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**DEVELOPING A SET OF INDICATORS TO MONITOR THE PERFORMANCE OF THE
PHARMACEUTICAL INDUSTRY**

Rishub Keelara*, Martin Wenzl*, Lisbeth Waagstein*, Marjolijn Moens*, Ruth Lopert*

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Authorised for publication by Stefano Scarpetta, Director, Directorate for Employment, Labour and Social Affairs.

(*) OECD, Directorate for Employment, Labour, and Social Affairs, Health Division

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Developing a set of indicators to monitor the performance of the pharmaceutical industry

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Abstract

The OECD's 2018 report entitled *Pharmaceutical Innovation and Access to Medicines* highlighted that public debates about pharmaceutical policy are often marked by a lack of authoritative and commonly accepted information, and that a set of agreed indicators would facilitate better informed, more fact-based pharmaceutical policy debates to benefit stakeholders, the public, policy-makers, and the pharmaceutical industry. The OECD undertook a feasibility study to establish a set of indicators to measure performance and resource allocation in the pharmaceutical industry. The work included an analysis of the indicators and their feasibility for regular reporting, a first iteration of the outputs, and an initial discussion of their implications. This Working Paper presents conclusions on the feasibility of populating indicators relating to inputs and activity of the pharmaceutical industry and considers how these, together with indicators of output and productivity, could support ongoing discussions of industry performance and inform fact-based policymaking.

Résumé

Le rapport de l'OCDE de 2018 intitulé *Pharmaceutical Innovation and Access to Medicines* soulignait que les débats publics sur la politique pharmaceutique sont souvent marqués par un manque d'informations faisant autorité et communément acceptées, et qu'un ensemble consensuel d'indicateurs pourrait alimenter des débats sur la politique pharmaceutique mieux informés et davantage fondés sur des faits, au bénéfice des parties prenantes, du public, des décideurs politiques et de l'industrie pharmaceutique. L'OCDE a entrepris une étude de faisabilité afin d'établir un ensemble d'indicateurs pour mesurer la performance et l'allocation des ressources dans l'industrie pharmaceutique. Le travail comprenait une analyse des indicateurs et la faisabilité de leur suivi régulier, une première itération des résultats, et une première discussion de leurs implications. Ce document de travail présente les conclusions sur la faisabilité de l'élaboration d'indicateurs relatifs aux intrants et à l'activité de l'industrie pharmaceutique et examine comment ces indicateurs, ainsi que les indicateurs de production et de productivité, pourraient soutenir les discussions en cours sur les performances de l'industrie et éclairer l'élaboration de politiques fondées sur des faits.

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This document presents supplementary material available online:
<https://www.oecd.org/health/Suppl-Mat-Monitor-performance-pharmaceutical-industry-2023.pdf>

Glossary of financial terms

Assets	Total balance of resources with economic value that a firm owns or controls at a given point in time with the expectation that it will provide a future benefit. Total assets are equal to total capital invested in a firm, which includes equity raised from shareholders and liabilities and debt raised from creditors.
Cost of capital	Cost to a firm in any given period for compensating shareholders and creditors for investing in the firm, expressed as a percentage of total capital invested in the firm. It represents the minimum return a firm needs to achieve to be economically viable. Cost of capital is typically estimated as a weighted average of the cost of debt, i.e. expenditure for interest payments to creditors, and the cost of equity, estimated based on a risk-free market return plus a firm-specific risk premium. The higher a firm's cost of capital, the higher risk of investing in it as perceived by investors.
Net cash flow from financing activities	All cash received or paid by a firm in a given period for funding itself. Inflows include cash received from issuing shares or debt. Outflows include cash used to pay dividends, repurchase shares, and repay debt. If more cash is used for paying shareholders and creditors than is received, net cash flow from financing activities is negative and vice versa.
Net cash flow from operating activities	All cash received or paid by a firm for conducting its ongoing and core business activities, such as manufacturing and selling goods or providing a service to customers. Inflows include cash received from customers for the sale of products. Cash outflows include cash used to pay suppliers and employees. If outflows exceed inflows, net cash flow from operating activities is negative and vice versa.
Gross operating margin	Profit margin, measured as the difference between revenue and the direct cost of goods sold, expressed as a percentage of revenue. The costs of goods sold includes costs directly associated with producing the goods and services a firm sells, including the cost of raw materials, direct labour in production and depreciation of capital equipment used for production.
Net operating margin	Profit margin, measured as the difference between revenue, direct cost of goods sold, and all operating expenditure (including all sales and marketing expenditure and, in the pharmaceutical industry, most R&D expenditure), expressed as a percentage of revenue.
Net return on assets	Return on assets after deducting the cost of capital. In competitive product and capital markets, returns on assets are expected to converge with costs of capital so that net returns on assets tend towards zero. A firm that generates a positive net return on assets generates economic profits, i.e. profits in excess of what is necessary to compensate shareholders and creditors for investing in the firm. A negative net return on assets indicates economic losses.

Return on assets Net profit margin expressed as a percentage of a firm's asset balance. It shows how well a firm deploys assets to generate profits.

Executive Summary

This paper presents the final report of a **feasibility study** whose objective was the development of a comprehensive set of indicators to monitor pharmaceutical industry performance, to better support informed debates in pharmaceutical policy. This included assessing the availability and utility of accessible data sources to construct and update these indicators. **The results confirm the feasibility of creating a set of indicators for the routine monitoring of pharmaceutical industry inputs and activity**, but also highlight the need for careful analysis and thoughtful interpretation to fully appreciate the implications for policy makers.

In this analysis, *inputs* encompass financial flows to the industry, such as revenue, tax credits, etc., while *activity* captures the purposes for which financial resources are deployed by firms, and includes both financial (e.g. R&D expenditure, cash outlays) and non-financial indicators (e.g. product development, clinical trials).

The development of the indicators drew on a variety of sources including official OECD statistics reporting aggregate data for the pharmaceutical industry at country level; clinical trial registry data compiled by WHO via the *International Clinical Trials Registry Platform* (ICTRP); prescription medicine sales data from the IQVIA MIDAS® database; firm-level financial data from the OECD *Bureau van Dijk* (BvD) *Orbis* and *Refinitiv Datastream* databases; and data from the *AdisInsight* proprietary database of drug development projects from Springer Nature. A key requirement was that data sources should be sufficiently granular to enable the analyses to explore the heterogeneity of the industry and its activities.

In addition to demonstrating the feasibility of deriving the indicators from the available data, a first iteration of the outputs was generated. The indicators (as well as methods and results) are presented according to the domains of *input* and *activity*, both financial and non-financial. Subject to data availability, indicators are reported for the years 2010 (beginning from 2005 for some of the financial indicators based on firm-level data) to 2020 or the latest year available.

An initial finding from this first iteration of indicators confirms that the **firms that make up the pharmaceutical industry are highly heterogeneous**. For example, publicly listed firms tend to spend more on R&D and operating expenses and less on production than their unlisted counterparts. A small group of large firms and publicly listed firms in OECD countries are the most profitable, and while older and larger publicly listed firms can finance themselves from revenue, younger and smaller firms tend to rely on capital markets for financing. Not surprisingly, perhaps, different types of pharmaceutical companies – manufacturers, generic companies, emerging biopharma research companies – all have different financing, investing, operating, and research behaviours, which cannot be adequately elucidated from aggregate figures. There also appear to be structural differences between pharmaceutical firms in OECD and non-OECD countries, with publicly listed firms in the latter being more manufacturing-focused and less R&D-focused.

In terms of financial *inputs*, in aggregate, **revenues from sales of products were the principal financing source** for the industry in the period analysed. Total revenue from prescription medicines increased by 47% from 2010 to 2021 (USD 815 billion to 1,196 billion, respectively, in 2015 USD at constant rates), with only a small decrease in 2012 (-1.6%). In 2021, the US market generated the highest overall revenue (USD 576 billion) and **OECD countries accounted for 78% of global revenue**. While the largest growth between 2010 and 2021 occurred in China (+181%), the United States market also grew faster (+49%) than OECD countries collectively (+42%). Originator medicines consistently accounted for nearly two thirds

of total revenues (66.2% in 2021), though this varied across therapeutic areas, with oncology originators generating the highest proportion (92% of total oncology revenue and 13.1% of total revenue overall).

The **net cash flows from financing activities** indicator suggests that the industry used more cash to pay shareholders and creditors than it raised from capital markets, **as aggregate values were negative** in all years analysed, except 2015 and 2020, and ranged from -6.0% of total assets in 2006 to +2.1% in 2015. Conversely, the **industry generated more cash from sales of its products than it spent on production and in operating expenditure, including R&D: net cash flows from operating activities were positive** in all years, ranging from 12.6% of total assets in 2008 to 7.6% of assets in 2020.

However, the **aggregate results obscure a substantial degree of heterogeneity at the firm level**. For example, at the median of the distribution, **net cash flows from financing activities** were consistently positive, and only firms in the lowest quartile (of the firm distribution in the indicator) exhibited consistently negative net cash flow from financing activities, similar to the aggregate. This suggests that a small number of large, mature and/or profitable firms used significant amounts of cash to pay shareholders and creditors, and these drove the aggregate patterns. The contrary was the case for **net cash flows from operating activities**, with a consistently positive aggregate driven by large and profitable firms, although the median was closer to zero. Overall, this suggests that **the majority of firms raised more cash from capital markets than they used to pay shareholders and creditors**, and only **about half the firms generated more cash from sales than they spent on operating activities**.

Although the data were limited, **direct subsidies by government, higher education and other sectors that fund R&D represented 10% of R&D expenditure**. Across a small number of OECD countries with available data¹, **tax credits for R&D were a relatively minor financing source**. However, this indicator does not capture major players, such as the United States, and thus is not currently suitable for routine reporting.

Among the financial indicators for industry *activity*, firm-level data suggest that in aggregate, **production costs accounted for 30% to 40% of revenue** of the pharmaceutical industry and **operating expenditure, including R&D expenditure, accounted for 40% to 50% of revenue**. **R&D expenditure** amounted to USD 148 billion in 2020 (or the latest year with available data), of which USD 129 billion was spent in OECD countries and USD 18.7 billion in China. R&D expenditure in the United States alone accounted for 69% of the OECD total, followed by Japan (10%) and Germany (6%). Between 2010 and 2019, R&D expenditure increased in real terms by 39% in OECD countries, and by 189% in China.

Among OECD countries with available data, **R&D expenditure accounted for 30% of gross value added (R&D intensity), which is higher than for any other industry**. However, this aggregate was heavily driven by the United States and Japan, with R&D intensities below 20% in all other OECD countries, except Belgium (27%) and Slovenia (23%). **Aggregate R&D expenditures were strongly driven by large and publicly listed firms headquartered in OECD countries**, while unlisted firms and firms headquartered in non-OECD countries spend little on R&D. Nevertheless, there is also a significant number of smaller firms that invest heavily in R&D but generate little revenue.

Overall, the pharmaceutical industry generated **net operating margins of between 10% and 20%** (as a proportion of total revenue) between 2005 and 2020, **higher than in most other industries** (including the aggregate of four other R&D-intensive industries), except the software industry, which generated comparable or higher net margins over the entire period. With a slight downward trend over time, pharmaceutical net operating margins had converged with those of other R&D-intensive industries by

¹ OECD countries with available data were Belgium, the Czech Republic, France, Greece, Hungary, Italy, Lithuania, Netherlands, Norway, Portugal, Slovak Republic, Slovenia, Sweden, and Türkiye. The interpretation of these results is significantly hampered by the lack of data from the United States, where large public funders, such as the National Institutes of Health (NIH), provide significant support for pharmaceutical research.

2017, with net operating margins equivalent to 3% to 9% of total capital invested. While **return on assets (ROA)** was also higher in the pharmaceutical industry than in most other industries early in the period, it had also converged with that of other R&D-intensive industries and the overall manufacturing sector by 2017. Analyses of profitability margins also suggest that there may be a structural difference between the pharmaceutical industries of OECD and non-OECD countries, with OECD countries home to a higher number of large and profitable as well as loss-making R&D-focused firms and a stronger presence of lower-margin manufacturing activities in non-OECD countries.

After deducting costs of capital to calculate **net ROA**, the results show that in aggregate, **there has been a downward trend in profitability. In aggregate, publicly listed firms in the pharmaceutical industry generated negative net ROA** in all years except 2006 (range -5.2% in 2018 to +0.5% in 2006), i.e. they made economic losses². **Cost of capital** represents the minimum return that is necessary for a firm to invest and is an indicator of investment risk associated with business expansions, accounting for equity and debt. Overall, the cost of capital in the pharmaceutical industry is comparable to other R&D-intensive industries, and since 2019, it has dropped to below the average of these other industries. This suggests that overall, **investors do not consider the pharmaceutical industry to be riskier** than other R&D-intensive industries. Aggregate cost of capital was relatively constant over the period of analysis, similar to other R&D intensive industries, suggesting that **a downward trend in net ROA can be attributed to a downward trend in returns or profits**, rather than an **increase in investment risk**. Importantly, however, the firm-level distribution was strongly skewed. **In all measures of profitability, large firms drove aggregates**, and while there were significant numbers of loss-making firms at the low end of the distribution, there were also a number that were profitable. Large pharmaceutical firms also have lower costs of capital than their smaller counterparts. In terms of **net return on assets (ROA)**, the lowest 75% of firms in the distribution were always loss-making, while **the top 10% consistently earned returns in excess of their costs of capital, with the 95th percentile ranging from 5% to 11%, and the 99th percentile approximately 20% to 50%**.

Given the underlying heterogeneity of firms in the sample, further analysis was conducted on a geographically-stratified random sample of 1000 firms to assess the feasibility of disaggregating the financial activity indicators by firm type. The indicators of Net ROA and net cash flows from operating and financing activities were disaggregated by firm type (e.g. manufacturer, research-based biopharmaceutical firms, large pharmaceutical conglomerates, contract research organisations,) and sub-type (publicly listed / unlisted, generic drugs, research-based). **Significant differences were found across different firm types for these indicators**. Most notably, manufacturing-based companies held consistent, but slim margins, while the performance of research-based companies differed widely by size. Smaller research-based firms typically had negative returns, positive net cash flows from financing activities, and negative net operating cash flows, while larger firms (defined as the top 15 revenue-generating conglomerates) had the contrary – positive returns, negative net cash flows from financing activities and positive net operating cash flows – thus, illustrating that **aggregate estimates do not adequately characterise the industry as a whole**. Further work to segment the financial analysis by pharmaceutical firm type and size and interpret the findings with respect to research activity and financing is warranted.

Non-financial indicators of industry *activity* also show that pharmaceutical **R&D activity has increased in the past decade**. By the end of 2021, 35 521 unique product-indication pairs were in active development, compared with fewer than 17 000 in 2011. **The number of new product-indication pairs that entered pre-clinical or clinical development increased by a factor of 4**, from approximately 2 000 in 2012 to more than 8 000 in 2020. Of 20 415 products in active development at the end of 2021, 89% originated exclusively within industry entities and 93% had at least one industry entity as an originator. Although data

² This is based on an ex-post analysis of profitability and cost of capital and does not take into account ex-ante market valuations of firms or assets, which are based on returns investors expect when investing in a firm or firms expect when making new investment decisions.

may somewhat overstate the role of the pharmaceutical industry in R&D relative to other entities, such as universities, hospitals and public research institutes, the industry plays a major role in R&D. **Oncology accounted for the largest proportion of product-indication pairs in every year since 2011**, and its importance has increased steadily, from 27% of all product-indication pairs in 2011, to 38% in 2020 and 40% in 2021. In fact, the top six disease categories (oncology; infectious and parasitic diseases; neurological conditions; endocrine, blood, and immune disorders; diseases of the musculoskeletal system and connective tissue; and cardiovascular diseases) remained the same throughout this period. Approximately 47% of the product-indication pairs in development at the end of 2021 were in pre-clinical phases, followed by phase 2 (19%), phase 1 (13%), and phase 3 (9%). OECD countries accounted for nearly 80% of all product development projects, with the United States representing 27% of the total. China attracted 6% of product development activities, more than any OECD country other than the United States. It should be noted that these results encompass all products in development, and do not take into consideration whether they ultimately entered the market. Furthermore, as this indicator measures the number of product-indication pairs, expanding indications for products in prominent therapeutic areas, such as oncology, could also contribute to the increase.

Of the **clinical trials of medicines** registered in the International Clinical Trials Registry Platform (ICTRP) that commenced recruitment since 2010 and were active or completed by the end of 2021, **48% had an industry entity as primary sponsor and 61% had industry involvement** (i.e. at least one industry entity as primary or secondary sponsor, or as a named funding source). This shows that both, industry and non-industry entities contribute significantly to clinical trial activity. The **number of new trials of medicines with industry involvement increased by 48% between 2010 and 2020**, to a total of 8 562, before declining again by -7% in 2021. **Oncology attracted the most trial activity in all years**, accounting for 25% overall. While neuropsychiatric conditions, infectious and parasitic diseases, and cardiovascular diseases were also in the top 4 until 2019, respiratory infections moved into second place in 2020, driven by COVID-19. Trial sizes varied over time, with initial estimates showing that the median number of participants in Phase 3 trials declined from years 2010 to 2021. While this could reflect a pivot toward niche markets and rare diseases, interpretation is limited by significant data quality issues and render it an unsuitable indicator for routine reporting at this time. Similar to products in development, the clinical trial data relate to all active trials, and do not take into account the complexity of the research or success of the trials. Importantly, this indicator, like those above, measures *activity* in the pharmaceutical sector, not *output*.

The results should be interpreted with caution. A comprehensive understanding of these indicators requires their closer examination within the context of the evolution of the pharmaceutical industry - of changing R&D priorities, product portfolios, and target markets. A common perception is that pharmaceutical companies invest over long periods of time to develop novel medicines, the most successful of which deliver profits for the firms and their investors. However, the reality is more complex. For example, smaller firms are increasingly driving early research and product development, while larger firms still attract the bulk of revenues (Congressional Budget Office, 2021^[1]). This manifests as larger companies investing less in developmental research and instead acquiring smaller biotech firms with patents and promising pipelines (Rossi, Thrassou and Vrontis, 2015^[2]; Congressional Budget Office, 2021^[1]). Furthermore, the increasing financialisation of large companies, as exhibited in the consistently negative net cash flows from financing activities, may be shifting their focus to more short-term sales and revenue-driving activities (Busfield, 2020^[3]). This can also be seen in the consolidation of portfolios and increased targeting of less competitive markets such as rare diseases (Ascher et al., 2016^[4]; Årdal, Lopert and Mestre-Ferrandiz, 2022^[5]). Many of these factors will influence performance and activity in complex ways that impact the indicators explored in this paper. Finally, it should be noted that the effects of the COVID-19 pandemic are not yet fully reflected in this analysis, as the time series in most datasets end in 2019 or 2020. The results are summarised in Table 1 below.

Table 1. Summary of key indicators

Based on data from 2010 to 2020 (from 2005 for selected firm-level financial indicators)

Domain	Indicator	Industry aggregate	Notes
Financial inputs	Revenue	+47% in global prescription medicine revenue in real terms (2010 – 2021) OECD countries accounted for 78% of global market	Consistent growth since 2010, except 2012 (-1.6%), to USD 1.296 billion in 2021 US highest share (57% of OECD, 44% overall), China highest growth (+181%)
	Net cash flows from financing activities	-6.0% of assets (in 2006) to +2.1% (2015) (publicly listed firms only)	Negative in all years except 2015 and lower than in most industries, except software. Driven by the most profitable quartile of firms, with positive cash flows in the upper 75% of firms.
	Direct subsidies for R&D	10% of R&D expenditure in 26 OECD countries	OECD aggregate driven by the United States (73% of OECD total), highest proportion of R&D expenditure in the UK (49%).
	Tax credits for R&D	USD 1.5 billion in tax credits for R&D (2019)	Data only available from 14 OECD countries (excluding the United States) accounting for 6% of R&D expenditure in OECD.
Financial activity metrics	Net cash flows from operating activities	7.6% of assets (in 2020) to 12.6% (2008) (publicly listed firms only)	Positive in all years and comparable to other R&D-intensive industries. Firm-level median close to zero – about half of firms have negative and half have positive cash flows. Aggregate driven by the largest 25% of firms that generated consistently positive net cash flows.
	Profitability	Gross operating margins: 51% (unlisted firms in 2015) to 70% (publicly listed firms in 2005) Net operating margins 10% (unlisted firms in 2019) to 20% (listed firms in 2009) Net returns on assets -5.2% (in 2018) to 0.5% (2006) (publicly listed firms only)	Downward trends in gross and net operating margins over time, convergence with other R&D-intensive industries. Net ROA at the 95 th percentile between 5% and 11%. Large and mature firms more profitable than small and young firms.
	Cost of capital	6.7% (in 2020) to 9.4% (2010) (publicly listed firms only)	Comparable to other R&D-intensive industries.
	R&D expenditure	USD 148 billion (2020 or latest available), USD 129 billion in OECD countries 39% real-term growth since 2010 R&D intensity 30% of gross value added in OECD countries	OECD aggregate and growth driven by publicly listed firms and the United States (69% of OECD), fastest growth in China. R&D intensity driven by United States and Japan, <20% in most OECD countries; OECD aggregate higher than in other industries.
Non-financial measures of R&D activity	No. of product development projects	35 521 product-indication pairs in active development in 2021 vs. 17 000 in 2011 89% originated with industry involvement 8 277 new product-indication pairs in active development in 2020 vs. 2 077 in 2012	Highest proportions in oncology and in the United States.
	No. of clinical trials	7 971 new medicines trials with industry involvement in 2021 vs. 5 790 Only 57% of all medicines trials with industry involvement	Highest proportions in oncology in all years, with a spike reflecting Covid-19 trials in 2020 and 2021.

Note: For details and sources, refer to the respective results section for each indicators.

Source: OECD analysis

1 Introduction

1. The OECD's 2018 report entitled *Pharmaceutical Innovation and Access to Medicines* (2018^[6]) noted that public debates about pharmaceutical policy are often marked by a lack of authoritative and commonly accepted information supporting the arguments of the stakeholders involved. Although divergent viewpoints are legitimate in public debates, stakeholders should be able to agree on a core set of underlying facts.
2. The lack of health policy-focused and commonly accepted information may undermine the ability of policy makers to make informed and balanced decisions. This is concerning because the functioning of the industry itself relies heavily on public policy, and the availability of effective medicines, which is dependent on a well-functioning industry and pharmaceutical market, has an immediate impact on the functioning of health systems. Health systems need the industry to provide a reliable supply of effective medicines to treat diseases and improve population health. One objective of public policy is to facilitate this, by maximising the output of the sector given the public and private resources invested.
3. Governments aim to achieve these goals through tight regulation of the sector and some significant public spending. Although private investment plays a major role, for example through venture capital and the stock market, large amounts of public funding also flow to the pharmaceutical industry. This includes direct public funding of pharmaceutical research, as well as R&D subsidies and tax credits. Across the OECD, direct government funding of health-related R&D represents more than USD 60 billion, or 0.1% of GDP. In addition, pharmaceutical markets in OECD countries are highly regulated, and a large share of pharmaceutical expenditure is funded through public or compulsory health financing schemes, which are a significant source of revenue and investment incentive for the industry. This environment calls for transparency with respect to the allocation of resources by the industry.
4. A set of agreed indicators would facilitate better informed, more fact-based pharmaceutical policy debates, and would therefore be of benefit to all stakeholders, including the general public, policy makers and the industry itself, and could also help restore and strengthen trust among them. It could also facilitate the establishment of a reporting cycle to generate and publish indicators periodically. A periodic reporting process would provide the additional benefit of generating longitudinal datasets that would enable trends to be assessed in addition to cross-sectional snapshots.
5. This working paper presents analyses undertaken to evaluate the feasibility of establishing a set of core indicators. Chapter 2 describes the conceptual basis and proposes a set of indicators. Chapter 3 identifies the data sources used to generate the indicators and assesses the feasibility of periodic reporting and analysis. Chapter 4 presents a first iteration of the indicators and discusses the results. Finally, Chapter 5 discusses the implications of the analysis and proposes a possible periodic reporting cycle.

2 Conceptual framework and selected indicators

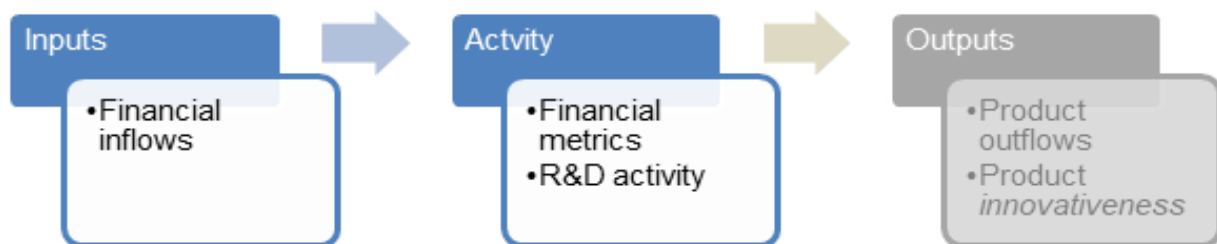
2.1 Selection of indicators takes a health policy perspective

6. The selection of indicators was guided by the principle that health policy aims to improve population health, and that access to effective medicines produced by a viable industry is an important contribution to achieving that objective. Indicators that would help policy makers understand whether the financial resources that flow to the pharmaceutical industry are deployed in ways that result in effective products for areas of need should therefore cover three domains (see Figure 2.1), measuring, from a health policy perspective:

1. All financial flows to the industry, which are considered *inputs*. This includes industry revenue, direct public funding of R&D or subsidies for other types of industry activity, and tax credits.
2. *Activity* indicators, which provide information about how financial resources are deployed by firms in the industry. These include financial indicators, such as industry R&D expenditure, other types of industry expenditure and cash outlays, and the proportion of industry revenue remaining as profit after investments are made and expenditures accounted for, as well as non-financial indicators of R&D activity, such as clinical trials.
3. *Outputs*, capturing information about the medicines the industry provides to health systems and their utility, in terms of health benefits they deliver.

7. Indicators explored in this working paper only address the *input* and *activity* domains of the framework shown in Figure 2.1. Financial flows to the industry, such as industry revenue, direct public funding of R&D or subsidies for other types of industry activity, and tax credits, are considered inputs. Activity indicators provide information about the purposes for which financial resources are deployed by firms in the industry. They include financial indicators, such as industry R&D expenditure, other types of industry expenditure and cash outlays, and what proportion of industry revenue remains as profit after investments are made and expenditures accounted for. They also include non-financial indicators of R&D activity.

Figure 2.1. Framework for defining indicators of resource allocation in the pharmaceutical industry from a health policy perspective



Note: The current analysis does not extend to indicators in the Output domain (in grey).

8. Table 2.1 provides an overview of all indicators across the input and activity domains that were proposed at the inception of the project. This draft report shows a first iteration of all indicators in Table 2.1 that are on non-shaded lines and explores the feasibility of calculating these indicators broken down by disease area, country or geographic region, and firm size or age, to reflect the heterogeneity in the industry. No data sources could be identified to construct an indicator of sales and marketing expenditure (shaded grey). All other indicators were derived from available data sources, as outlined in Table 3.1.

