

Paper for first consideration from the Transfer Pricing
Subcommittee

Transfer Pricing and the Pharmaceutical Industry

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Executive Summary

This report was prepared by the UN Transfer Pricing Subcommittee in response to the need, often expressed by developing countries, for practical guidance in applying the arm's length principle to the pharmaceutical industry. All tax administrations, but particularly those from developing countries, face resource and capacity constraints in a specialized area such as transfer pricing. This makes it important to ensure that limited resources are targeted as efficiently and effectively as possible. Given the importance of the pharmaceutical industry to all countries, both developed and developing, this paper intends to provide practical guidance for this industry.

The guidance in this document commences by describing the global value chain of the industry and its value drivers. The document then considers transfer pricing issues for the pharmaceutical industry. Practical issues relating to transaction delineation, comparability analysis, and the application of transfer pricing methods in the pharmaceutical industry are addressed.

It should be noted that the analysis contained in this document may not reflect particularities specific to all countries, but instead takes a systematic approach of describing the most pertinent features of the pharmaceutical industry and related transfer pricing issues. It is important to highlight that the United Nations Practical Manual on Transfer Pricing for Developing Countries ("the UN TP Manual") (2021) is applicable to the pharmaceutical industry and the guidance provided in this report is based on, and should be read in conjunction with, the UN TP Manual.

A list of the abbreviations used in this report is attached as Appendix 1 and a glossary of key terms used in the report is attached as Appendix 2.

1. Introduction

1.1. The pharmaceutical industry

The pharmaceutical industry, which is part of the life sciences sector¹, is dedicated to the discovery, development, manufacturing, marketing and distribution of pharmaceutical products (drugs) used for medical purposes in the treatment or prevention of diseases.

Pharmaceutical products contain an active pharmaceutical ingredient (API) that is designed to treat a disease or medical condition. Pharmaceutical products are normally separated into two broad categories: chemical (small molecule) or biological (large molecule), corresponding to the API's characteristics.² Historically, pharmaceutical companies were built on chemical APIs and biotechnology companies delivered products derived from living organisms (biological APIs). Since most large pharmaceutical companies nowadays use both technologies,³ the term “pharmaceutical industry” used in this report includes both pharma and biotechnology firms.

1.2. Segments in the pharmaceutical industry

The pharmaceutical industry can be viewed through a number of lenses depending on how the industry is segmented. One common classification depends on whether the manufacturer developed the API, the pharmaceutical product, and obtained patent protection, or instead used the same API formula to create a generic drug. A second classification depends on whether a prescription from a medical professional (e.g., a doctor) is or is not needed to purchase the pharmaceutical product.

Novel, generic, and orphan pharmaceutical products

i. Originator and generic drugs

The pharmaceutical industry has consisted historically of two types of firms: originator companies and generic drug companies.⁴ When a new or novel API emerges from the pharmaceutical R&D process, the pharmaceutical company (the “originator”) patents the API as a “generic substance” with a generic name. If the originator company develops a pharmaceutical product using this API, a trademark is attached to the product and the product is sold by the patent owner or one or more licensees under the trademark. Originator companies discover new drugs to meet clinical needs, apply for patent protection to exclude imitators, and then either manufacture, market and sell the

¹ The life sciences sector encompasses a broad range of industries including the pharmaceutical industry, biotechnology, nutrition and chemical manufacturing sector.

² BCC Research Staff (June 2019). Markets at a Glance: Pharmaceuticals. Report Code: PHM213A.

³ Segal., T. (2022). Biotech vs. Pharmaceuticals: What's the Difference? Investopedia. Available from <https://www.investopedia.com/ask/answers/033115/what-difference-between-biotechnology-company-and-pharmaceutical-company.asp>

⁴ Collins, M., and Wundisch, K. (2004). Transfer Pricing in the Ethical Pharmaceutical Industry. International Bureau of Fiscal Documentation (IBFD). Section 2.1.2. Competition from Generics.

drugs or license the API formula during the life of the patent. These products are referred to as “novel” or “branded” or “originator” drugs. They are typically protected by patents on their products and/or processes for several years, with the length varying by product (type), country, and patent organization. The typical patent length in most countries is 20 years but can be significantly shorter depending on how long it takes to develop and receive government authorization to sell a new product (cf. sections 3.1 and 4.2 for a discussion on patents).

