefits of offshoring and underestimated the advantages of retaining manufacturing at home. For pharmaceutical companies, the interviews highlighted ensuring product quality in a highly regulated sector as a motivation for re-shoring or retaining production in the United Kingdom, as well as more effective waste and inventory management (Theyel, Hofmann and Gregory, 2018[81]). In the post-COVID context, decisions to re-shore may also be motivated by the increased frequency of disruptions to global supply chains; rising labour, transport and insurance costs; and government incentives to relocate production (Somoza Medina, 2022[79]).

The pros and cons of re-shoring/near-shoring:

In a study on antibiotics in Sweden, Baraldi, Ciabuschi and Fratocchi (2023[77]) suggested that re-shoring or near-shoring production could reduce delivery times, increase the ability to adapt to sudden changes in demand, and lower supply chain risks by bringing the different stages of the supply chain (MAHs, FPPs, and APIs) closer. Strengthening regional and domestic supply chains could create a more geographically diverse production structure, while reducing the dependence on a small number of suppliers in Asia. In addition, in the specific case of antibiotics, re-shoring or near-shoring production may result in reducing environmental impact, which is crucial to containing the alarming levels of antibiotic resistance caused by uncontrolled discharges in open waters at offshore locations (Baraldi, Ciabuschi and Fratocchi, 2023[77]).

However, the study also noted that these advantages must be weighed against certain negative effects, such as increases in direct costs leading to more expensive medicines, and expensive investment (including for the training of skilled workers and specialists). For policy makers, the advantages (security of supply, job creation, expansion of local industry) must also be weighed against potentially costly subsidies or the risk of international trade disputes (Baraldi, Ciabuschi and Fratocchi, 2023[77]). In addition, it can be argued that higher production costs in re-shored locations will not address the key commercial issue of low margins for off-patent medicines such as antibiotics. Baraldi, Ciabuschi and Fratocchi (2023[77]) concluded that, in the case of Sweden, the domestic market size is not large enough to counterbalance the investments needed to re-shore manufacturing, and that relocation decisions would be more attractive if conceived at a supra-national level. Barbieri et al. (2020[80]) also highlight that it may be challenging to re-locate a whole supply chain within the borders of a single nation, and for this reason, effective co-operation between nations in nearby macro-regions might be the key to promoting near-shoring initiatives.

Sanchez and Muzzio (2021[82]) discuss the limitations and challenges of re-shoring the production of off-patented pharmaceutical products to the United States. The main constraint is the lack of local availability of intermediate materials used for the synthesis of APIs. Other constraints identified were taxes and tariffs, access to technologies for API manufacturing, the environmental impact of API manufacturing resulting from waste generation, the availability of skilled workforce, and regulatory constraints (Sanchez and Muzzio, 2021[82]).

A report by Ernst & Young (Stark and Botos, 2021[83]) illustrated the high costs and time associated with the extension of available capacity or the development of new facilities for the production of APIs (small molecule), drug substance (biopharma) and formulation in the United States. According to this report, upgrading an existing small molecule API facility could take 12 to 18 months and would cost between USD 15 and 150 million. Creating a new facility for the same purpose would raise costs to between USD 300 million and 1.5 billion and take 48 to 60 months. Gaining the necessary regulatory approvals would take several additional months (from 9 to 18 months). The costs of upgrading or creating a facility to produce a drug substance for a biological product would be even higher. These estimates do not cover the costs of producing the finished products (i.e. formulation). In addition, these estimates do not consider the challenges highlighted above with respect to the availability of skilled workforce and local availability of intermediate materials. Developing the full pharmaceutical ecosystem and training new workers can substantially increase the costs and time needed to expand existing capacity or build new facilities.

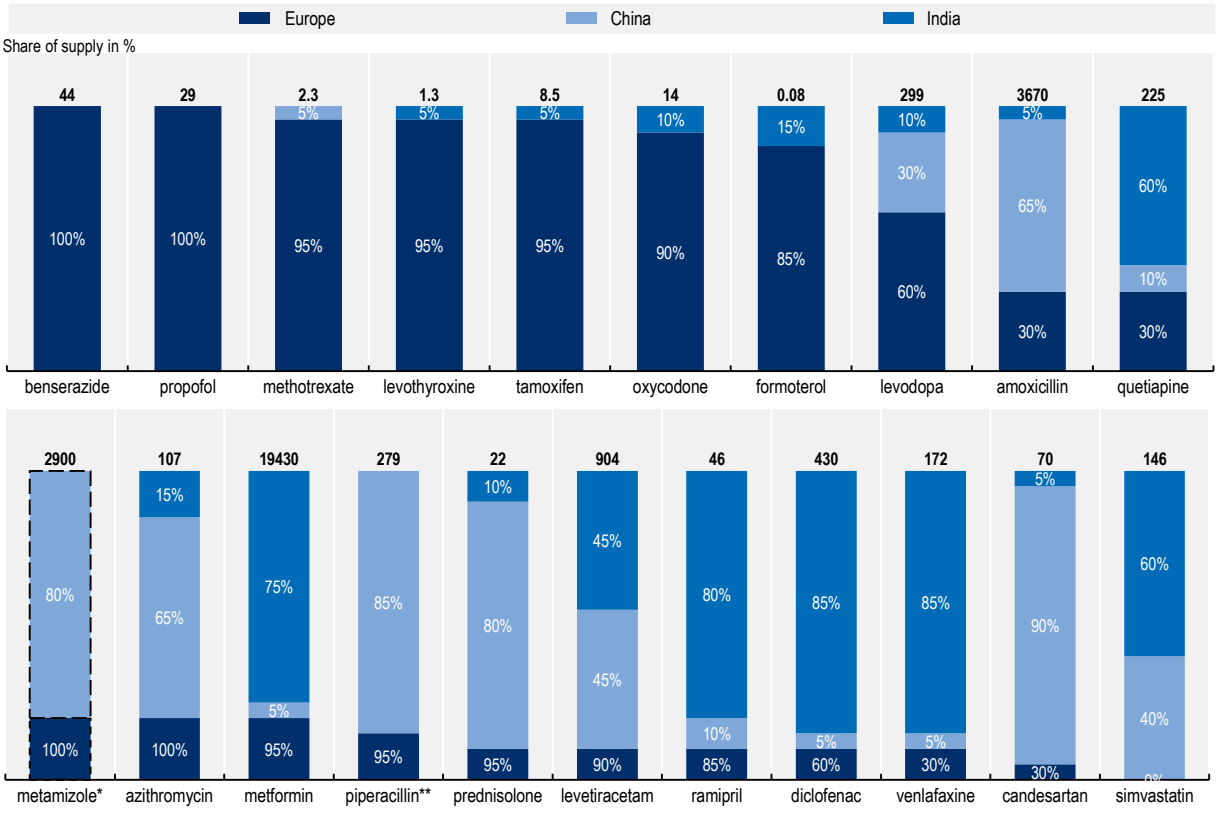
Another study by Berger (2018[84]) highlighted that relocating antibiotic API production in Europe might not be economically feasible due to high costs and the lack of availability of some inputs. The report suggested that in the case of generic cephalosporins (a class of antibiotics), local production in Germany of quantities sufficient to serve the German market would involve transferring EUR 55 million to private companies (equivalent to additional costs of 46 cents per daily drug dose) to cover the operational costs.

This suggests that public financial support should target medicines with evidence of vulnerable supply chains, as all shortages do not result from “offshored” production. In a 2020 study on API provenance of products supplied in the EU market, Mundicare highlighted that two-thirds of the certificates issued to

produce APIs for products marketed in Europe[6] were held by Asian manufacturers, many of them located in two regions of India and China (Progenerika, 2020[85]). API manufacturing was quite concentrated with more than half of all APIs produced by only 1 to 5 suppliers. However, the report looked more closely at supply chains for 21 critical APIs and showed wide variations in the countries involved in their production (Figure 2.2). Policy making in this domain should be informed by reliable and granular information on supply chains and should prioritise the diversification of supply.

Figure 2.2. Provenance of API supply for medicines in Europe

Estimated share of supply for European demand by regions



Note: Data labels at the top show total European demand in tonnes. API active pharmaceutical ingredient.
* Estimation, Data basis limited; ** API mainly in combination with Tazobactam (exclusively produced in Asia).
Source: Reproduced from Progenerika (2020[85]), *Where do our active pharmaceutical ingredients come from? – A world map of API production,* https://progenerika.de/app/uploads/2020/11/API-Study_long-version_EN.pdf.

Box 2.4. Country examples of re-shoring and near-shoring policies

Program for Promoting Investment in Japan to Strengthen Supply Chains

Since the 1980s, Japanese industries have increasingly transferred manufacturing to neighbouring China, which has led to increased dependence on Chinese imports. In 2020, after the outbreak of COVID-19, Japan introduced policy incentives to on-shore production of goods considered essential, including for public health. The project, which was included in Japan's substantial COVID-19 relief package, reserved JPY 220 billion (USD 2.1 billion) to support companies that decided to move production to the country. The measure also included USD 220 million in incentives to support near-shoring initiatives in countries that are part of the Association of Southeast Asian Nations (ASEAN). Among the medical products that received funding for relocation to Japan were antigen and PCR test kits, medical gloves, and low-temperature logistics refrigerators (Ministry of Economy, 2023[86]).

United States' Supply Chains

In the United States, Presidential Executive Order 14 017, signed on 24 February 2021, initiated a 100-Day Supply Chain Review covering four critical groups of products: semiconductors, large capacity batteries, critical minerals and materials, and pharmaceuticals and APIs. The objective was to identify vulnerabilities, assess risks, and develop strategies to promote resilience. Recommendations from the Review led to the establishment by the US Department of Health and Human Services (HHS) of a public-private consortium for advanced manufacturing and on-shoring of domestic essential medicines production. The first task of the consortium was to identify the medicines to be prioritised. In addition, funds were committed to develop novel platform technologies to increase domestic capacity for the production of APIs. As of June 2023, over USD 500 million had been invested. An additional action was the launch of a National Biotechnology and Biomanufacturing initiative in 2022, aimed at increasing R&D and growing domestic biomanufacturing capacity. In November 2023, more measures to support the domestic production of APIs and pharmaceuticals were announced as part of the creation of a Council on Supply Chain Resilience, including broadened use of the Defense Production Act to enable investment in the production of essential medicines and critical inputs. Finally, through the CHIPS and Science Act (2022), the United States provided support for the domestic manufacturing of semiconductors, including those needed for the production of medical devices (The White House, 2023[87]).

France Relance and France 2030

As the fifth largest manufacturer of medicines globally, France has seen its share of the global pharmaceutical market wane in recent decades, with many companies moving production offshore to reduce costs. Led by the Ministry of Economics and Finance, France's COVID-19 relief package (i.e. France Relance) included incentives to support the relocation of manufacturing in strategic sectors through co-financing schemes with manufacturers. By June 2023, EUR 800 million had been awarded in aid, as well as EUR 1.7 billion of productive investment in the health sector. Launched in 2022, France 2030 is a parallel large-scale investment project in the re-industrialisation of the country, focusing on investing in manufacturing modernisation and capacity-building in different sectors, including medical products. In June 2023, a list of 50 medicines whose production *should* be relocated or reinforced was identified, commencing with a smaller list of 25 essential medicines that includes antibiotics (e.g. amoxicillin), urgent care medicines (e.g. morphine, propofol, clonazepam) and oncology drugs (e.g. oxaliplatin and busulfan). France 2030 has an allocated budget of EUR 7.5 billion to be spent over the next seven years (Ministère de l'Économie, 2023[45]; Ministère de l'Économie, 2022[88]).

European Chips Act

The European Chips Act (Regulation 2023/1 781) establishes a framework for the semiconductor ecosystem in the EU and acknowledges the importance of secure supply for the manufacturing of medical devices. The second pillar of the Act foresees some support to attract investments and to develop EU production capacity.

2023 European Commission's communication on addressing shortages in the EU

In a recent communication, the European Commission announced a number of strategies to address shortages, including boosting Europe's capacity to produce and innovate in the manufacturing of critical medicines and ingredients, through national and EU financial support. The Commission advocates for co-ordinated action to define criteria and priorities for such actions (European Commission, 2023[1]).

Sources: As cited. See also Annex A.

Because of the constraints and challenges of re-shoring strategies, some scholars suggest that policy makers should instead focus on policies that promote innovation, digitalisation, and the improvement of professional skills. This could lead to greater productivity in developed economies that would indirectly stimulate the repatriation of manufacturing processes (Somoza Medina, 2022[79]). With the expanded use of digital and Industry 4.0 technologies (e.g. robotics, automation, computerised manufacturing, 3D printing, artificial intelligence, etc), some authors suggest that the input cost advantages of offshoring locations may be reduced (Dachs, Kinkel and Jäger, 2019[89]; De Backer and Flaig, 2017[90]).

2.2.2. Encouraging flexibility and agility into the system

Encouraging agility and flexibility into the system can also help to reduce risks of potentially harmful supply disruptions. The sections below discuss the use of trade facilitation and regulatory co-operation, as well as co-ordinated and efficient stockpiling strategies and the harnessing of digital technologies.

Trade facilitation to allow movement of supply

Trade facilitation encompasses a series of policies and border measures aimed at reducing the time and cost of moving goods. The WTO Trade Facilitation Agreement (TFA), which entered into force in 2017, includes provisions encouraging countries to take action to streamline and harmonise export and import processes, including through co-operation between customs authorities. Trade facilitation measures are important for the smooth functioning of medical supply chains and contribute to flexibility by allowing firms to easily move final products and inputs where they are needed (OECD, 2018[91]). The implementation of the TFA and additional measures that countries can take to automate and simplify border processes for the movement of medical products are part of the package of trade policy measures that can contribute to resilience (OECD, 2020[92]).

While progress has been recorded across all regions in the areas of information availability, simplifying and harmonising documents, and automating and streamlining procedures, there is still a gap between the regulatory frameworks and their implementation in some countries (Sorescu and Bollig, 2022[93]). It should be kept in mind that each additional day spent in clearing products at a border translates into additional costs, including additional inventories to continue to meet demand.

In addition, reducing tariffs and non-tariff measures (NTMs) on exchanges of medical goods and services can further increase the level of flexibility and the potential for firms and markets facing shortages to source from alternative partners. The 1994 Agreement on Trade in Pharmaceutical Products is a sectoral initiative by which some WTO Members agreed to eliminate or reduce tariffs on a list of finished pharmaceutical products and APIs or chemicals used by the pharmaceutical industry. While trade barriers have been

significantly reduced by some countries, there are still tariffs and NTMs on essential medicines (OECD, 2023[94]).