Table 2.1. Proposed list of indicators across input and activity domains, and dimensions of disaggregation

Domain	Type of indicator	Indicators	Industry total	By disease area	By country / geographic region	By firm size / age
Inputs	Financial inflows	Revenue	√	√	√	
		Cash inflows from operating and financing activities	√		√*	√
		Direct subsidies Tax credits	√		√	
Activity	Financial metrics	Research & development (R&D) expenditure	√	√	√	√
		Sales & marketing expenditure	√			
		Cash outflows for operating and financing activities	√		√*	√
		Cost of capital	√			√
	Profitability	√		√*	√	
	Non-financial measures of R&D activity	Number of product development projects	√	√	√	
		Number of clinical trials	√	√	√	
Number of people enrolled in clinical trials		√	√	√		

Notes: Data sources could not be identified for sales and marketing expenditure (shaded dark grey).

* For these financial indicators based on firm-level data, only a breakdown between OECD and non-OECD countries is reported.

Source: Authors

2.2 Presenting a global picture of ‘the industry’

9. In general, indicators have been constructed to monitor the global pharmaceutical industry in aggregate. The “pharmaceutical industry” is generally defined, in line with existing OECD classification systems of economic activity, as the aggregate of all firms in the business enterprise sector whose main

activity is the production of medicines for human use.³ The business enterprise sector comprises all entities capable of generating a profit or other financial gain for their owners.⁴

10. However, *'the pharmaceutical industry'* is highly heterogeneous, and individual firms vary both in their nature and the activities in which they engage, thus necessitating some disaggregation to inform policy. This feasibility study therefore aimed to disaggregate indicators to identify and monitor separately relevant segments of the industry as discussed below and outlined in Table 2.1. Data availability nevertheless constrained the scope for disaggregation to some degree. Methods and disaggregation for each indicator are discussed in more detail in Chapter 3.

11. Most importantly, one objective of this feasibility study was to identify and generate indicators of the R&D-based industry, which comprises the subset of pharmaceutical firms that specialise mainly in R&D, product development and/or in manufacturing and selling of novel medicines that benefit from patent protection and regulatory exclusivities, also referred to as 'originator' products. Where data permitted, indicators were generated separately for the R&D-based industry and the segment of the industry that specialises in the manufacture and sale of generics or biosimilars, which enter the market after the loss of exclusivity of the relevant originator product. In addition, the industry comprises firms that differ, for example, in terms of maturity, i.e. from early-stage start-ups to mature multinationals; or in terms of ownership and financing, including firms that are privately held and those that are listed on public stock markets. Where data permitted, indicators aimed to provide insights into these differences.

12. The industry is also more active in some countries than in others, which may reflect differences in the availability and costs of production factors or market size, as well as of policies to attract and support industry activities. Thus, it also made sense to disaggregate certain indicators by country. Where possible and relevant, indicators were also disaggregated by disease area, to illustrate the relative importance accorded to each of them, and to assess the extent to which these reflect population health needs.

13. Where data permitted, the pharmaceutical industry was also compared to the four other R&D intensive and high-tech industries below, which are characterised by significant R&D expenditure. These are shown in aggregate and/or individually where relevant.

- Manufacture of computer, electronic and optical products (ISIC Division 26, NACE Code 26);
- Manufacture of air and spacecraft and related machinery (ISIC Group 303, NACE Code 303);
- Manufacture of medical and dental instruments and supplies (ISIC Group 325, NACE Code 325); and,
- Software publishing (ISIC Group 582, NACE Code 582).

14. Finally, where possible, the pharmaceutical industry was also compared to the aggregate of all manufacturing industries (ISIC Section C, NACE Code C) and to the aggregate of all other non-financial sectors of the economy, excluding pharmaceuticals. It should be noted that industry codes are not well-defined categories, so other research or health-based firms may be included.

³ The pharmaceutical industry is defined as, ISIC Code 21 "Manufacture of basic pharmaceutical products and preparations" in all aggregate data; All firms assigned to NACE codes 2110 "Manufacture of basic pharmaceutical products", 2120 "Manufacture of pharmaceutical preparations", and 7211 "Research and experimental development on biotechnology" in firm-level microdata; or in data that do not include commonly accepted industry codes, in particular data about R&D activities, all entities that are part of the business enterprise sector, as determined by the OECD Secretariat.

⁴ This is a precis of the full, formal definition. The classification of all business enterprise entities into distinct industries, including the pharmaceutical industry, is based on existing taxonomies used in OECD and other international statistics that are disaggregated by industry, such as ISIC Rev. 4 industry codes used in the OECD System of National Accounts (SNA) and OECD R&D Statistics, and NACE Codes. For a more detailed discussion, see the OECD Frascati manual (OECD, 2015, pp. 81-107⁽⁷⁾)

3 Data sources

15. This section describes the data sources used in the construction of each indicator. Indicators are presented separately for the *input* and *activity* domains. The same firm-level datasets were used for all firm-level financial indicators, including cash flow from financing and operating activities, R&D expenditure, profitability, and cost of capital. A summary of data sources is provided in Table 3.1, and methods for the calculation of indicators are outlined in the [Supplementary Material](#).

3.1 Inputs

16. Indicators of inputs include revenue, cash flow from financing activities, direct subsidies for R&D and tax credits for R&D, as shown in Table 2.1.

3.1.1 Revenue

17. This indicator reports global **industry revenue** in a cross-sectional view of the latest year with data and in a longitudinal view for the years 2010 to 2020. Revenue is defined as the aggregate sales of all pharmaceutical firms, at ex-factory prices. Revenue from current sales is a major source of funding for mature pharmaceutical firms that hold marketing authorisation for one or several medicines.

Data Sources

18. The primary data source considered for the indicator of **industry revenue** is aggregate data from the OECD National Accounts database (based on the System of National Accounts [SNA] framework). OECD National Accounts provide data on economic output by country, as a component of GDP, and the Supply and Use Tables (SUT) of the SNA provide estimates of industry output, at ex-factory prices by 2-digit ISIC Rev.4 codes.⁵ Revenue is approximated using industry output reported in SNA and SUT data, defined as the goods produced within an establishment that become available for use outside that establishment, plus any goods produced for the establishment's own use. The main advantage of the SNA and SUT is their 'whole economy' approach rooted in the standard national accounts methodology and using standard product and industry classifications. More information on the definitions and methods used for SNA / SUT data are available in the [Supplementary Material](#).

19. A secondary data source, provided by IQVIA, estimates revenue at ex-factory level based on invoice prices reported in purchases by downstream stakeholders of the distribution chain, including wholesalers, pharmacies and hospitals, after adjustments for distribution chain mark-ups (excluding rebates or discounts). This secondary data source was required for two main reasons. First, the SNA and SUT data are limited by lack of timeliness and a lack of granularity at the level of the pharmaceutical industry. SNA and SUT data typically become available with a lag of at least one to three years. Recent data at the level of the pharmaceutical industry are not available for all OECD and non-OECD countries with major pharmaceutical markets. Second, no breakdowns by products of a given industry are available from SNA data; the data source therefore does not permit the disaggregation of sales by disease area. One limitation of the IQVIA data source is that it only includes sales revenues from prescription medicines, while

⁵ For SUT data, also see Discussion Paper DELSA/HEA(2019)14, presented at the joint Workshop of the Expert Group on Pharmaceuticals and Medical Devices and the Working Party on Health Statistics in October 2019. Data from SNA Supply-Use tables (SUT) have also been evaluated as a possible source for estimating total pharmaceutical expenditure.

companies in the sample may derive revenues from over-the-counter products or from other medical products and devices. In our estimates, these sales are not taken into account, however related activities will be taken into account in other cash flows. Limitations of the IQVIA methodology and further definitions are outlined in the [Supplementary Material](#).

20. Data on pharmaceutical expenditure from the OECD System of Health Accounts (SHA) may also be used as another secondary data source, for instance to estimate the share of generics in total industry revenue. Pharmaceutical expenditure exceeds industry revenue in any given country because expenditure includes margins of entities in the distribution chain, including wholesalers and retail pharmacies, and value added tax (VAT) where applicable. These need to be accounted for when using expenditure data to estimate industry revenue at ex-factory prices.

3.1.2 Net cash flows from financing activities

21. This indicator reports industry **net cash flows from financing activities** in a longitudinal view for the years 2005 to 2020, to provide insight into how the industry finances itself. The indicator shows the relative importance of cash inflows from financing activities, capturing the component of financial flows between the industry and capital markets.

22. Firms can fund themselves from various sources, including capital markets, where venture capitalists, private equity, and investors in public stock and debt/bond markets provide financing. These cash inflows may be particularly important for immature firms that invest in the development of a single or small number of R&D projects but do not yet have sales from existing products to fund these investments. However, firms can also fund themselves from the sale of products. This can be a major source of funding for mature pharmaceutical firms that hold marketing authorisation for one or several medicines and is captured by cash flows from operating activities (see Section 3.2.1).

Data Sources

23. Firm-level microdata from the OECD Capital Market Series dataset, Refinitiv Datastream database were used to construct an unbalanced panel dataset for the indicator of cash flow from financing activities. Net cash flows for financing activities, including debt and equity, were computed as a ratio of total assets in aggregate for the pharmaceutical industry for each year (2005 to 2020). Data are only available for publicly listed firms. The OECD-Orbis Corporate Finance dataset, the other source of firm-level financial data available to the OECD Secretariat, contains no detailed cash flow variables. Further information on data coverage and methodology are available in [Supplementary Material](#).

3.1.3 Direct subsidies for R&D

24. This indicator reports **direct subsidies to the pharmaceutical industry for R&D** in a cross-sectional view of the latest year with data, and in a longitudinal view for the years 2010 to 2020. Pharmaceutical firms receive funding from non-industry entities for performing R&D, which can be a significant source of funding in particular for young firms that have product candidates at various stages of their development pipeline but generate no or little revenue from sales. Funding can be provided by governments and their agencies, higher education institutions, and private non-profit entities, such as philanthropic organisations.

Data sources

25. Data on **direct subsidies to the pharmaceutical industry for undertaking R&D** can be extracted from the OECD Research & Development Statistics (RDS). The main advantage of OECD RDS data is that they provide aggregate estimates of R&D expenditure in the business enterprise sector (BERD)

according to the standards defined in the Frascati manual (OECD, 2015^[7]), which ensures a high level of consistency and comparability over time and across industries and countries. These data have previously been used to report total R&D expenditure in the pharmaceutical industry across OECD countries, and to compare the R&D intensity of the pharmaceutical industry with other R&D-intensive industries.⁶

26. The main drawback of OECD RDS is that data become available with a significant time lag, and that data availability and geographic coverage decrease with increasing levels of disaggregation, which is a particular problem for the pharmaceutical industry (see Section 4). Some data gaps can be filled by using data published by national statistics and other agencies, for instance the United States, which alone accounts for two-thirds of total pharmaceutical BERD in OECD countries (OECD, 2021^[8]). For the United States, the National Science Foundation (NSF) publishes data on business and industry R&D, based on the national Business Enterprise Research and Development Survey and its predecessors, which include estimates of BERD broken down by industry and funding source (see (NSF, 2021^[9])).

27. While the pharmaceutical industry may also receive subsidies of a different nature and for purposes other than R&D, no data source could be identified to construct an indicator of direct subsidies overall, regardless of their purpose.

28. Further information on data definitions and methods is available in [Supplementary Material](#).

3.1.4 Tax credits for R&D

29. This indicator reports **tax credits** from which the pharmaceutical industry benefits as a result of undertaking R&D. Tax credits are an indirect means of incentivising private sector activities, and governments of OECD countries have increased their use significantly since the year 2000 (OECD, 2020^[10]; OECD, 2020^[11]; OECD, 2021^[12]). In addition to direct subsidies, they can represent a major source of public sector support for the pharmaceutical industry.

Data sources

30. Data from the official OECD R&D Tax Incentives Survey are the primary data source for this indicator. Based on this survey, the OECD compiles from national statistical agencies country-level estimates of Government Tax Relief for R&D Expenditure (GTARD) and estimates the implied marginal tax subsidy rates for R&D. GTARD is a measure of the cost to governments (or benefit to firms) of provisions that imply a more favourable treatment of R&D activities relative to otherwise comparable activities that do not qualify as R&D.⁷ The main limitation of this data source is geographic coverage at the disaggregated level of the pharmaceutical industry and lack of data for a longitudinal view. Until 2021, these statistics were only compiled for entire national economies but not disaggregated to the industry-level. From 2022, data are available for 14 to 15 OECD countries for a number of R&D-intensive industries, including pharmaceuticals. This set of countries includes the United States and a number of EU Member States in which the pharmaceutical industry has a significant R&D footprint, including Belgium, France, Italy and Sweden.

31. Estimates from the MicroBERD project, undertaken under the auspices of the OECD Working Party of National Experts on Science and Technology Indicators (NESTI), could serve as a secondary data source for this indicator. MicroBERD investigates the structure, distribution and concentration of business R&D, the sources of R&D funding, and the incidence and impact of public support for business R&D,

⁶ See OECD (OECD, 2021, pp. 244-45^[8]; Galindo-Rueda and Verger, 2016^[27]). R&D intensity is defined as business enterprise R&D expenditure as a share of gross value added in the same industry. R&D intensity in the pharmaceutical industry is compared to the electronic & optical products and the air & spacecraft industries; and the wider economic sectors of manufacturing (including pharmaceuticals); mining & quarrying; total services; utilities; agriculture; forestry & fishing; and construction.

⁷ See OECD (2021^[12]) for a more detailed discussion of relevant definitions. Activities that qualify as R&D are generally defined according to the OECD Frascati manual (OECD, 2015^[7]).

complementing data from official surveys with estimates based on administrative microdata (OECD, 2020_[10]). The use of MicroBERD estimates increases the geographic coverage of the indicator. However, neither official survey nor MicroBERD data are currently available for a number of OECD countries in which the pharmaceutical industry has a significant R&D footprint, including Japan, Germany, Switzerland, Korea and Denmark. Further information and methodology are available in [Supplementary Material](#).

3.2 Activity

32. Indicators of activity include the financial indicators of cash flow from operating activities, profitability and cost of capital, sales & marketing expenditure, and R&D expenditure; and the non-financial indicators of R&D activity, number of product development projects, number of clinical trials and the number of people enrolled in clinical trials, as shown in Table 2.1.

3.2.1 Net cash flows from operating activities

33. This indicator reports **industry cash flows** from operating activities in a longitudinal view for the years 2005 to 2020, to provide insight into whether the operations of the industry result in net cash in- or outflows. It shows the relative importance of cash in- and outflows from operating activities, capturing financial flows to and from the industry that result from the operating activities of pharmaceutical firms, including cash inflows from product sales and outflows to cover costs of production and for operating expenses, including R&D.

34. Firms can fund themselves from various sources, including from the sale of products. This can be a major source of funding for mature pharmaceutical firms that hold marketing authorisation for one or several medicines. Firms also rely on funding from capital markets, where venture capitalists, private equity investors, and investors in public stock markets and debt/bond markets provide financing. These cash inflows may be particularly important for immature firms that invest in the development of a single or small number of R&D projects but do not yet have sales from existing products to fund these investments themselves.

Data sources and methods

35. The same data source and methods are used as for the indicator of cash flow from financing activities (see above).

3.2.2 Profitability

36. Indicators of **profitability** report the performance of the pharmaceutical industry through four different measures, in a longitudinal view for the years 2005 to 2020, and provide a comparison of the pharmaceutical industry with other industries and the wider economy. The following metrics are reported:

- **Gross operating margin:** profitability after production costs only.
- **Net operating margin:** profitability after all operating costs, including production costs, R&D costs and other operating expenditure, including expenditure for sales & marketing.
- **Return on assets (ROA):** profitability for investors, in terms of net margin relative to the total capital invested, including debt and equity financing.
- **Net return on assets, i.e. ROA less cost of capital (COK):** risk-adjusted profitability for investors, in terms of net margin relative to the cost of total capital invested, which increases with investment risk.

Data sources

37. Measures of profitability are based on an unbalanced panel of firm-level microdata from the OECD Orbis and Refinitiv Datastream databases.

- OECD Refinitiv Datastream is used to generate all measures listed above for firms that are **publicly traded** on stock exchanges, with cost of capital (COK) extracted from Bloomberg and completed with information from the FactSet database where necessary.
- OECD Orbis is used for estimating gross and net operating margins and returns on equity and assets (ROE and ROA), only for firms that **are not publicly listed**.

38. The panel dataset based on OECD Capital Market Series dataset, Refinitiv Datastream contains financial information of all publicly listed firms. It covers 50 087 unique non-financial firms.

39. OECD Orbis contains data on nearly 400 million firms, both those that are publicly listed and unlisted. This enables an analysis of not only the large, listed firms that are likely to drive the industry aggregate, but also of less mature and smaller pharmaceutical or biotechnology firms, including those active in earlier-stage R&D, and smaller manufacturing firms. This has the advantage of avoiding survivor bias by also capturing small firms that may fail before they grow and list on public stock markets. However, by definition, shares in privately owned firms have no publicly available price. It is therefore not possible to estimate their cost of capital (COK) with commonly accepted asset pricing models, and no net ROE or ROA can be estimated. Additional information on the databases and methodology is available in [Supplementary Material](#).

3.2.3 Cost of capital

40. Cost of capital is constructed as the weighted average cost of capital (WACC), i.e. the mean of cost of equity and cost of debt weighted by the respective shares of equity and debt in total capital. It is reported in terms of an aggregate and a mean across all firms in the pharmaceutical industry for each year in the period 2005 to 2020. Because cost of capital is estimated as an annual percentage of capital invested at the firm level, an aggregate measure of cost of capital for the entire industry is constructed by computing a weighted mean across all firms, where each firm is weighted for its share of total assets in the aggregate of assets for all firms. The median and quartiles are computed to show the distribution across firms.

41. Cost of capital for publicly listed firms was retrieved from Bloomberg at the firm level. This database contains the actual cost of debt based on interest expenditure reported by firms and estimates of the cost of equity, based on the Capital Asset Pricing Model (CAPM) commonly used in financial markets.

3.2.4 Sales & marketing expenditure

42. No suitable data sources could be identified to generate an indicator of sales & marketing expenditure.

3.2.5 Research & development (R&D) expenditure

43. This indicator reports total **R&D expenditure** incurred by the industry. Investment in R&D is an activity of the R&D-based pharmaceutical industry that is of key importance in health policy, as it is expected to result in new and effective medicines. This indicator facilitates the assessment of trends in R&D expenditure over time, and by comparison with other types of expenditure, the importance of R&D *vis-a-vis* other purposes to which resources are allocated. R&D expenditure is also compared with that of other industries. Using aggregated data, the indicators include R&D expenditure (BERD) and R&D intensity. Using firm-level data, R&D intensity in the pharmaceutical industry only, defined as R&D expenditure as a share of revenue, was calculated. Further information on data sources and methodology are available in [Supplementary Material](#).

Data sources

44. The OECD Research & Development Statistics (RDS), including the Analytical Business Expenditure on Research and Development Database (ANBERD), is the primary data source for this indicator. OECD RDS provides a wide range of data on the resources devoted to R&D in all OECD countries and selected non-member economies.⁸ Data are aggregated at the country- and industry-level according to standards in the Frascati manual (OECD, 2015^[7]).

45. As previously noted, an advantage of OECD RDS data is that they provide aggregate estimates of R&D expenditure in the business enterprise sector by industry, including pharmaceuticals.⁹ These data have previously been used to report total R&D expenditure in the pharmaceutical industry across OECD countries and to compare the R&D intensity of the pharmaceutical industry to other R&D-intensive industries.¹⁰

46. The main drawback of OECD RDS is that data become available with a significant time lag and that data availability and geographic coverage decrease with increasing level of detail. An inherent source of inaccuracy in R&D expenditure data stems from the fact that expenditure can be assigned to a given industry based either on the “main activity” of each of the firms in an industry (i.e. all expenditure reported by a given firm is allocated to a single industry corresponding to the firm’s industry classification), or on a “industry orientation”-basis (i.e. the reporting firm distributes its R&D expenditure across the different lines of business for which the R&D is relevant in terms of the industry ultimately served or the type of product embodying the outcome of the R&D) (OECD, 2015^[7]). Availability of data using the “industry orientation” classification is much more limited than when using the “main activity” classification; per May 2021, only five OECD countries¹¹ reported pharmaceutical R&D expenditure according to this classification. Further information on the distinction between the definitions and their impact is in [Supplementary Material](#).

47. The OECD Orbis and the Refinitiv Datastream databases, which provide a large volume of firm-level data, are secondary data sources for this indicator. A key advantage of also using firm-level data is that such microdata enable the analysis of the distribution of R&D expenditure across firms within the pharmaceutical industry. A major drawback of such data is that they report expenditure according to accounting standards, such as IFRS and US GAAP, with some divergence from the standards for reporting of R&D expenditure in the OECD Frascati manual (OECD, 2015^[7]). R&D expenditure reported according to the Frascati manual represents a monetary measure of R&D activity that reflects when and where the activity takes place, by virtue of the principle that expenditure be recorded in the country and year in which the R&D activity takes place. Accounting measures of R&D expenditure, on the other hand, represent expenditure on an accrual basis reported by the firm that incurs the expenditure, which does not necessarily coincide with the year in which the activity took place nor with the geographic location of the activity. Further information on the limitations of accounting standards in interpreting expenditure is available in [Supplementary Material](#).

No data source could be identified to disaggregate R&D expenditure by disease area.

3.2.6 Number of product development projects

48. This indicator tracks the number of drug development projects, in terms of the number of drug candidates in active development for a given indication each year. Drug development projects are one of the most direct measures of activity in the pharmaceutical industry, and it is important to understand where,

⁸ See <https://www.oecd.org/sti/inno/researchanddevelopmentstatisticsrds.htm>.

⁹ See Note 6.

¹⁰ See OECD (2019, pp. 214-15^[22]; Galindo-Rueda and Verger, 2016^[27]). R&D intensity is defined as business enterprise R&D expenditure as a share of gross valued added in the same industry. R&D intensity in the pharmaceutical industry is compared to the electronic & optical products and the air & spacecraft industries; and the wider economic sectors of manufacturing (including pharmaceuticals); mining & quarrying; total services; utilities; agriculture; forestry & fishing; and construction.

¹¹ Belgium, the Czech Republic, Finland, France and Portugal.

when, and by whom these drugs are developed. The indicator is reported in a cross-sectional view of the latest year and in a longitudinal view for the years 2011 to 2021. A full list of sub-group analyses and further information on the methodology can be found in [Supplementary Material](#).

Data Sources

49. Drug development projects were identified using the proprietary AdisInsight database curated by Springer Nature.¹² AdisInsight tracks commercial drug development projects from discovery to market launch worldwide based on publicly available information. The main advantage of the AdisInsight Database is the robustness of the data and the use of structured and unstructured primary sources curated by a team of editors.¹³ Information is summarised by drug candidate, in product profiles that contain, among other things, details about product characteristics, the development stages for the diseases being investigated, and the organisations involved in the development of the product. More information on the dataset and methodology is included in [Supplementary Material](#).

3.2.7 Number of clinical trials

50. This indicator tracks the number of clinical trials, in terms of new trials that started recruiting participants in a given year and are either still actively recruiting or have been completed.

Data Sources

51. Data from the International Clinical Trials Registry Platform (ICTRP) were used to construct the indicator of the **number of clinical trials**. ICTRP is a project of the Health Metrics and Measurement cluster of the World Health Organization (WHO), which aims to facilitate registration of all clinical trials and the public accessibility of that information.¹⁴ However, ICTRP is not a primary trial register, but rather a single point of access to trial registration data that unifies data from primary registers. The latter are maintained by authorities in various WHO member countries and must, in order to be recognised as a primary register by WHO, meet certain criteria set by the International Committee of Medical Journal Editors (ICMJE), related to content, quality and validity, accessibility, unique identification, technical capacity and administration. As such, ICTRP provides a rich set of clinical trial data with broad geographic coverage and across a number of disaggregations, such as therapeutic area, sponsor, etc. Another advantage of ICTRP is that the data are publicly available and downloadable free of charge. Further information about the data fields and methodology are provided in [Supplementary Material](#).

3.2.8 Number of subjects enrolled in clinical trials

52. This indicator tracks the number of participants enrolled in clinical trials, in terms of new trials that started recruiting participants in a given year and were still actively recruiting participants or have been completed. Trial size is useful for pharmaceutical industry activity as it is an indirect indicator of cost and consequently, R&D investment.

¹² For a brief overview of AdisInsight, see <https://adisinsight.springer.com/help>.

¹³ This data source was chosen from a range of sources offered by commercial vendors of data related to the R&D pipeline because of its comprehensiveness and high level of detail. The WHO Global Observatory on Health R&D also uses AdisInsight to monitor the pipeline of health products. See: <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/health-products-in-the-pipeline-from-discovery-to-market-launch-for-all-diseases>.

¹⁴ See <https://www.who.int/clinical-trials-registry-platform/about>

Data Sources

53. Data from the International Clinical Trials Registry Platform (ICTRP) are used to construct the indicator of the **number of participants enrolled in clinical trials**, similar to in ‘Number of Clinical Trials’. In addition, a variable on “Interventional”, which includes clinical trials designed to test the effectiveness of a therapeutic intervention (i.e. drug) against a control or other sample, or “Observational” trials meant to observe changes in the sample of participants before or after some intervention usually over long periods of time and with larger groups of participants, was available for use in the analysis. The methodology for the indicator calculation is available in [Supplementary Material](#).

Table 3.1. Data sources and feasibility

Each data source examined to potentially support the indicators and analysis are presented below with their feasibility for use.