When the patent protection expires for the originator drug, any firm (the “generic drug company”) can copy the generic substance and sell a replica drug under the generic name or under a new trademark. The generic drug has the same API formula as the brand-name pharmaceutical product and is created to be the same also in terms of its product characteristics (e.g., dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use). Having the same product characteristics demonstrates bioequivalence, i.e., the generic and brand-name medicines are substitute products (they work in the same way and provide the same clinical benefits).⁵ However, generic medicines do not have to repeat the same clinical trials that are required of the original brand-name medicines in terms of demonstrating safety and effectiveness and thus do not incur the same up-front R&D and regulatory costs as originator firms.

Compared with their generic competitors, originator firms face additional challenges:⁶

- The time and cost involved to bring a new drug to market. On average, only one out of every 20 drugs that enter clinical testing will be approved for marketing, and it takes 10 to 12 years to bring a new drug to market at a cost of up to 1.5 to 2 billion USD.⁷
- Price controls and the buying power of third-party payers (e.g., insurance companies) as they are often looking for cost savings.
- The need to have several R&D projects simultaneously to ensure “pipeline” in terms of the number of approved new drugs.
- The efforts and costs associated with complying to regulatory requirements of national government agencies and international organizations.

Because generic medicines do not have to repeat the same clinical trials that are required of brand-name medicines in terms of demonstrating safety and effectiveness, the cost structure of generic drug companies differs substantively from originator companies. However, multiple generic drugs may be approved based on the same API, creating

⁵ U.S. Food & Drug Administration. Generic Drugs: Questions & Answers. Available from <https://www.fda.gov/drugs/frequently-asked-questions-popular-topics/generic-drugs-questions-answers#q1>.

⁶ Kellogg, V. (January 2020). ROI in Pharmaceutical R&D: How to Halt the Decline. Chapter 3. Challenges Facing Pharma and Biotech Companies. BCC Publishing Report Code PHM218A

⁷ Harrer, S., Shah, P., Antony, B., and Hu, J. (August 2019). Artificial Intelligence for Clinical Trial Design. Trends in Pharmacological Sciences. Vol. 40. Issue 8.

competition in the marketplace that results in lower prices.⁸ Multiple firms can enter the market as long as they have regulatory approval. As a result, generic prices are typically much lower than the originator drug price, providing additional competition to existing producers.

ii. Orphan drugs

In addition to novel and generic drugs, there are also a third category of so-called “orphan drugs”, which are designed to target rare diseases and disorders where “rare” is defined as less than 200,000 patients. Given the small potential market compared with the costs of developing an API and pharmaceutical product, few private firms are willing to enter this market segment without additional financial support. In addition, few consumers could financially bear the costs of purchasing these drugs. As a result, some governments provide incentives to pharmaceutical firms for the development of orphan drugs and may also bear some of the per-patient costs.⁹

Over-the counter vs prescription drugs

Pharmaceutical products can also be segmented into categories depending on whether a medical professional is required to write a prescription for the medicine.

A prescription drug is a pharmaceutical product that can only be supplied to a patient by the written prescription of an authorized health professional such as a physician or dentist. In many countries prescription drugs are registered with a government authority and may have a specific registration number. For a prescription drug to be registered it must be supported with evidence including clinical trials to ensure the efficacy of the drug. The government authority assesses the evidence provided to determine whether the drug will be registered. It is usually a requirement that the benefits of a drug proposed for registration outweigh the potential risks of using the drug. Some drugs treating life-threatening conditions may receive fast-track approval depending on the registration authority. Examples of prescription drugs in many countries are antibiotics and blood pressure tablets.