Facilitating the exchange of medicines between countries on a voluntary and solidarity basis can also be relevant in addressing localised shortages and limiting wastage of essential products. Although countries are able to send donations of excess supplies to regions in need, this process usually involves complex regulatory procedures that could be streamlined, particularly in the case of health emergencies. One possible solution would be to implement frameworks that would allow countries to signal a need for specific products, and for donating countries to send such items in a more timely and less bureaucratic fashion. The EU Voluntary Solidarity Mechanism for medicines is one example of an institutionalised system that facilitates such exchanges between member countries. Introduced in October 2023 as a new tool of the Union Civil Protection Mechanism, it allows Member States to signal a need for products in shortage and to co-ordinate transfers and deliveries. The centralised body responsible for the EU-level stockpile, the European Response Co-ordination Centre (ERCC), is tasked with providing logistical support. A series of criteria that are evaluated by the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) are also in place to make sure the mechanism is only activated by member countries as an option of last resort (EMA, 2023[95]).

Regulatory co-operation and flexibility

Co-operation and co-ordination between regulatory agencies have been ongoing for many years and can take different forms. Regulatory agencies responsible for the approval (and post-approval changes) of medicines and medical devices have different capabilities, approaches, evidentiary requirements, and assessments. The OECD's *Pharmaceutical Innovation and Access to Medicines* report (2018[96]) highlighted areas and initiatives in which regulatory authorities have been co-operating, through harmonising various regulatory standards and the establishment of shared working arrangements and in some cases, mutual recognition agreements. In addition, Section 2.2.1 above on *Encouraging improvements in quality management* describes regulatory co-operation for manufacturing site inspections and guidance for quality management systems for medicines and medical devices.

Regulatory co-operation and flexibility can also contribute to mitigating the impact of potential or actual supply disruptions on patients. A 2020 cross-sectional study on measures to address medicine shortages (primarily pre-COVID-19) found that 20 of 24 countries had previously enacted simplified procedures for marketing authorisation and distribution of imported substitute products, including exceptions to packaging and labelling requirements, and the acceptance of information leaflets in other languages (Vogler and Fischer, 2020[7]). The COVID-19 pandemic demonstrated the usefulness of added regulatory flexibility to enhance security of supply of essential products. Building on the positive experience from COVID-19 and to support longer and medium-term resilience of supply chains of critical medicines in the EU, a Joint Action on regulatory flexibilities is planned to be launched in 2024 (European Commission, 2023[1]). Another Joint Action aims to support the Co-ordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network (CHESSMEN) through seven different work packages between 2023 and 2026 (Annex A). As part of this, regulatory agencies in CHESSMEN intend to work together to identify countries' best practices in managing and preventing medicine shortages.

In addition to multi-language packaging, the idea of electronic package leaflets (or electronic product information or e-leaflets) has been discussed by stakeholders as a potential tool to facilitate imports of medicines from abroad and shifting of stock between countries in times of shortage, particularly for hospital products. Here, healthcare providers (or in some cases, patients) would be able to scan a barcode to access information related to the product in electronic form. Healthcare professionals would still be able to communicate the necessary information about the product to the patient and print out consumer product information leaflets when prescribing or dispensing. Product information (including on quality and safety) is updated throughout the product life cycle, and having electronic information would facilitate

dissemination of up-to-date information (and in several languages) in a timely manner. It would also be in line with the digital health transition and is envisaged to reduce costs and have environmental benefits. Thus far in Europe, and as described in a recent commentary by Skogman-Lindqvist et al. (2023[97]), implementation of digital leaflets has been limited to pilot projects in hospital settings, as package leaflets are a legal requirement in the European Union. For example, Belgium, Luxembourg, Spain, the Baltics (Estonia, Latvia and Lithuania) and Iceland have ongoing pilot initiatives targeting hospital products. Several countries have also developed websites or apps for use by patients and/or healthcare professionals (Germany, Finland, Sweden, Norway, Denmark) (ibid.). In other countries, e-leaflets are already implemented. In Japan, digitalisation of package inserts (i.e. inserts with information on precautions for prescribed medicines and medical devices, intended for use by health professionals) started in August 2021, with access to their contents available on the Pharmaceuticals and Medical Devices Agency website via scanning the GS1[7] barcode on the outer box (Nagaoka and Takamine, 2022[98]). The transition to digital package inserts was completed in Japan in July 2023. In Australia, e-leaflets have been in use for several years, and from September 2023 printed product information for injectable medicines (e.g. vaccines) that are administered in hospitals is no longer required (TGA, 2023[99]).[8] In summary, implementation of digital leaflets could be implemented more readily at least for medicines administered by health professionals, for example vaccines, whereby there is substantial diversity in presentation and packaging and labelling requirements between countries (even within Europe). It is also a step towards common packaging, which would have the benefit of reducing waste and facilitating the movement of products across countries.

Using vaccines as an example, the harmonisation of regulatory requirements and enhancing systems for mutual recognition outside times of crisis could aid the resilience of vaccine supply chains and reduce bottlenecks in supply. As described in Chapter 1, vaccine manufacture is highly concentrated geographically and among companies, with the complexity of production and testing resulting in long lead times and difficulty in scaling up production quickly (e.g. in response to unpredictable increases in demand). Frequent post-approval changes are required to be submitted by manufacturers (e.g. due to improvement in facilities, changes in equipment or process, quality control issues, changes in testing or suppliers etc.), affecting many different licenses (Pasté et al., 2022[100]). ICH and WHO have made progress towards greater global harmonisation of regulatory requirements and standards, but despite this, national requirements (particularly for older vaccines) remain variable, and post-approval changes complex. As suggested by vaccine manufacturers, better alignment of post-approval changes could facilitate improved product availability (Pasté et al., 2022[100]; Jongh et al., 2021[20]). Another suggestion is to promote the implementation of mutual recognition agreements (or reliance mechanisms) between authorities for approvals of these post-approval changes, as well as for independent batch releases by official medicines control laboratories (Pasté et al., 2022[100]).

Using plasma-derived medicinal products (PDMPs) as an example, harmonisation and streamlining of the regulatory framework for plasma donation would directly impact the amount of the final product that is obtained (Kluszczynski, Rohr and Ernst, 2020[101]). To guarantee patient safety, regulatory requirements in certain countries and regions are stringent, and manufacturers must comply with multiple overlapping regulations at different jurisdictional levels (regional-national-local). For example, the EU Blood Directive (2002/98/EC) provides clear quality and safety standards for the collection, testing, processing, storage, and distribution of human blood and blood components. However, EU countries must not only comply with the EU Common Codex, the EU Blood Directive, and Annex 14 of EU Good Manufacturing Practice (GMP) applying to medicinal products derived from human blood or plasma. They should also comply with requirements of the WHO Annex 4 Guidelines for sampling of pharmaceutical products and related materials,[9] the ICH), the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guide to Inspections of Source Plasma Establishments and Plasma Warehouses, the EDQM, and the EMA. Streamlining the regulatory environment for plasma could help to avoid overlapping requirements and double compliance standards.

Since fractionation and purification processes need to meet high quality and maximum safety standards, PDMPs require licensing by regulatory bodies such as the EMA and the US FDA. For this, manufacturing sites need to undergo regular inspections (Kluszczynski, Rohr and Ernst, 2020[101]; Strengers, 2023[102]). In the EU for example, marketing authorisation is obtained on completion of the plasma master file (PMF) in accordance with Commission Directive 2003/63/EC, in which the manufacturer must submit all the required scientific data on the quality and safety of its plasma (EMA, 2023[103]). However, biennial inspections of fractionation plants have resulted in a huge backlog for plasma manufacturers, as the availability of inspectors is limited and there are no mutual recognition agreements between regions, such as the United States and EU that frequently trade plasma. Such an agreement would carry the benefit of reducing duplication of inspections by the regulatory authorities.

Beyond that, the EU Directive does not differentiate between whole blood and plasma donations, although both products are different in terms of manufacturing and usage. While plasma undergoes a rigorous fractionation and a multi-step purification process with several inactivation steps, the same does not apply to blood donations. Despite that, both products face similar regulatory treatment with respect to safety requirements even though an assessment of over 12 million plasma donations showed that donor adverse events are rare and 99.84% of the donations safe (Purohit et al., 2023[104]). In that regard, separate regulatory environments for blood and plasma collections, where the latter face less stringent requirements in light of purification and inactivation steps that they undergo during the manufacturing process, could aid in mitigating supply bottlenecks for PDMPs.

Certain donor requirements, including compensation schemes, and rules regarding the frequency and volume of donations, could also be reconsidered. Policies to increase the security of supply need to consider the importance of public awareness and willingness to donate, while protecting citizens from commercialisation of the human body. For example, at EU-level the Blood Directive is currently being revisited to propose a system of reasonable and proportional monetary compensation for donors' expenses and inconvenience (European Commission, 2022[105]). To date, only the United States and four European countries (Austria, Czechia, Germany and Hungary) that allow for private collection of plasma, offer monetary compensation.[10] In other countries where collection is administered by public entities, tax benefits, free public transport, compensated leave or other compensation may be applied. This is only meant to cover the expenses incurred and give recognition to the time spent and the inconvenience of donation. A relevant EU project (SUPPLY) is currently underway that aims to investigate what measures can be taken to strengthen voluntary non-renumerated plasma collection capacity in Europe (European Blood Alliance, 2024[106]). Furthermore, the frequency and volume of donations that are allowed per donor differ across countries. The regulated frequency of possible donations according to respective national laws varies from one plasma donation every 14 days in Czechia, France, Italy and the Netherlands, to a maximum of 60 donations per year in Germany -i.e. one donation every 6 days (Kluszczynski, Rohr and Ernst, 2020[101]).

Promoting appropriate inventory strategies to ensure contingency planning

Inventories are the first layer in risk management strategies (Sodhi and Tang, 2021[107]). Pharmaceutical companies maintain inventories to cover annual demand for their products and can generally absorb small variations in demand through these buffer stocks. Their finished product inventories are generally higher than those for consumer goods: 60 to 90 days as opposed to 10 to 40 days (Argiyantari, Simatupang and Hasan Basri, 2020[108]). However, the cost of inventories quickly becomes prohibitive, and inventories cannot address extremes of demand during a global crisis. When there is a large spike in demand, companies with large inventories can supply consumers for a few more days or weeks, but eventually shortages are unavoidable (Choi et al., 2023[109]). In its February 2023 guidance, the EMA recommended that MAHs and manufacturers should assess their own inventory strategies to ensure a margin of contingency stock, particularly for important medicines (see Annex Table 2.A.1).

While lean management was criticised during COVID-19, it is actually a strategy that allows firms to quickly adjust to disruptions, in particular because it implements decentralised decision-making and promotes the continuous improvement of production processes in close co-operation with suppliers (Birkie, 2016[110]). Lean management is not about holding no inventory, but creating efficient supply chains (Choi et al., 2023[109]). For example, lean management was essential for Moderna to create the new mRNA vaccine supply chains during COVID-19 (Mixson, 2023[111]). That said, it is important for firms to regularly review their inventory strategies to ensure that they have adequate levels of stock for business continuity in routine circumstances, acknowledging that other risk management strategies are necessary in major health crises.

The intensive globalisation of medical supply chains, and increased pressure for efficiency gains and lower prices for pharmaceuticals, have led to reduced inventory levels in companies. Seasonal or unexpected variations in demand are in principle anticipated by manufacturers, and regular risk management systems by actors in the supply chain can be effective in dealing with volatile demand on a small or medium scale. Yet, in various scenarios (e.g. sudden change in clinical guidelines, public health crisis etc), demand for certain essential products can increase dramatically, and within a very short time frame. Close and timely collaboration between manufactures and national authorities is critical to ensuring continued supply of essential medicines.

Ensuring co-ordinated and efficient stockpiling in collaboration with companies

Stockpiling of essential medicines and other medical goods is increasingly used as a risk management tool to mitigate the effects of sudden increases in demand and/or disruptions caused by supply chain failures. In general, seasonal or unexpected volatility in demand on a small or medium scale are managed at company level. However, with more dramatic increases in demand during health crisis scenarios, national risk management policies are required (OECD, 2021[112]).

OECD countries have implemented national stockpiling systems, with variable scope, objectives, governance, and financing arrangements (see Annex A for some examples in Australia, Canada, Colombia, Korea, Spain, Switzerland and the United States; and Box 2.5 for a review of existing or planned stockpiling systems in the context of antimicrobial resistance (AMR) in the EU). Management of stockpiles can be the responsibility of public health authorities, or manufacturers, or both. When stockpiling is fully managed by governments and financed with public funds, health authorities at different levels (federal, regional, and local) are responsible for selecting and procuring essential products. This is the case in Denmark, Lithuania, Portugal, Norway and Slovenia with respect to stockpiling antibiotics against AMR. When private firms are required to maintain publicly mandated stockpiles, these can either be implemented through privately-owned physical stockpiles (i.e. MAHs and/or wholesalers are required to increase their inventories to a certain level) or through pre-arranged reserves with firms. Examples of the former can be found in France and Finland, and pre-arranged reserves in Hungary and Iceland. Mixed models with different levels of public and private arrangements may be found in the United States, Australia, Belgium and Poland (European Commission, 2022[113]; Australian National Audit Office, 2021[114]; Congressional Research Service, 2023[115]).

All stockpiling governance systems must integrate both manufacturer and government strategies to ensure well-balanced, efficient, and sustainable medical reserves. Mandatory stockpiling policies must therefore take a careful approach to suppliers' incentives and limitations, to avoid posing excessively cumbersome burdens on manufacturers, which can in turn increase the risk of shortages. Countries adopt different approaches to ensure compliance by companies in the case of privately managed schemes. In Finland, for example, funding is provided through direct payments or compensation through higher prices for manufacturers that are required to stockpile products. France, on the other hand, exercises compliance by levying fines against firms that do not abide by the regulations (European Commission, 2022[113]).