Domain	Indicator	Data Source	Feasibility	Sufficient for analysis
Financial inputs	Revenue	OECD Systems of National Accounts (SNA) and Supply and Use Tables (SUT)	OECD collected data using industry output as a measure of revenue. Lack of timeliness and granularity at the industry, disease area, and country levels. Currently insufficient data available for 2021 and 2020.	No
		IQVIA Prescription Medicine Revenue	Estimates revenue at ex-factory prices through reported purchased by distributors (wholesalers, providers, etc.). Data are timely and available in multiple disaggregations: country, disease area, drug type, company, etc.	Yes
		OECD System of Health Accounts (SHA)	OECD collected data on expenditure in the health sector, to supplement other sources on the share of generics in total industry revenue. Considerable time lags and possible overlap with IQVIA.	No
	Net cash flow from financing activities	OECD-ORBIS Corporate Finance dataset	Contains information for unlisted firms, however no detailed cash flow data are available.	No
		OECD Capital Market Series dataset, Refinitiv Datastream	Data available for publicly listed firms with cash inflow / outflow information for financing activities (including debt and equity) at firm level and historically.	Yes
	Direct subsidies for R&D	OECD Research and Development Statistics (RDS) – Business Enterprise Sector (BERD)	OECD managed data with aggregate estimates of BERD according to Frascati Manual Standards. Issues with timeliness (lag in collection/reporting) and gaps at lower disaggregations that can be supplemented with other public sources.	Yes
	Tax credits for R&D	OECD R&D Tax Incentives Survey – Government Tax Relief for R&D Expenditure (GTARD)	OECD led survey collection of GTARD which estimates marginal tax subsidies for R&D. Data are available as a cross-section for the latest year at the industry-level disaggregation for 14-15 OECD countries. Sufficient for analysis (without time component).	Yes (with limitations)
		MicroBERD	OECD-STI led database currently in development. Would use microdata to provide more detail about business R&D including the sources, incidence / impact of public spending, etc. Not currently available.	No
	Net cash	OECD-ORBIS	Contains information for unlisted firms, however no	No

Domain	Indicator	Data Source	Feasibility	Sufficient for analysis
Financial activity metrics	flows from operating activities	Corporate Finance dataset	detailed cash flow data are available.	
		OECD Capital Market Series dataset, Refinitiv Datastream	Data available for publicly listed firms with cash inflow / outflow information for financing activities (including debt and equity) at firm level and historically.	Yes
	Profitability	OECD-ORBIS Corporate Finance dataset	Data on gross operating margin, net operating margin, return on assets (ROA), net ROA available in Orbis for unlisted firms. Sufficient for profitability analysis.	Yes
		OECD Refinitiv Datastream, Bloomberg, FactSet	Data on gross operating margin, net operating margin, return on assets (ROA), net ROA available in Refinitiv (listed firms). Cost of capital supplemented with Bloomberg and Factset.	Yes (for profitability analysis)
	Cost of capital	Bloomberg	Data available for cost of equity and cost of debt in Bloomberg for listed companies.	Yes (for analysis and construction of WACC)
	Sales & Marketing Expenditure	-	No suitable data sources could be identified to generate an indicator of sales & marketing expenditure.	No
	Research & development (R&D) expenditure	OECD Research and Development Statistics	OECD collected data on R&D expenditure in the business sector. Disaggregated by geography (OECD and non-member countries) and industry-levels, but not disease-level.	Yes
		OECD-ORBIS Corporate Finance dataset	Firm-level microdata available on R&D expenditure, but based on accounting standards not Frascati Manual standards. Unavailable at disease level.	Yes
		OECD Capital Market Series dataset, Refinitiv Datastream	Firm-level microdata available on R&D expenditure, but based on accounting standards not Frascati Manual standards. Unavailable at disease level.	Yes
	Non-financial measures of R&D activity	Number of product development projects	AdisInsight Database (Springer Nature)	Detailed, audited data collected by Springer Nature on drug development projects available historically and by firm, therapeutic area, drug type, drug status, phase, geography and more.
Number of clinical trials		International Clinical Trials Registry Platform (ICTRP)	WHO led registry of clinical trial data with historical capture of trial information and status. Several disaggregations available (condition level, phase, trial size, sponsors, etc.), however, some are cleaner and more accessible than others.	Yes
Number of people enrolled in clinical trials		International Clinical Trials Registry Platform (ICTRP)	WHO led registry of clinical trial data with historical capture of trial information and status. Several disaggregations available (condition level, phase, trial size, sponsors, etc.) however some are cleaner and more accessible than others. Available for analysis, though significant cleaning required for trial size.	Yes

Note: Cells shaded grey indicate their omission from further analysis. 'OECD Refinitiv Datastream' refers to the same database 'OECD Capital Market Series dataset, Refinitiv Datastream' but shortened for legibility.

4 Results

54. This section describes initial results for each indicator, based on available data. Indicators are presented separately for the *input* and *activity* domains.

4.1 Inputs

4.1.1 Revenue

55. OECD SNA data were not used for the indicator of industry revenue because of the lack of geographic coverage and timeliness of the data. At the time of drafting, data for only 3 countries were available in 2021, and in 2020, only for a total of 20 OECD and non-OECD countries and excluding several countries that host large pharmaceutical sectors (China, Denmark, Germany, India, Japan and Switzerland).

56. Industry revenue data from IQVIA were available for the global market for prescription medicines and for the 15 largest national markets for the years 2010 to 2021. The data were also broken down by disease area, for the top 20 diseases ranked by revenue, and by revenue from sales of originator and generic products. Overall, the granularity and coverage of the data would support regular reporting of this indicator. However, it should be noted that revenue calculated from this data source may be overstated due to the omission of discounts and ex-post rebates.

57. Global revenue from prescription medicines was estimated at USD 1,296 billion in 2021, a 46.8% increase since 2010 (USD 815 billion, in adjusted 2015 constant rates). In 2021, the United States was the largest market, reaching USD 576 billion (44% of global revenue), followed by China with USD 120 billion (9%). Within OECD countries, the United States accounted for 57% of total revenue, followed by Japan (7.5% OECD, 6% of global revenue), and Germany (6.1% OECD, 4.8% global), France (4.1% OECD, 3.2% global), and Italy (3.6% OECD, 3% global). The aggregate of OECD countries not in the top 15 accounted for 8.8% of global revenues.

58. Global revenue is consistently driven by revenue from originator medicines. In 2021, global revenue from originator prescription medicines reached nearly USD 858 billion (66.2% of total revenue) compared to USD 437 billion (33.8%) from generic medicines. These proportions did not vary significantly over time. In 2010, originator medicines accounted for 68% of global revenue which slightly decreased to 62% in 2016 but increased steadily through 2021.

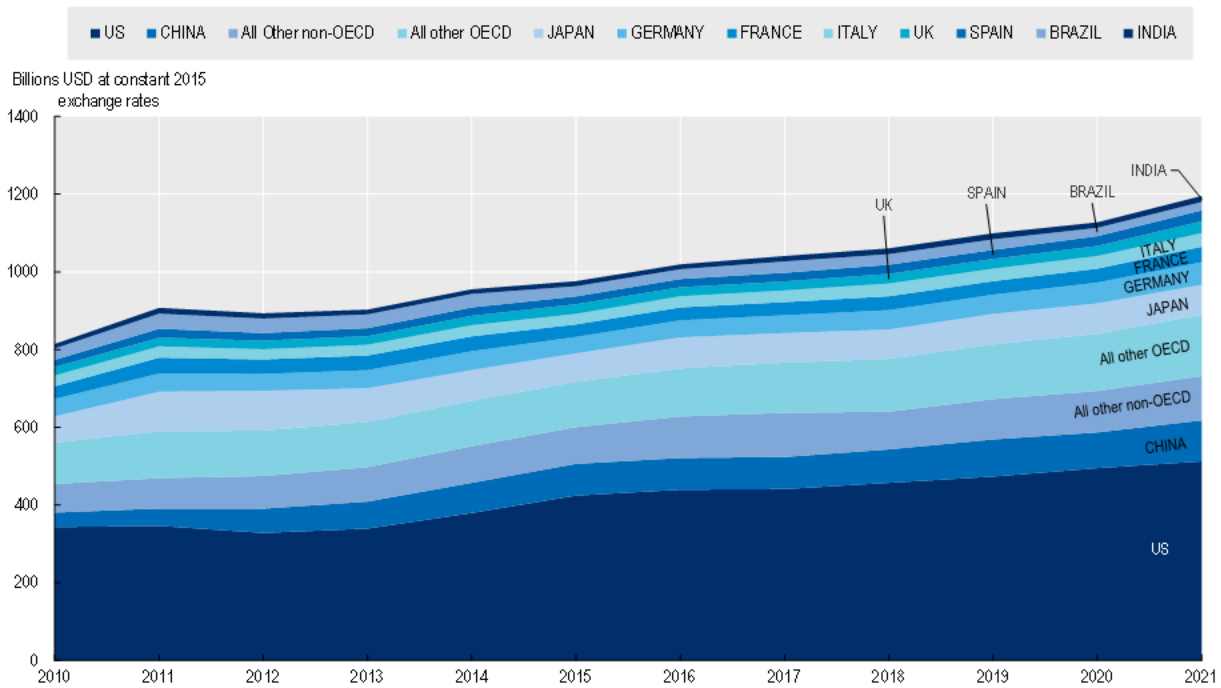
59. Annual growth rates varied widely between countries and years from -39% to +51%. OECD countries saw increases in revenue by 42% from 2010 to 2021, which is below the overall increase of 46.8%. The largest growth occurred in China, where prescription medicines revenue increased by 181% since 2010, while the Russian market contracted by 30%. Several OECD countries also experienced high growth rates, including the United States (49%), Spain (49%), the United Kingdom (40%), and Korea (34%). Figure 4.1 below displays each country's prescription medicines revenue from 2010 to 2021 in USD (constant 2015 exchange rates), the sum of which is the estimate of global revenue.

60. Using the same data, prescription medicine revenue was disaggregated by therapeutic area. Of the top 20 therapeutic areas, *oncology* accounted for the largest share of revenue in 2021, with USD 185 billion globally (14% of total revenue). *Antidiabetics* and *immunology* were next highest with USD 128 billion (10%) and 126 billion (9.8%), respectively. Since 2010, the largest increases in revenue were seen

in immunology (+411%), bisphosphonates, tumour-related and bony metastases (+354%), and oncology (+186%), while the markets for *lipid regulators* and *anti-ulcerants* showed the largest declines, at -54% and -40%, respectively. Figure 4.2 displays the changes in revenue over time by disease area in USD (constant 2015 exchange rates).

61. The proportion of revenue driven by originators *vis a vis* generics¹⁵ varied widely across therapeutic areas (Figure 4.3). In 2021, the therapeutic area with the highest revenue from originator medicines was oncology (USD 169 billion, 92% of total oncology revenue and 13.1% of total revenue overall), while the highest revenue from generic medicines was for pain medication (USD 40.8 billion, 68% of total pain revenue and 3.2% of total revenue overall). As a proportion of total revenue by therapeutic area (share of revenue from originators), vaccines and immunology had the highest proportions (99.6% and 98.8%, respectively). Bisphosphonates, tumour-related & bony metastases as well as antibacterials had the highest proportions of generic revenue (99.6% and 76.8%, respectively), however, it should be noted that these are both quite small and only represent 2.2% of total revenue.

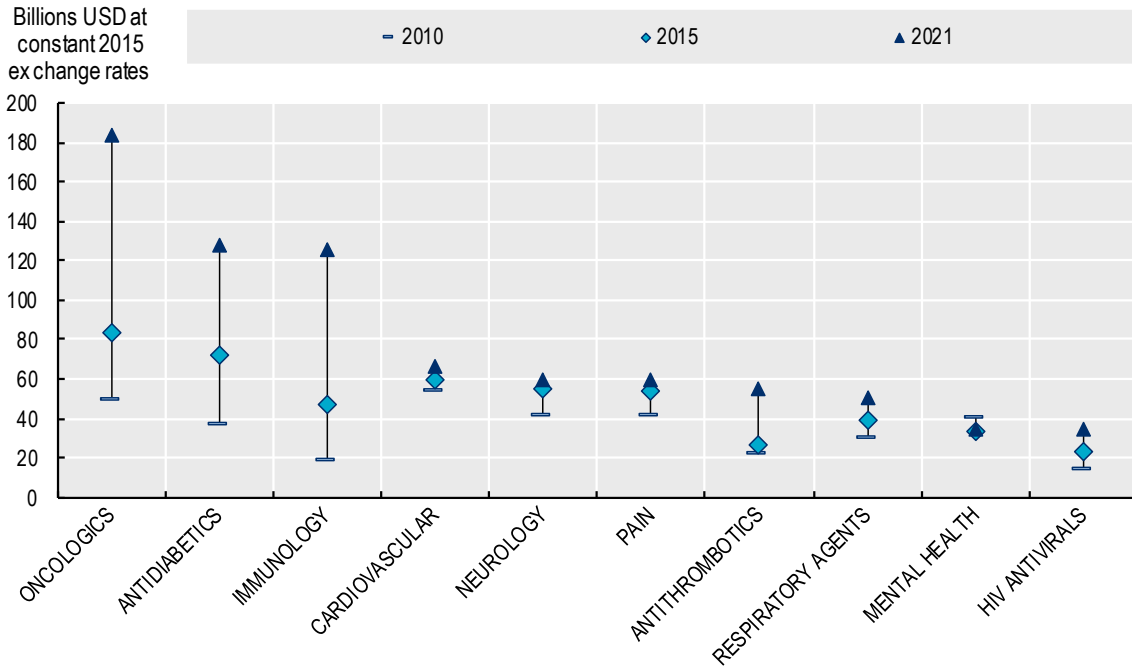
Figure 4.1. Total revenue from prescription medicines by country / region, 2010 – 2021



Note: includes the top 15 largest markets and additional aggregates for remaining OECD and non-OECD countries.
 Source: OECD Analysis based on IQVIA data.

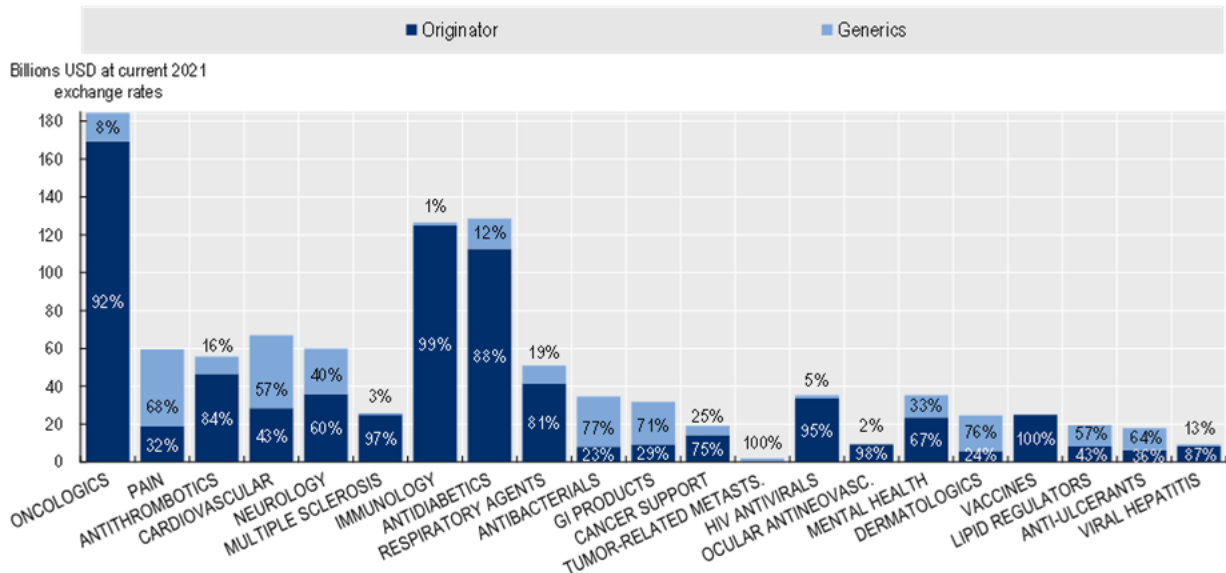
¹⁵ Categorisation of generics source data listed in [Supplementary Material](#).

Figure 4.2. Total revenue from prescription medicines by therapeutic area, 2010 – 2021



Note: Includes the top 10 therapeutic classes (by total revenue).
 Source: OECD Analysis based on IQVIA data.

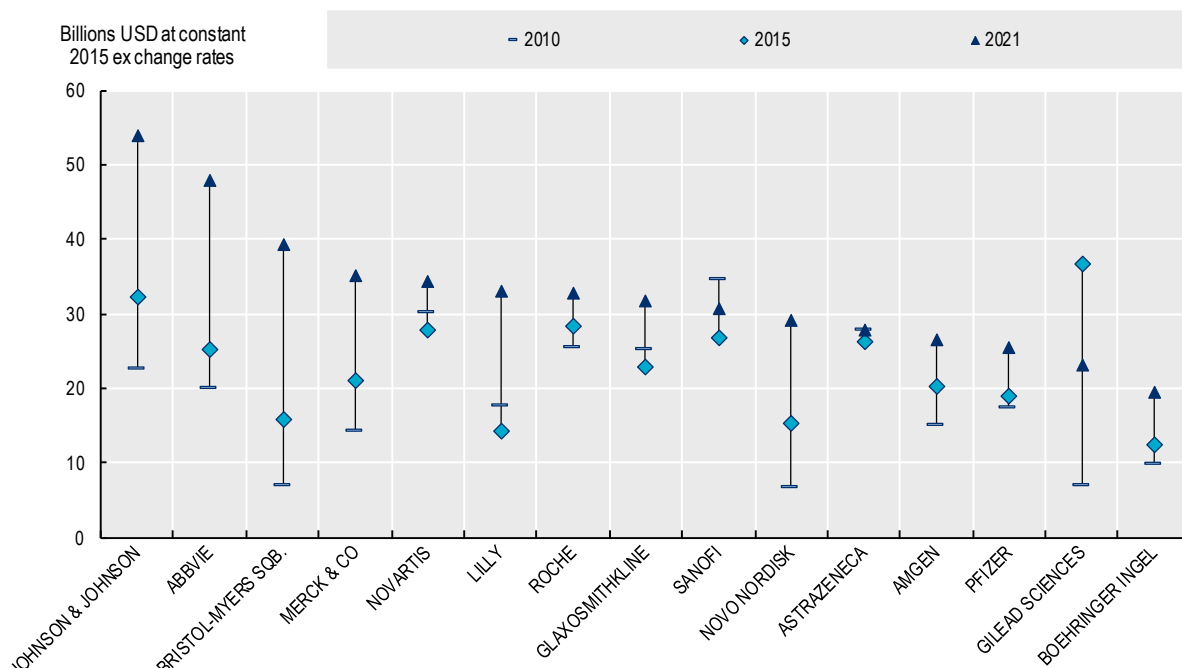
Figure 4.3. Total revenue from prescription medicines in 2021 by therapeutic area and originator v. generic sources



Note: Includes the top 20 therapeutic classes. Originator and Generic categories mapped based on existing sub-category definitions provided by IQVIA
 Source: OECD Analysis based on IQVIA Data

62. Global revenue from prescription medicines was also disaggregated across the top 15 firms, which together accounted for 42% of total revenue in 2021 across all therapeutic areas and regions. Of these, in 2021, Johnson & Johnson had the largest market share at 4.6% of total market (USD 59.7 billion) followed closely by AbbVie (4.1%, USD 53.6 billion) and Bristol Myers Squibb (3.3%, USD 43.2 billion). Growth rates since 2010 varied widely across firms. Bristol Myers Squibb had the highest growth of 456%, followed by Novo Nordisk (335%) and Gilead Sciences (240%). Only revenues of Sanofi (-11.4%) and AstraZeneca (-0.32%) declined since 2010. Figure 4.4 shows revenues from prescription medicines for the top 15 firms over the time period in USD billions (constant 2015 exchange rates).

Figure 4.4. Global revenue from prescription medicines by firm, 2010 – 2021



Note: Includes total revenue from prescription medicines from the Top 15 Corporations.

Source: OECD Analysis of IQVIA data

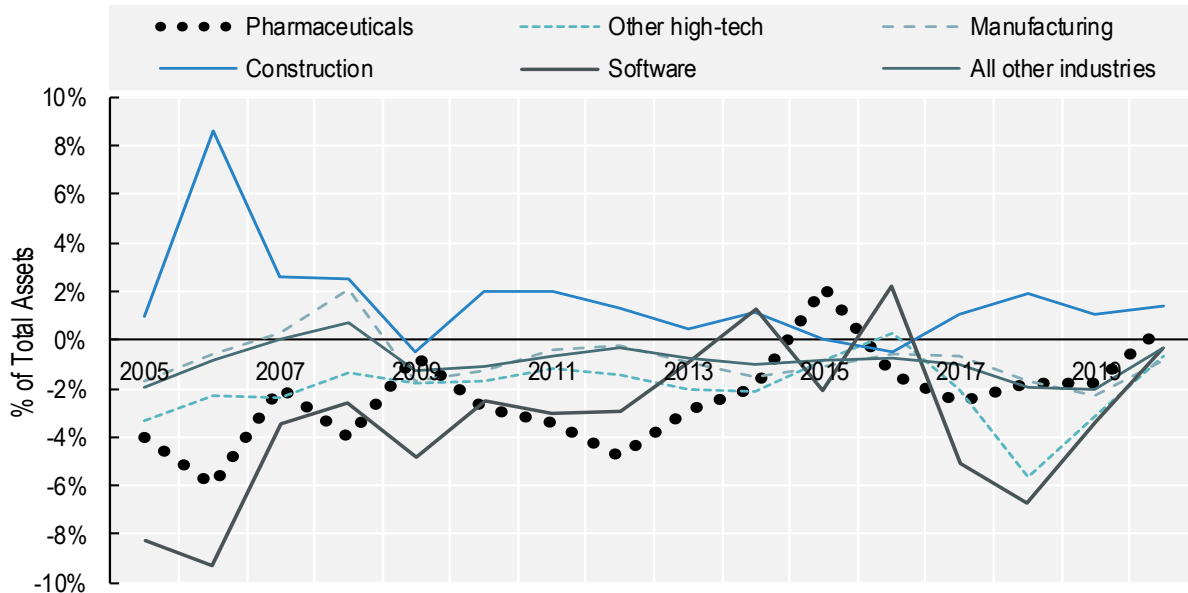
4.1.2 Cash flow from financing activities

63. Between 2005 and 2020, data were available for an average of 1 285 publicly listed pharmaceutical firms per year (range 1 040 in 2005 to 1 895 in 2020) across the 40 countries included. However, while the sample does not include pharmaceutical firms from all these countries in all years, the data were adequate in coverage and granularity to enable reporting of this indicator (see [Supplementary Material](#)).

64. In aggregate, the pharmaceutical industry generated negative net cash flows from financing activities in all years, except in 2015 and 2020, meaning that, on balance, the industry used more cash to pay shareholders and creditors than it raised from capital markets. Net cash flows from financing activities ranged from -6.0% of total assets in 2006 to +2.1% of total assets in 2015 as shown in Figure 4.5. Compared to other industries, the pharmaceutical industry tended to be at the lower end of the range for this indicator. Only the software industry had lower negative cash flows from financing activities in some years while cash flows in other R&D-intensive industries were also negative in most years but closer to zero. The total manufacturing sector and the aggregate of all industries excluding pharmaceuticals had cash flows from financing activities that were close to zero, while construction was the only sector that had positive net cash flows in most years.

Figure 4.5. Aggregate net cash flows from financing activities in the pharmaceutical and other industries

As a percentage of total assets, publicly listed firms only, 2005 to 2020



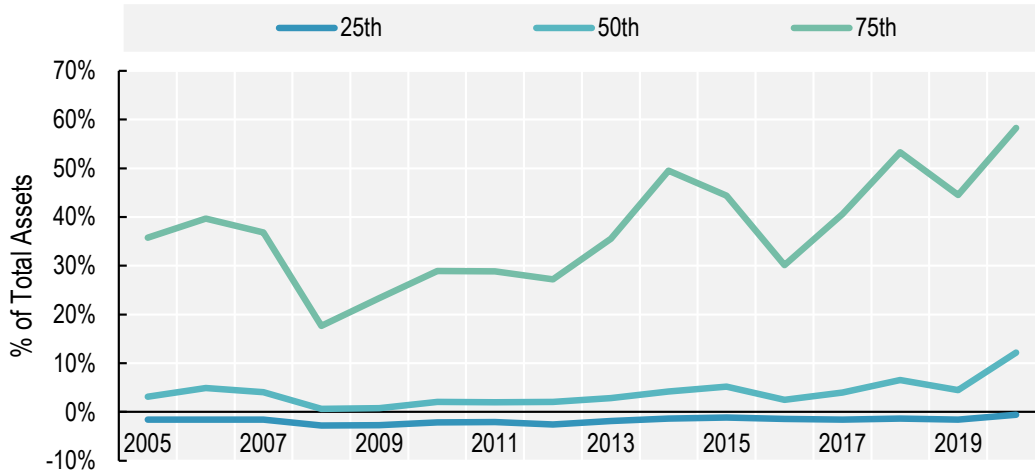
Notes: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries show the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software.

Source: OECD analysis based on Refinitiv Datastream data

65. The distribution across firms is strongly skewed. The median of the distribution was consistently positive, while only firms in the lowest quartile exhibited consistently negative net cash flow from financing activities (Figure 4.6), suggesting that the majority of firms raised more cash from capital markets than they used to pay shareholders and creditors. This implies that the aggregate pattern was likely driven by a small number of large firms and profitable firms that use significant amounts of cash for paying shareholders and creditors. This is confirmed by a sub-group analysis by size and age of firms, with older and larger firms having lower cash-flow-to-asset ratios than younger and smaller firms. A sub-group analysis by return on assets, one measure of profitability, confirms that only the most profitable 25% of firms had consistently negative cash-flow-to-asset ratios, in the range of -4% to -11% in the years 2005 to 2020, while firms in the 3rd quartile of the profitability distribution had ratios close to zero, and the lower half of the distribution had positive ratios.

Figure 4.6. Firm-level distribution of net cash flows from financing activities in the pharmaceutical industry

As a percentage of total assets, publicly listed firms only, 2005 to 2020

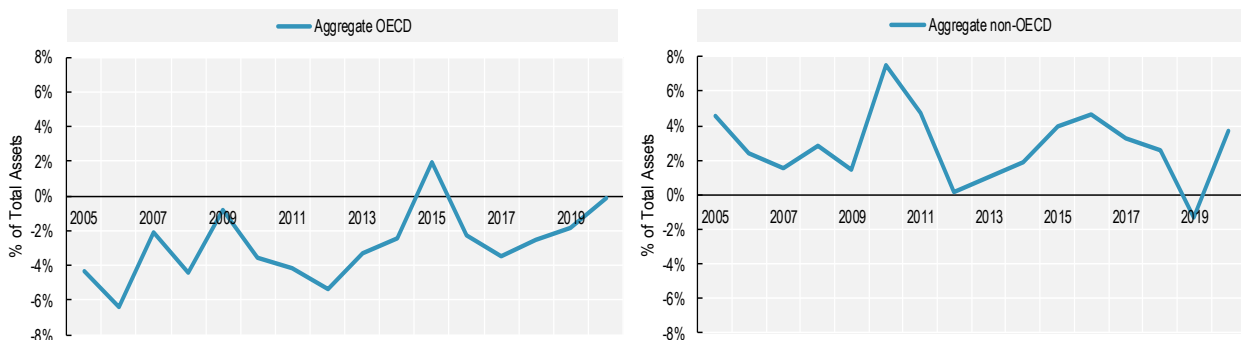


Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia) by percentiles of firms across the distribution of the cash flow from financing activities by total assets indicator.
Source: OECD analysis based on Refinitiv Datastream data

66. There were also marked differences between firms in OECD and non-OECD countries. While the majority of pharmaceutical firms are headquartered in OECD countries and the aggregate across OECD countries is similar to that of the entire sample, firms headquartered outside of OECD exhibited consistently positive net cash flows from financing activities, in all years except 2019, ranging from +7.5% of total assets in 2010 to -1.3% in 2019 (Figure 4.7). The distribution across firms also shows a different pattern in non-OECD countries, with the median remaining close to 0% over time.

Figure 4.7. Aggregate cash flow from financing activities in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of total assets, publicly listed firms only, 2005 to 2020



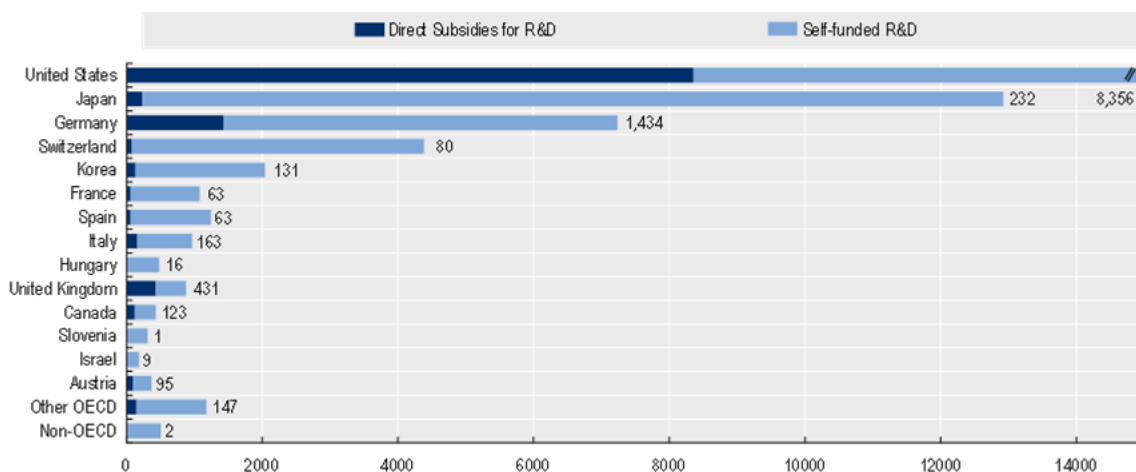
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).
Source: Source: OECD analysis based on Refinitiv Datastream data

4.1.3 Direct subsidies for R&D

67. R&D expenditure data broken down by funding source were available from OECD R&D Statistics for a total of 25 OECD countries and 2 non-OECD countries in at least one year between 2016 and 2019, with data for most countries from 2017. These were combined with US data published by the National Science Foundation (NSF). However, no data were available for Belgium, Denmark or China, which together represent a considerable proportion of total R&D expenditure in the global pharmaceutical industry. Despite this, analysis and reporting of this indicator was possible for the pharmaceutical industry. Data availability did not allow for comparing the pharmaceutical industry with other research-intensive industries.