Non-prescription medicines, also known as over-the counter (OTC) drugs do not require a prescription from a medical professional. Governmental regulations differ between countries on how these drugs can be accessed. OTC products are typically sold in pharmacies, though some countries may also allow these products to be sold in drugstores, supermarkets or convenience stores. There are countries that further distinguish into pharmacist-only OTC drugs, which are drugs that don't require a prescription but may only be purchased by customers who have spoken with the on-duty pharmacist. Other countries don't have this distinction as OTC drugs can only be

⁸ U.S. Food & Drug Administration. Generic Drugs Facts. Available from <https://www.fda.gov/drugs/generic-drugs/generic-drug-facts>.

⁹ Countries that subsidize the development of orphan drugs include the United States, United Kingdom, and the Netherlands. See Cohen, J.P., and Felix, A. (January 2014). Are payers treating orphan drugs differently? Journal of Market Access and Health Policy.

bought in pharmacies. Examples of OTC drugs include, for example, low dosage pain medication.

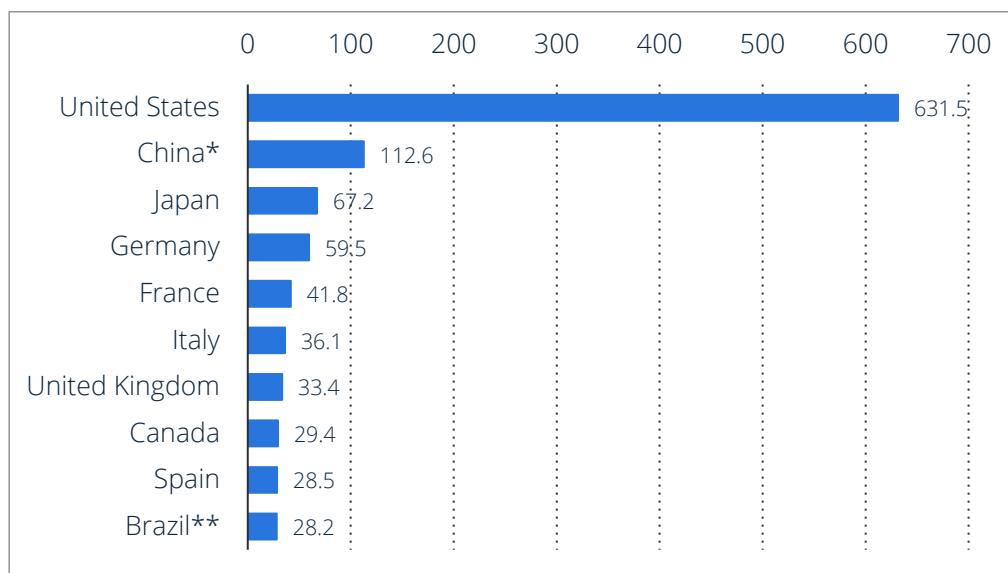
OTC products are thus much more readily available to consumers than prescription medicines, and also are usually relatively affordable vis-à-vis prescription drugs. In many cases, products that were once available only as a prescription drug become OTC products. OTC products may be protected by patents, but this is less likely as compared to prescription drugs.

1.3. Statistics on the pharmaceutical industry

Sales and market share

In 2021, worldwide revenues of the pharmaceutical industry totaled 1.42 trillion U.S. dollars; this includes both originator and generic pharmaceutical products, whether they require a prescription or are sold as OTC medicines.¹⁰ While the United States has the largest share of revenues (43.7%) and five of the ten largest pharma multinationals (MNEs) are headquartered there, other countries' markets have also grown dramatically over the last decades. China now ranks second in terms of market revenues.¹¹

Figure 1: Pharmaceutical markets by revenues, Top 10 countries, 2022 (billions U.S. dollars)¹²



¹⁰ Statista (2023). Global pharmaceutical industry - statistics & facts. Available from [Global pharmaceutical industry - statistics & facts | Statista](https://www.statista.com/statistics/1000000/global-pharmaceutical-industry-statistics/). See also <https://www.zippia.com/advice/us-pharmaceutical-statistics/>.