Government managed and financed stockpiles faced challenges when dealing with extreme shocks in demand. The US Strategic National Stockpile (SNS) and the Australian National Medical Stockpile (NMS) are two national stockpiling strategies in which almost all stocks are managed by public authorities[11] (see

Annex A for further information on these systems). Evaluations of both schemes' performance during the COVID-19 pandemic showed that narrow stockpiling objectives limited the implementation of pre-established plans during the crisis (Australian National Audit Office, 2021[114]; Congressional Research Service, 2023[115]). Co-ordination with stakeholders was also considered a major challenge for the effective functioning of the SNS and the NMS. For the latter, a public audit suggested that health authorities should conduct regular deployment drills, and that deployment plans should be based on a strategic analysis of risk in co-ordination with relevant stakeholders. The evaluation of the US system by Handfield et al. (2020[116]) noted structural deficiencies in both supply- and demand-side stakeholder engagement. A lack of market intelligence and information on supply capacity and constraints severely limited the SNS' capability to procure essential products. At the same time, the absence of strategic forecasting with users (e.g. hospitals and other healthcare suppliers) and of barcode-tracking for inventory management hampered its ability to anticipate shortages and other supply needs. The financial sustainability of national stockpiles has also been questioned, especially when comparing requirements to address a wide range of crises with available resources. Although the appropriation for the SNS in 2022 was USD 845 million, government projections from 2019 stated that USD 1.04 billion would have to be spent to secure stocks for anthrax and smallpox alone (Congressional Research Service, 2023[115]). Prioritising essential products for stockpiling and rotating stocks can help ensure more efficient application of this policy option.

Switzerland maintains a compulsory rolling stock system for essential goods, which includes a diverse set of medicines such as anti-infectives, analgesics, selected vaccines, and veterinary medicines. While public authorities determine the products and volumes that must be stockpiled, stocks are maintained and owned by private firms. The Federal Office of National Economic Supply (FONES) can order the release of privately held supplies when faced with a shortage. During the first months of the COVID-19 pandemic, the Swiss Federal Office of Public Health (FOPH), in partnership with FONES, developed a prioritisation strategy to allocate essential medicines to hospitals facing shortages. This strategy also allowed for a better monitoring of available supply and current demand. After the first wave of 2020, FOPH developed a catalogue of 30 APIs that were considered relevant to respond to the pandemic. Strict weekly monitoring of stocks, deliveries and demand for these products was implemented. These rolling stockpiles were considered an efficient and effective strategy for responding to shortages during COVID-19. However, public audits noted a lack of international co-ordination and global market oversight as key areas of improvement (FOPH, 2022[117]).

In July 2023, Australia implemented new minimum stockholding requirements for MAHs. This policy targets predominantly lower priced medicines that are subject to more frequent shortages. Manufacturers of certain medicines are required to hold either four or six months of stock in the country. The government supported the investment of the industry in meeting these requirements through one-off price increases on 1 October 2022 and the establishment of "floor price" protections for lower cost medicines – medicines subject to stockholdings will not be subject to future price reductions, and the approved ex-manufacturer prices will not fall below AUD 4 per pack (Pharmaceutical Benefits Scheme, 2023[118]). A review of the effectiveness of the minimum stockholding requirements is planned 24 months after its implementation.

The sustainability and efficiency of stockpiling schemes could likely benefit from increased cross-country co-operation and joint initiatives. Increased volumes of national or subnational stockholdings of supplies for essential medical products may produce counterproductive outcomes, such as shortages of such products for regular use, price hikes, and wastage of unused stock. Stockpiling at the individual institution (e.g. hospital) level can also be an issue, as was seen during the COVID-19 pandemic. A 2021 study on global health security identified that among OECD countries, only Chile, Costa Rica and Luxembourg[12] did not provide any evidence of implementing a stockpile for medical countermeasures (GHS, 2021[119]). International co-operation can therefore help mitigate the inefficiencies of such schemes, pooling procurement for stocks and co-ordinating more rational and equitable allocation of resources across countries according to pre-established guidelines. The mechanism created for medical countermeasures in Europe provides a good example of co-ordinated stockpiling (see Chapter 3).

Box 2.5. Review of existing or planned stockpiling systems in the EU, in the context of antimicrobial resistance (AMR)

To inform a feasibility assessment on the stockpiling of antimicrobials against antimicrobial resistance (AMR), a HERA commissioned study published in September 2022 reviewed existing and planned stockpiling systems at the individual EU member state and EU-wide level, as well as other relevant stockpiling systems more broadly (European Commission, 2022[113]). In a survey focusing on anti-microbials conducted by the European Medicine Agency's (EMA) Medicine Shortages Single Point of Contact (SPOC) Working Party, 13 of 20 EU and EFTA respondent countries reported a national stockpile that included antimicrobials (including finished products and/or APIs). The findings are summarised below and in Table 2.3, although the report noted that the analysis of public and privately-owned stockpiles is limited by lack of transparency.

Governance model

- *Physical stockpile managed by public authorities and fully financed by public (national) funds:* Denmark, Lithuania, Norway, Portugal, Slovenia
- *Privately-owned physical stockpiles* (i.e. whereby obligations are placed on marketing authorisation holders and/or wholesalers to increase their inventories to a certain level): France, Finland, the Netherlands
- *Pre-arranged reserves:* Hungary, Iceland
- *Mixed stockpile governance system* (i.e. public and/or private and/or pre-arranged reserves)*:* Belgium, Sweden, Poland

Table 2.3. Presence and governance model of national antimicrobial stockpile in 20 EU/EFTA countries

	AUT	BEL	HRV	CZE	DNK	FIN	FRA	DEU	HUN	IRL	LVA	LTU	NDL	POL	POR	SVN	SWE	ESP	ISL	NOR
Public physical stockpile		√			√							√		√	√	√	√			√
Private physical stockpile						√	√						√	√			√			
Pre-arranged reserve/ access agreement		√							√					√					√	
No national antimicrobial stockpile	√		√	√				√		√	√							√		

National health authorities managed the stockpiles in most countries; regional-level stockpiles were also noted by Denmark and Sweden; a few countries (Austria, Finland and Norway) reported hospital-level stockpiles.

Funding / reimbursement arrangements

Limited survey data on funding arrangements indicated that public-sector physical stockpiles were fully financed by national (public) funds. For privately managed stockpiling systems, in some cases governments reimburse firms through direct payments, or compensate payers through higher prices

(Finland). In France, no compensation is provided for mandatory stockpiling, and compliance is exercised through the levying of fines against firms that do not adhere to the regulations.

Stock management

To avoid waste and ensure efficiency in stockpile management, most countries reported having rotating stocks, with medicines nearing their expiry date reintroduced to the market through wholesalers or through direct transfers to hospitals. Publicly-owned stockpiles have also reported donating medicines to third countries. Privately-owned stockpiles tend to rotate stock into the commercial supply chain, with countries imposing different requirements regarding stockpile volumes.

As part of broader analyses of stockpiling systems included in the report, there is also an estimate of the inventory stockpiled by different actors in the antibiotic commercial value chain. According to this estimation, pharmacists typically stock around one to four weeks of antibiotics, wholesalers one month, manufacturers around 60 to 90 days based on expected demand, fill and finish facilities around three months of APIs, and API manufacturers around one month of input supplies (European Commission, 2022[113]).

Source: Adapted from European Commission (2022[113]), HERA AMR feasibility study on stockpiling, https://op.europa.eu/en/publication-detail/-/publication/712bbfff-801e-11ed-9887-01aa75ed71a1.

Public information on the costs of stockpiling is sparse. The U.S. Congressional Research Service estimated that the annual budget for the National Stockpiling System and the BioShield Project[13] amounted to around USD 1.7 billion (i.e. about USD 5 per inhabitant) in 2021, without accounting for supplemental budget allocated to respond to COVID-19 (Congressional Research Service, 2023[115]). Only a proportion of stockpiled medicines will be cycled out to the US health system, while others will be retained for exceptional events and may never be needed. In Australia, the Australian National Audit Office estimated the value of products in the national stockpile in 2019 at AUD 123.1 million (USD 85.5 million, or USD 3.4 per inhabitant) (Australian National Audit Office, 2021[114]). An academic study of the economics of PPE stockpiling in the United States observed that purchasing PPE to stockpile was far less costly than purchasing it at much higher prices during a pandemic. Based on observed prices of PPE before and during the COVID-19 pandemics, the authors estimated that procuring an adequate PPE stockpile in advance at non-pandemic prices would cost only 17% of the projected amount needed to procure it at current pandemic-inflated prices, and that maintaining the stockpile would be cheaper than real-time purchases even if it was not needed for another 35 years (Dow, Lee and Lucia, 2020[120]).

Evidence of the cost-effectiveness of stockpiling is even more difficult to find. Plans-Rubio (2020[121]) looked at the cost-effectiveness of several preparedness strategies, including stockpiling of vaccines, antiviral treatments, and ventilators. The author highlighted several difficulties in estimating cost-effectiveness, including the fact that the virulence and infectiousness of the next pandemic pathogen is unpredictable and that many assumptions have to be formulated to take these uncertainties into account. In addition, the effectiveness of the stockpiled vaccines on the circulating pathogen cannot be known in advance (Plans-Rubió, 2020[121]). Another short paper observes that the incremental cost-effectiveness of stockpiling pneumococcal vaccines to prevent secondary bacterial infections (especially *Streptococcus pneumoniae* infections) during past influenza pandemics is very dependent on the replacement costs of the stockpile (Dhankhar, Dasbach and Elbasha, 2009[122]).

Harnessing digital technologies to improve the flexibility and agility of supply chains

A large body of literature highlights the important role of digital technologies in improving supply chain resilience (Ivanov, Blackhurst and Das, 2021[123]). Digital technologies help firms increase their dynamic capabilities, such as flexibility and agility, as well as providing more visibility in the supply chain, as described in Section 2.1.1. For example, AI-driven technologies offer the capacity to learn from real-time data and to adjust decision-making to react rapidly to disruptions, enhancing visibility and real-time co-ordination and providing adaptive capabilities to build supply chain resilience (Belhadi et al., 2021[124]). Big data analytics and blockchain are two other digital technologies that are mentioned for the improvement of visibility in the supply chain and the early detection of disruptions and variations in demand. More simply, the use of digital product information in e-leaflets can facilitate the swift movement of goods across borders to areas in need (see Section 2.2.1 on *Regulatory co-operation and flexibility).* The use of digital technologies for supply chain resilience relies on harmonised approaches to health data governance across the supply chain.

These technologies can also benefit national or international health agencies. During the COVID-19 pandemic, the Pan-American Health Organization implemented two AI solutions into their existing planning infrastructure to facilitate the expedited procurement of medical products by member states, including COVID-19 vaccines. The first platform assisted the purchase of strategic products by automating the order requisition process, and the other generated advance shipment notifications (PAHO, 2023[125]). The Vaccine Innovation Prioritisation Strategy (VIPS), a collaboration between Gavi, WHO, Bill & Melinda Gates Foundation, United Nations Children's Fund (UNICEF) and PATH (formerly known as the Program for Appropriate Technology in Health), has been exploring the use case for barcodes on vaccines and the feasibility of their implementation. Automated stock and inventory management was highlighted as a possible use case at the 2023 Vaccine Industry Consultation meeting held in September 2023 (UNICEF, 2023[126]).

The deployment of digital technologies in the health sector is an ongoing process driven by innovative firms. However, there are regulatory issues for which governments can provide support, in particular in relation to the transmission and sharing of data. Supply chain data are less sensitive than patient health data, yet they are subject to regulations and standards across borders. Ensuring the security and interoperability of data exchanges requires appropriate regulatory environments both at national and international level. While health-specific regulations are developed to improve the traceability of medicines (e.g. the U.S. Drug Supply Chain Security Act), facilitating exchange of data along the supply chain could also play a role in resilience. There are opportunities for alignment with the OECD Council Recommendation on Health Data Governance (2016[127]) and for governments to work within their countries to harmonise policies and standards for health data across supply chains. Further, to enable cross-border collaboration of supply chains, there are opportunities for cross-border harmonisation of health data governance in alignment with the OECD Council Recommendation.

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Annex 2.A. EMA's good practices for industry

Medicine shortages are a complex global problem, with many different supply chain actors involved. In February 2023, the European Medicines Agency published a *Good practices for industry for the prevention of human medicinal product shortages* (2023[128]), which outlines the general roles and responsibilities of different supply chain actors[14] in preventing and mitigating shortages, and proposes some best practices. While these good practices were developed for the European context, they have global relevance. Annex Table 2.A.1 summarises the main takeaways from this document as they pertain to marketing authorisation holders, manufacturers, and wholesale distributors. These preventive strategies are aimed at addressing the underlying root causes of shortages, such as quality and manufacturing issue, unexpected increases in demand, regulatory issues, and distribution issues. It is important to recognise, however, that there is no "one-size-fits-all approach", and several strategies may need to be employed to respond to a shortage.