68. Across the 26 OECD countries, the pharmaceutical industry received USD 11.5 billion in external funding for R&D in 2019 or the latest year with available data, representing just under 10% of total R&D expenditure. This includes domestic funding by government, higher education, and private non-profit sectors as well as funding from foreign sources. R&D subsidies for the industry in the United States alone accounted for 73% of the OECD total, similar to the US proportion of R&D expenditure; the United States accounted for just under 70% of total R&D expenditure in OECD countries, followed by Germany (13%) and the United Kingdom (5%). The proportion of pharmaceutical industry R&D funded by external sources varied considerably between countries. Subsidies accounted for 1% of R&D expenditure in Japan and 2% in Switzerland, but 20% Germany, and as much as 49% in the United Kingdom (Figure 4.8). Current aggregate OECD data are only available through 2019, so do not capture the effects of the Covid-19 pandemic. Governments subsidised the development of Covid-19 vaccines generously and reduced investment risk for firms through advance purchase commitments.

Figure 4.8. Direct subsidies for R&D and total R&D in the pharmaceutical industry in million USD at current purchasing power parities (PPPs), 2019 or latest year available



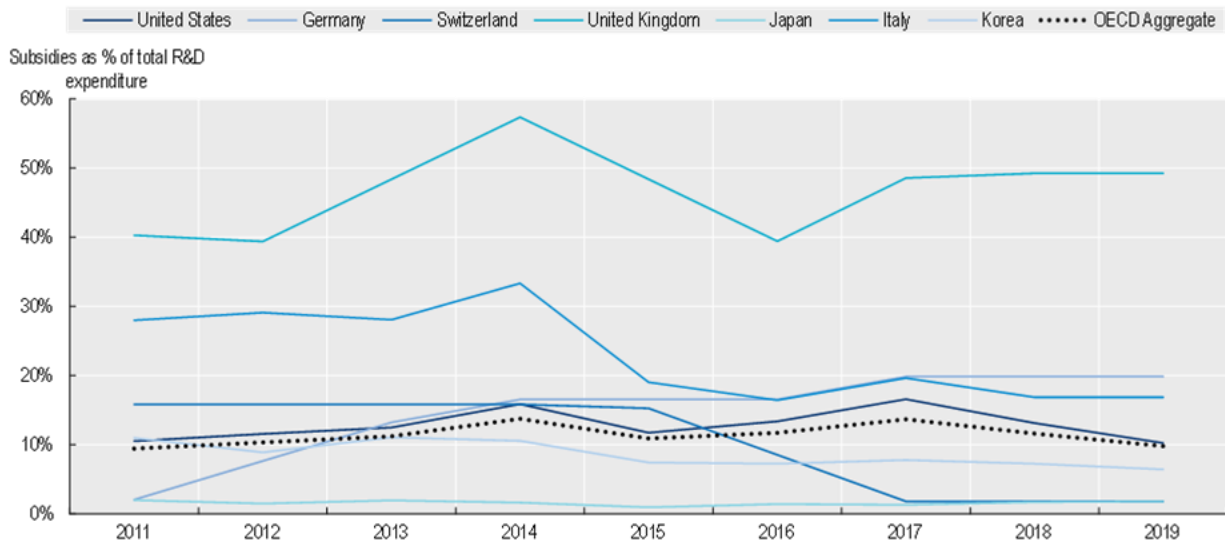
Note: Data labels correspond to direct subsidies. For the United States, self-funded R&D stands at 73 299 million USD. The graph includes 26 OECD countries, all with data on total R&D expenditure (see below) except Belgium, Denmark, Ireland, Mexico and the Netherlands. Non-OECD countries are Chinese Taipei and Romania.

Source: OECD R&D Statistics, R&D expenditure by industry and funding source

69. Since 2011, R&D subsidies for the pharmaceutical industry in OECD countries with available data have increased by 69% in real terms, i.e. at constant purchasing power parities (PPPs). Subsidies nearly doubled in absolute terms and increased from 9% to 14% of R&D expenditure between 2011 and 2017, then declined by 12% between 2017 and 2019. Trends in the OECD aggregate are strongly driven by the

United States, where subsidies increased until 2017 but declined between 2017 and 2019 in both, absolute terms and as a proportion of R&D expenditure. To the extent that data are available, there appeared to be a notable upward trend in Germany, with nearly a 10-fold increase from USD 116 million in 2011 to USD 1.1 billion in 2017; no data were available for subsequent years. (Figure 4.9) shows trends in R&D subsidies for selected countries as a proportion of total R&D expenditure in the industry between 2011 and 2019.

Figure 4.9. Trends in direct R&D subsidies to the pharmaceutical industry by country, 2011 – 2019



Note: The OECD aggregate includes 26 countries, all with data on total R&D expenditure (see below) except Belgium, Denmark, Ireland, Mexico and the Netherlands. Non-OECD countries are Chinese Taipei and Romania. Missing data points were filled using linear interpolation when data were available on both sides of the missing year(s). If the times series for a country ends before 2019, missing data are imputed by maintaining a constant proportion of R&D subsidies in total R&D expenditure.

Source: OECD R&D Statistics, R&D expenditure by industry and funding source

4.1.4 Tax credits for R&D

70. Recent data from the OECD R&D Tax Incentives Survey were only available for 14 OECD countries, which did not include the United States¹⁶, sufficient to report this indicator as a cross-section only¹⁷. Collectively, these 14 countries accounted for approximately 6% of R&D expenditure by the pharmaceutical industry across the OECD in 2019 (USD 8.4 billion).

71. In 2019, pharmaceutical firms in these 14 countries benefited from a total of USD 1.5 billion in tax credits for R&D, equivalent to approximately 18% of their R&D expenditure in the same year (Figure 4.10). This was a higher proportion than in the total manufacturing sector and comparable to the computer and electronics industry, but lower than in the chemicals industry.

72. The magnitude of R&D tax credits relative to R&D expenditure varied considerably between countries, ranging from less than 1% to 74%. This variation in the implied ratio of R&D tax support to R&D expenditure is influenced by several factors such as cross-country differences in the uptake of R&D tax incentives, generosity of R&D tax relief as well as conceptual differences in business expenditures

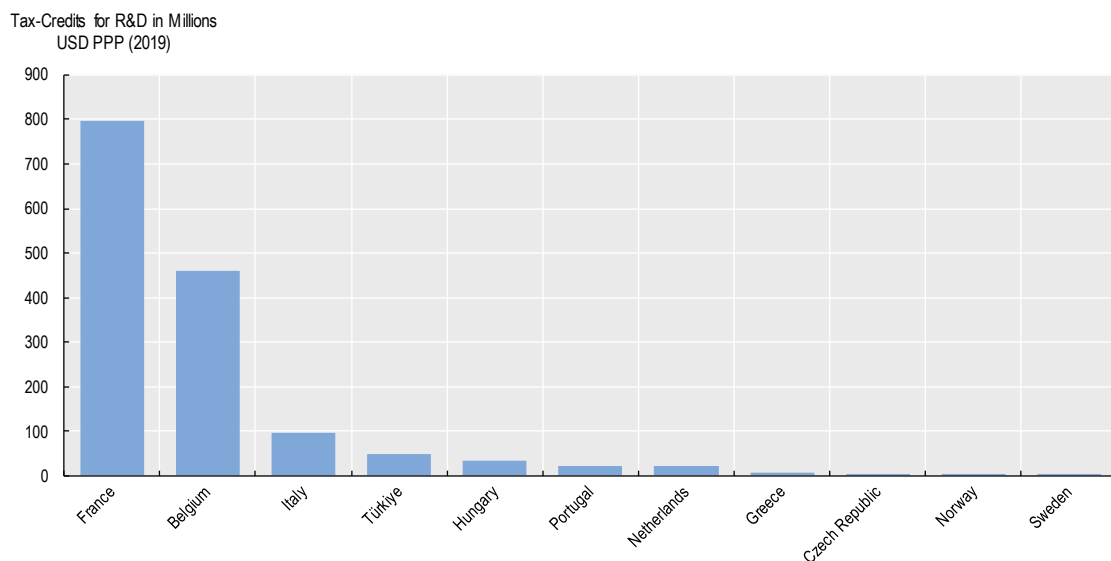
¹⁶ Belgium, the Czech Republic, France, Greece, Hungary, Italy, Lithuania, Netherlands, Norway, Portugal, Slovak Republic, Slovenia, Sweden and Türkiye.

¹⁷ As the survey is ongoing, more data may yet become available for longitudinal analysis.

qualifying for R&D tax relief and total amount of R&D performed by business in a given country (OECD, 2021_[12]). Moreover, the allocation of business R&D expenditures to the pharmaceutical industry on a main activity basis (see Section 3.2.5 Research & development (R&D) expenditure) results in the exclusion of pharmaceutical-oriented R&D conducted in enterprises classified in other industries, such as R&D services (ISIC Rev.4 72). This can lead to a higher implied ratio of R&D tax support to R&D expenditure in the pharmaceutical sector. As this indicator is still in development, more time is needed to confirm the feasibility of regularly reporting tax credits for R&D as a proportion of total R&D expenditure in the pharmaceutical industry.

Figure 4.10. R&D tax credits in the pharmaceutical industry

14 OECD countries in 2019, in USD millions at current purchasing power parities (PPPs)



Note: No data available for the United States and 13 other OECD countries. This is an experimental indicator. International comparability may be limited, e.g. due to variations in the industry definitions adopted for R&D tax relief reporting purposes. For more information on R&D tax incentives, see <http://oe.cd/rntax>.

Source: OECD R&D Tax Incentive Database

4.2 Activity

4.2.1 Cash flow from operating activities

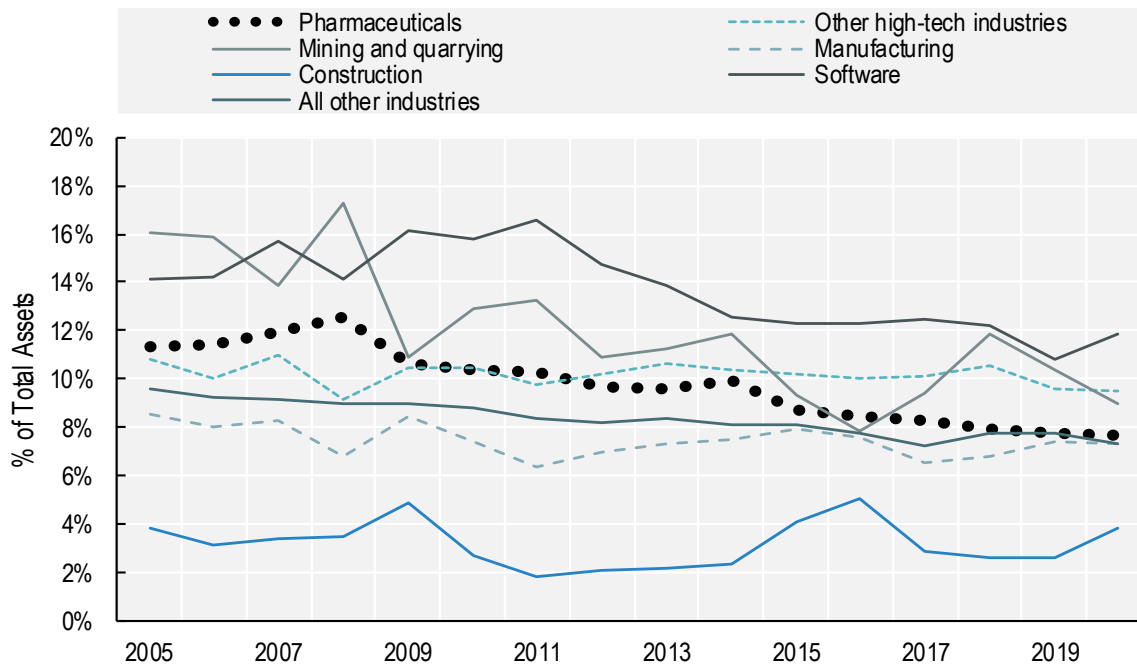
73. Between 2005 and 2020, data are available for an average of 1 292 publicly listed pharmaceutical firms per year (range 1 042 in 2005 to 1 902 in 2020) across the 40 countries included. However, while the sample does not include pharmaceutical firms from all countries in all years (see [Supplementary Material](#)), it was considered adequate in coverage and granularity to report this indicator.

74. In aggregate, the pharmaceutical industry generated positive net cash flow from operating activities in all years, ranging from 12.6% of total assets in 2008 to 7.6% of assets in 2020 (Figure 4.11). This means that, on balance, operating activities are consistently a net financing source for the industry – the industry generates more cash from sales of its products than it spends on production and for operating expenditure, including R&D. Compared to other industries, the pharmaceutical industry is close to the aggregate of other R&D-intensive industries, while only the software industry generated higher net cash flows from

operating activities. Higher net operating cash flows were also generated in the mining and quarrying industry. The total manufacturing sector and the aggregate of all industries excluding pharmaceuticals also had positive net cash flows from operating activities but lower than the pharmaceutical industry.

Figure 4.11. Aggregate net cash flows from operating activities in the pharmaceutical and other industries

As a percentage of total assets, publicly listed firms only, 2005 to 2020



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries shows the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software. Source: OECD analysis based on Refinitiv Datastream data

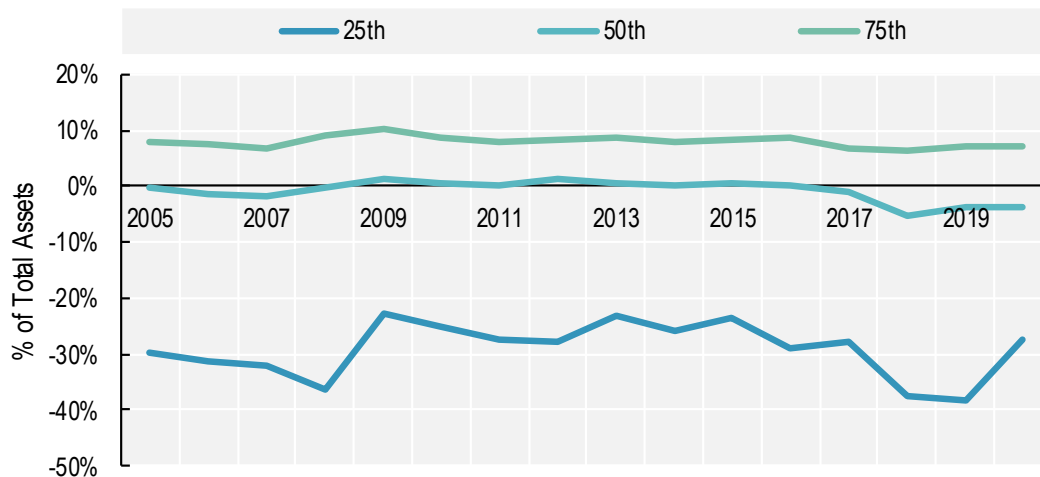
75. The distribution of net cash flows from operating activities across firms was skewed. While the median of the distribution tended to be close to zero over time (maximum of +1.3% of total assets in 2012 to -3.9% of total assets in 2020), the lowest 25th percentile of firms were consistently negative (between -23% to -38% of total assets), while the upper 75th percentile were in the range of +6% to +10% and more comparable to the aggregate (Figure 4.12). This suggests that nearly half of all firms spend more cash on operating activities than they generate from the sale of products (have negative net operating cash flows), and that the positive aggregate is driven by a small number of large firms that have significant amounts of cash from sales as a net financing source (have positive net operating cash flows).

76. This was confirmed by a sub-group analysis by size, with only the quartile of largest firms exhibiting consistently positive net cash flows from operating activities. A sub-group analysis by return on assets, a measure of profitability, showed that firms in the upper half of the profitability distribution consistently generated positive net cash flows from operating activities, while cash flows in the 2nd quartile fluctuated around zero and the least profitable 25% of firms generated net cash flows of between -40% and -70% of assets. The pattern was less clear in a sub-group analysis by firm age. While mature firms generated, in aggregate, relatively constant positive net cash flows from operating activities over the time period

analysed, younger firms also generated positive aggregate cash flow from operating activities, but with a declining trend over time.

Figure 4.12. Firm-level distribution of net cash flows from operating activities in the pharmaceutical industry

As a percentage of total assets, publicly listed firms only, 2005 to 2020



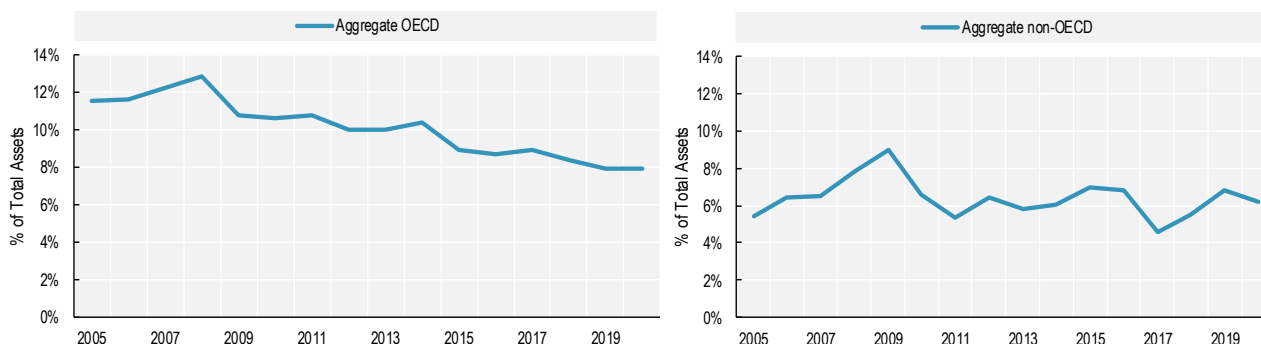
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia) by percentiles of firms across the distribution of the cash flow from operating activities by total assets indicator.

Source: OECD analysis based on Refinitiv Datastream data

77. In aggregate, the pattern is comparable in OECD and non-OECD countries, with consistently positive net cash flow from operating activities between 2005 and 2020. However, firms in non-OECD countries had somewhat lower ratios of cash flow from operating activities to total assets (Figure 4.13). There was also a marked difference in the distributions of firms between OECD and non-OECD countries. While a majority of firms in OECD countries exhibited negative net cash flows from operating activities in the period analysed, the vast majority of firms headquartered outside the OECD exhibited positive net cash flows, with even the 25th percentile of firms close to, but above zero. Firms outside the OECD are also more homogenous, with the distribution showing a much smaller range between quartiles (Figure 4.14). It is not clear from the analysis what is driving this pattern. It could be driven by a more manufacturing-focused and less R&D-intensive industry outside the OECD, with fewer firms generating little or no sales while having to finance investments in R&D and production capacity. Furthermore, firms in OECD countries have wider distribution of operating activities but an overall higher aggregate than those in non-OECD countries, suggesting that there are a small number of large, successful firms driving the OECD aggregates.

Figure 4.13. Aggregate net cash flows from operating activities in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of total assets, publicly listed firms only, 2005 to 2020

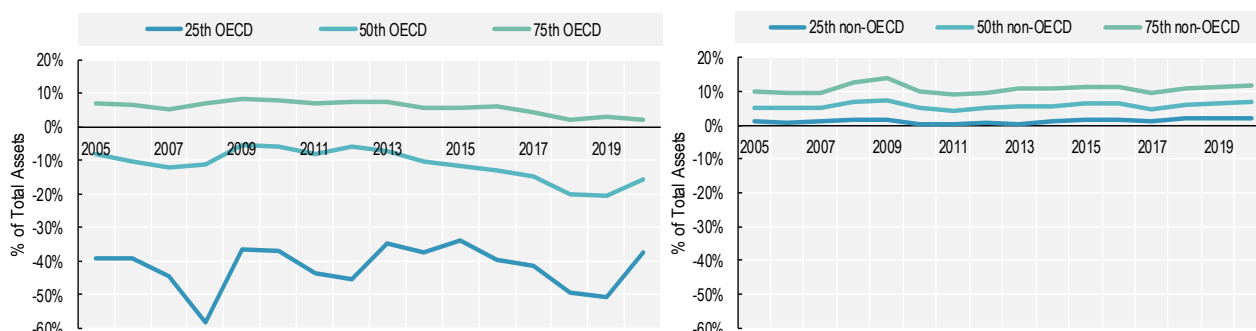


Note: Indicator is measured as a percentage of Total Assets. Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: Source: OECD analysis based on Refinitiv Datastream data

Figure 4.14. Firm-level distribution of net cash flows from operating activities in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of total assets, publicly listed firms only, 2005 to 2020



Note: Indicator is measured as a percentage of Total Assets. Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: Source: OECD analysis based on Refinitiv Datastream data

4.2.2 Profitability

Gross operating margin

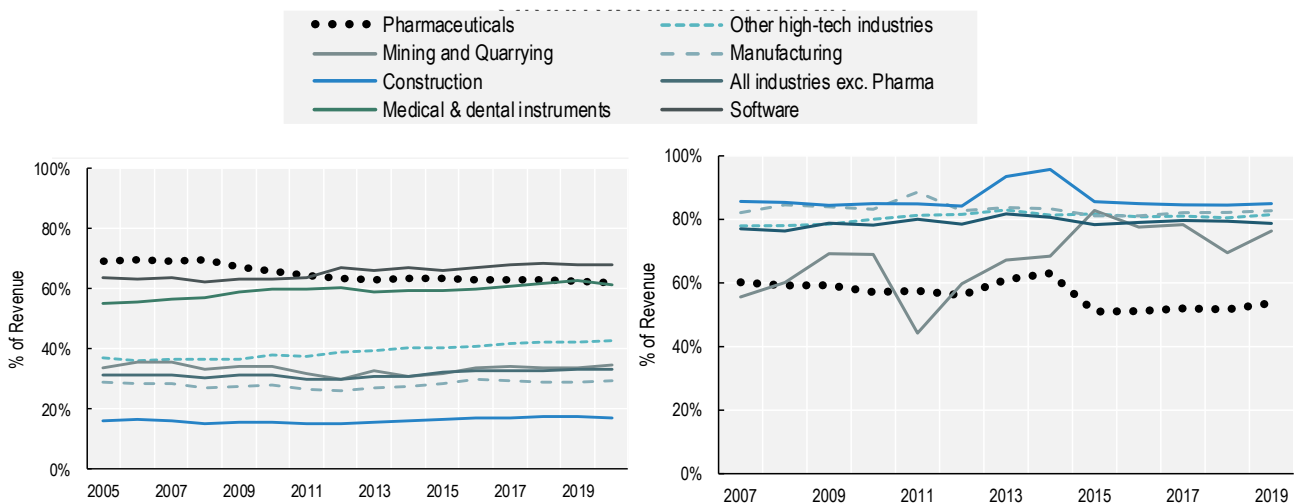
78. Between 2005 and 2020, data are available from Refinitiv Datastream for an average of 1 186 publicly listed pharmaceutical firms per year (range 967 in 2005 to 1 566 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all countries in all years (see [Supplementary Material](#)). From OECD-Orbis, data are available for an average of 4 966 unlisted pharmaceutical firms per year in the period 2007 to 2019 (range 8 610 in 2014 to 1 547 in 2019) across the 40 included countries. The availability of microdata across the two datasets supports the feasibility of reporting this indicator.

79. In aggregate, publicly listed firms in the pharmaceutical industry generated gross margins between 62% and 70% between 2005 and 2020. This means that, in aggregate, publicly listed pharmaceutical firms

sold their products at approximately 2.6 to 3.3 times their cost of production. Although there was a slight downward trend over time, gross margins were significantly higher than in most other industries, including the aggregate of four other R&D-intensive industries and the total manufacturing sector (Figure 4.15). Among other R&D-intensive industries, only the software and medical & dental instruments industries generated comparable gross operating margins, with the former exceeding pharmaceuticals since 2012 and the latter below pharmaceuticals for most of the period but with a converging trend. Unlisted firms were less profitable in aggregate, with gross margins ranging from 51% to 61%, i.e. revenue that is equivalent to 2 to 2.6 times the cost of production. This is at the lower end of the range when compared with other industries. The decline after 2014 should be viewed with some caution as the sample size in OECD Orbis changed significantly between 2014 and 2015, and the change may be partly driven by a change in the composition of the sample.

Figure 4.15. Aggregate gross margin in the pharmaceutical and other industries

As a percentage of revenue (sales), publicly listed firms 2005 to 2020 (left), and unlisted firms 2007 to 2019 (right)

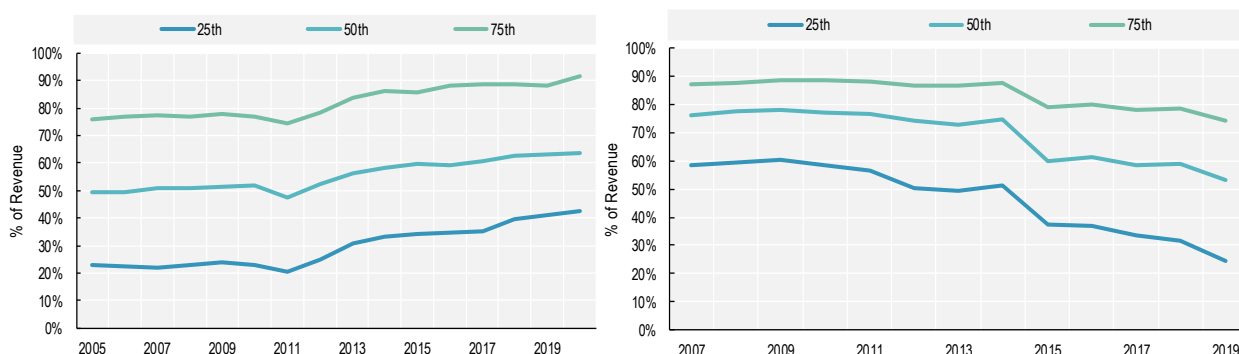


Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries shows the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software. Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

80. The distribution across publicly listed firms appeared to be relatively even across the sample (Figure 4.16), albeit with a median below the aggregate, suggesting that the aggregate was driven by larger and more profitable firms. This was confirmed by a sub-group analysis across the distribution of the gross operating margin indicator, with the largest 25% of firms clearly generating higher gross margins than the smallest 75% of firms. The distribution of unlisted firms, on the other hand, exhibited the opposite pattern, with the aggregate below the median and with greater skewness (see also Figure 4.16). This suggests that there is a significant number of small but profitable firms, but that the aggregate is driven by larger and less profitable firms. This was confirmed by a sub-group analysis by firm size, with the largest 25% of firms (by total assets) generating lower gross margins than the remaining three quarters. The pattern was less clear by firm age, with the most profitable firms generally found toward the middle of the age distribution.