¹¹ Pharmanews Intelligence (2023). Comparing Global Pharmaceutical Markets: US, UK, and China. Available from [Comparing Global Pharmaceutical Markets: US, UK, and China \(pharmanewsintel.com\)](https://pharmanewsintel.com/comparing-global-pharmaceutical-markets-us-uk-and-china/). See also [China Briefing \(November 2022\). How Big Is China's Biopharma Market? Available from https://www.china-briefing.com/news/china-booming-biopharmaceuticals-market-innovation-investment-opportunities/](https://www.china-briefing.com/news/china-booming-biopharmaceuticals-market-innovation-investment-opportunities/).

¹² IQVIA (2023). Revenues of leading 10 national pharmaceutical markets worldwide in 2022 (in billion U.S. dollars). May. ID 266469. Prices are reported at the ex-manufacturer level (price when sold from manufacturer to wholesaler or direct to pharmacies).

Table 2 provides data at the regional level on pharmaceutical markets in 2022 in billions of US dollars. The largest market is North America (455.09 billion USD) followed by Asia (434.16 USD billion).

Table 2: Pharmaceutical markets by region, 2022 (billions U.S. dollars)¹³

Region	2022
Sub Saharan (Region)	20.658
* East & Central Africa	6.3
* West Africa	8.3
* Southern Africa	7.4
Asia (Region)	434.161
* Northeast Asia	258.3
* Southeast Asia	27.7
* South Asia	38.9
Europe (Region)	390.8
* Western Europe	290.1
* Emerging Europe	88.2
Latin America (Region)	66.303
MENA (Region)	39.856
* Middle East	38.3
* North Africa	12.1
North America (Region)	455.093

Pharmaceutical exports and imports

Tables 3 and 4 provide publicly available data on the top 20 countries in terms of exports and imports of pharmaceutical products in 2021.¹⁴ Figures are reported in millions of U.S. dollars. Trade balance is defined as exports minus imports, so a negative trade balance means that imports exceed exports of pharmaceutical products. Large exporting countries can also be large importing countries; for example, the United States and

¹³ Sources are BMI (2023). Global Pharmaceuticals Report, Q3. Page 26; BMI (2023). Sub-Saharan Africa Pharmaceuticals Report, Q3. Page 28; BMI (2023). MENA Pharmaceuticals Report, Q3. Page 28; BMI (2023). Latin America Pharmaceuticals Report, Q3. Page 25; BMI (2023). Europe Pharmaceuticals Report, Q3. Page 34; BMI (2023). Asia Pharmaceuticals Report, Q3. Page 15.

¹⁴ OEC (2021). Which countries export Pharmaceutical products? Available from https://oec.world/en/visualize/tree_map/hs92/export/show/all/630/2021/.

Germany are in the top three countries for both exports and imports. Trade flows include both unfinished and finished products.

**Table 3: Exports and imports of pharmaceutical products, Top 20 countries, 2021
(millions U.S. dollars)**

Top 20 Exporting Countries			Top 20 Importing Countries		
	Country	Exports		Country	Imports
1	Germany	\$115,465.16	1	United States	\$145,321.68
2	Switzerland	\$90,226.55	2	Germany	\$76,636.18
3	United States	\$81,586.31	3	Belgium	\$44,025.24
4	Belgium	\$71,103.13	4	Switzerland	\$40,208.23
5	Ireland	\$70,635.72	5	France	\$34,890.99
6	France	\$39,098.65	6	China	\$34,120.29
7	Italy	\$38,152.76	7	Italy	\$30,333.39
8	China	\$36,021.11	8	Japan	\$30,252.16
9	Netherlands	\$35,585.56	9	United Kingdom	\$28,793.44
10	United Kingdom	\$24,800.78	10	Netherlands	\$27,011.22
11	Spain	\$22,414.83	11	Spain	\$24,291.10
12	India	\$21,704.55	12	Canada	\$17,762.91
13	Denmark	\$18,531.62	13	Russia	\$12,242.23
14	Singapore	\$16,294.93	14	Ireland	\$10,987.46
15	Austria	\$14,714.88	15	Brazil	\$10,591.12
16	Sweden	\$11,522.91	16	Australia	\$10,384.04
17	Japan	\$10,220.48	17	Austria	\$10,348.58
18	Canada	\$9,669.13	18	Poland	\$10,019.41
19	South Korea	\$9,428.77	19	South Korea	\$9,743.98
20	Slovenia	\$8,402.58	20	Turkey	\$7,356.04