Annex Table 2.A.1. Supply chain actors and their respective roles and responsibilities related to medicine shortages in Europe

Summary of information in the European Medicines Agency's *Good practices for industry for the prevention of human medicinal product shortages.*

Actor	Main roles and responsibilities (related to shortages)	Recommendations on best practices to prevent or mitigate shortages (numbers refer to the specific recommendation in the guidance)
Marketing authorisation holders	- hold product marketing authorisation - overall end-end oversight (national and global) of the supply chain from manufacturing to end user - obligations for continued supply, within limits of their responsibilities - oversight over demand-supply - require their stakeholders to have standards (e.g. quality culture) to prevent shortages	(1) notify potential or actual shortage as soon as possible in advance of any shortage (3) increase the accuracy of shortage notification detail provided (e.g. manufacturing delays, affected API manufacturing sites) (4) ensure role-specific shortage prevention plan, covering sourcing of APIs all the way through to wholesale distributors (5) ensure role-specific shortage management plan (6) optimise quality management systems to strengthen reliability and resilience of supply (7) assess own inventory strategies and ensure appropriate contingency stock to allow for unexpected delays, particularly for clinically important medicines (8) improve intra-company communication as well as communication between MAH, relevant manufacturing sites, and wholesaler (and NCA as appropriate) (9) ensure stock allocation practices between countries consider clinical need (10) companies involved in parallel trade should monitor and inform of any situation that may be a risk to public health, and seek advice from the relevant authorities
Manufacturers	- actual producers of medicinal product or API (includes contract manufacturers, producing on behalf of MAHs) - in-depth knowledge of manufacturing processes and any inherent issues that could lead to a shortage - oversight over demand fluctuation	(1) notify potential or actual shortage as soon as possible in advance of any shortage (4) ensure role-specific shortage prevention plan, focusing on product-specific parameters for risk management, manufacturing capabilities, sourcing of raw materials, market trends, marketing activities etc (5) ensure role-specific shortage management plan (6) optimise quality management systems to strengthen reliability and resilience of supply (7) assess own inventory strategies and ensure appropriate contingency stock to allow for unexpected delays, particularly for

Actor	Main roles and responsibilities (related to shortages)	Recommendations on best practices to prevent or mitigate shortages (numbers refer to the specific recommendation in the guidance)
		clinically important medicines (8) improve communication between relevant manufacturing sites, MAH, and wholesaler (and NCA as appropriate)
Wholesaler distributors	- interface between MAH or manufacturers and those who supply medicines to the public (e.g. pharmacies, hospitals) - obligations for continued supply (subject to national provisions) - visibility of stock levels and product flow to identify early signal of potential shortages	(1) notify potential or actual shortage as soon as possible in advance of any shortage (4) ensure role-specific appropriate shortage prevention plan, covering vulnerabilities from receipt of the medicine, storage, to delivery (5) ensure role-specific shortage management plan (8) develop a system based on criteria of available stock vs. deliveries to identify and communicate potential disruptions to suppliers (and NCA if appropriate)

Note: MAH Marketing Authorisation Holder; API active pharmaceutical ingredient; NCA national competent authority.
The guidance from which this information is summarised refers to a broad definition of a shortage "a shortage of a medicinal product for human of veterinary use occurs when supply does not meet demand at a national level".
Source: Summarised from EMA (2023[128]), *Guidance for industry to prevent and mitigate medicine shortages,* www.ema.europa.eu/en/news/guidance-industry-prevent-mitigate-medicine-shortages.

Notes

[1] In the EU, marketing authorisation can be obtained through one of three processes. The centralised procedure is mandatory for all new active substances indicated for conditions that include cancer, diabetes, neurodegenerative diseases, and viral and autoimmune diseases, as well as medicines derived from biotechnology processes, advanced-therapy medicinal products and orphan medicines. It may also be used voluntarily for other products. As a result, almost all products containing new active substances are approved by this route (about 80 per year). However, the vast majority of product approvals are granted at the national level through decentralised procedures, or in a small number of cases via mutual recognition (usually over 1 000 products per year). These procedures mainly concern generic medicines or similar applications (799 procedures in 2020). For more information see https://health.ec.europa.eu/system/files/2023-05/mp_ia_revision-pharma-legislation_annex_5_en.pdf.

[2] In EU countries, 8% of the reported causes of shortages mentioned distribution issues as the root cause of shortages (Jongh et al., 2021[20]).

[3] See the Pharmaceutical Group of the European Union's (PGEU) position paper, available at www.pgeu.eu/wp-content/uploads/2020/08/PGEU-Statement-on-the-potential-use-of-the-EMVS-to-monitor-shortages.pdf.

[4] The implementation has been progressive, with the obligation for placing the UDI carriers in medical devices and IVDs applying according to different deadlines: Implantable devices and Class III devices by 26 May 2021; Class IIa and Class IIb devices by 26 May 2023; Class D IVDs: 26 May 2023; Class I devices by 26 May 2025; Class C and B IVDs by 26 May 2025; and Class A IDVs by 26 May 2027.

[5] The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), established in 1990, gathers representatives of regulatory authorities and of industry. ICH has been working on guidance to improve quality and safety of pharmaceutical development and their regulation, with the aim to harmonise existing practices and requirements.

[6] Certificate of suitability to the monographs of the European Pharmacopoeia (CEP). The analysis related to around 550 APIs involved in the production of generics in Europe.

[7] The use of the GS1 coding system, rather than QR codes, was implemented considering the opinions of the industry. GS1 codes have been used for production distribution and control in the pharmaceutical industry, with a precedent not set in the case of QR codes. Adoption of QR codes were considered to involve large costs and times to change product design.

[8] Product information leaflets provide scientific information about safe and effective use of prescription medicines, and are primarily used by health professionals. Injectable products used by patients will still have a printed copy of the product information.

[9] WHO Annex 4 Guidelines for sampling of pharmaceutical products and related materials requires equal treatment of whole blood and plasma donation, even though only the latter is manufactured.

[10] In European countries, compensation is based on fixed rate allowance usually following the minimum salary in the relevant country. In the United States, compensation schemes are more flexible.

[11] In the case of the United States, vendor-managed inventories account for 10% of current SNS contracts and are directly funded by SNS These inventories are reportedly particularly useful in maintaining a rotating system, which avoids storage of expired medicines and waste (ASPR, n.d.[129]).

[12] Taking into consideration OECD's assessment of Luxembourg's response to the COVID-19 pandemic, work is underway in Luxembourg to set up a system for the supply and storage of critical medical products. The project has been approved by the Government Council, with a bill expected to be tabled in the first quarter of 2024 (personal communication, 2023).

[13] The SNS includes medicines and vaccines approved by the FDA and other medical countermeasures, while the Bioshield project adds 22 products to the SNS, including vaccines against anthrax and smallpox and treatments for anthrax, botulism, nerve agents, radiation, and thermal burns.

[14] Roles and responsibilities are described for the following supply chain actors: marketing authorisation holders, manufacturers, wholesale distributors, national competent authority, European Medicines Agency, national health service provider, Ministry of Health, healthcare professionals, and patient representative groups.

3 Developing additional crisis capabilities

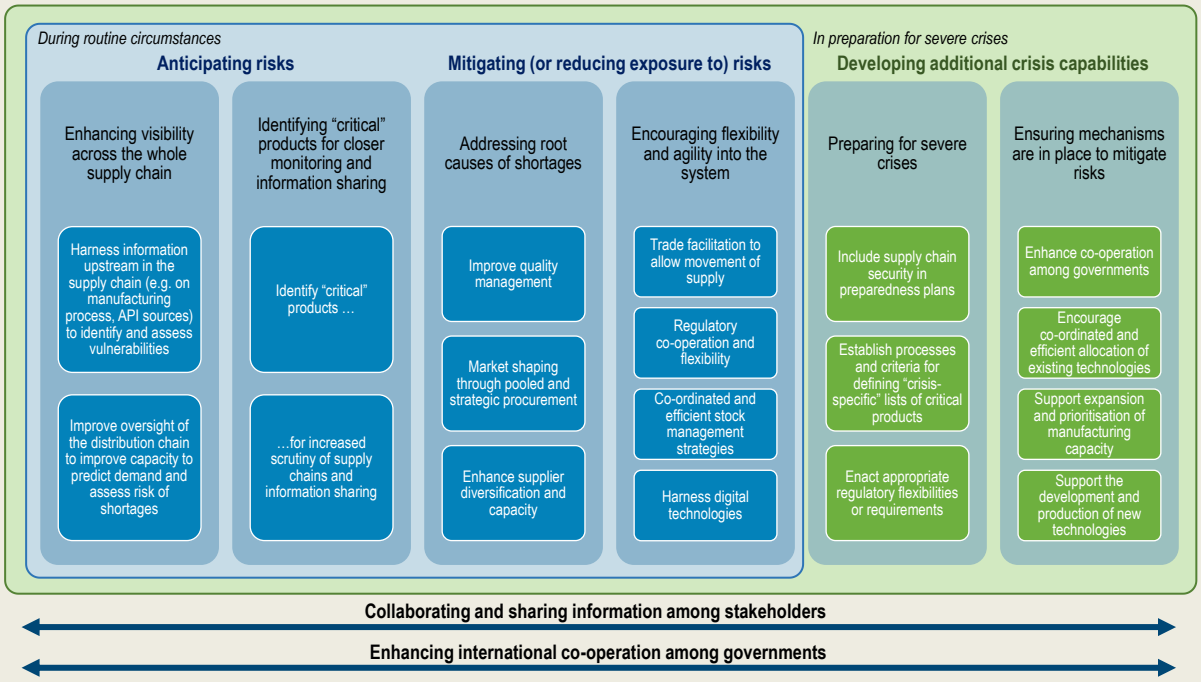
This chapter focuses on additional actions needed to anticipate and mitigate the impact of severe crises on medical supply chains. These actions go above and beyond the foundational supply security policies already discussed in the previous chapter. First, this chapter explores how to be better prepared for faster and more agile responses to crises. It then describes mechanisms to mitigate the risk of shortages and ensure equitable access to existing and newly developed technologies that populations need. This chapter has a focus on co-operation among governments and collaboration with the private sector.

Key findings

Anticipating and mitigating the impact of a severe crisis on medical supply chains requires additional efforts, building on the initiatives to anticipate, avert and mitigate the impact of shortages described in Chapter 2, to (1) prepare for more rapid responses and to (2) implement mechanisms to reduce the impact of the crisis on population health (see Figure 3.1 for an analytical framework). International co-operation and close collaboration between the private sector and governments are important to ensure a cohesive, collective, and efficient response.

- Preparedness plans should include specific measures to address supply chain issues. Stakeholders could work on the establishment of processes and criteria for defining **lists of critical products specific to different emergency situations** and to **put in place mechanisms to monitor international and regional flows** of the selected products. These lists could also be used for cross-county pooled procurement, for example at the European level. Policy makers could also agree in advance on rules and processes to deploy appropriate regulatory flexibilities or requirements in times of crisis to ensure needed products can be distributed without compromising quality.
- Policy makers should also ensure that mechanisms are in place to **facilitate worldwide access and fair allocation of existing technologies**, and to support R&D efforts and encourage technology transfer of technologies developed during the crisis (such as new vaccines or treatments).
    - Countries should agree on mechanisms to **co-operate, share information** on supply and demand, and refrain from exacerbating supply chain issues through panic buying and export restrictions. Multilateral or regional trade agreements or mutual recognition agreements (MRA), for example, could contain health-related provisions encouraging countries to co-operate to ensure the continuity of supply of medical goods.
    - Policy makers may need to **support the expansion of production capacity** in cases of surging demand and **mandate the prioritisation of the medical sector** for the supply of raw materials and electronic components by subcontractors. Preparing and implementing appropriate legislation in advance would facilitate rapid responses by policy makers and other stakeholders.
- **Governments may need to support the development of new vaccines and treatments in response to specific crises**. In doing so, they should reinforce existing mechanisms to facilitate equitable access, such as knowledge sharing, voluntary licensing, and technology transfer, using mechanisms that can be activated immediately in the event of a crisis.

Figure 3.1. Analytical framing of policies to improve medical supply chain security



Note: API active pharmaceutical ingredient. "Routine circumstances" refers to routine or "business as usual" situations in which minor or major supply disruptions occur absent a major crisis. Severe crises refer to major events (e.g. pandemic, other type(s) of major events or health threats).

Chapter 3 focuses on policies to address sudden surges of demand due to regional or global crises. While the policies outlined in Chapter 2 are at the foundation of building more resilient supply chains, anticipating and mitigating the impact of severe crises on supply chains requires additional effort. The objective is to be better prepared for faster and more agile responses (Section 3.1) and to ensure equitable access to the (existing and newly developed) technologies that populations need (Section 3.2) – Annex A supplements discussions in this Chapter, presenting examples of national and cross-country initiatives. For minor disruptions (e.g. a severe seasonal influenza season), firm inventories may be adequate and there may be no need for governments to intervene. More serious crises (e.g. epidemics, localised natural disasters) may require additional capacity, and governments will have a role in complementing the actions from the private sector. In an extreme crisis (e.g. a global pandemic), these strategies will be inadequate to avert disruptions, and standby capability will be required (Sodhi and Tang, 2021[1]). Governments have a central role in organising emergency supply chains and working with industry and relevant international organisations, if necessary, to develop these additional capabilities in advance.

3.1. Preparing for severe crises

To deal with major crises, governments need to develop plans for different types of future health crises in which they identify their role in securing access to essential products and clarify the organisation of emergency supply chains with the private sector. In doing so, the role of governments in securing access before crises take place may be seen as threefold.

First, governments need to incorporate supply chain issues in their general and health-specific risk prevention strategies. This is where reviews of vulnerabilities and assessments of potential additional capacity are relevant and can be undertaken jointly with the private sector. The sharing of information is key to ensuring that governments know in advance the nature and extent of disruptions and fluctuations in demand that can be absorbed by private sector risk management strategies, and those that will require government intervention. Some investment in monitoring information systems may also be needed to enable governments to assess the severity of a health crisis in terms of security of supply and identify when emergency plans have to be deployed.

The second role of governments is to produce clear guidelines that define risk management structures, processes, and responsibilities, so that when a crisis occurs, procedures can be immediately triggered without the need to define roles and responsibilities. These guidelines can also help the private sector in organising its own risk management strategies and knowing what to expect in a crisis. Guidelines pertaining to access to essential medical products can include emergency procurement procedures (such as centralising the purchase of emergency supplies, undertaking centralised price tracking and quality verification, etc.); template agreements that can be used with domestic and foreign suppliers; descriptions of communication channels; and methods by which firms can access regulations and decisions adopted as part of emergency procedures.

The third and most complex role of governments is to create an "industry commons"[1] (Sodhi and Tang, 2021[1]) and to enter into upstream agreements and advanced planning with firms on emergency supply chains and the repurposing of existing manufacturing capacity. Large-scale crises involve spikes in demand that cannot be addressed by stockpiling strategies and regular risk management strategies. Production has to be ramped up to levels well beyond normal market demand and this requires the deployment of manufacturing capacity. Planning for repurposing in advance, and having agreements in place with firms to do so, is the most efficient way of preparing for large-scale crises. However, this requires close co-operation with the private sector and firm-specific partnerships and contracts that are challenging for governments to put in place, especially when there is no crisis, and investing resources in such efforts may not appear as a priority.

The sections below highlight the need to consider supply chain security explicitly in preparedness plans (Section 3.1.1), to define governance and processes to establish lists of critical products tailored to specific health emergencies (Section 3.1.2), and to enact additional regulatory flexibilities or requirements to respond to large scale events (Section 3.1.3).

The importance of enhancing medical supply chain security and preparing for future crises is recognised in international co-operation fora (G7, G20, International Health Regulations) (see Box 3.1).