Figure 4.16. Firm-level distribution of gross operating margin in the pharmaceutical industry

As a percentage of revenue (sales), publicly listed firms 2005 to 2020 (left), and unlisted firms 2007 to 2019 (right)



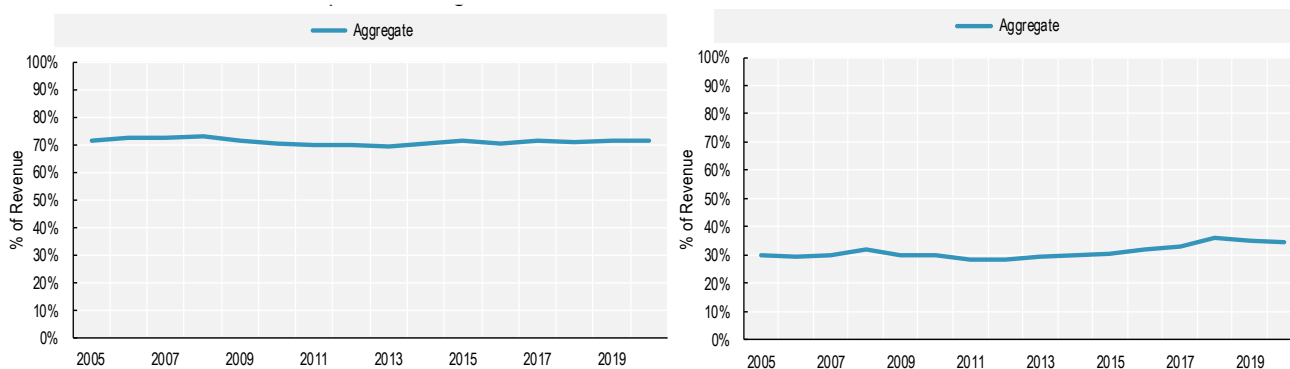
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia) by percentiles of firms across the distribution of the gross operating margin by total assets indicator.

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

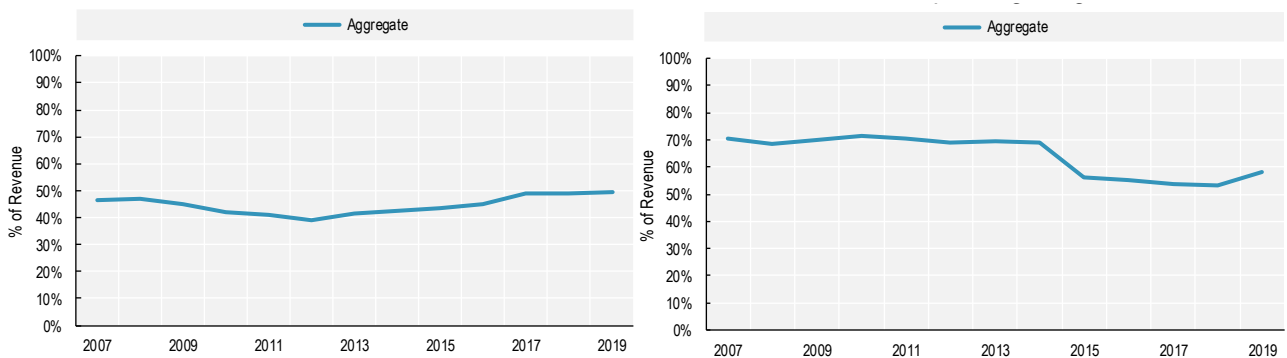
81. Publicly listed firms headquartered in OECD countries were significantly more profitable in aggregate than their counterparts in non-OECD countries, consistently generating gross margins close to 70% between 2005 to 2020 vs 30% to 36% in non-OECD countries. The opposite pattern was apparent for unlisted companies, where aggregate gross margins were between 40% and 50% in OECD countries vs 50% to 70% in non-OECD countries (Figure 4.17). It is unclear from the analysis why this is the case, but may be an artefact of firm size, with OECD countries home to larger publicly listed firms, and with differences in size less marked for unlisted firms. It could also be related to different business models, e.g. a higher proportion of R&D-focused firms among publicly listed firms in OECD countries, which sell more expensive products. Again, the OECD Orbis samples for non-OECD countries changed in size significantly between 2014 and 2015, so the apparent decline between these years may be influenced by a change in the composition of the sample.

Figure 4.17. Aggregate gross operating margin in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of revenue (sales), publicly listed firms 2005 to 2020, OECD countries (left) and non-OECD countries (right)



As a percentage of revenue (sales), unlisted firms 2007 to 2019, OECD countries (left) and non-OECD countries (right)



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

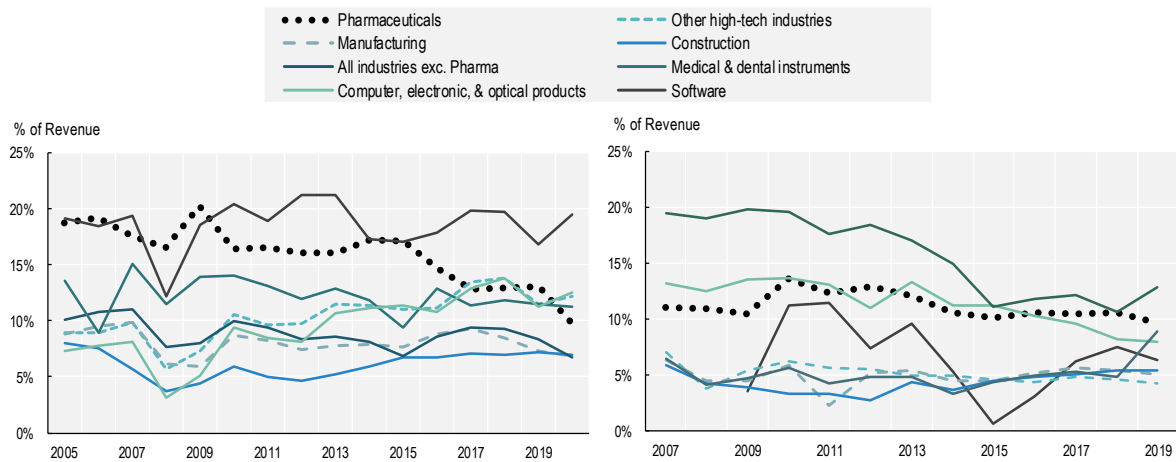
Net operating margin

82. Between 2005 and 2020, data were available from Refinitiv Datastream for an average of 1 320 publicly listed pharmaceutical firms per year (range 1 071 in 2005 to 1 837 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all countries in all years (see [Supplementary Material](#)). From OECD-Orbis, data are available for an average of 7 368 unlisted pharmaceutical firms per year in the period 2007 to 2019 (range 9 923 in 2014 to 3 756 in 2019) across the 40 countries included. The availability of microdata across the two datasets supports the feasibility of reporting this indicator.

83. In aggregate, publicly listed firms in the pharmaceutical industry generated net margins between 10% and 20% between 2005 and 2020 (Figure 4.18). This means that, in aggregate, publicly listed pharmaceutical firms retain between one-tenth and one-fifth of their revenue as profits after deducting the costs of production and all current operating expenses, including R&D and sales, marketing and administrative (SG&A) expenditure. A comparison with the gross operating margin analysis (see above) also reveals that publicly listed firms spend more on operating expenditure (approximately 46% to 53% of revenue between 2005 and 2020) than on production (30% to 38% of revenue in the same period). Net margins were higher than in most other industries until 2016, including the aggregate of four other R&D-intensive industries, except the software industry, which generated comparable or higher net margins in the entire period. With somewhat of a downward trend in pharmaceuticals over time, net margins had converged with other R&D-intensive industries by 2017, including with margins in the medical & dental instruments and the computer industries. Unlisted firms were less profitable in aggregate, with net margins ranging from 10% to 14% between 2007 and 2019 (also see Figure 4.18). This was also higher than in most other industries in the entire period, near the net margin of the computer and electronics industry, but below that of the medical and dental instruments industry. Unlisted pharmaceutical firms spent a comparable proportion of their revenue on operating expenditures, so that lower net margins were mainly driven by higher costs of production and thus lower gross operating margins (see above).

Figure 4.18. Aggregate net operating margin in the pharmaceutical and other industries

As a percentage of revenue (sales), publicly listed firms (left) and unlisted firms (right)



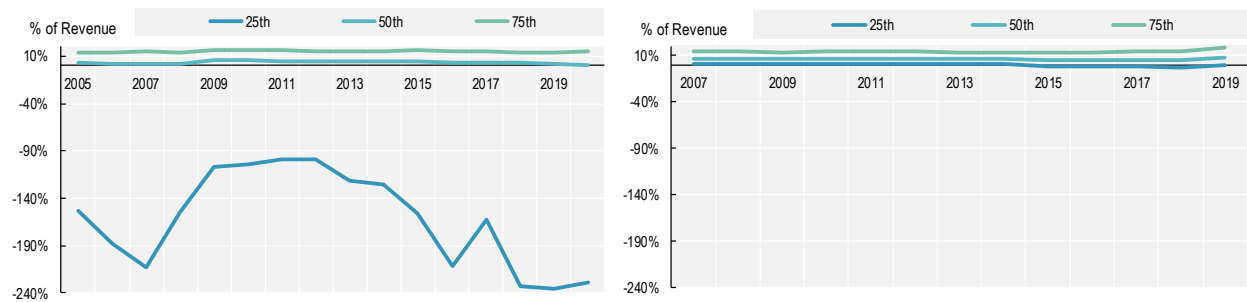
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries shows the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software. Data outliers for unlisted firms in the software industry in 2007 and 2008 were excluded from the figure (right panel).

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

84. The distribution across publicly listed firms was strongly skewed, with the 75th percentile close to the aggregate. The median was just above zero, meaning that nearly half of all firms are loss-making (Figure 4.19). This suggests that larger and more profitable firms drove the aggregate measures while loss-making firms are smaller and have a small effect on the aggregate, which was confirmed by a sub-group analysis by firm size. Net operating margins are positively correlated with firm size, with only the largest quartile of firms having clearly generated positive net margins in aggregate while the lowest quartile of the size distribution made net losses in aggregate. The largest publicly listed firms were thus clearly the most profitable, both in terms of gross and net operating margins. The distribution of unlisted firms, on the other hand, exhibited a rather different pattern, with little skewness, the 25th percentile close to zero and the aggregate above the median. This suggests that the majority of firms were profitable and that larger and more profitable firms drove the aggregate. This is confirmed by a sub-group analysis by firm size, with the largest quartile of firms having generated higher net margins than the remaining three quarters of the size distribution. It is notable that the largest unlisted firms were also the least profitable in terms of gross operating margin (see above), suggesting that these firms spend more on production than on operating expenditure relative to their revenue, i.e. they sell products that are expensive to produce relative to their selling prices but require fewer resources in R&D or sales. The pattern is less clear by firm age, with comparable net operating margins across the age distribution.

Figure 4.19. Firm-level distribution of net operating margin in the pharmaceutical industry

As a percentage of revenue (sales), publicly listed firms (left) and unlisted firms (right)

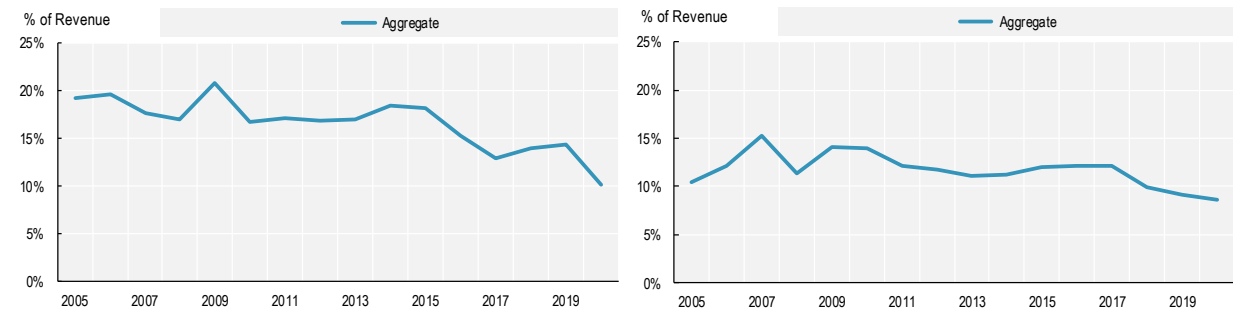


Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia) by percentiles of firms across the distribution of the net operating margin by total assets indicator.
 Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

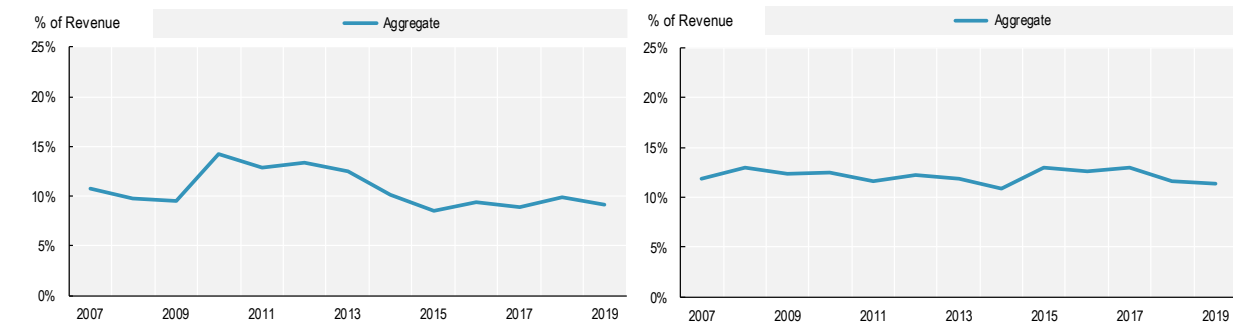
85. Publicly listed firms headquartered in OECD countries were more profitable in aggregate than their counterparts in non-OECD countries especially until 2015, with net margins between 17% and 21% vs. 10% to 14% in non-OECD countries, while there has been some convergence since then due to a decline in net margins of firms in OECD countries. This was not true for unlisted companies, where aggregate net margins were somewhat higher in non-OECD countries in most years, albeit with differences being small (Figure 4.20).

Figure 4.20. Aggregate net operating margin in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of revenue (sales), publicly listed firms, OECD countries (left) and non-OECD countries (right)



As a percentage of revenue (sales), unlisted firms, OECD countries (left) and non-OECD countries (right)



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

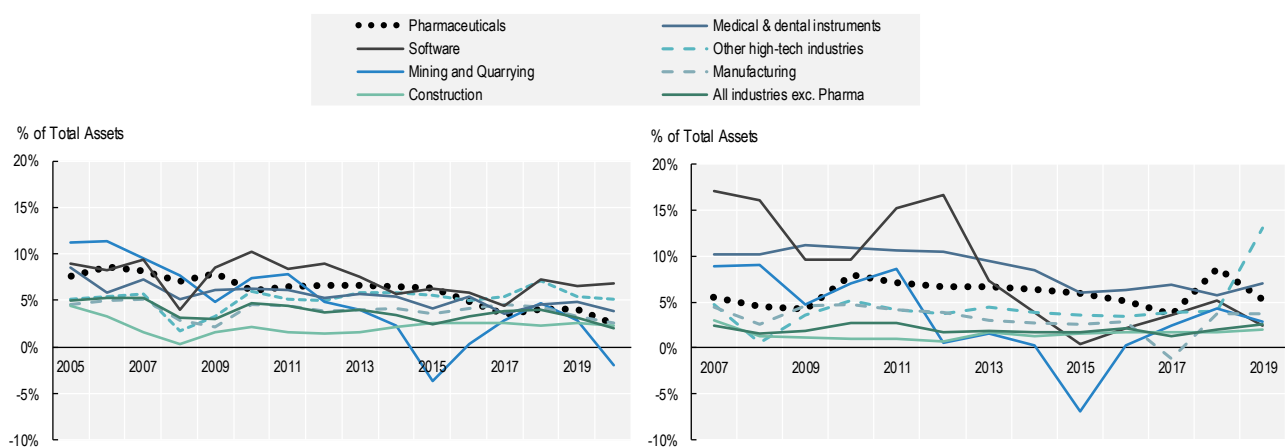
Return on Assets

86. Between 2005 and 2020, data are available from Refinitiv Datastream for an average of 1 387 publicly listed pharmaceutical firms per year (range 1 108 in 2005 to 1 905 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all of these countries in all years (see [Supplementary Material](#)). From OECD-Orbis, data are available for an average of 9 086 unlisted pharmaceutical firms per year in the period 2007 to 2019 (range 5 763 in 2019 to 11 078 in 2014) across the 40 countries included. The availability of microdata across the two datasets supports the feasibility of reporting this indicator.

87. In aggregate, publicly listed firms in the pharmaceutical industry generated returns on assets between 2.5% and 8.6% between 2005 and 2020 (Figure 4.21). This means that, in aggregate, publicly listed pharmaceutical firms generated annual net operating margins equivalent to 3% to 9% of their total assets. Until 2010, returns of publicly listed firms were higher in pharmaceuticals than in most other industries, including the total manufacturing sector and the aggregate of four other R&D-intensive industries, but comparable to the mining & quarrying, software and medical & dental instruments industries. With somewhat of a downward trend over time, returns were comparable to other R&D-intensive industries between 2010 and 2016 and dropped below the aggregate of these industries, closer to the total manufacturing sector after 2017. Firms frequently list R&D expenditure or activity as an asset, a practice known as capitalisation. Overall, the aggregate effect of capitalising R&D expenditure was small and resulted in higher or lower returns on assets depending on the year (see Box 4.1). Unlisted firms generated returns on assets of between 4% and 9% between 2007 and 2019 with no clear trend. This remained above returns of most other industries, including total manufacturing and the aggregate of four other R&D-intensive industries, but below returns in the medical & dental instruments industry in most of the period. While returns in the software industry were higher than in pharmaceuticals until 2013, the opposite is true since 2014. However, this trend should be viewed with caution as the sample composition in OECD Orbis has changed over time, including a significantly higher number of firms from China in later years.

Figure 4.21. Aggregate returns on assets in the pharmaceutical and other industries

As a percentage of total assets, publicly listed firms 2005 to 2020 (left), and unlisted firms 2007 to 2019 (right)

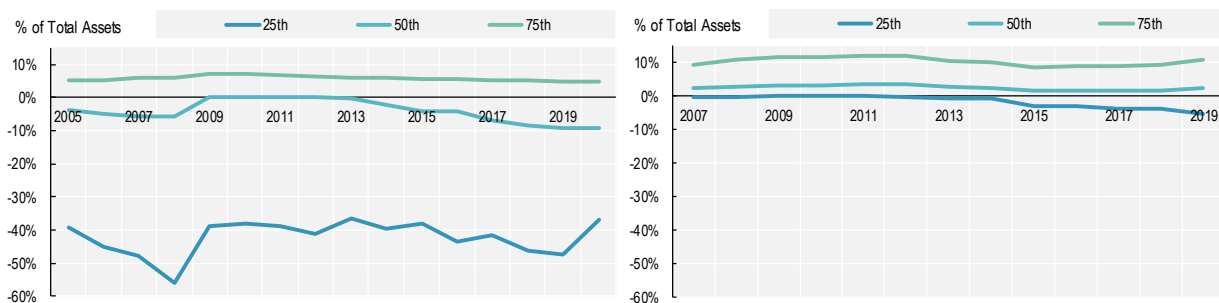


Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries shows the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software. A data outlier for the aggregate of unlisted firms in other R&D-intensive (high-tech) industries in 2019 was excluded from the figure (right panel). Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

88. The distribution of RoA across publicly listed firms was strongly skewed, with the 75th percentile close to the aggregate, a median close to but below zero in most years and a significant number of loss-making firms (Figure 4.22). This suggests that the aggregate was driven by larger and more profitable firms, which was confirmed by a sub-group analysis by firm size. Only the largest 25% of firms clearly generated positive returns on assets in aggregate while the lower 75% of the size distribution was making net losses in aggregate. The largest publicly listed firms were thus clearly the most profitable, even after accounting for the larger amounts of capital invested in them. However, the accounting treatment of R&D expenditure can have a significant effect on return on assets at the firm level, and a simulation suggests that for most firms the prevailing accounting treatment, which requires recognition of R&D as expenditure in the current period, leads to an understatement of returns on assets (see Box 4.1). The distribution of unlisted firms, on the other hand, exhibited a rather different pattern, with the 25th percentile close to zero and the aggregate above the median. This suggests that the majority of firms were profitable and that the aggregate was driven by larger and more profitable firms. This is confirmed by a sub-group analysis by firm size, with the largest quarter of firms having generated higher aggregate RoA than the remaining three quarters of the size distribution and the lower half of firms in the size distribution making losses in their respective aggregates. The pattern is less clear by firm age, with comparable returns on assets across the age distribution.

Figure 4.22. Firm-level distribution of return on assets in the pharmaceutical industry

As a percentage of total assets, publicly listed firms (left) and unlisted firms (right)



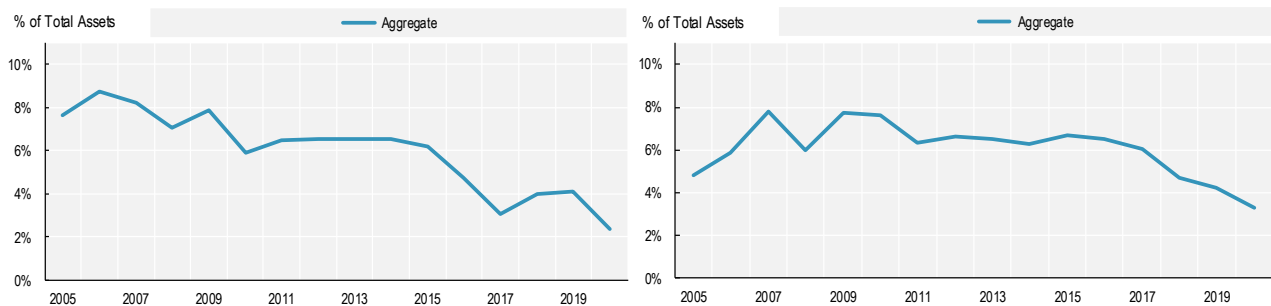
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

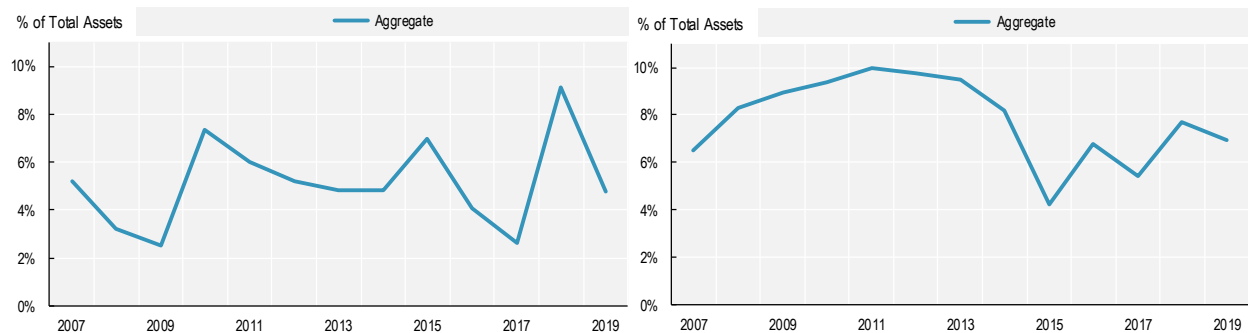
89. Over the entire period, there was no marked difference in aggregate returns on assets generated by publicly listed firms headquartered in OECD countries and their counterparts in non-OECD countries; in both, OECD and non-OECD countries, aggregate return on assets fluctuated between approximately 2% and 8% (Figure 4.23). However, while publicly listed firms in OECD countries were more profitable than in non-OECD countries earlier in the period analysed, their profitability declined to levels below that of firms in non-OECD countries by 2017. For unlisted firms, on the other hand, returns on assets were somewhat higher in non-OECD countries, particularly prior to 2015. However, the trend since 2015 in non-OECD countries should be viewed with caution, as the sampling method in OECD Orbis changed between 2014 and 2015, and the trend may be driven in part by changes in the composition of the sample.

Figure 4.23. Aggregate returns on assets in the pharmaceutical industry in OECD and non-OECD countries

As a percentage of total assets, publicly listed firms, OECD countries (left) and non-OECD countries (right)



As a percentage of total assets, unlisted firms, OECD countries (left) and non-OECD countries (right)



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis data.

Net Return on Assets

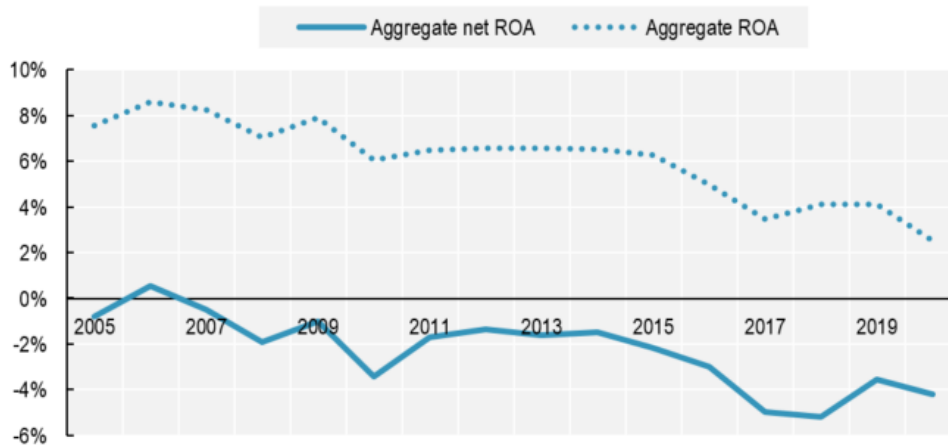
90. Between 2005 and 2020, data are available from Refinitiv Datastream for an average of 1 318 publicly listed pharmaceutical firms per year (range 957 in 2005 to 1 889 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all these countries in all years (see [Supplementary Material](#)). Overall, the availability of microdata across the two datasets supports the feasibility of reporting this indicator.

91. In aggregate, publicly listed firms in the pharmaceutical industry generated negative net returns on assets in all years except 2006 (range -5.2% in 2018 to +0.5% in 2006) (Figure 4.21). This means that based on an ex-post analysis, publicly listed pharmaceutical firms overall made economic losses as their returns on assets invested were lower than the returns investors demanded given the perceived risk of investing in the industry¹⁸. Because the aggregate cost of capital was relatively constant in the period analysed (see below), the downward trend can be attributed to a downward trend in profitability, rather than an increase in investment risk.

¹⁸ This does not take into account ex-ante market valuations of firms or assets, which are based on returns investors expect when investing in a firm or firms expect when making new investment decisions.