Box 3.1. Securing medical supply chains is a priority in international co-operation fora

G20 and G7

The G20 meetings hosted by Indonesia (2022) and India (2023) were instrumental in fostering global co-operation among the world's largest economies in order to address supply chain issues in the aftermath of the COVID-19 pandemic. According to the chair's summary of the 2023 Health Ministers meeting, one of the three focus areas of work was "*Strengthening Co-operation in the Pharmaceutical sector with focus on availability & access to safe, effective, quality and affordable Medical Countermeasures – VTDs (Vaccines, Therapeutics, and Diagnostics)"* (G20, 2023[2]). With respect to medical supply chains, ministers prioritised discussions that recognised the need for a broader manufacturing base for essential products, particularly in developing countries. The strengthening of local and regional health product manufacturing capacity and co-operation was highlighted as a relevant concern. The summary also encouraged the development of multi-stakeholder collaboration to promote R&D, diversify manufacturing networks, and strengthen the resilience and transparency of global supply chains. It recognised the relevance of inter-agency work and partnerships in global health, such as GAVI, CEPI, and the Global Fund, and their collaborations with WHO, UNICEF and member states.

Unlike those of the G20, recent G7 meetings have not focused specifically on the topic of medical supply chains. During the 2023 G7 Health Ministerial meeting held in Nagasaki, Japan, participants emphasised the importance of multi-stakeholder engagement to promote equitable and rapid access to safe and effective medical countermeasures (Ministry of Health, Labour and Welfare, 2023[3]). The WHO Access to COVID-19 Tools Accelerator (ACT-A) was underscored as a strong example from which countries could draw insights. Although medicines were not mentioned explicitly, G7 leaders focused their discussions on measures to improve the security of supply chains to avoid dependency on one or only a few countries for essential products. The 2021 G7 Health Ministers meeting was an important forum for discussing the relevance of strengthening global supply chains to increase and diversify the production of COVID-19 vaccines, and to recognise the threat posed by shortages and the lack of diversified supplies of antimicrobials.

Reforms of the International Health Regulations (IHR) and the development of a new Pandemic Treaty

With the onset of the COVID-19 pandemic and the recognition of shortcomings in international co-operation to address global health threats, WHO and its member states initiated a process to draft and negotiate a new agreement on pandemic preparedness and response. The process is being led by an intergovernmental negotiating body (INB), representing all regions of the world. In February 2023, the INB released its "conceptual zero draft" of the text, capturing the key topics to be discussed further by negotiators (WHO, 2023[4]). Article 6 of the document proposed the establishment of a WHO Global Pandemic Supply Chain and Logistics Network, within which parties would co-operate on assessments of supply vulnerabilities and implement agreed policies in the event of a future pandemic. Proposed measures include examining the types and volumes of products to be included in collective stockpiling schemes; mapping manufacturers and suppliers of strategic medicines and estimating demand; identifying the most efficient multilateral purchasing mechanisms (including pooled procurement schemes); and developing a system to ensure the fair allocation of products. The text also includes provisions committing the parties to refrain from imposing regulations that affect the trade of pharmaceutical raw materials and ingredients. The INB is expected to submit its final document to the World Health Assembly in May 2024 (WHO, 2023[5]).

In accordance with the World Health Assembly Decision WHA75(9) on Strengthening WHO preparedness for and response to health emergencies, and in parallel with the development of a new pandemic treaty, a WHO working group with representatives from all member states has been studying

potential amendments to the International Health Regulations (IHR) (2005) since October 2022. The IHR is a legally binding international law instrument which defines countries' rights and obligations during public health emergencies of international concern and determines specific rules in regard to health measures for international travellers and goods. The latest amendment proposals were submitted by a wide range of WHO member countries and considerably increase the scope of the IHR, including the addition of measures to ensure the supply for essential products (WHO, 2022[6]). For example, WHO would be responsible for carrying out assessments of the affordability and availability of health products required to respond to the international health threat, and to develop allocation plans to ensure equitable access for all parties to the IHR. More complex topics, such as the recommendations for exemptions in national intellectual property regulations to facilitate the manufacture and export of health products, are also present in the draft text. The proposed amendments are currently undergoing technical review by the WHO secretariat and should be considered by member states during the 77th World Health Assembly in May 2024.

3.1.1. Including supply chain security in preparedness plans

Prior to the COVID-19 pandemic, several OECD countries had undertaken some degree of pandemic preparedness planning. Of 23 countries who responded to the OECD Resilience of Health Systems Questionnaire 2022, 91% stated that they had a national plan motivated by WHO recommendations (70%), strong national/political will (61%), and their experience of the 2009 H1N1 pandemic (61%). Many of these included provisions with respect to testing and laboratories (~70%), stockpiles of vaccines and medicines (about two-thirds); personal protective equipment (PPE) procurement and logistics (~50%), vaccines and other medicines' logistics during the pandemic (~40%) and respirators supply strategies (~40%). A smaller proportion had planned for emergency approval processes for vaccines and medicines (~30%), vaccine and other medication R&D (~30%), and PPE production and/or trade (~30%). About half of these plans included a strategy for international co-operation (OECD, 2023[7]).

In Europe, the Health Emergency Preparedness and Response Authority (DG-HERA), part of the European Commission, was established in 2021 to ensure the availability of medical countermeasures (MCMs) in the event of future public health emergencies. In terms of preparedness, HERA works on the identification and assessment of different types of potential threats (i.e. pathogens with pandemic potential; chemical, biological, radiological and nuclear threats; and antimicrobial resistance) and on the organisation of epidemiological surveillance. It supports R&D for the development of medical countermeasures, and works with industry to identify potential vulnerabilities in supply chains and to prepare for capacity expansion for manufacturing of MCMs in case of need. HERA also works on the preparation of critical lists of medicines and medical devices needed to respond to crises (see Section 3.1.2 below) and for inclusion in EU-wide stockpiles. HERA publishes annual reports on the State of Health Preparedness (European Commission, 2022[8]).

At the 2021 North American Leaders' Summit (NALS), leaders from Canada, Mexico and the United States agreed to convene a Public Health Supply Chain Dialogue under the North American Plan for Pandemic and Animal Influenza (NAPAPI) Health Security Working Group. This Dialogue took place on 10 November 2022. Representatives from the three countries convened to discuss challenges, lessons learned, and opportunities for further trilateral discussion and collaboration, including providing support for a revision of NAPAPI in 2023. The revised NAPAPI will strengthen North America's ability to respond to health security threats, including influenza and other serious communicable disease outbreaks (Gobierno de Mexico, 2021[9]).

3.1.2. Establishing processes to define lists of critical products to respond to emergencies

The development of lists of critical medical products to respond to severe emergencies and major crises can be used to address two objectives. One is to guide stockpiling, the other is to support efforts to ensure supply chain security. For example, WHO recently defined a list of products for radiological and nuclear emergencies that it recommends stockpiling nationally (WHO, 2023[10]). In 2012, PAHO developed an Emergencies and Disasters Essential Medicines List (EDEML) for Caribbean countries to facilitate rapid procurement to support the provision of urgent medical care in the acute phase of a crisis and to maintain care for people with chronic diseases under treatment (PAHO, 2012[11]).

Some OECD countries have been working on establishing similar lists. As discussed in Chapter 2, the United States has established a list of medical products that should be available at all times in the country, including all of the inputs that are critical for their production (active pharmaceutical ingredient, raw material). This list preferences products used in the acute treatment of severe conditions, as well as those required for protection against certain infectious diseases, and chemical, biological, radiological, and nuclear threats. Supply chains for some of these products are being analysed (FDA, 2022[12]).

In Europe, two steering groups are responsible for developing lists of critical medicines and medical devices to respond to major events or public health emergencies. The objective is not to stockpile all these medical products, but to ensure continuous access during a crisis:

- The Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG), comprising members of all EU Member States, the Commission, and the European Medicines Agency (EMA), is responsible for ensuring a robust response to *medicine* supply issues caused by "major events" or public health emergencies. While the latter are declared based on specific criteria,[2] "major events" can encompass a broad range of situations, such as environmental or biological events, or incidents affecting the supply of essential medicines in more than one Member State. The MSSG is responsible for establishing lists of critical medicines that must be monitored on declaration or recognition of a public health emergency or major event (EMA, 2023[13]). To help the creation of these future lists, the MSSG published in July 2022 a list of "main therapeutic groups" in crisis preparedness. This list includes the relevant subgroups (at anatomic therapeutic classification (ATC) Level 3) considered necessary for emergency care, intensive care, and surgery, and is based on a well-defined process and published methodology (EMA, 2022[14]; EMA, 2022[15]). Lists of critical medicines for mPox and COVID-19 were published in August 2022, but are already obsolete.
- The Executive Steering Group on Shortages of Medical Devices (MDSSG), established in March 2023, supports the EMA's mandate to ensure a robust response to *medical device* supply issues caused by public health emergencies (EMA, 2023[16]). The group is responsible for establishing a list of critical medical devices for monitoring on declaration of a public health emergency; ensuring supply and demand tracking to facilitate rapid identification and mitigation of shortages; reporting and offering recommendations on mitigation measures; and proposing EU-level actions to address shortages of these vital medical devices. The methodology for establishing the list of critical medical devices was published in June 2023 (EMA, 2023[17]). Public health emergency critical devices lists will be tailored to respond to specific emergencies.

In addition, European legislation[3] foresees the development of an IT platform to facilitate collection of information on shortages of, and supply and demand for, medicinal products, including information on marketing status (including withdrawals and cessations of supply), from both industry and Member States The platform is expected to become operational in February 2025. The objective is to monitor, prevent, and manage (1) shortages of products on the critical medicines lists during a public health emergency or major event, and (2) actual and threatened medicine shortages in one or more EU Member States that could give rise to a major event or public health emergency.

3.1.3. Enacting appropriate regulatory flexibilities or requirements

Responses to emergency situations may require some additional regulatory flexibilities or requirements, while ensuring that patient safety is not compromised. Policy makers could agree in advance on rules and processes to be able to use these appropriately in times of crisis. For example, this may include authorising the use of alternative products already approved by a regulatory agency (or having WHO pre-qualification) where shortages occur due to failures in supply. For example, during the COVID-19 crisis, Canada authorised quantities of propofol from alternative suppliers on the basis of having marketing authorisation in the EU. This may also take the form of accelerated or exceptional processes to approve the use of newly developed products during emergency situations. The EMA's implementation of rolling reviews and the US Food and Drug Administration's (FDA) use of Emergency Use Authorizations (EUA) for COVID-19 technologies are examples.

All these decisions, however, represent trade-offs demanded by emergency situations. In the United States, the Department of Health and Human Services (HHS) authorised emergency use of in-vitro diagnostics (IVDs), PPE and other medical devices, as well as medicines for use during the COVID-19 outbreak (HHS, 2020[18]). EUAs may be issued for medical products which "may be effective", – representing a lower level of evidence compared to the "effectiveness" standard normally required for product approvals (FDA, 2017[19]). In the EU, Member States were allowed to approve medical devices that had not yet undergone conformity assessment in case they were urgently needed and no alternative was available. Some COVID-19 IVDs are reported to have been approved early in March 2020 according to standards lower than those prevailing for diagnostic tests (Blakely et al., 2022[20]). Some goods approved hastily were later recalled (e.g. masks in the Netherlands and in the United States). In Australia, the Therapeutic Goods Administration (TGA) introduced an expedited recall pathway to respond to complaints of poor safety or performance within 24 hours (Blakely et al., 2022[20]).

While additional flexibilities may be necessary, they can pose additional risks and should be removed when the crisis is over. While many of the products needed during pandemics are consumables and will not remain in the health system, others such as ventilators, infusion pumps, haemodialysis devices, and left ventricular support systems, are likely to remain in use in hospitals, even though their safety-performance profile may be inferior to that of other available products (Blakely et al., 2022[20]). Hospitals, which often faced higher than usual acquisition prices and operate under tight budgetary pressure in many countries, are not likely to replace them prior to obsolescence.

Blakely et al. (2022[20]) suggest a number of policy options to limit the drawbacks of additional flexibilities during severe crises. The first option is to annually review the scope of medical devices eligible to use these expedited pathways during a crisis to ensure they target the appropriate ones. The second is to require additional evidence retrospectively for items intended for long term use, and the third is to support hospitals in ensuring the removal and replacement of devices where necessary (ibid.)

Other flexibilities may be less problematic. This could include the simplification or acceleration of regulatory processes, for example, to enable the sale of medicines with foreign packaging and labelling or to permit the exceptional importation of products. It is important for regulatory agencies to have the imprimatur to apply regulatory flexibilities in the event of critical supply chain disruptions.

Responses to emergency situations may also require the gathering of additional information. In the United States, for example, requirements to notify potential medical device shortages emergency situations was implemented to facilitate prevention measures.

3.2. Ensuring mechanisms are in place to mitigate risks of shortages

The sections below discuss mechanisms for mitigating the risks of severe crises, including the importance of enhancing co-operation among governments to prepare for crises (Section 3.2.1), to encourage co-ordinated and efficient allocation of existing technologies (Section 3.2.2), to support expansion and prioritisation of manufacturing capacity (Section 3.2.3), and to support the development and production of new technologies and encourage technology transfer (Section 3.2.4).

3.2.1. Enhancing co-operation among governments to prepare for crises

Many of the issues affecting the security and resilience of supply chains (and by extension, the policies needed to address them) lie outside health systems. Co-operation among governments in areas such as trade policy, trade facilitation, transport and infrastructure (both physical and digital) can also increase preparedness by keeping markets open, addressing disruptions, and facilitating the movement of essential medical products during crises.

The first objective of such co-operation is to improve transparency, which is critical in helping governments manage fast-evolving crises. This includes sharing lessons learned, building confidence in supply and trust in global markets, and helping to avoid harmful policy choices such as panic buying or hoarding by governments. International initiatives or forums can offer a framework for co-operation, similar to that of the Agricultural Market Information System (AMIS) initiative in the case of agricultural and food markets (Box 3.2).

International co-operation can also lower barriers to trade and investment in essential products, as well as their main inputs, in order to optimise sourcing opportunities and access for all countries, consistent with the objective of many trade and investment agreements. However, strengthening the resilience of key global value chains may require new commitments from countries to prevent disruptions to markets, such as the use of export restrictions. In the World Trade Organization (WTO), the Ottawa Group (a group of 13 WTO members) launched a global Trade and Health Initiative in 2020 that aimed at developing a list of actions and potentially new commitments to facilitate trade in essential medical products (Ottawa Group, 2020[21]).

The COVID-19 pandemic offers a striking example of how trade barriers can affect the supply of medicines. As previously noted, the early stages of the pandemic saw countries imposing lockdowns and travel bans, with consequent disruptions to transport, freight, logistics and customs activities which adversely affected the movement of goods across borders (including raw materials, components, and finished products). These were followed by export restrictions that reduced access to essential medical products and exacerbated shortages (Hoekman, Fiorini and Yildirim, 2020[22]). Outside COVID-19, many essential medicines not only remain subject to substantial tariffs, but also to a range of non-tariff measures (NTMs) that go beyond the imposition of quality standards (OECD, 2023[7]). Restrictive measures such as these can not only contribute to scarcity in international markets, but can also raise prices and reduce availability in non-producing countries. No country is self-sufficient in the production of all necessary medicines or their constituents, and trade is therefore essential to ensure the continuity of supply chains.

Trade agreements, whether multilateral, regional or bilateral, include general exceptions and specific exceptions related to health that allow countries to take measures, such as export restrictions, during crises. Some trade agreements, such as the Japan-Australia Economic Partnership Agreement (JAEPA), have specific provisions to ensure stable supply of energy and mineral resources and to prevent the introduction of export restrictions when there are disruptions. Co-operation mechanisms and commitments to resort to reasonable measures that take into account the availability of products for partners during a crisis could also be envisaged for medical supply chains in regional trade agreements or at the multilateral level.

At the regional level, the Free Trade Commission of the Canada-US-Mexico Agreement (CUSMA) issued a decision in February 2023 to encourage Coordination and Consultation on North American Trade Flows in Emergency Situations (Government of Canada, 2023[23]) Under this decision, the partners have agreed to create new mechanisms to consult with sub-national governments and key stakeholders in the event of supply chain disruptions, and to create a new Trilateral Co-ordination Sub-Committee on Emergency Response to share information and co-ordinate activities related to matters affecting trade in emergency situations. The Canada-US Working Group on Supply Chains (established in 2021) supports both bilateral efforts to facilitate trade but also broader regulatory co-operation looking at stockpiling and regulatory flexibility (The White House, 2022[24]).

Finally, governments also play a pivotal role through trade facilitation measures, as these ensure the swift movement of goods across borders. Measures designed specifically for crises, such as fast clearance procedures or accelerating certification processes, can help mitigate disruptions that affect international trade flows and are complementary to the regulatory flexibility described in Chapter 2. Trade facilitation measures have generally proven to be more efficient when they are co-ordinated across countries, and even more so when they are included in a series of initiatives taken to promote co-operation, regulatory convergence, and the harmonisation of rules.

Box 3.2. Enhancing transparency and policy co-ordination: The experience of the Agricultural Market Information System (AMIS)

The Agricultural Market Information System (AMIS) initiative was created by the G20 in 2011 in response to the food price crisis of 2007/08 and 2010. AMIS assesses global supplies for major staple crops (wheat, maise, rice and soybeans) and provides a platform to co-ordinate policy action in times of market uncertainty. By enhancing transparency and policy co-ordination, AMIS prevented disruptions and price hikes for food during COVID-19.

How does AMIS work?

To gather information on food supplies, AMIS relies on the Global Food Market Information Group which is composed of technical representatives from the 28 AMIS members. The Information Group provides comparable and timely information on markets (supply, demand, stocks and prices) and on policies put in place by countries that affect markets (e.g. duties, export restrictions, price caps, etc.). The Rapid Response Forum is composed of senior officials from AMIS participants. It promotes early discussion about disruptions and critical market conditions, as well as ways to address them. Finally, AMIS has a Secretariat that involves 10 international organisations (including the OECD).

Feasibility for medical products

Given the positive experience with AMIS, it has been suggested that a similar initiative be established for essential medical products. However, the agricultural and medical sectors are different in a number of ways. AMIS focuses on a limited number of products that are inputs for the food industry and for which production and market information were already being collected by participating countries or international organisations. Medical supply chains are more complex and collecting similar information for a variety of essential medical products would be challenging. It would involve working closely with the private sector and setting up a fit-for-purpose mechanism for collecting information. It would also involve countries' obtaining legal authorities to collect the necessary information, as well as the funding to set up and maintain the infrastructure. Nevertheless, having a forum where major producers of medical products could co-ordinate their policies and address crises could be regarded as a valuable avenue for improving medical supply chain security.

Source: Agricultural Market Information System – AMIS (2023[25]), *Homepage,* www.amis-outlook.org/

3.2.2. Encouraging co-ordinated and efficient allocation of existing technologies

Regional stockpiling and pooled procurement can be considered useful means of ensuring access to technologies in cases of large surges in demand. However, stockpiling critical products at country level can have a negative impact on available supply. Regional stockpiling may be considered a more pragmatic option, provided that the rules for the allocation of products in times of crises are well-defined.

Launched in 2019, rescEU is one example of a multi-country stockpiling mechanism that aims to provide essential material and human resources to respond to a diverse range of emergencies. The initiative is part of the EU Civil Protection Mechanism, a co-ordination strategy to ensure rapid emergency responses. The European Commission funds the collective stockpile and 9 Member States hold the physical stockpiles, assuming both logistics and procurement responsibilities. Countries propose which products should be stockpiled and provide appropriate logistics and interoperability with EU systems. rescEU acts as an option of last resort for member and associated countries that lack sufficient capacity to respond to emergencies (European Commission, 2022[26]). EU countries made extensive use of the system during COVID-19. Notably, rescEU focused on providing PPE, ventilators, and protective masks, although it also stockpiled and delivered medicines. The scheme also supports some non-EU countries (Glencross, 2022[27]). As part of the package of measures introduced by the European Commission's communication on medicine shortages (2023[28]), a common strategic approach to medicine stockpiling is planned for the first half of 2024.

In the European Union, a process for joint procurement agreements to secure access to MCMs in the event of a crisis was established just after the 2009 H1N1 outbreak. This mechanism was activated during the COVID-19 pandemic, allowing the Commission to procure COVID-19 vaccines on behalf of Member States. The EU strategy aimed to secure timely access to affordable vaccines through advance purchase agreements (APA). A steering board with representatives from each member state and the Commission provided oversight of the procurement process and validated contracts prior to signature. To facilitate timely access, the Commission Decision that approved the agreement with Member States for vaccine procurement included (1) speed of delivery and (2) capacity to supply through the development of production capacity within the EU, as two criteria to be applied in financing contracts with manufacturers. A report by the European Court of Auditors highlighted that in the first half of 2021 the EU faced vaccine delivery issues with Janssen and AstraZeneca vaccines, having only received a third of contractually agreed volumes by the end of June 2021. The auditors recognised that the Commission had limited leverage to overcome supply challenges, as no supply chain risk analyses had been carried out prior to signing contracts with manufacturers (European Court of Auditors, 2022[29]). The report called for a more complete evaluation of the joint procurement scheme, including benchmarking with other procurement processes. Nevertheless, EU Member States can engage in the collective procurement of MCMs on a voluntary basis, and some did so to procure mPox antivirals, for example.

3.2.3. Supporting expansion and prioritisation of manufacturing capacity

COVID-19 vaccines were developed and manufactured in record time. There was no vaccine for SARS-CoV-2 at the beginning of the outbreak in December 2019, but by May 2022, 15.2 billion doses had been produced.[4] This feat was achieved through close collaboration with the private sector. In the United States, the US Department of Defense and the Department of Health and Human Services worked together and used the Defense Production Act (DPA) to assist companies in expediting the process of developing and manufacturing COVID-19 vaccines (Bown, 2022[30]). During "Operation Warp Speed", the government provided subsidies to seven companies for R&D and completion of clinical trials, and, for biotech companies without manufacturing capacity, for outsourcing of production. Further funding was provided through priority-rated contracts to speed up manufacturing for the most promising candidates at the end of Phase 3 trials. This funding allowed the shifting of financial risks from the firms to the government, and accelerated the development and production of vaccines.

In the EU, a Task Force for Industrial Scale-up of COVID-19 vaccines was set up in February 2021 by the Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs (European Commission, 2021[31]). The Task Force worked closely with the industry to ramp up production. In particular, it helped to address about 150 bottlenecks identified in production capacity and supply chains, such as the sourcing of bioreactor bags, vials, low dead space syringes, and lipids for mRNA vaccines. In co-operation with national authorities, the Task Force also helped to launch new production facilities and supported manufacturers in the signature of APA with EU countries. The EU became the biggest producer and exporter of COVID-19 vaccines (based on data from WTO-IMF COVID-19 Vaccine Trade Tracker, as of May 2022). As documented by Bown and Bollyky (2021[32]), the scaling up of manufacturing was achieved through efforts of firms who established efficient supply chains through outsourcing, partnerships, and international production networks. However, the support of governments was key in assisting firms and speeding up the process.

During crises, market dynamics can become obstacles to rapidly increasing the production of essential medical products that experience strong surges in demand. In severe cases, governments must have effective policy tools to ensure that such products are prioritised in access to raw materials and other components that might otherwise be provided to speed up manufacturing to other industry sectors. In the United States, the DPA allows federal agencies to require companies to prioritise government contracts deemed essential to address national emergencies. For example, from April to May 2020, seven new public contracts priority-rated under the DPA to provide a total of 137 431 new ventilators by the end of 2020 were signed with manufacturers, both to support healthcare providers and to replenish the Strategic National Stockpile (FEMA, 2021[33]). Priority-rated contracts also allow orders to take preference over other contracts with respect to delivery. This could, for example, facilitate access to semiconductors for the medical device industry, which faces challenges in the supply of these products, as they are in high demand from other sectors (car and aviation industry). In interviews with manufacturers, it was noted that the prioritisation provided by the DPA was effective in supporting security of supply for ventilators. A 2021 report by the US Government Accountability Office (2021[34]) also confirmed with manufacturers that priority ratings had helped ensure the continuous supply of ventilators in the United States. However, despite the potential benefits of priority setting for the production of essential products during crises, the use of such instruments should be evaluated carefully and follow strict pre-determined rules. Public intervention in industrial production has the potential to disrupt the supply of other products that may be essential to respond to the crisis and can result in unanticipated consequences for other manufacturing sectors.

Emergency situations have also led some countries to resort to involving other industry sectors in contributing to national efforts to secure the provision of much needed health products. In the United Kingdom, for example, the National Health Service launched the “Ventilator Challenge”, a call for manufacturers outside the health sector to begin producing ventilators to treat severely ill COVID-19 patients. The initiative was led by the UK Cabinet Office and, together with a similar initiative by the Department of Health and Social Care, had an initial target of 30 000 ventilators. Mainly as a result of quality issues, the ventilator challenge fell well short of reaching its goal (European Parliament, 2021[35]). However, manufacturers’ interest in the project and relatively strong preparedness to respond to the government request have led experts to predict that re-shoring efforts in the United Kingdom could increase in the near future (European Parliament, 2021[35]). A UK Government audit of the programme noted that the cost of the programme was GBP 277 million. It also mentioned that the government accepted higher levels of risk by signing contracts without a previous evaluation of which products would actually work. However, it concluded that the Cabinet Office took reasonable approaches to control the programme’s costs and that it adapted its initial urgent demand after realising it would not be necessary to purchase that quantity of new ventilators (National Audit Office, 2020[36]).

While the above examples illustrate measures that were taken during the COVID-19 crisis, the expansion and prioritisation of manufacturing capacity can be planned in advance for other types of crises, and

co-ordinated across countries. In addition to the regulatory co-operation described in Chapter 2, strategies aimed at diversifying supply (including through additional domestic capacity) and creating an "industry commons"[1] could also benefit from more international co-ordination and global initiatives.

3.2.4. Supporting the development and production of new technologies and encouraging technology transfer

International co-operation already plays an important role in the financing of clinical R&D, notably in therapeutic areas that are neglected by the private sector, due to high risks and/or low market prospects. Describing all initiatives would be beyond the scope of this report but an evaluation of what took place during the COVID-19 pandemic may be useful in preparing for future severe crises.

For example, the Coalition for Epidemic Preparedness Innovations (CEPI), a non-profit foundation with donors from the public, private and philanthropic sectors, was established after the 2014 Ebola outbreak to develop vaccines to prevent and respond to emerging infectious diseases, and to "secure access to such products for the populations who need them". CEPI focuses on the generation of clinical trials, knowledge, and investigational vaccines, and its contracts include obligations for grantees to ensure equitable access to developed products, including commitments to provide affordable access to populations in need (see Chapter 13 in (OECD, 2023[7])).

During the COVID-19 pandemic, CEPI contributed to the financing of COVAX, the international partnership to develop, manufacture, procure, and distribute COVID-19 vaccines, and Moderna and AstraZeneca also benefited from modest contributions from CEPI. Despite this, high-income countries were able to secure higher number of doses of these vaccines than low- and middle-income countries. CEPI recently developed a new Strategic plan, which includes establishing networks and partnerships to address several objectives including the promotion of equitable access and relies on decentralised manufacturing, building R&D capacity in low- and middle-income countries, and supply reservations (OECD, 2023[7])

Voluntary licensing of new technologies is another avenue for expanding production capacity. Through a voluntary licence agreement, a company holding intellectual property rights on a product allows another company to manufacture this product and sell it in a set of countries, most often with small royalty payments. The Medicines Patent Pool (MPP), supported by Unitaid and several governments, has been working on framework agreements with pharmaceutical companies to allow generic manufacturers to produce medicines and sell them to low-income countries specified in the agreements. To date, the MPP has signed agreements with 20 patent holders for 13 HIV antiretrovirals, one HIV technology platform, three hepatitis C direct-acting antivirals, a tuberculosis treatment, a cancer treatment, four long-acting technologies, 3 oral antiviral treatments for COVID-19 and 15 COVID-19 technologies (Medicines patent pool, 2023[37]). The MPP awarded a record number of 72 sublicenses for COVID-19 therapeutics. These cover 119 low-income countries, and more than 4.35 billion people, for at least one of the three COVID-19 therapeutics, with royalty payments waived until WHO declares the end of COVID-19 as a public health emergency of international concern (USITC, 2023[38]).