Figure 4.24. Aggregate net returns on assets in the pharmaceutical industry

Publicly listed firms only, 2005 to 2020



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and Bloomberg

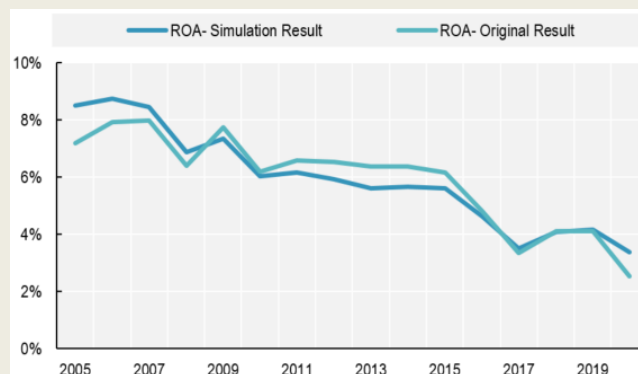
Box 4.1. The effect of capitalising R&D expenditure on aggregate profitability is small

A simulation of the effect of capitalising R&D expenditure was performed using a sample of 1 310 to 1 905 publicly listed firms from the Refinitiv Datastream dataset between 2005 and 2020, accounting for more than 90% of total R&D expenditure in the pharmaceutical industry (see Section 4.2.4). In aggregate, the net effect on return on assets remained below 1 percentage point in all years except 2005 (+1.3 pts), with small negative effects from 2009 to 2016 and positive effects in the remaining years (Figure 4.25). A hypothesis that prevailing accounting standards overstate returns on assets in the pharmaceutical industry is therefore not supported. Further information on the motivation and methodology are available in the [Supplementary Material](#).

Capitalisation increased total assets by between 29% to 36% per year and operating margins by between 17% and 71%. It should also be noted, however, that effects can be much more significant for individual firms. Capitalising R&D expenditure increased return on assets at the 25th, 50th and 75th percentiles of the firm distribution with a particularly strong effect at the lower end of the distribution (+22 pts to +36 pts at the 25th percentile).

Figure 4.25. Effect of capitalising R&D expenditure on aggregate returns on assets in the pharmaceutical industry

Publicly listed firms only, 2005 to 2020



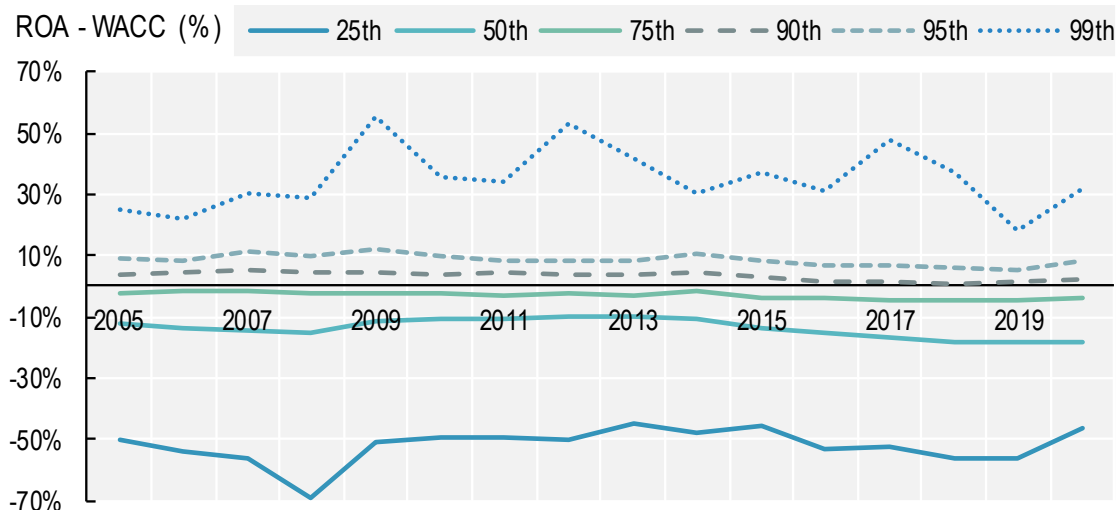
Note: ROA is return on assets

Source: OECD analysis based on Refinitiv Datastream. More detail on the methods of the analysis is available in the [Supplementary Material](#).

92. However, the distribution across publicly listed firms was strongly skewed. While the majority of firms generate economic losses, which are significant at the low end of the distribution, there is a small group of firms at the top end of the distribution that generate returns in excess of their cost of capital. The 90th percentile was consistently above zero, meaning that the top 10% of firms generate returns in excess of what investors demand given their investment risk. The 95th percentile ranged from 5% to 11% while the 99th percentile ranged from approximately 20% to 50% (Figure 4.26). With an aggregate above the mean, this also suggests that larger firms tend to be towards the upper end of the profitability distribution. A sub-group analysis by firm size shows a clear gradient by firm size, with net return on assets increasing from the first quartile (smaller firms) to the fourth quartile (larger firms) in the size distribution. The age distribution exhibits the same pattern, with increasing net return on assets from first quartile (younger firms) to the fourth quartile (older firms); since this pattern is not apparent in the return on assets measure, it can be assumed that less mature firms have higher investment risks reflected in higher costs capital.

Figure 4.26. Firm-level distribution of net returns on assets in the pharmaceutical industry

Publicly listed firms only, 2005 to 2020



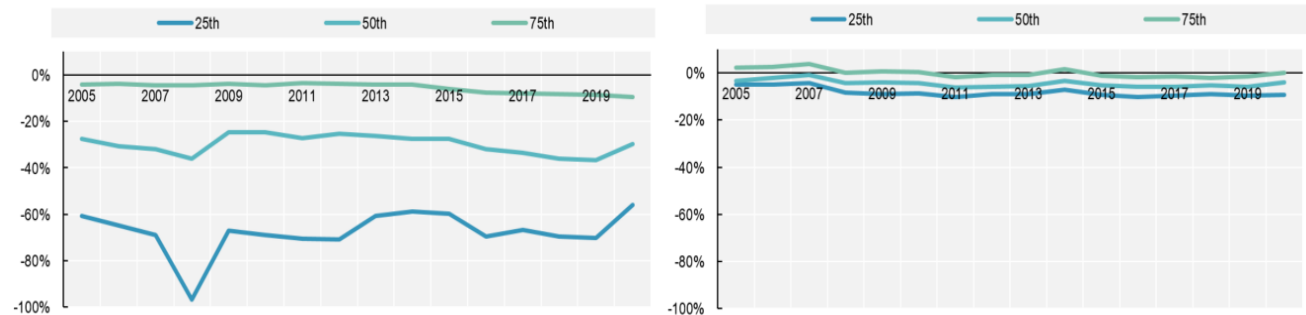
Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

Source: OECD analysis based on Refinitiv Datastream and Bloomberg

93. While the majority of firms in non-OECD countries also generate economic losses, the median in non-OECD countries is closer to zero and there is less dispersion in the firm-level distribution compared to OECD countries (Figure 4.27). Also, albeit negative, the 25th percentile of firms in non-OECD countries is higher than in OECD countries and the 75th percentile fluctuated closer to zero. This suggests that there is a much smaller proportion of firms making economic losses and a higher proportion of economically profitable firms in non-OECD countries, despite comparable aggregate returns on assets (see above). This also suggests that there is a structural difference between the pharmaceutical industry in OECD and non-OECD countries.

Figure 4.27. Firm-level distribution of net returns on assets in the pharmaceutical industry in OECD and non-OECD countries

Publicly listed firms only 2005 to 2020, OECD (left) and non-OECD (right)



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Net ROA is expressed as a percentage determined from subtracting WACC from ROA.

Source: OECD analysis based on Refinitiv Datastream and Bloomberg

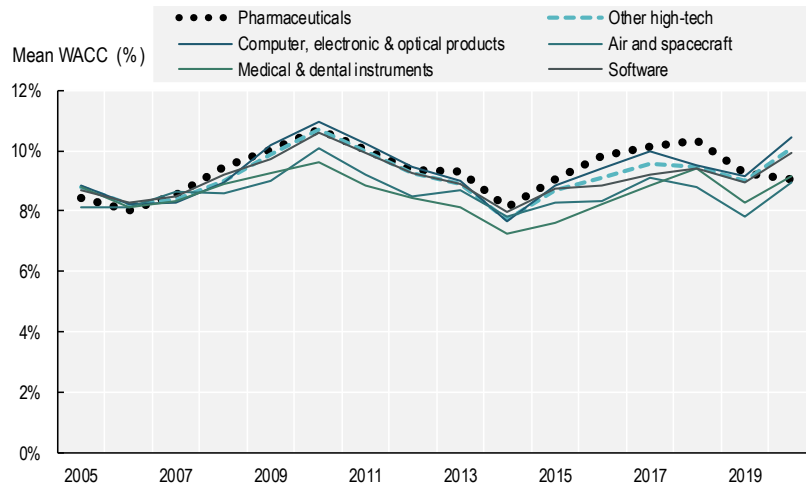
4.2.3 Cost of capital

94. Between 2005 and 2020, data were available from Bloomberg for an average of 1 318 publicly listed pharmaceutical firms per year (range 958 in 2005 to 1 890 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all of these countries in all years (see [Supplementary Material](#)). Overall, the availability of microdata across the datasets supports the feasibility of reporting this indicator.

95. The mean across all firms of firm-level weighted average cost of capital (WACC) in the pharmaceutical industry ranged from 8.0% to 10.7% between 2005 and 2020. This was generally close to the mean WACC across other R&D-intensive industries and, since 2008, somewhat higher than in manufacturing of air & spacecraft and medical & dental instruments. While the WACC in the pharmaceutical industry was somewhat higher than in other R&D-intensive industries between 2013 and 2019, it dropped to below that of other industries in 2020 (Figure 4.28). The WACC was somewhat lower for firms headquartered in OECD countries than for firms in non-OECD countries, however, this difference was also small.

Figure 4.28. Mean of firm-level weighted average cost of capital (WACC) in the pharmaceutical and other R&D-intensive industries

Publicly listed firms only, 2005 to 2020

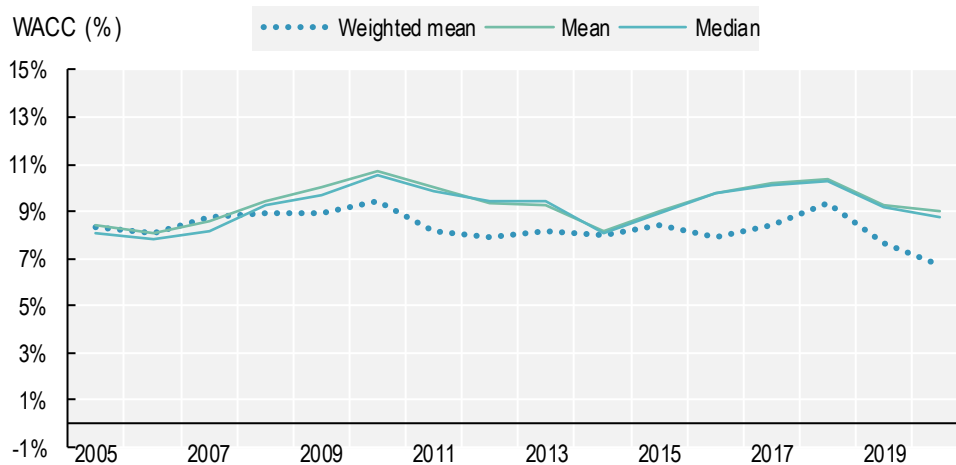


Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). Other high-tech (R&D-intensive) industries shows the aggregate of manufacture of computer, electronic and optical products; manufacture of air and spacecraft and related machinery; manufacture of medical and dental instruments and supplies and software. Source: OECD analysis based on Refinitiv Datastream and Bloomberg databases

96. There was little skewness in the distribution across firms in the pharmaceutical industry, with a median close to the mean and the 25th and 75th percentiles approximately 2 percentage points from the mean and median. However, a mean weighted for capital invested in each firm was below the unweighted mean and median since 2007 (Figure 4.29). The weighted mean is an aggregate measure of cost of capital for the industry. A lower weighted mean implies that larger firms, which tie up more capital and drive this measure, have a lower WACC than smaller firms and that the WACC for the industry as a whole is below that of the average firm in the industry.

Figure 4.29. Aggregate, mean and median cost of capital in the pharmaceutical industry

Publicly listed firms only, 2005 to 2020



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia). *Weighted mean*, as referred to in the figure above, is the mean WACC, weighed by total assets, across all firms in the aggregate. *Mean* in the figure refers to an unweighted mean WACC across all firms, and *Median* signifies the midpoint of the distribution of WACC across firms.

Source: Source: OECD analysis based on Refinitiv Datastream and Bloomberg databases

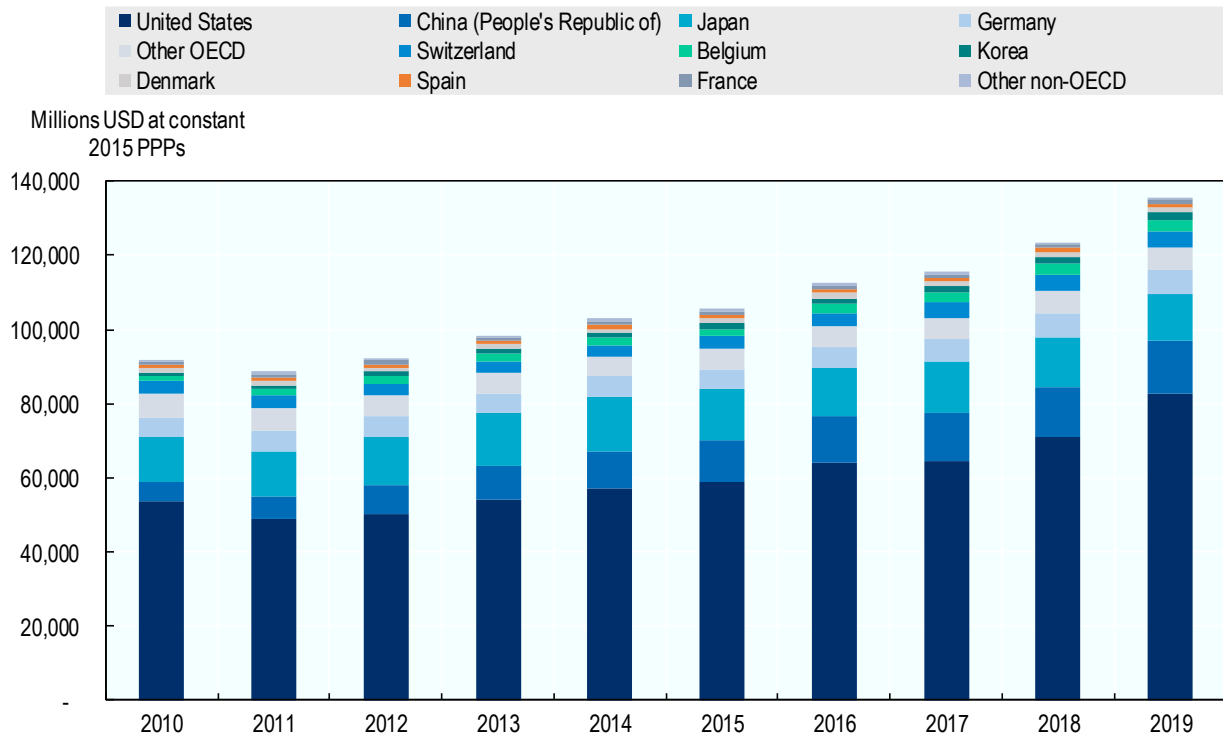
4.2.4 Research & development (R&D) expenditure

OECD R&D Statistics

97. R&D expenditure data from OECD R&D Statistics were available for a total of 33 OECD countries and four non-OECD countries in at least one year between 2017 to 2020, with data for most countries available from 2019. Across these 37 countries, the pharmaceutical industry spent USD 148 billion on R&D in the latest year with available data, of which USD 129 billion was spent in OECD countries. R&D expenditure in the United States alone accounted for 69% of the OECD total, followed by Japan (10%) and Germany (6%). R&D expenditure by the pharmaceutical industry in China amounted to USD 18.7 billion in 2020, making it the country with the second highest expenditure, ahead of Japan and Germany.

98. Since 2010, R&D expenditure by the pharmaceutical industry in OECD countries with available data has increased by 39% in real terms, i.e. at constant purchasing power parities (PPPs). Following a decline between 2010 and 2011 and annual growth rates of 2% to 6% from 2012 to 2017, growth accelerated to 11% from 2018 to 2019. Growth of the OECD aggregate is strongly driven by the United States, which accounted for 62% of R&D expenditure in the OECD in 2010 but where expenditure grew more rapidly between 2010 and 2019 than in other countries. Some smaller OECD countries exhibited rapid growth in this period, including Poland (161%), Chile (136%) and Korea (114%). However, their share of the OECD aggregate remains small. By far the most significant growth was observed in China, where R&D expenditure increased from USD 4.9 billion (in constant 2015 PPPs) to 14.2 billion in 2019 (189%). Figure 4.30 shows the trend in R&D expenditure between 2010 and 2019 for the top countries.

Figure 4.30. Trend in R&D expenditure in the pharmaceutical industry by country, 2010 - 2020



Note: Includes 33 OECD countries, all except Australia, Colombia, Costa Rica, Luxembourg and New Zealand. Other non-OECD countries include Chinese Taipei, Romania and Singapore. Missing data in any given country and year are replaced with values from the most recent year available.

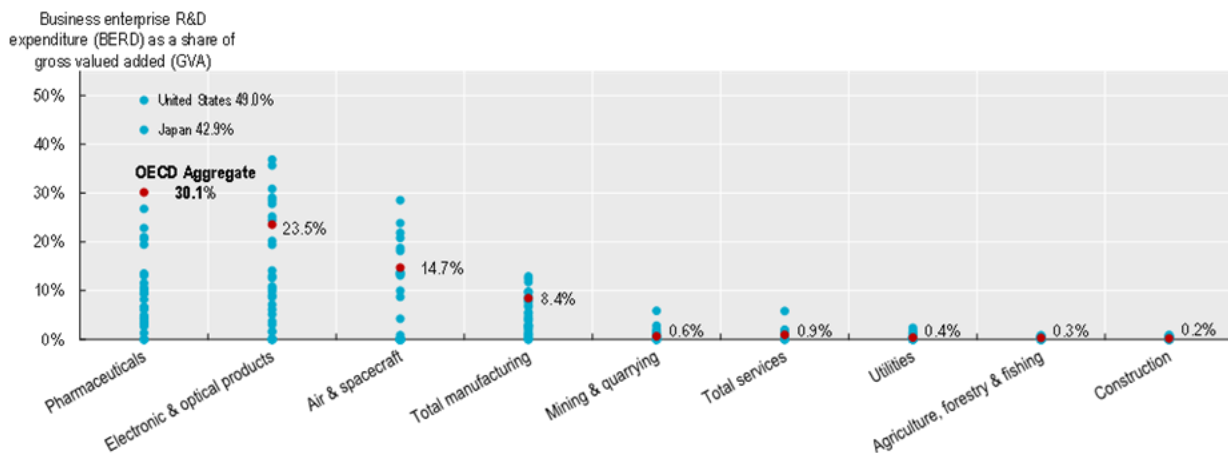
Source: OECD Analytical Business Enterprise R&D (ANBERD) database

99. Recent data on business enterprise R&D expenditure (BERD) and gross value added (GVA) at the industry-level were available for 17 OECD countries for the air & spacecraft; and between 32 and 37 OECD countries for all other industries. In aggregate across OECD countries for which recent data are available, the pharmaceutical industry spent a higher proportion of its gross value added (GVA) on R&D than other industries. R&D intensity was 30% of GVA in 2019 (or the latest year of data available between 2017 and 2020), compared to 24% in the computer & optical products, 15% in the air & spacecraft, and 8% across all manufacturing industries (Figure 4.31).

100. It should be noted that the OECD aggregate for the pharmaceutical industry is heavily driven by the United States and Japan, which together accounted for nearly 80% of aggregate BERD across OECD countries, and in which R&D intensity stood at 49% and 43% respectively. R&D intensity in all other OECD countries was below the aggregate, led by Belgium (27%), Slovenia (23%) and Sweden (19%). In other industries, the aggregate is less driven by outliers and closer to the centre of the distribution across countries.

101. Outside the OECD, R&D intensity can be assumed to be driven by China. However, no recent GVA data are available with which to compute R&D intensity.

Figure 4.31. R&D intensity in the pharmaceutical and other industries of OECD countries, 2019 or nearest year



Note: The air & spacecraft, electronic & optical products, and pharmaceuticals industries are sub-categories of total manufacturing. All other industries are at the same level as total manufacturing. The OECD aggregate based on available BERD and GVA data across 17 countries for air & spacecraft; and between 32 and 37 countries for all other industries.

Source: OECD Analytical Business Enterprise R&D (ANBERD), Structural Analysis (STAN) and System of National Accounts (SNA) databases.

Firm-level data

102. Between 2005 and 2020, data are available from Refinitiv Datastream for an average of 1 386 publicly listed pharmaceutical firms per year (range 1 108 in 2005 to 1 904 in 2020) across the 40 countries included. However, the sample does not include pharmaceutical firms from all of these countries in all years (see [Supplementary Material](#)). From OECD-Orbis, data are available for an average of 7 653 unlisted pharmaceutical firms per year in the period 2007 to 2019 (range 3 882 in 2019 to 11 565 in 2019), including firms whose R&D expenditure is assumed to be zero when data are missing, across the 40 countries included. Because GVA data are not consistently available in firm-level datasets, R&D intensity estimates based on firm-level data are expressed as R&D expenditure as a proportion of revenue.

103. A comparison with aggregate OECD R&D Statistics, using output rather than GVA as denominator, showed that firm-level data are likely to understate R&D intensity in recent years. It is not clear from this analysis why this is the case but could be driven by a number of factors. First, firm-level data report R&D expenditure and revenue according to accounting standards (see [Supplementary Material](#)), which differ from definitions of business enterprise R&D expenditure (BERD) and output in OECD statistics. Second, firm-level data include not only firms assigned to NACE industry codes 2110 and 2120 but also 7211 “Research and experimental development on biotechnology” while aggregate OECD statistics only include ISIC industry code 21 “Manufacture of basic pharmaceutical products and preparations” (see Section 2); in OECD statistics data are available only at the level of the entire ISIC division 72 “Scientific research and development”, which would not allow identifying a more narrow sector of research in biotechnology. Third, the geographic scope differs slightly; while OECD R&D Statistics cover all OECD countries except Australia, Colombia, Costa Rica, Luxembourg and New Zealand, the OECD Orbis and Refinitiv Datastream samples include Australia, Colombia, Luxembourg and New Zealand but do not include Chile, Costa Rica, Poland and Türkiye. Fourth, and importantly, the OECD Orbis and Refinitiv Datastream samples may not be representative of the entire pharmaceutical industry in all countries. A comparison with aggregate OECD R&D Statistics shows that R&D intensity might be particularly understated in the United States, which accounts for more than two-thirds of R&D expenditure across OECD countries. While OECD R&D Statistics suggest that BERD in the United States increased from 24% to 28% of output in the pharmaceutical industry between 2010 and 2019, firm-level data yield estimates of R&D expenditure in the

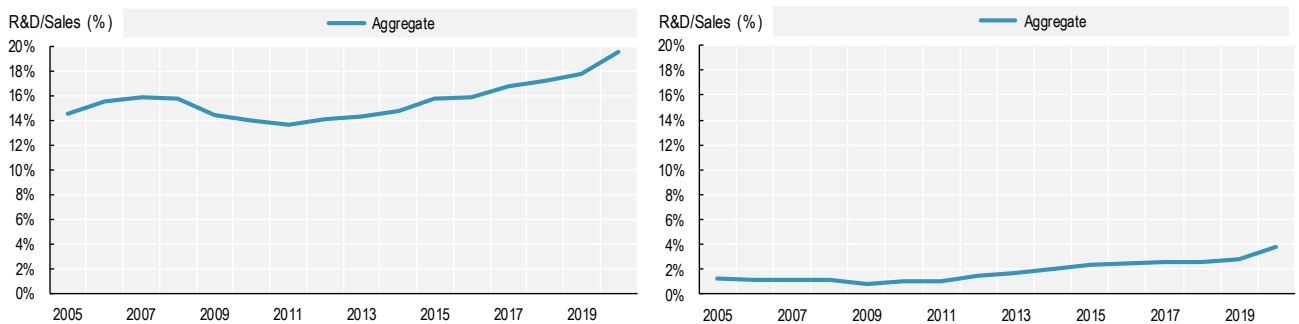
range of 17% to 24% of revenue in the same years. Furthermore, missing firm-reported R&D expenditure was assumed as zero rather than missing, which might introduce bias into some estimates.

104. Consequently, estimates of R&D intensity presented below should therefore be interpreted with caution. However, these limitations above notwithstanding, the estimates provide useful insights into differences between OECD and non-OECD countries, publicly listed and unlisted firms, and into the distribution across firms, none of which is apparent from aggregate OECD statistics.

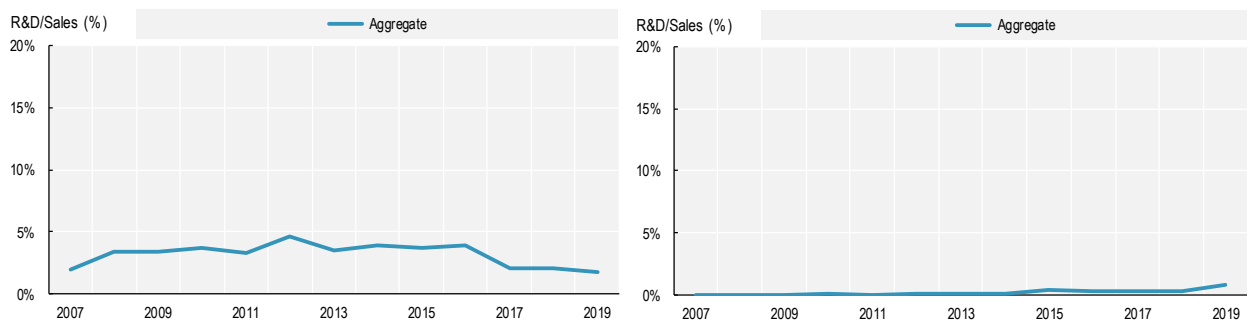
105. Aggregate R&D expenditure reported by pharmaceutical firms in the Refinitiv and Orbis samples is heavily driven by firms that are publicly listed and headquartered in OECD countries. Firms in OECD countries accounted for between 95% (in 2019) and 99.5% (2007) of total expenditure, and publicly listed firms in OECD countries for between 91% (in 2011) and 97% (2007) of the total. In aggregate, R&D intensity of publicly listed firms was between 12% and 16% as a share of sales between 2005 and 2020. R&D intensity was higher in OECD countries, where publicly listed firms exhibited intensities of between 14% and 20% of revenue between 2005 and 2020 with an upward trend since 2011 vs. approximately 1% in non-OECD countries until 2011 and also an upward trend since then, having reached 4% by 2020 (Figure 4.32). For unlisted firms, R&D intensity remained in a range of 2% to 5% between 2007 and 2019 in OECD countries, and below 1% in non-OECD countries (Figure 4.32). Due to treating missing R&D expenditure as 0, there could be additional bias from the composition of firms in the respective samples.

Figure 4.32. Aggregate R&D intensity in the pharmaceutical industry in OECD and non-OECD countries

In % of revenue, publicly listed firms, OECD countries (left) and non-OECD countries (right)



In % of revenue, unlisted firms, OECD countries (left) and non-OECD countries (right)



Note: Due to data availability, R&D intensity is expressed as a proportion of revenue, not of gross value added (GVA) so it is not comparable to the aggregate results in Figure 4.32. Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) and 6 non-OECD countries (Brazil, China, India, Indonesia, Romania and Russia).