In addition, the WHO COVID-19 Technology Access Pool (C-TAP) was established in 2020 to facilitate faster equitable and affordable access to COVID-19 health products for all countries. C-TAP is currently endorsed by 45 WHO member states, and works with UNDP, the Medicines Patent Pool, the UN Technology Bank and Unitaid (WHO, 2023[39]). The idea was to establish a single global platform through which developers of COVID-19 therapeutics, diagnostics, vaccines and other health products could share their intellectual property, knowledge, and data with quality-assured manufacturers through public health-driven, transparent, voluntary, and non-exclusive licences. C-TAP provides support for technology transfer agreements and voluntary licensing, as well as patent pooling.

Technology transfer hubs can facilitate the sharing of knowledge, data, intellectual property rights (IPRs) and know-how for the development and manufacture of health technology products. WHO has announced

it intends to establish several hubs, and the first, Afrigen, has been established in South Africa, to expand the capacity of low- and middle-income countries to develop COVID-19 mRNA vaccines and to scale up manufacturing. This will include the transfer of a comprehensive technology package, appropriate training and any licenses required to facilitate production and export of mRNA vaccines to low- and middle-income countries (WHO, 2021[40]).

Although these initiatives do not primarily target OECD countries as beneficiaries, expansion of manufacturing capacity may relieve some pressure on supply chains in the face of increasing global demand for medicines and other medical products, and in case of emergencies. In addition, knowledge sharing has the potential to contribute to a more global response to future pandemics or other emergencies. These initiatives also address the quest for more equitable access to medicines and medical countermeasures in an increasingly connected world.

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Notes

[1] An “industry commons” consists for governments to establish and institutionalise emergency preparedness measures with the private sector. According to Sodhi and Tang (2021[41]), these measures should address stockpiling (e.g. what quantity of goods should be stockpiled), backup capacity (e.g. which firms are expected to produce more) and standby capabilities (e.g. what resources can be freed if the emergency demand exceeds the combined stockpile and capacity). A strategy needs to be discussed and agreed with the private sector before a crisis occurs.

[2] The criteria are defined in Article 12(1) of Decision No 1 082/2013/EU.

[3] Article 13 of Regulation 2020/0321.

[4] According to WTO-IMF COVID-19 Vaccine Trade Tracker.

Annex A. Landscape analysis

Table A A.1. National initiatives for improving supply chain security

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Stockpiling	Minimum stockholding requirements (Australian Department of Health and Aged Care, 2023[1]), [2023-]	Australia	Establish supply buffer for low-cost medicines: – Manufacturers of low-price, shortage-prone drugs required to maintain stockpiles of 4 to 6 months supply. – Manufacturers' investments in stockholding mechanisms will be financed by a one-off price increase for medicines with ex-manufacturer price of < AUD 4 (~USD 2.60).	Designated criteria for determining which medicines and brands are subject to the stockholding requirement (noting that all prescription medicines in Australia are branded). A designated "responsible person" from the manufacturer must disclose its compliance with stockholding requirements to health authorities.	Around 3 000 brands for different medicines are included in the designated stockholding list.
Stockpiling	National Medical Stockpile (NMS) (Australian Department of Health and Aged Care, 2023[2]), [2012-]	Australia	Support front-line health services with additional resources when facing national health emergencies. Guarantee the continuous supply of medicines nationally, in a country highly dependent on imports. – The stockpile provides PPE, medicines, vaccines and antidotes where commercial supplies are unavailable and there is demonstrable need for the products.	The stockpile is managed by the Department of Health and Aged Care. Inventories are dispersed around the country in undisclosed locations, and stocks are released at the request of state and territory governments.	In late December 2019, the stockpile's inventory was valued at AUD 123 million (USD 87.8 million) (Australian National Audit Office, 2021[3]). The first large scale use was during the 2009 H1N1 influenza outbreak, when 900 000 courses of antivirals were distributed (ibid). During COVID-19, the stockpile was focused on purchasing PPE. Narrow stockpiling objectives and eligibility criteria for healthcare providers to receive goods from the stockpile during the pandemic were found to be obstacles in internal audits.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Visibility, Onshoring/ re-shoring	Drug Shortages Task Force (Government of Canada, 2023[4]), [2022-]	Canada	Consider novel approaches for addressing shortages and improving supply chain resilience for medical products, including initiatives for improved communication and transparency of shortages, greater supply chain visibility and the use of safety stocks for some essential drugs.	The task force engages provincial and territorial governments, industry stakeholders, healthcare system partners, patient groups and academia to develop a long-term strategy.	An online consultation received 160 written submissions, with the highest share coming from industry (45%). Respondents highlighted the need for increased transparency on shortages, including where products are available and possible alternatives. Increased visibility of inventory level data at different points of the supply chain was also raised as a necessary improvement, including improved tracking systems. Stakeholders also indicated the need for a list of essential drugs that could be subject to additional measures in case of shortages, and recommended improvements to shortage reporting requirements. Finally, stakeholders stressed the need for reinforced domestic manufacturing capabilities and procurement practices that also prioritise security of supply (Health Canada, 2023[5]).
Stockpiling	National Emergency Strategic Stockpile (NESS) (Public Health Agency of Canada, 2022[6]), [1952-]	Canada	Guarantee supply of essential medical equipment and pharmaceuticals to provinces and territories. – NESS also works as the sole provider of some niche medical countermeasures, such as vaccines and antidotes and antivirals to respond to emergencies.	In Canada, emergencies are first managed at local level; managing healthcare systems is a shared responsibility of provinces and territories. If assistance is needed, provinces and territories can ask the federal government for support through the NESS.	N/A

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Stockpiling	Centro de Reservas del Sector de Salud (CRSS) (Ministerio de Salud y Protección Social, n.d.[7]), [2010-]	Colombia	Support hospitals with medicines, PPE, antidotes and other medical products during health emergencies or disaster situations. Provide specialised teams to support disaster response efforts.	Stockpiles are maintained by the Ministry of Health and Social Protection and managed by the Centre of Communication and Co-ordination for Health Sector Emergency Response, which is responsible for supplying regional stockpiling centres. Stockpiles function at both national and regional levels.	N/A
On-shoring/ re-shoring	France 2030 (Ministry of Finance, 2023[8]), [2022-]	France	Support the development of strategic industrial sectors and ensure supply of key products and raw materials, such as semiconductors, batteries, and essential medical products. Guarantee access to medical products through public-private investments in France and Europe.	The France 2030 investment project is led by the General Investment Secretariat (SGPI), under the authority of the Prime Minister's office.	A first investment of EUR 50 million for re-shoring projects has been announced. 50 medications have been selected to receive reshoring investment under the programme, of which 25 are already in process (Ministère de l'Économie,, 2023[9]).
On-shoring/ re-shoring	France Relance (France Stratégie, 2021[10]), [2020-]	France	Support the relocation of manufacturing in strategic sectors in France through co-financing.	The initiative is led by the Ministry of the Economy, which published a call for applications from companies seeking funding.	By February 2022, 106 projects in health had been awarded public grants of EUR 158 million, accompanied by EUR 561 million from industry stakeholders (France Relance, 2022[11]). 18 of the projects are aimed at re-shoring the production of 35 different APIs in France (ibid). A new paracetamol API factory with capacity to supply a third of Europe's requirements for the product will be established in France with subsidies from this programme.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Visibility	TRACStock (LEEM, 2021[12]), [2020-]	France	Allow companies to share information of their stocks with competent authorities, particularly the medicine agency, in a confidential data environment managed by a trusted third party. – TRACStock focuses on "Medicines of major therapeutic interest" (list of ~450 medicines established by the industry). – The platform should be able to anticipate the possibility of shortages based on the data provided, and recommend alternative therapeutics, where available.	Implemented by *Les Enterprises du Medicament* (LEEM), an organisation representing 260 pharmaceutical companies. Manufacturers are responsible for providing information to the system regarding supply shortages. Only France's regulatory agency, ANSM, has full access to the platform.	TRACStock has been focusing on monitoring stocks of, and demand for COVID-19 products in hospitals. By late 2023, more than 1 200 medications and 108 manufacturers are connected to TRACStock (LEEM, 2023[13]).
Visibility	DP-Rupture (LEEM, 2019[14]), [2013-]	France	Create links between pharmacists, industry providers, and national regulators to monitor the timeliness of pharmaceutical delivery to pharmacies across the country. – Allows hospital pharmacists and practitioners to signal supply issues to the supplier and the competent authorities (ANSM). – Allow companies to have a clearer picture of products' supply and distribution, allowing them to communicate supply disruptions to pharmacists in advance.	A platform implemented by France's National Chamber of pharmacists.	262 retail pharmacists, 4 hospital pharmacies, 4 wholesale distributors and 50 laboratories participated in a trial phase in 2014. During this trial, 1944 shortage declarations were made, with nervous and cardiovascular system medicines the most widely reported (Bordas, Duplay and Buxeraud, 2014[15]).

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
On-shoring	Program for Promoting Investment in Japan to Strengthen Supply Chains (Ministry of Economy, Trade and Industry, 2023[16]), [2020-]	Japan	Secure a domestic production base of essential products in case of emergencies. Support businesses in building new plants and new facilities to produce essential materials in Japan, based on companies' own judgements to strengthen supply chains.	The Ministry of Economy, Trade and Industry is responsible for selecting applicants to receive government subsidies in order to secure domestic production bases. A third-party committee of experts was tasked with selecting the companies that would receive government subsidies	57 companies were selected in July 2020 to receive JPY 57 billion (USD 537 million) from government subsidies to secure domestic production bases. The current list of health-related products includes PPE, reagents for PCR tests, and logistics kits for pharmaceuticals (e.g. cold chain), syringes etc.
Stockpiling	Korea National Stockpile (OECD, 2020[17]), [Start date unclear]	Korea	Stockpile a variety of medicines and other essential medical products.	The Ministry of Food and Drug Safety develops a list of the essential medical products that must be stockpiled. Stocks are maintained by both national and local authorities. National legislation provides that the stockpiling for disaster management must be reviewed every year by the agency responsible for keeping such stocks.	The list of essential medicines stockpiled currently contains 351 different products (Ministry of Food and Drug Safety, 2019[18]). Recent measurements of volumes of stockpiled antivirals indicated quantities sufficient for 26% of the population, above the WHO-recommended level of 20%.
Visibility	Availability of information on manufacturers' location for API and other components of authorised medicines by the Medicines and Medical Devices Safety Authority (MEDSAFE) (MEDSAFE, 2021[19]), [Start date unclear]	New Zealand	Provide publicly available information on manufacturers' names and locations for APIs, finished dosage forms, packaging, and testing, and sites of domestic product release, among other essential data.	The database is maintained by MEDSAFE, New Zealand's regulatory agency for medicines and medical devices.	Supply chain information is made available to the public. The database does not provide any additional data on volume and manufacturers' name and location for excipients.
Stockpiling, on-shoring	Strategic Reserve based on National Industrial Production Capacities (RECAPI) (Ministerio de la Presidencia, Relaciones con las Cortes y Memoria Democrática, 2021[20]), [2021-]	Spain	As part of a wider reform of the national security system, ensure the supply of essential products to the Spanish economy and essential public services, including medical products. Identify essential industrial resources for all sectors of government and establish basic production capacities to guarantee supply of essential products during exceptional circumstances.	An inter-ministerial council, with the support of an operational secretariat, is responsible for establishing the strategies and priorities of the RECAPI strategy.	A methodology for conducting dependency mapping of pharmaceuticals and API is currently being developed.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Stockpiling, visibility	Switzerland stockpiling system (FOPH, 2022[21]) [1951-]	Switzerland	Guarantee the uninterrupted supply of essential medicines.	Stockpiles are maintained and owned by private firms, but the Federal Office of National Economic Supply (FONES) determines the products and volumes that should be kept in a rolling stock system. A diverse set of medicines is included, as well as selected vaccines, and veterinary medicines. FONES orders the release of privately held supplies when faced with a shortage.	During the first months of the COVID-19 pandemic, the Swiss Federal Office of Public Health (FOPH), in partnership with FONES, developed a prioritisation strategy for allocating essential medicines to hospitals facing shortages. The rolling stock scheme allows for better monitoring of overall supplies and demand for essential medicines by public health authorities. A catalogue of 30 APIs essential to respond to the COVID-19 pandemic that would require stockpiling was developed after the first wave in 2020. Strict weekly monitoring of stocks, deliveries and demand for these products was implemented. Rolling stockpiles were considered an efficient and effective strategy to respond to shortages during COVID-19. However, international co-ordination and global market oversight have been identified as key areas for improvement in public audits.
On-shoring/ re-shoring	Reshoring UK (Reshoring UK, n.d.[22]), [2014-]	United Kingdom	Connect manufacturers with trusted suppliers that match their requirements. Encourage UK companies to engage with domestic manufacturers in their supply chain.	A public-private collaboration of industrial engineering associations manages Reshoring UK initiatives.	N/A
Onshoring/ reshoring	Life Sciences Sector Deal (Office for Life Sciences, 2018[23]), [2018]	United Kingdom	Increase the country's attractiveness for domestic production of advanced therapies.	The life sciences sector deal is part of the UK Government industrial strategy. It combines input from industry, academia, and charity partners to determine the areas for funding prioritisation.	GBP 181 million (USD 241 million) was reserved by the UK Government to support growth in life sciences manufacturing. Industry stakeholders from have also announced a series of investments in line with the government priorities.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Onshoring/ reshoring	Manufacturing USA (Deloitte, 2017[24]), [2014-]	United States	Increase competitiveness of US manufacturing. Facilitate the scaling-up of production and improving the cost-effectiveness of innovative technologies. Accelerate the development of an advanced manufacturing workforce.	Public-private collaborations form eight institutes, each focused in one area of innovation and/or manufacturing. These institutes form networks for collaboration among stakeholders from academia, industry, and government.	By late 2016, the US Government had committed USD 600 million in investments towards the initiatives of the institutes. This investment was matched by USD 1.3 billion in investments from industry and other stakeholders.
Stockpiling	Strategic National Stockpile (SNS) (ASPR, n.d.[25]), [1999-]	United States	Provide emergency medical supplies to states and local health jurisdictions in the event of a bioterrorist attack or other public health emergency.	The stockpile is managed by the Administration for Strategic Preparedness and Response (ASPR). The list of products to be stockpiled is defined by the HHS Secretary following advice by an inter-agency working group (generally including medicines, vaccines, medical products, and ancillary supplies) Most supplies are stored in SNS-managed physical storages facilities, but vendor and user-based inventories are also used. Vendor-managed inventories account for 10% of current SNS contracts and are directly funded by the SNS.	During the recent mPox outbreak, the SNS provided 1 million vials of JYNNEOS vaccines (CDC, 2022[26]). During the COVID-19 pandemic, the SNS focused on supplying PPE to all US states, the country's four largest cities, and other jurisdictions in need. The stockpile proved to be ill-prepared and lacking sufficient resources to respond effectively to the COVID-19 pandemic. Management of the stockpile has been reported to be inefficient.

Note: This list of initiatives should not be considered to be exhaustive. NA not applicable or not available; PPE personal protective equipment; API active pharmaceutical ingredient.
Exchange rates have been converted to USD using the OECD Statistics database and based on the average rate for the year the initiative was first implemented.

Table A A.2. Regional and multi-country initiatives for improving supply chain security

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Procurement	Gulf Co-operation Council (GCC) (DeRoeck et al., 2006[27]), [1978-]	Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, Yemen, and the United Arab Emirates	Ensure availability of quality medicines at lower prices. Ensure continuous supply of medicines and medical products throughout the year. Standardise procurement policies, processes, and quality, price and manufacturers of medicines used in GCC countries.	GCC Executive Board, supported by committees with representatives from all countries for each step of the tendering process. Countries must first inform on their public sector vaccine demand. The GCC centralises the tender and bid process, however each country contracts and pays suppliers individually. Member countries are required to purchase at least 60% (by value) of their total needs for each product category. Contracts with pre-selected providers are awarded based on best price.	By 2003, 10 tenders had been issued, covering 8 900 different products worth USD 508 million.
Visibility	European Shortages Monitoring Platform (ESMP) (European Council and Parliament, 2022[28]), [Implementation planned for 2025]	EU	Create a single European platform to exchange information on essential medicines during public health emergencies (PHE) and major events, using a standardised minimum information set MAHs must provide to regulators. – The dataset will include information on supply and demand for critical medicines considered relevant during a PHE or major event, in addition to the identification of its API manufacturing sites, details of alternative medicinal products, and other essential data.	The system will be established and managed by the EMA. Primarily, national competent authorities and single points of contact in MAHs will be the main providers of information to the ESMP. The ESMP will also be capable of processing information received directly from MAHs, wholesale distributors and other relevant entities.	Under current plans, only information on medicines identified as essential to respond to a PHE or a major event, and medicines for which shortages could give rise to a PHE/ major event will be collected by ESMP. The 2023 European Commission Pharmaceutical Legislation reform aims to expand the use of the platform to non-critical scenarios. The platform is planned for implementation from 2025.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
On-shoring/ re-shoring	EU Important Projects of Common European Interest (IPCEI) for the pharmaceutical industry (European Commission, n.d.[29]), [2022-]	EU	Identify industrial sectors considered strategic for the European economy and competitiveness. Support the development of technologies and production capacity for strategic medical products. Contribute to the objectives of the European Health Union and the Industrial Strategy for Europe.	Selected projects are agreed and funded by EU member states, which also determine the main areas of focus and the selection of projects to be funded.	16 EU countries have agreed to continue work towards deployment of the IPCEI for the pharmaceutical industry. IPCEIs are considered excessively bureaucratic to implement. They are mainly aimed at developing innovative projects. Although these have the potential to become long-term investments, they may not solve current shortages affecting older technologies.
Visibility	Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) (EMA, 2023[30]), [2022-]	EU	Provide oversight of the supply of medicines for the European market in response to crises. Develop lists of pharmaceutical or therapeutic subgroups considered essential for emergency care, surgery, and intensive care, which will also inform the establishment of ad hoc lists of critical medicines to be monitored during major crises or public health events. Advise the Commission regarding scenarios that should be recognised as “major events”, in accordance with Reg EU 123/2022. Co-ordinate activities to prevent and mitigate the effects of medicine shortages.	MSSG is a permanent executive body of the EMA. It includes representatives from each EU member state, a delegate from the European Commission and a delegate from the EMA. Wherever possible, decisions are adopted by consensus, otherwise by an absolute majority.	Since its implementation, regular MSSG meetings have monitored the availability of essential medical products to respond to ongoing health emergencies, such as COVID-19 and mPox. Following a surge in respiratory infections, since November 2022 the MSSG has been monitoring the supply of amoxicillin-containing antibiotics in the EU. After exchanges with EU Member States and taking account of regulatory flexibilities and increases in supply, the MSSG determined that the current shortage should not be considered a major event.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Stockpiling	rescEU (European Commission, 2022[31]), [2019-]	EU countries and, in some cases, non-EU countries such as Montenegro, North Macedonia and Ukraine	Provide countries with essential material and human resources to respond to emergencies. Support can only be approved when countries' own resources are not able to fully respond to the emergency.	Stockpiles are held in 9 EU member countries, which are also responsible for their maintenance, logistics and procurement. The European Commission provides funding for the programme. Countries request assistance to the Emergency Response Co-ordination Centre (ERCC), a EU body responsible for co-ordinating civil protection activities. ERCC evaluates the ability of rescEU resources to support the country's request and deploys the resources.	The stockpile has been a key element in the EU's response to the pandemic, supplying various EU and non-EU countries with PPE, ventilators, and protective masks. rescEU has supported Ukraine with ventilators, infusion pumps, masks and gowns since the beginning of the war in the country. To date there are no reports of rescEU providing countries with medicines, although they are also stockpiled.
Visibility	Heads of Medicine Agency (HMA) – European Medicines Agency (EMA) Joint Task Force on Availability of Authorised Medicines for Human and Veterinary Use (TF AAM) (HMA, n.d.[32]), [2016-]	EU	Provide strategic guidance for structural actions to be taken outside crises in order to address shortages of medicines in Europe. Work as a "supply and availability" hub that tracks information for different EU-level projects. Provide guidance for stakeholders on how to address different shortage situations.	The Taskforce comprises a Steering Committee and two thematic working groups (availability and supply disruptions, and communications). The Steering Committee is composed of representatives from EU Member States and HMA bodies, and co-chaired by an HMA representative and an EMA senior staff member.	The Taskforce's 2021-25 work programme includes drafting proposals for the new EU pharmaceutical legislation on preventing and managing shortages, assessing which recommendations of a European Commission report on root causes of shortages can be implemented, and establishing the EU list of critical medicines (EMA, 2022[33]). The Taskforce has organised workshops with stakeholders from EU Member States to debate better practices, discuss challenges and develop strategies to prevent and manage shortages. Multiple guidance documents have been published to support different stakeholders in managing and communicating shortages both among themselves and with the public.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Procurement	EU Directive recommending the preferential use of Most Economically Advantageous Tender (MEAT) procedures in public procurement (European Parliament and the Council of the European Union, 2014[34]), [2014-]	EU	Award tender contracts based on criteria other than price (i.e. adapt tendering criteria to the context). Utilise the procurement process to incentivise firms to achieve other policy objectives, such as more secure or more environmentally friendly supply chains.	National competent authorities or ministries of health define the organisation of tenders and the definition of award criteria.	Despite the EU directive, the uptake of MEAT has been limited. The extent to which security of supply has been included as a criterion is unknown (Vogler, Salcher-Konrad and Habimana, 2022[35]). MEAT only applies to public procurement, which accounts for significant market share in EU countries, especially for older off-patent products used in hospitals, the sector most severely affected by shortages.
Cooperation	Coordination and Harmonisation of the Existing Systems against Shortages of Medicines – European Network (CHESSMEN) (2023[36]), [2023-2026]	21 EU member states and 1 EEA country	Coordinate joint action by European countries against medicine shortages. Support the harmonisation of definitions and standards by collecting country-specific data and definitions. Identify countries' best practices in managing and preventing medicine shortages.	The initiative brings together participating countries and 5 affiliated entities under the co-ordination of the Italian Medicines Agency (AIFA). With co-funding and support from the European Commission, 7 different work packages led by different European national regulatory authorities are responsible for carrying out CHESSMEN's focus areas of work. The initiative is planned to last for 3 years.	N/A
Procurement	Baltic Procurement Initiative (Estonian Ministry of Foreign Affairs, 2021[37]), [2012-]	Estonia, Lithuania and Latvia	Joint procurement of medical products, secure access, and better prices for medicines. Facilitate mutual "lending" of medicines to partner countries facing shortages.	For each period, countries agree to jointly tender for medical products, and a lead country is selected to procure on behalf of others.	Since its implementation, the initiative has conducted four tenders for different vaccines that have been considered successful. Award criteria other than price have rarely been considered, and security of supply has not yet been used.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Procurement	Pan-American Health Organization (PAHO) revolving fund (PAHO, 2021[38]), [1977-]	41 countries in Latin America and the Caribbean	Support smaller countries' access to essential vaccines through a regional collective purchasing process. Achieve lower prices through collective bargaining. Provide technical expertise in procurement to countries with lesser resources. When feasible, ensure security of supply by awarding more than one bidder for a certain product. Ensure consistency and continuity in countries' vaccination programmes by allowing them to receive deliveries before reimbursing the fund. Support countries' efforts and expertise to forecast demand for vaccines.	Country annual vaccine demand forecasts are submitted to PAHO, which consolidates purchase orders and conducts the entire tendering process up to delivery to countries. From a list of pre-qualified bidders, the one offering the lowest price is awarded the contract. PAHO pays manufacturers up front and is only reimbursed by countries after delivering the purchased products.	47 types of vaccines were procured from 38 providers in 2021, amounting to USD 1.07 billion. 100 million people have been impacted by the regional revolving funds. Regular demand forecasting for vaccines, with technical assistance provided by PAHO, has provided more certainty for manufacturers. Vaccine shortages and delays in delivery were already reported. During periods of surges in demand, vaccine manufacturers were not able to meet PAHO's requests on time.
Procurement, visibility	Nordic Pharmaceutical Forum (NPF) (Nordic Pharmaceutical Forum, 2023[39]), [2015-]	Norway, Denmark, Sweden, Iceland, and Finland (observer)	Increase participants' purchasing power through collective bargaining and ensure security of supply. Focus on purchasing older medicines. The initiative also serves as a platform for sharing information on horizon scanning, manufacturing, and logistics. Supply chain security and environmental award criteria were also included in tenders.	A steering group chaired by Denmark co-ordinates the tendering process. Participating countries can join individual tenders voluntarily.	A pilot programme helped the setting of priorities for the joint procurement processes and an extensive market survey with suppliers was held to inform the procurement process. Two successful joint tenders for off-patent medicines have been concluded. Procurement agencies in smaller countries have been able to leverage partner countries' expertise.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Visibility	Centre for Information on the Supply of Medicines (CISMED) (Consejo General de Colegios Oficiales de Farmacéuticos, 2023[40]), [2019-]	Spain (also collaborating with France, Italy, and Portugal)	Anticipate shortages by allowing pharmacies to report real-time daily information on patient-level supply issues. Exchange information on shortages faced by countries and support standardisation in recognising and reporting shortages, and methods for quantifying supply problems. Expand this system to all European countries in future.	The original system was managed by the General Pharmaceutical Council of Spain. A joint initiative between Spain and three other European countries to exchange information based on the CISMED design comprises entities representing pharmacies in each of the collaborating countries. The project is part of the Digital Health Europe twinning scheme, with funding from the European Commission.	The cross-country collaboration has demonstrated the feasibility of information-sharing between countries on shortages in medical supply chains (e.g. a comparative analysis of shortages identified a large increase in shortages of neurology medications in all four countries between 2019 and 2020). Digital Health Europe states that the system was particularly relevant in the context of the COVID-19 pandemic.
Visibility	Canada-U.S. Working Group on supply chains (The White House, 2022[41]), [2021-]	United States and Canada	Enhance co-operation between the two countries, whose supply chains are deeply interconnected, through economic analysis of risks and mapping of key supply chains, including critical medicines, medical devices and PPE. Identify areas for greater alignment between the countries in regulatory requirements and manufacturing of essential medical products.	The working group is composed of representatives from the United States and Canada, with a mandate to provide analyses and recommendations.	A progress report released in November 2022 has led to closer collaborations between the US Administration for Strategic Preparedness and Response (ASPR), Health Canada, and the Public Health Agency of Canada on stockpiling and regulatory flexibilities for critical medical supply chains.

Policy Area	Initiative (main source), [start/end dates]	Scope of implementation	Aims and objectives	Governance	Outcomes and limitations
Visibility	USAID Global Health Supply Chain Program (GHSC) (USAID, 2023[42]), [this programme started in 2015, although programmes under this umbrella had existed before-]	Funded by the US Government, the programme is present in more than 65 low- and middle-income countries in Latin America, Africa, Asia and Oceania.	Achieve more resilient health supply chains by providing modern procurement and quality assurance tools, and other country-specific technical assistance. – The GHSC programme also provides tools standardising the information on medical products to facilitate co-operation between supply chain operators, improve planning and avoid duplication of data. Ensure continued availability of medicines for HIV, family planning, maternal and child health, and emerging public health threats.	A series of 8 complementary projects are managed by the United States Agency for International Development.	The procurement funding branch of GHSC has delivered health commodities worth USD 4.4 billion since its creation. In 2022, global standards for product identification, location identification and product master data for health commodities were implemented in 10 countries, which helped improve the availability of products in health supply chains. The project has also explored ways to increase regional production capacity in Africa for essential medicines such as antiretrovirals.

Note: This list of initiatives should not be considered to be exhaustive. NA not applicable or not available; PHE public health emergency; MAH marketing authorisation holder; API active pharmaceutical ingredient.
Exchange rates have been converted to USD using the OECD Statistics database and based on the average rate for the year the initiative was first implemented.

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OECD Health Policy Studies

Securing Medical Supply Chains in a Post-Pandemic World

Secure medical supply chains are a cornerstone of resilient health systems. Medical supply chains are complex and internationalised, often involving many suppliers. The COVID-19 pandemic, which combined an unprecedented surge in demand with interruptions in supply and trade, exacerbated pre-existing, rising shortages of essential medicines, such as antibiotics and anaesthetics, and generated shortages of medical devices, such as face masks and respirators. This report offers insights into the risks and vulnerabilities of the supply chains of medicines and medical devices. Policy options to anticipate and mitigate risks of shortages of medicines and medical devices, both routinely and in the context of severe crises, are analysed. Most importantly, the report shows that strengthening the long-term resilience of medical supply chains requires collaborative approaches that balance measures best undertaken by the private sector with those more appropriately managed by governments or supranationally.

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