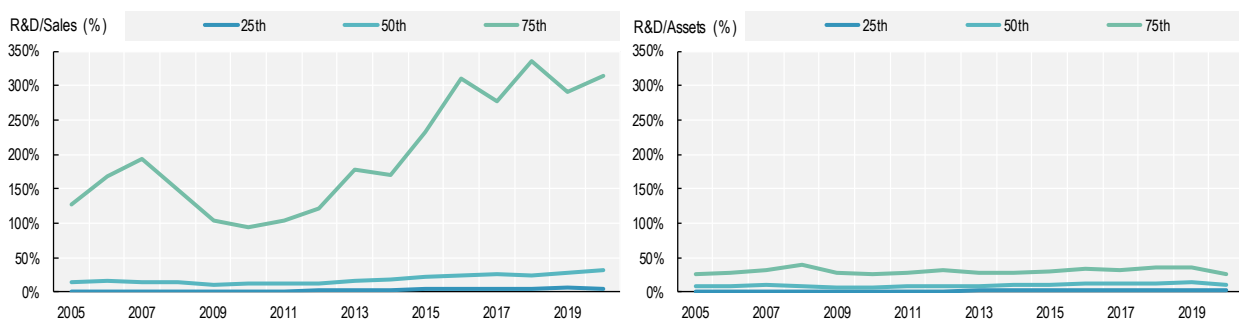
Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

106. Among publicly listed firms in OECD countries, the median was close to the aggregate R&D intensity until 2012 but has increased more rapidly since then, reaching 32% of revenue by 2020 vs. an aggregate

of 20%. Throughout the entire period, the distribution exhibits a long tail towards the top-end: the 75th percentile increased from 100% of revenue in 2011 to more than 300% in 2020 (Figure 4.33). This may reflect a significant number of relatively immature firms that invest heavily in R&D but generate little revenue. Expressing R&D intensity in terms of total assets confirms the notion that the upper end of the distribution is dominated by firms that generate little revenue; while skewness towards firms with high R&D intensity is also present, the 75th percentile was between 25% and 40% of assets in the same period (Figure 4.33).

Figure 4.33. Firm-level distribution of R&D intensity in the pharmaceutical industry in OECD countries

Publicly-listed firms only, in % of revenue (left) and in % of assets (right)



Note: Includes 34 OECD (all countries except Chile, Costa Rica, Poland and Türkiye) countries.

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis

107. A sub-group analysis by firm size revealed that the aggregate was clearly driven by large firms, with the aggregate R&D intensity across all firms close to that of the largest 25% of firms, while the smallest 25% of firms exhibited R&D intensities equivalent to 50% to 160% of revenue. However, a sub-group analysis by firm age showed no clear pattern until 2013, with R&D intensities in each age group that were comparable to the overall. Only since 2014 did the youngest 25% of firms exhibit higher aggregate R&D intensities (between 17% and 25% of revenue) while the remaining 75% of firms in the age distribution continued to have R&D intensities close to the aggregate across all firms. Firms with high R&D expenditure relative to their revenue are thus not necessarily younger firms.

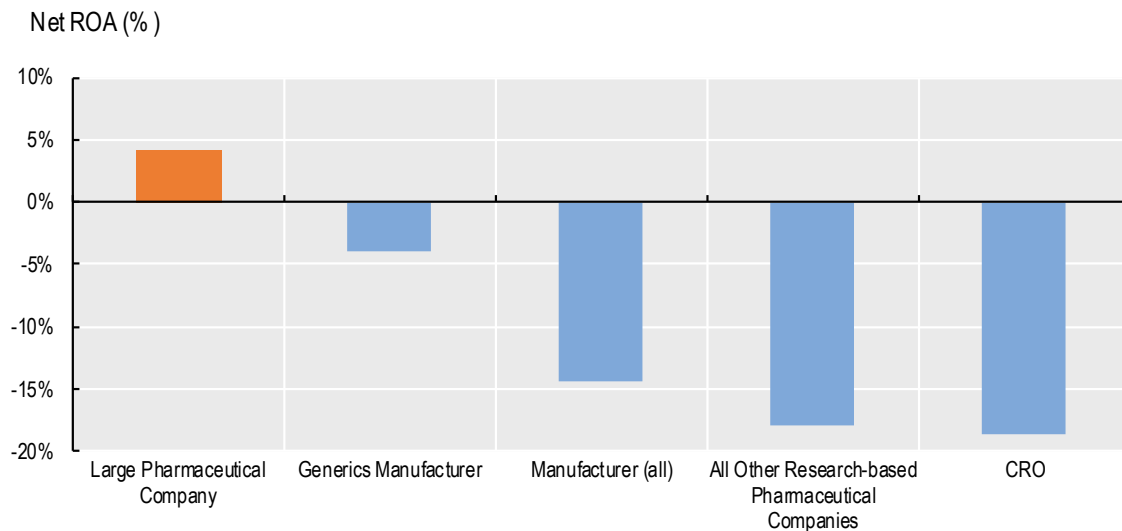
4.2.5 Further disaggregation by firm type

108. As discussed through the financial activity indicators, the presence of heterogeneity across firm types in the sample skews the aggregate results and challenges interpretation of the findings. A supplementary analysis was conducted to assess the degree to which different organisations within the firm sample were positioned with respect to the indicators. As it was not possible to map the entire sample beyond the NACE industry codes, a random, geographically-stratified sample of 1000 firms was selected. As there was no data readily available to categorise the firms into measurable categories, all firms were manually reviewed and mapped to overarching firm archetypes that include different firm types in the pharmaceutical industry (further information on methods is available in the [Supplementary Material](#)). The firm archetypes included are:

- **Manufacturers (all):** all firms whose predominant activity is the manufacturing of pharmaceutical products with little to no research activity. This group includes publicly listed, unlisted, and generic firms

- **Generic manufacturers:** a subset of firms in *Manufacturers (all)* that specifically mention the production of generic, off-patent products, or 'active' molecules.
- **Large Pharmaceutical Companies:** The top pharmaceutical firms by sales revenue. These firms have multiple roles, most notably in the research, development, and production of originator medicines. The firms included are: Johnson & Johnson, Bristol-Myers Squibb, AbbVie, Merck & Co, Novartis, Eli Lilly, GlaxoSmithKline, Sanofi, Novo Nordisk, Amgen, Pfizer, and Gilead Sciences.
- **All Other Research-Based Pharmaceutical Companies:** all other pharmaceutical, biopharmaceutical, and biotechnology companies directly involved in the research and development of drugs or interventions.
- **Contract Research Organisations (CROs):** firms that are contracted to oversee a research element such as clinical or other downstream drug development stages, but are not originators of new products.

Figure 4.34. Net Return on Assets (ROA) by Firm Type (2019)



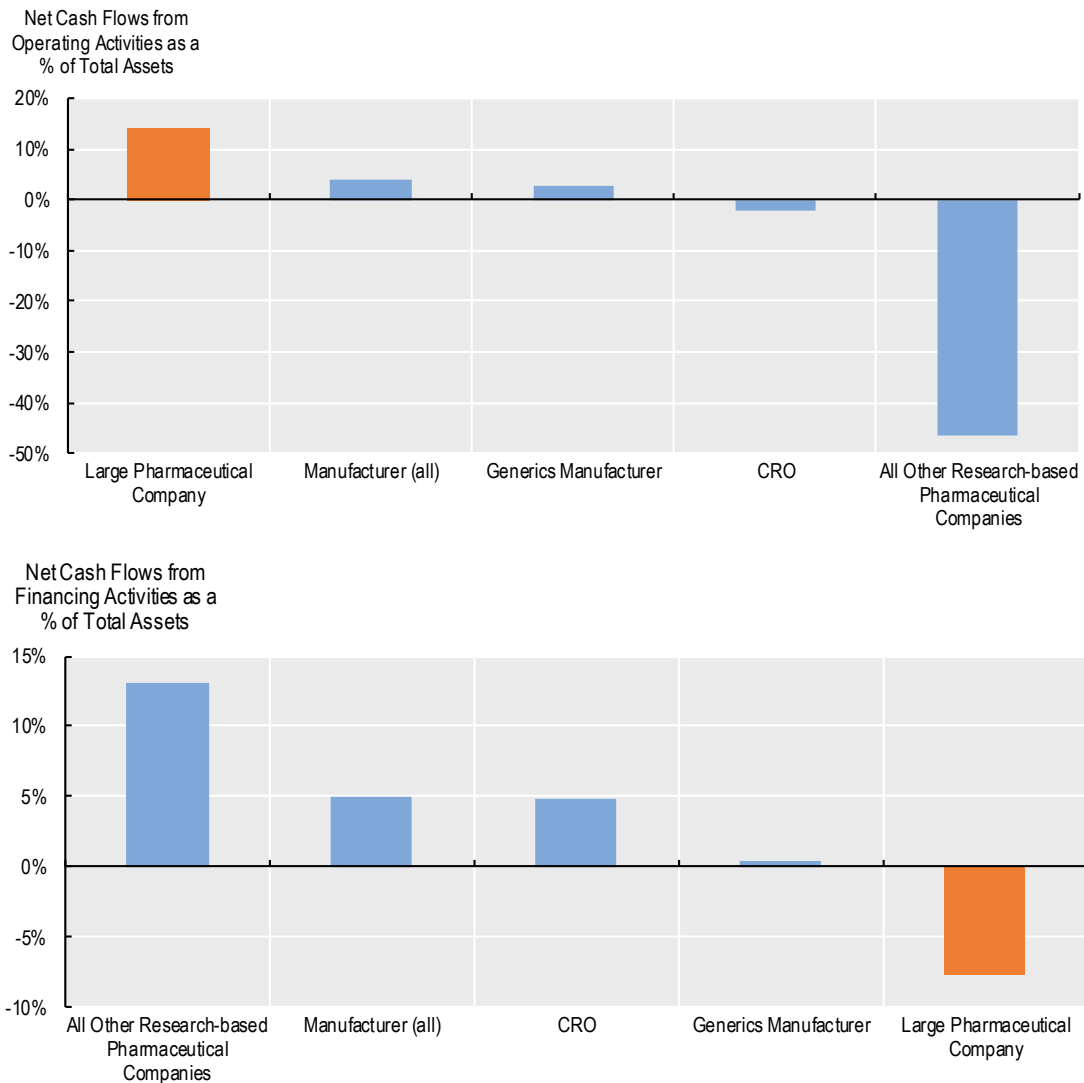
Note: Based on averages by disaggregated firm subgroup, restricted to publicly listed firms. Net ROA (%) is the difference between ROA and the Cost of Capital (WACC).

Source: OECD analysis based on Refinitiv Datastream, year 2019

109. Net ROA, as a measure of profitability, varies widely by firm size as discussed in previous sections (see Figure 4.34), and results in similar heterogeneity when compared to the aggregate measures and large pharmaceutical companies as a driving outlier. The difference in average profitability across different firm types suggests the need for segmentation both in analysing and interpreting the financial information further. It should be noted that this sample was restricted to publicly listed firms in the Refinitiv Database and might not consider all relevant subsidiaries. Further work could address the creation of more granular and measurable categories of firm types and structures across the industry, as well as the expansion of the analysis to the entire sample (both in number of firms and years). Selection of the uppermost segment by revenue introduces a bias, but the respective roles and sizes are comparable, and more work can be done to categorically measure firm size, structures, and characteristics within subgroups. This result highlights the heterogeneity among research-based companies and across the industry as a whole.

Figure 4.35. Cash Flows from Financing and Operating Activities by Firm Type (2019)

Net cash flows from operating activities (top) and financing activities (bottom) in relation to firm type



Note: Based on averages by disaggregated firm subgroup. Net operating cash flows includes unlisted and listed firms, while net financing cash flows only includes listed.

Source: OECD analysis based on Refinitiv Datastream and OECD Orbis, year 2019

110. Net cash flows from financing and operating activities exhibited similar heterogeneity across different firm types as well as outlier behaviour from large pharmaceutical companies (lesser effect in operating cash flows). Operating cash flow is a measure of regular business income-generating activities and can vary widely across different types of firms in the industry. Smaller research-based pharmaceutical companies are more likely to be investing in R&D for new products than earning profits from existing products, while larger companies, which may have developed patented products via research or M&A, are able to maintain a positive cash flow through revenue (Figure 4.35 top). Net cash flows from financing activities accounts for cash raised from investors, including equity and debt, as well as cash outflows, including payments to shareholders and to creditors for servicing debt. Large pharmaceutical companies are the only group to have significantly negative cash flows, meaning more funds are paid to shareholders

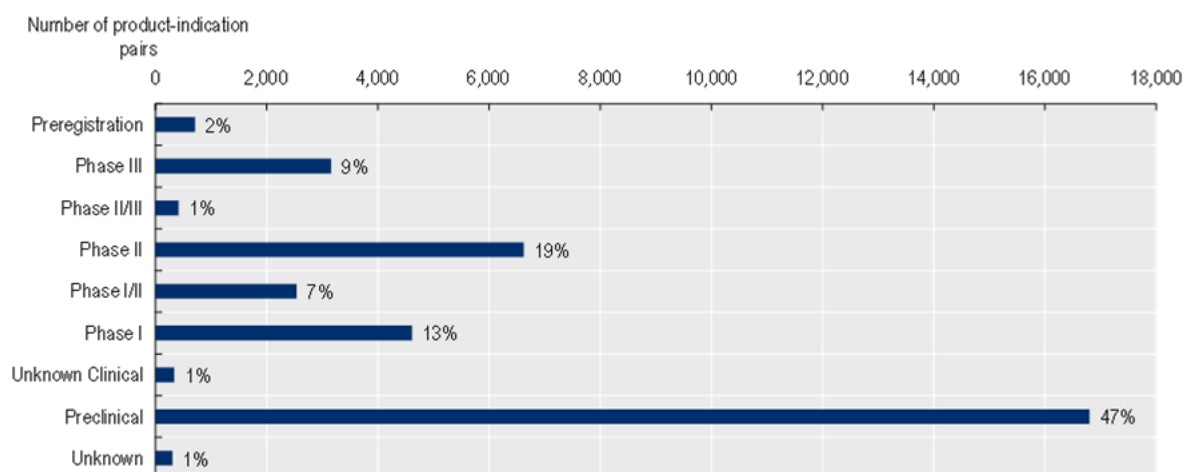
than are brought in from capital markets (Figure 4.35 bottom). It should be noted that the net cash flows from financing activities analysis was restricted to public firms in the Refinitiv Database.

111. This was an experimental analysis and further consideration is needed. The initial results highlight the heterogeneity of firm types across the financial activity indicators as well as the distinct behaviour of large pharmaceutical companies. This suggests that among firms considered to constitute the pharmaceutical industry, there are different models of financing and operating behaviour; and thus, these groups should be studied independently rather than through aggregate indicators across the industry. These analyses, however, were limited by resource and data constraints and are not currently feasible for any further interpretation or reporting. Further work should be done to categorically map a larger sample of firms to distinct, granular firm types with longitudinal observations and individual structure considerations to determine distinctive behaviour within the indicators.

4.2.6 Number of product development projects

112. By the end of 2021, data from the AdisInsight database showed 20 415 medicines or vaccines in active and commercial product development. These products development projects covered a total of 35 521 unique product and indication combinations. Approximately 47% of these product-indication pairs were in pre-clinical development, followed by phase 2 (19%) and phase 1 (13%).

Figure 4.36. Product-indications in active development by phase, as of 31st of December 2021



Note: Excludes products that have already received marketing authorisation or have been launched.

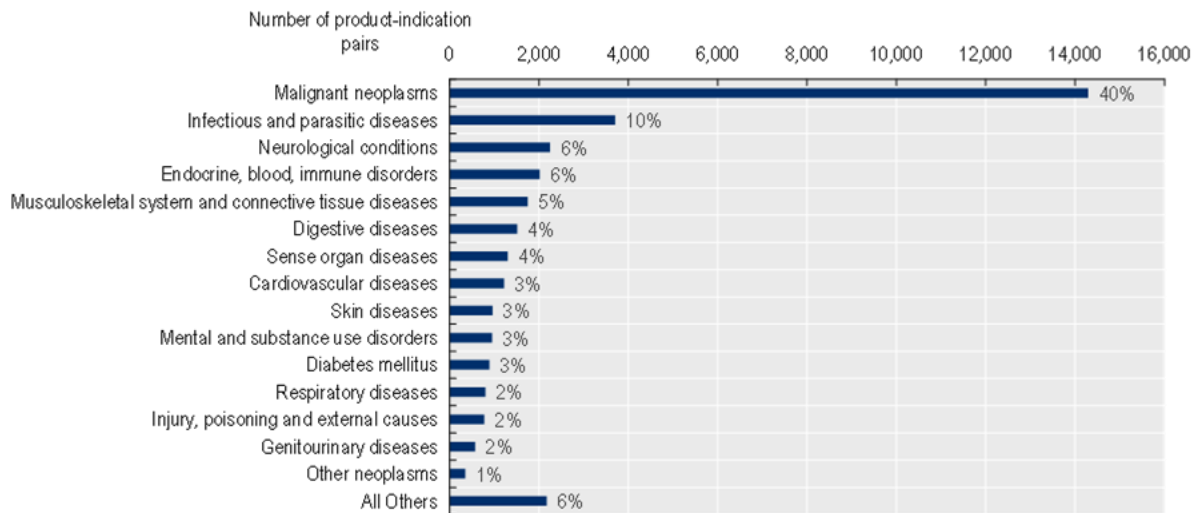
Source: OECD analysis based on AdisInsight data

113. Non-communicable diseases accounted for 81% of product-indication pairs while communicable, maternal, perinatal and nutritional conditions accounted for 12% (the remaining 7% were related to injuries and unclassified indications). Cancer was the disease category that attracted by far the most product development, representing 40% of the total, followed by infectious and parasitic diseases (10%), and neurological conditions (6%) (see Figure 4.37). Overall, 12,824 products (63% of the total) were new molecular entities (NMEs),¹⁹ accounting for two-thirds of all product-indication pairs. Approximately 2,000 orphan indications were in active development (6% of all product-indication pairs).

¹⁹ NMEs are medicines whose active moiety has never been approved by the European Medicines Agency (EMA) in the European Union or the Food and Drug Administration (FDA) the United States.

114. The pharmaceutical industry plays a major role in product development. Of 20 415 products in active development, 18 127 (89%) originated exclusively from entities that were part of the industry (88% of all product-indication combinations), and 18 918 (93%) had at least one entity that was part of the industry as an originator (92% of all product-indication combinations). Information about current IP ownership was only available for a small subset of the data (6,252 product-indication pairs, representing 18% of the total). Among those with data available, more than 98% were currently owned by the industry. It should be noted that the AdisInsight dataset may somewhat overstate the role of the pharmaceutical industry because it tracks only product development projects that are deemed to be commercial, i.e. excluding, for example, medicines that are developed in a purely academic setting or with not-for-profit objective. However, given the broad range of data sources reviewed by Springer Nature to curate the AdisInsight database (see Section 3.2.6), it can be assumed to provide a reasonably complete view of the development pipeline.

Figure 4.37. Product-indication pairs in active development by level-2 disease category, as of 31st of December 2021

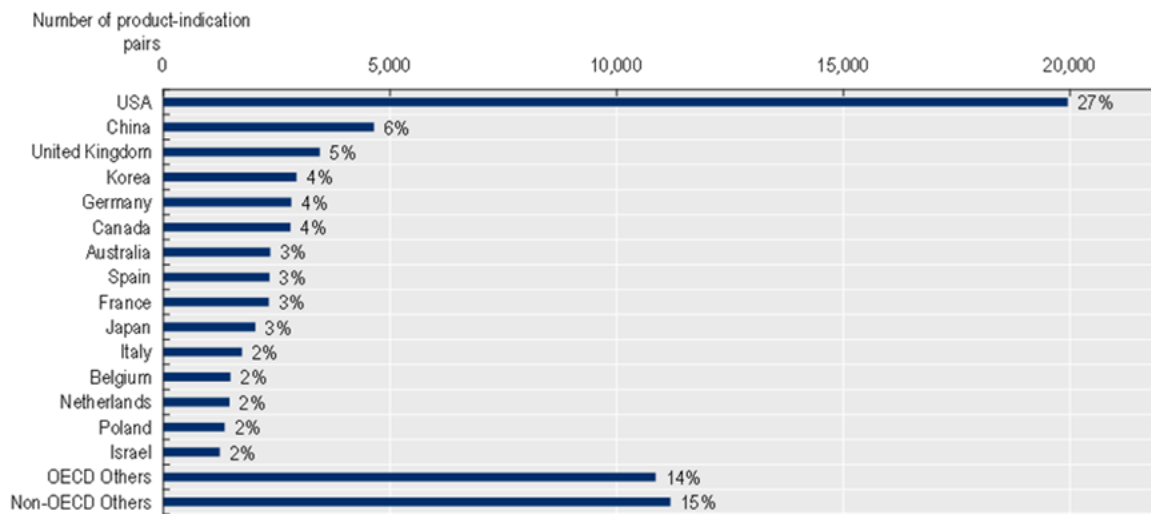


Notes: Excludes products that have already received marketing authorisation or have been launched. Shows the top 15 categories with all others aggregated into “All Others”.

Source: OECD analysis based on AdisInsight data

115. Many product development projects are active in several countries. On average, a given product-indication pair was in development in just over two countries (mean number of countries: 2.1). When counting the unique combinations of active product-indication pairs and countries, OECD countries host 79% of all product development projects, with the United States alone accounting for 27% of the total, followed by the United Kingdom (5%), Korea (4%) and Germany (4%) (Figure 4.38). China attracted 6% of product development, which is more than any OECD country except the United States.

Figure 4.38. Product-indication pairs in active development by country of development, as of 31st of December 2021

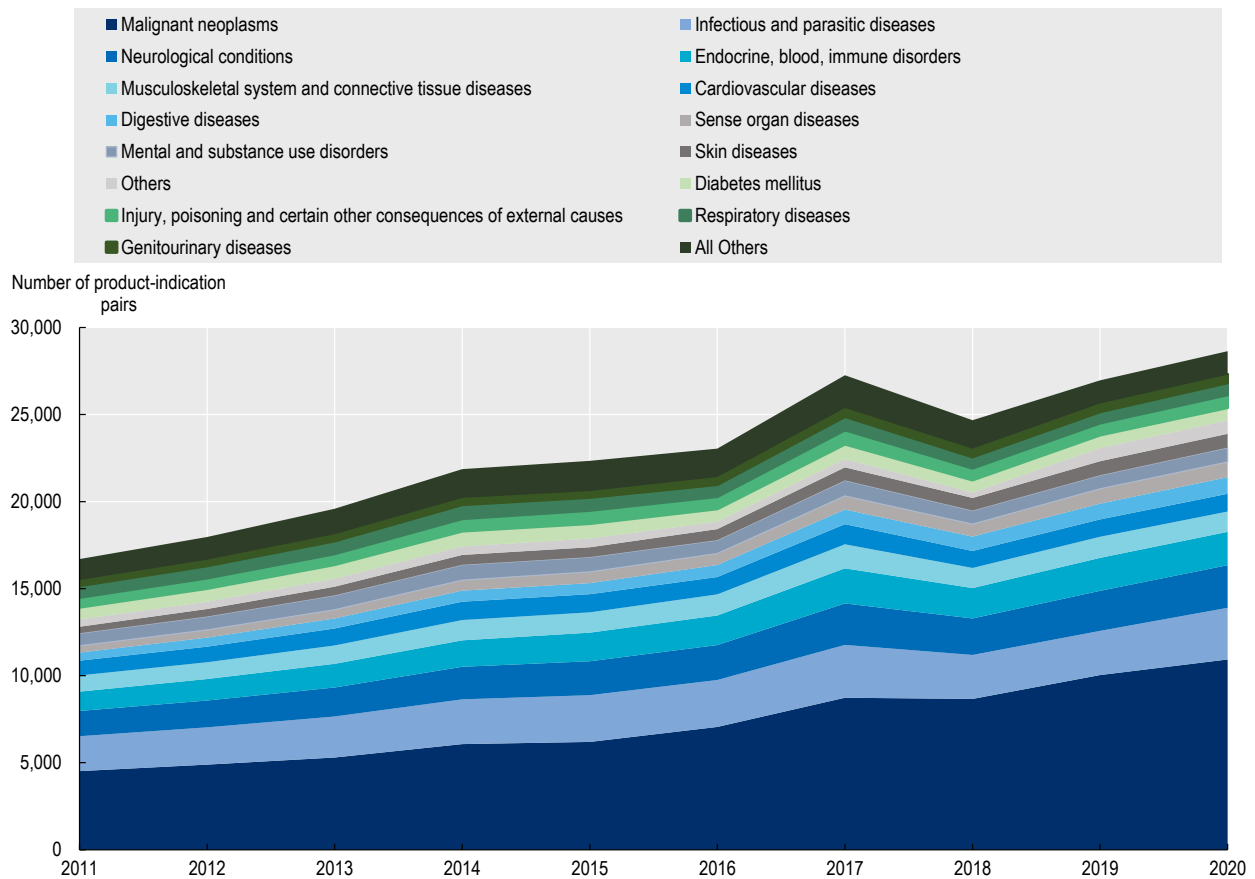


Notes: Excludes products that have already received marketing authorisation or have been launched. Country shares are based on unique combinations of product-indication/country. Shows the top 15 countries only, with all others aggregated into the “OECD Others” and “Non-OECD Others” categories.

Source: OECD analysis based on AdisInsight data

116. In terms of disease focus, product development priorities have not changed dramatically since 2011 (Figure 4.39). Cancer accounted for the largest share of product-indication pairs in every year since 2011, and has increased steadily, from 27% of all product-indication pairs in 2011, to 38% in 2020 and 40% in 2021. The following five of the top six disease categories (infectious and parasitic diseases; neurological conditions; endocrine, blood, and immune disorders; diseases of the musculoskeletal system and connective tissue; and cardiovascular disease) in 2011 also remained unchanged through 2020, although their combined share of product-indication pairs declined from 38% in 2011 to 33% by 2020, mainly attributable to declining numbers in infectious and parasitic diseases and diseases of the musculoskeletal system and connective tissue. While there was also little change in the composition of the top 15, digestive diseases, sensory organ diseases, and skin diseases rose in the rankings, while the rankings of mental and substance use disorders, diabetes mellitus, and respiratory diseases, declined. Collectively, the top 15 (including cancer) continued to account for nearly 95% of all product-indication pairs in development throughout the time period, with the increase in cancer activity offset by a decline across the next 14 disease categories. It should be noted that due to the classification of product-indication pairs, expanding the number of indications for the same product might also contribute to the increase.

Figure 4.39. Product-indication pairs in active development by level-2 disease category over time, 2011 – 2020

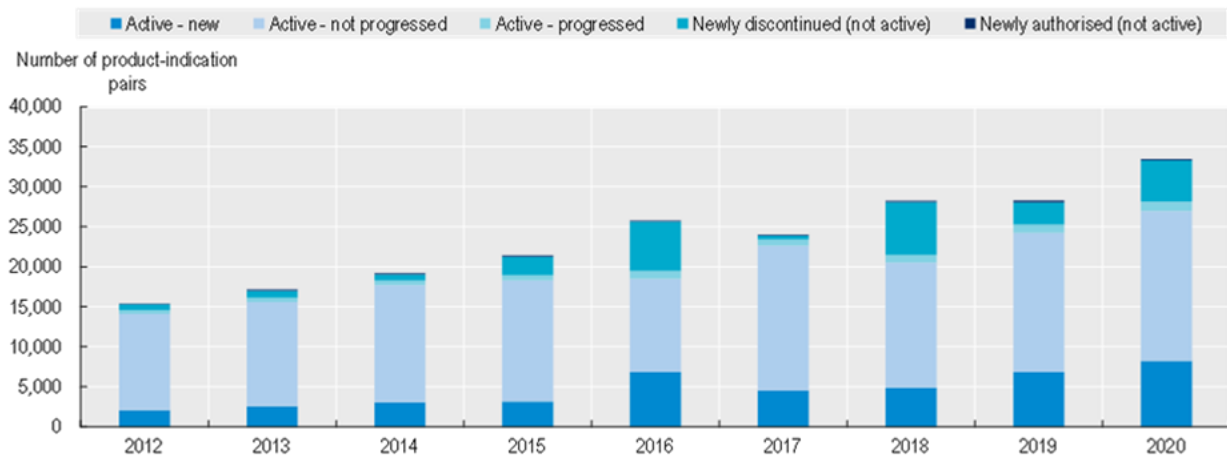


Notes: Excludes products that have already received marketing authorisation or have been launched. Shows the top 15 categories with all others aggregated into “All Others”.

Source: OECD analysis based on AdisInsight data

117. Between 2012 and 2020, the total number of product-indication combinations that are in active development nearly doubled, from 14 544 in 2012 to 28 187 in 2020. In any given year, the majority of active development projects are pre-existing projects that remain in active development. However, the number of new projects that enter active pre-clinical or clinical development has also increased, from 2 077 in 2012 (14% of all active product-indication combinations) to 8 227 (29% of the total) in 2020, following a spike of 6 808 product-indication combinations (35% of the total) in 2016. Between 2012 and 2020, 88 to 262 product-indication combinations received marketing authorisation per year (0.7% to 1.2% of product-indication combinations in active development in the prior year); 459 to 1 191 progressed to a subsequent development phase per year (3.5% to 5.1% of product-indication combinations in active development in the prior year); and development was discontinued for 759 to 6 612 product-indication combinations per year (5% to 32% of product-indication combinations in active development in the prior year). Figure 4.40 the number of product-indication combinations that are newly authorised and in active development every year between 2012 and 2020 as well as those for which development is discontinued.

Figure 4.40. Development progression of product-indication pairs, 2012 – 2020



Note: Includes only product-indication combinations with data in all consecutive years of active development. Product-indication combinations that are newly authorised or discontinued in a given year are no longer counted in subsequent years.

Source: OECD analysis based on AdisInsight data

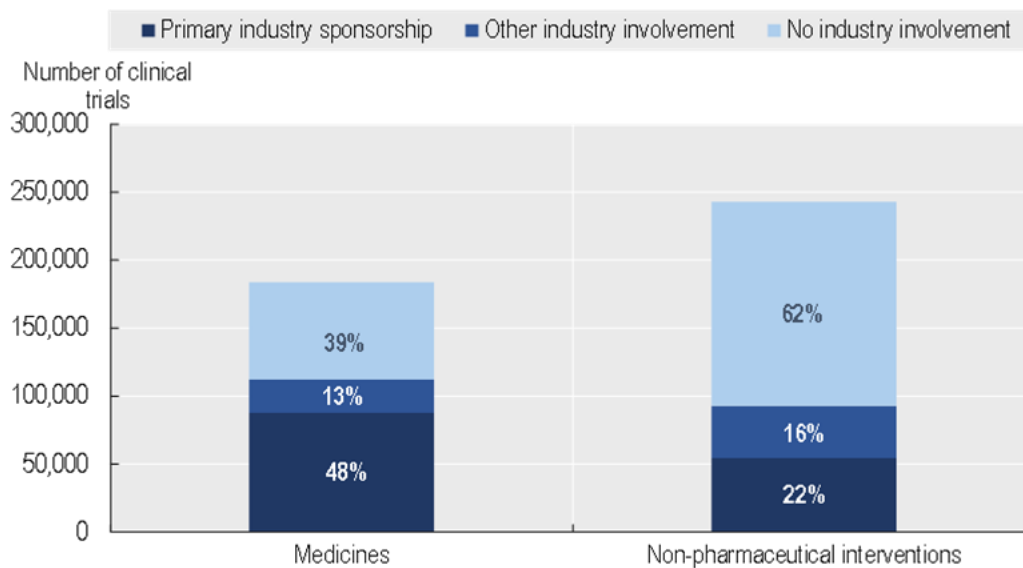
4.2.7 Number of clinical trials

118. The ICTRP dataset contained records of 757 481 clinical trials by the end of 2021. Of these, 592 401 (78%) could be unambiguously assigned to a starting year between 2010 and 2021 based on the field that captures the date of enrolment of the first participant (19% had started recruiting before 2010 and the remaining 3% had missing or ambiguous data in the field capturing the year of first recruitment).

119. Of the 592 401 trials that started recruiting in 2010 or later, 426 603 (72%) were identified as having been completed or as actively recruiting by the end of 2021 (the remaining 28% had a non-active status, including trials that had not started recruiting or were withdrawn).

120. Text-mining algorithms developed by the Secretariat identified among the 426 603 trials that began recruiting between 2010 and 2021, and were active or completed by 2021; 183 733 trials of medicines (43%), 141 943 trials with an industry entity as a primary sponsor (33%), and 204,974 (48%) with industry involvement, i.e. with at least one an industry entity as primary or secondary sponsor or as named source of financial support. Among all trials of medicines, 48% had primary industry sponsorship and 61% had industry involvement vs. 22% and 38% respectively of trials of other types of interventions. Figure 4.41 compares the number of trials with primary industry sponsorship, with and without industry involvement, and between medicines and non-pharmaceutical interventions.

Figure 4.41. Number of active or completed clinical trials by industry sponsorship or involvement, as of 2021



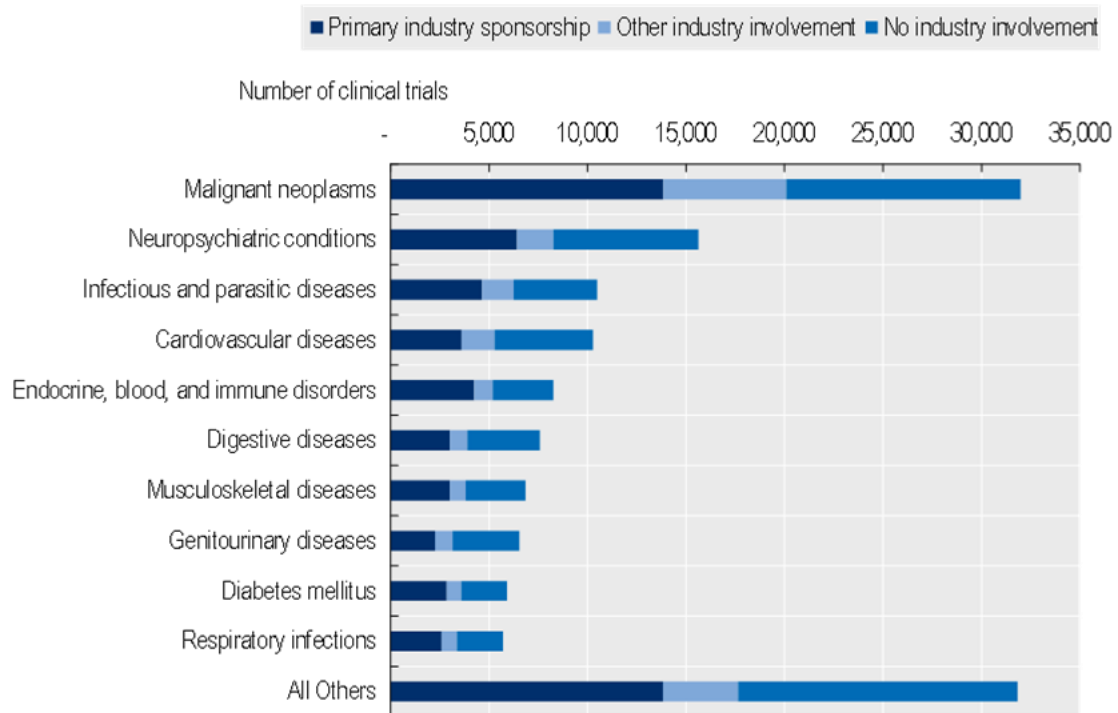
Note: Includes all trials that started recruiting between 2010 and 2021 and were active or completed by 2021. Interventions and trial sponsors are categorised by a text-mining algorithm developed by the OECD; accuracy is <100%.

Source: OECD analysis based on ICTRP data provided by WHO

121. The number of new trials of medicines increased from 18 428 in 2010 to 27 895 in 2020 (+51%), before declining to 26 002 in 2021. However, the increase was smaller than in the number of trials of non-pharmaceutical interventions in the same period, which nearly tripled between 2010 and 2020 before also declining in 2021.

122. A total of 141 091 medicine trials active or completed since 2010 (77% of the total) could be assigned to a disease category by WHO based on the information in ICTRP (the disease was not identified unambiguously in the remaining 23%). Among these 141 091 trials, non-communicable diseases accounted for 81% of all trials of medicines, while maternal, perinatal and nutritional conditions accounted for 16% and the remaining 2% were related to injuries and uncategorised indications. Oncology attracted by far the most trial activity, representing 23% of the total in the period 2010 to 2021, followed by neuropsychiatric conditions (11%), infectious and parasitic diseases and cardiovascular diseases (both 7%) (Figure 4.42). Overall, 57% of trials had industry involvement. Among the top 10 disease areas, the highest proportion of trials with industry involvement were found in oncology (63% of all trials), followed by endocrine, blood, and immune disorders (63%) and diabetes mellitus (61%); the lowest in genitourinary diseases (48%), cardiovascular diseases and digestive diseases (both 51%) (see also Figure 4.42). Trials of medicines without industry involvement focused on the same top 4 disease categories as those with industry involvement, but oncology and infectious and parasitic diseases accounted for a smaller proportion of the total than trials with industry involvement (20% vs. 25% and 7% vs. 8%), while the proportions of trials in neuropsychiatric conditions and cardiovascular diseases were slightly higher (12% vs. 10% and 8% vs. 7% respectively).

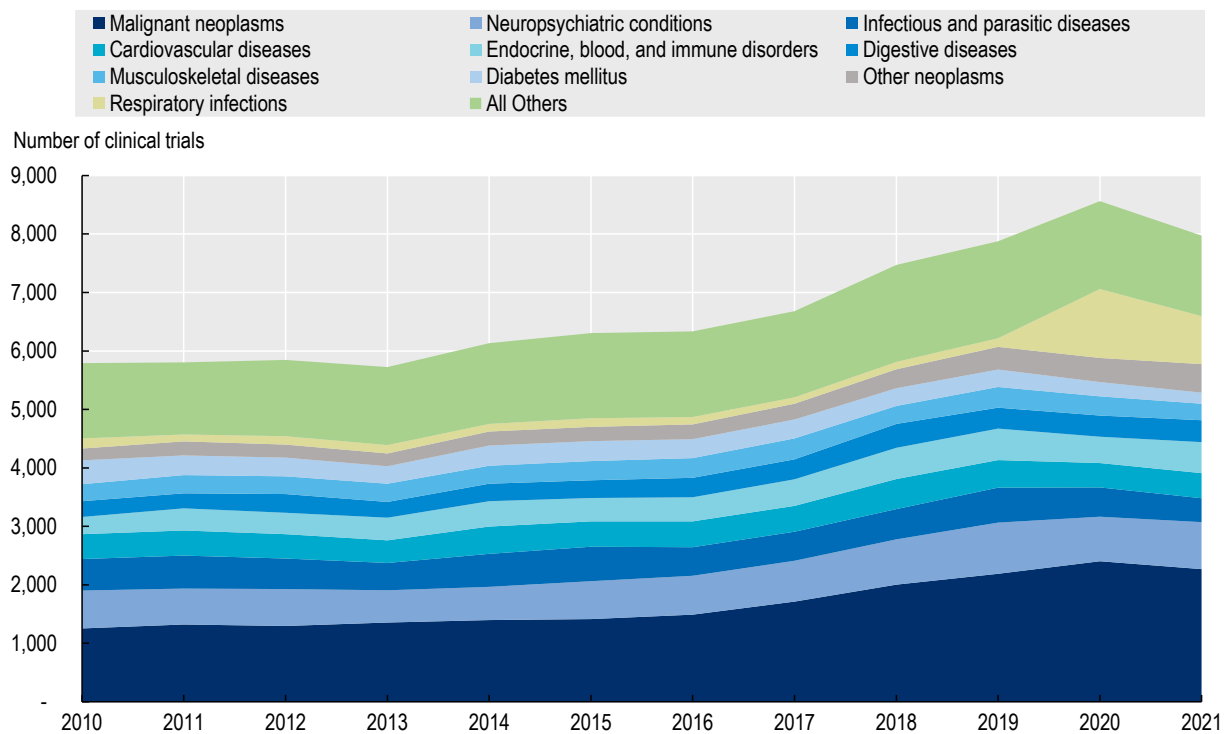
Figure 4.42. Number of clinical trials by level-2 disease category and industry involvement



Note: Includes all trials that started recruiting between 2010 and 2021 and were active or completed by 2021. Excludes 42 642 trials (23% of the total) that could not be assigned to a disease category by WHO based on free text fields in ICTRP that capture information about the disease. Source: OECD analysis based on ICTRP data provided by WHO

123. The number of trials of medicines with industry involvement increased from 5 790 trials that began recruiting in 2010 to 8 562 with first recruitment in 2020 (+48%), before declining to 7 971 in 2021 (-7%) (Figure 4.43). Until 2019, the importance of oncology increased steadily, from 22% of trials in 2010 to 28% in 2019, while the proportion of the other three of the top 4 diseases (neuropsychiatric conditions, infectious and parasitic diseases, and cardiovascular diseases) remained constant. Changes since 2018 exhibit a spike in trials of treatments for respiratory infections, driven by COVID-19: while respiratory infections represented 2% of all trials of medicines with industry involvement until 2019, they represented 14% in 2020 (second only to oncology, 1,179 trials with first recruitment in 2020) and 10% in 2021 (822 new trials). Meanwhile, the number of new trials in the previous top 4 disease categories remained constant or declined between 2019 and 2021.

Figure 4.43. Number of active or completed clinical trials with industry involvement by year of first recruitment and level-2 disease category



Note: Includes all trials that started recruiting between 2010 and 2021 and were active or completed by 2021. Excludes 42,642 trials (23% of the total) that could not be assigned to a disease category by WHO based on free text fields in ICTRP that capture information about the disease. Source: OECD analysis based on ICTRP data provided by WHO

4.2.8 Number of subjects enrolled in clinical trials

124. The trial size sample was limited to ‘Active’, ‘Interventional’, and ‘Drug’ trials, yielding 166,385 clinical trials in total. Initial results yielded a median (50th percentile) trial size of 72 participants per clinical trial (interquartile range 35 – 184). The trials were disaggregated into Phases 1 – 4, with the largest trials occurring in Phase 3 (median: 145 participants) and the smallest trials in Phase 1 (median: 36 participants). Phase 3 trials median trial sizes declined overall, from 200 in 2010 to 158 in 2021, with trials with industry involvement showing a slightly more pronounced decline. When broken down by disease area, the top category was *noncommunicable diseases* with a median of 1 915, but this was considered an outlier due to the low number of observations. The next highest overall was *respiratory infections* (median: 120 participants).

125. However, several issues were observed with the data that impact the feasibility of the indicator for regular reporting. The sample was highly skewed, with median trial sizes far lower than means, suggesting a large number of trials with very few participants. The variables used in this analysis did not appear to have been entered or reported consistently and subsequently required extensive cleaning and manipulation. The results shown here should therefore be interpreted with caution. Further analysis of this sub-sample is needed to assess the feasibility of median trial size as a reliable indicator for future reporting.

5 Conclusion and discussion

5.1 Conclusion

126. This working paper presents the findings of a feasibility study whose objective was to develop a comprehensive set of indicators to monitor pharmaceutical industry performance and support better informed debates in pharmaceutical policy. It focused on two domains of measurable performance in the pharmaceutical industry: *inputs* and *activity*. Inputs include financial flows to the industry, such as revenue, tax credits, etc., while activity captures the purposes for which financial resources are deployed by firms in the industry, which includes both financial (e.g. R&D expenditure, cash outlays) and non-financial activities (e.g. product development, clinical trials). A first iteration of the results for these indicators was generated and is summarised in Table 5.1.

Table 5.1. Summary of Key Indicators

Based on data from 2010 to 2020 (from 2005 for selected firm-level financial indicators)

Domain	Indicator	Industry aggregate	Notes
Financial inputs	Revenue	+47% in global prescription medicine revenue in real terms (2010 – 2021) OECD countries accounted for 78% of global market	Consistent growth since 2010, except 2012 (-1.6%), to USD 1.296 billion in 2021 US highest share (57% of OECD, 44% overall), China highest growth (+181%)
	Net cash flows from financing activities	-6.0% of assets (in 2006) to +2.1% (2015) (publicly listed firms only)	Negative in all years except 2015 and lower than in most industries, except software. Driven by the most profitable quartile of firms, with positive cash flows in the upper 75% of firms.
	Direct subsidies for R&D	10% of R&D expenditure in 26 OECD countries	OECD aggregate driven by the United States (73% of OECD total), highest proportion of R&D expenditure in the UK (49%).
	Tax credits for R&D	USD 1.5 billion in tax credits for R&D (2019)	Data only available from 14 OECD countries (excluding the United States) accounting for 6% of R&D expenditure in OECD.
Financial activity metrics	Net cash flows from operating activities	7.6% of assets (in 2020) to 12.6% (2008) (publicly listed firms only)	Positive in all years and comparable to other R&D-intensive industries. Firm-level median close to zero – about half of firms have negative and half have positive cash flows. Aggregate driven by the largest 25% of firms that generated consistently positive net cash flows.
	Profitability	Gross operating margins: 51% (unlisted firms in 2015) to 70% (publicly listed firms in 2005) Net operating margins 10% (unlisted firms in 2019) to 20% (listed firms in 2009) Net returns on assets -5.2% (in 2018) to 0.5% (2006) (publicly listed firms only)	Downward trends in gross and net operating margins over time, convergence with other R&D-intensive industries. Net ROA at the 95 th percentile between 5% and 11%. Large and mature firms more profitable than small and young firms.
	Cost of capital	6.7% (in 2020) to 9.4% (2010) (publicly listed firms only)	Comparable to other R&D-intensive industries.
	R&D expenditure	USD 148 billion (2020 or latest)	OECD aggregate and growth driven by publicly listed

		available), USD 129 billion in OECD countries 39% real-term growth since 2010 R&D intensity 30% of gross value added in OECD countries	firms and the United States (69% of OECD), fastest growth in China. R&D intensity driven by United States and Japan, <20% in most OECD countries; OECD aggregate higher than in other industries.
Non-financial measures of R&D activity	No. of product development projects	35 521 product-indication pairs in active development in 2021 vs. 17 000 in 2011 89% originated with industry involvement 8 277 new product-indication pairs in active development in 2020 vs. 2 077 in 2012	Highest proportions in oncology and in the United States.
	No. of clinical trials	7 971 new medicines trials with industry involvement in 2021 vs. 5 790 Only 57% of all medicines trials with industry involvement	Highest proportions in oncology in all years, with a spike reflecting Covid-19 trials in 2020 and 2021.

Note: For details and sources, refer to the respective results section for each indicators.

Source: OECD analysis

127. These analyses have confirmed the feasibility of creating a set of indicators for the routine monitoring of pharmaceutical industry performance and activity. Only one proposed indicator (clinical trial size) was not considered currently feasible for routine collection, and a second (tax subsidies for R&D) requires further development. However, while the construction and population of the selected indicators is feasible, further work is needed to fully understand how these indicators are affected by changes in the structure and composition of the industry and the resultant policy implications.

5.2 Discussion and avenues for further work

128. It is well recognised that the pharmaceutical industry is highly complex and, as this analysis has confirmed, highly heterogeneous, spanning a wide variety of activities and firm types. While this analysis provides a first iteration of indicators related to inputs and activity of the industry, the results must be interpreted with caution for at least two reasons. First, the heterogeneity of the industry is reflected in marked skewness of most of the indicators that are based on firm-level data, suggesting that a more disaggregated analysis by the sub-sector of the industry is warranted and would likely be more policy-relevant than industry aggregates. Second, the results should also be interpreted in the context of current trends in the pharmaceutical industry, not all of which have yet been elucidated in the development of this initial set of indicators. Additional analytical work is therefore required to develop a final set of indicators offering a more complete and sufficiently nuanced understanding of the functioning of the industry to inform evidence-based policy making. Continuing work could progress along the following avenues.

129. First, indicators in the *output* domain are required to understand the productivity of the industry and its contribution to effective health systems. More information on how drugs produced by the industry are 'innovative', clinically beneficial to patients, and address health need, will provide context to how and where the most significant research and development are driven by the industry.

130. Second, further disaggregation of the first iteration of indicators will be necessary to appropriately reflect the heterogeneity of the pharmaceutical industry and the variety of activities and firm types that constitute the industry as a whole. This is particularly necessary for the financial indicators related to inputs and activity, including but not limited to revenue, R&D subsidies, net cash flows from financing and operating activities, and profitability. As shown in Section 4.2.5, the industry comprises R&D-focused firms of varying sizes, manufacturing focused-firms that produce various types of medicines or ingredients, manufacturing firms focused on generics and biosimilars, large and diversified firms and contract research

organisations. Firms in these sub-categories may not only differ in terms of their business and financing models but are also subject to different policy incentives and forms of regulation within the 'ecosystem' of pharmaceutical policy. They therefore need to be analysed separately. Thus far, disaggregation of the industry into these sub-sectors has only been possible with a small sample of firms and for those indicators that report profitability in terms of net return on assets (RoA) and net cash flows from financing and operating activities, providing an incomplete picture of the activities of each sub-sector. The analysis should be completed with a larger sample of firms and for all relevant indicators.

131. Third, in addition to its intrinsic complexity, some commentators in policy debates and a number of prior studies based on small samples of firms suggest that the pharmaceutical industry might currently be undergoing considerable evolution (Congressional Budget Office, 2021^[1]; Attwood, Rask-Andersen and Schiöth, 2018^[13]; Keenan, Monteath and Wójcik, 2022^[14]). This may include increasing financialisation and extensive M&A activity, and an increasing focus on niche markets. It is therefore important to attempt to assess which additional indicators might help to elucidate these changes and how this evolution may manifest itself in the indicators discussed in this paper.

132. Financialisation refers to the increasing role of financial motives, financial markets, and financial institutions in the operation of domestic and international economies (Epstein, 2005^[15]; Busfield, 2020^[16]). This phenomenon may affect *inputs* to, *activity* of, and *outputs* of the industry, and therefore pharmaceutical policy. It may, for instance, result in an increasing allocation of cash for rewarding shareholders rather than funding investments such as R&D; in strategic shifts in R&D toward M&A; or in terms of upward pressures on market valuations, and therefore firm revenues and, of crucial importance to access and affordability of medicines, product prices. Additional measures that capture indicators such as the volume of M&A transactions and their valuations, the extent of stock buy-backs or shareholder structures could explicate to what extent financialisation is present in the pharmaceutical industry. An indicator that captures asset and firm valuations could also shed light onto profitability relative to *ex-ante* profit expectations by markets in addition to the *ex-post* and accounting-based view taken in the Net Return on Assets (Net RoA) indicator discussed in this paper.

133. Some tentative evidence of financialisation can already be derived from the indicators discussed in this paper. For example, public firms that are highly financialised will distribute most, if not all, of their profits to shareholders through cash dividends and/or stock buybacks. The cash flow indicators developed in this working paper reflect this: in nearly all years analysed, the pharmaceutical industry, as a whole, used more cash to pay shareholders and creditors than it raised from capital markets, an aggregate pattern driven by a small number of large, mature, and profitable firms that generate significant amounts of cash from the sale of products. When firms buy back their own stock, cash is distributed to shareholders, which increases the value of equity (without the issue of additional shares), consolidates ownership, and may attract future investors, however, without generating any additional assets of economic value. From 1981 to 2018, the proportion of profits in the top segment (S&P 500) of US firms spent on stock buybacks increased by 59%, while the proportion spent on dividends remained nearly the same (Lazonick et al., 2019^[17]). This activity extends to the pharmaceutical industry as well. A 2018 study based on a limited sample of US pharmaceutical companies, found that 57% of profits earned from 2009-2018 were spent on buybacks, which was 14% more than the amount spent on R&D and far above levels of buybacks seen in other technology and research-driven industries (Lazonick et al., 2019^[17]). Importantly, financialisation in the pharmaceutical industry is often perceived to occur at the expense of innovation: it is easier to propagate firm value through mechanisms like stock buybacks than long-term internal investments in R&D (Keenan, Monteath and Wójcik, 2022^[14]). However, the indicator of R&D expenditure shows a continued upward trend so that a claim that cash outflows to investors come at the price of declining R&D expenditure cannot be readily supported by this first iteration of indicators. The indicators that track the number of R&D projects and clinical trials also exhibit upward trends. However, all of these indicators measure R&D activity; they neither provide a measure of 'innovation' nor of industry output. Future work on developing indicators of

outputs will provide more context around the possible effects of financialisation on industry output in terms of effective medicines that are made available to patients.

134. One aspect of the *output* domain of indicators is the increasing development of products for niche markets. In order to secure market capitalisation, pharmaceutical companies allocate resources to consolidating portfolios and may increasingly target less competitive markets such as rare diseases (Ascher et al., 2016^[4]; Årdal, Lopert and Mestre-Ferrandiz, 2022^[5]). Orphan medicines, or medications targeted towards rare diseases or conditions (e.g. fewer than 200 000 patients in the US, fewer than 5 per 10 000 population in the EU), have been an increasing area of focus for pharmaceutical companies in recent years, measured as orphan-designated new molecular entities (NME) (Attwood, Rask-Andersen and Schiöth, 2018^[13]). There are many reasons for focusing on orphan drugs and rare diseases including addressing unmet need, but there are also considerations of first mover advantage, higher willingness to pay, challenges in developing novel drugs for common chronic diseases, and favourable financial or policy incentives (e.g. US Orphan Drug Act of 1983, EU Orphan Regulation of 2020). This is also manifested as targeted acquisitions of smaller biotech or biopharma research companies focused on orphan drugs, such as AstraZeneca's USD 39 billion acquisition of Alexion Pharmaceuticals, a rare disease biopharma research company, in 2021.

135. In the context of this paper, the targeting of niche markets will be evident in both non-financial and financial activity indicators. Shifting from larger therapeutic areas to orphan drug research affects resource allocation decisions in multiple ways. For example, this could impact indicators such-as firm-level R&D expenditure, government tax subsidies, number of products in development, operating cash flows, and cost of capital, however the direction and extent of these effects are still not understood. Subsequent work will attempt to elucidate how *outputs* relate to the indicators discussed in this paper and how they may be interpreted in the context of longitudinal changes in the industry.

5.3 Future reporting process

136. Subject to funding, the indicators presented in this paper could be updated on a biennial basis and published electronically on the OECD website. This could be undertaken in parallel with the biennial publication of *Health at a Glance*, with a first update in 2025.

137. In the next phase of this work, the analysis will be expanded to include *outputs* and to further assess the feasibility of a more complete industry disaggregation, as discussed above. Outputs capture information on medicines developed by industry and their utility and benefits to patients and health systems. Together with the analyses presented in this working paper, these will provide a more complete picture of the performance of the pharmaceutical industry.

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