The countries with the largest positive trade balances (net exports) are Ireland, Switzerland, and Germany. The countries with the largest negative trade balances (net imports) are the United States, Japan, and Russia.

**Table 4: Trade balances for pharmaceutical products, Top 20 countries, 2021
(millions U.S. dollars)**

Positive Trade Balance		Negative Trade Balance			
Country	Trade Balance	Country	Trade Balance		
1	Ireland	\$59,648.26	1	United States	(\$63,735.37)
2	Switzerland	\$50,018.31	2	Japan	(\$20,031.68)
3	Germany	\$38,828.98	3	Russia	(\$9,727.45)
4	Belgium	\$27,077.89	4	Brazil	(\$9,234.35)
5	India	\$18,362.71	5	Canada	(\$8,093.78)
6	Denmark	\$12,074.50	6	Australia	(\$7,934.92)
7	Singapore	\$12,064.26	7	Poland	(\$5,816.94)
8	Netherlands	\$8,574.33	8	Saudi Arabia	(\$5,583.18)
9	Italy	\$7,819.36	9	Turkey	(\$5,405.35)
10	Sweden	\$5,770.95	10	Mexico	(\$4,803.54)
11	Austria	\$4,366.30	11	United Kingdom	(\$3,992.66)
12	France	\$4,207.66	12	Indonesia	(\$3,673.29)
13	China	\$1,900.82	13	Philippines	(\$3,663.16)
14	Slovenia	\$1,443.14	14	Taiwan, Province of China	(\$3,628.18)
15	Hungary	\$485.32	15	Vietnam	(\$3,622.52)
16	Greece	\$380.38	16	Romania	(\$3,458.14)
17	Malta	\$188.25	17	Egypt	(\$3,454.14)
18	Anguilla	\$12.32	18	Pakistan	(\$3,281.92)
19	San Marino	\$12.06	19	Colombia	(\$3,225.48)
20	American Samoa	\$6.43	20	Czechia	(\$3,187.54)

Global revenues by market segments

Table 5 provides data on global revenues for the prescription and over-the-counter (OTC) segments of the pharmaceutical market for the years 2020, 2021, and 2022. Prescription drug sales were approximately 88 percent of global sales during this period; the remainder (12%) were sales of OTC medicines. Patent-protected prescription drugs represented about 77 percent of prescription drug sales, with the remainder split between generics (8%) and orphan (15%) prescription drugs.

Table 5: Sales of pharmaceutical products by market segment, 2020-2022¹⁵
(billions U.S. dollars and % market)

	Billions of US Dollars			Share of Total Market		
	2020	2021	2022	2020	2021	2022
Total prescription drug sales revenues worldwide	893.0	1024.0	1,058.0	88.0%	88.8%	88.5%
* Prescription drugs (excluding generics and orphan drugs)	689.0	794.0	817.0	67.9%	68.9%	68.4%
* Generic prescription drugs	74.0	82.0	85.0	7.3%	7.1%	7.1%
* Orphan prescription drugs	130.0	148.0	156.0	12.8%	12.8%	13.1%
Over-the-counter (OTC) pharmaceuticals revenue worldwide	121.5	129.1	137.0	12.0%	11.2%	11.5%
Total Prescription and OTC pharmaceuticals revenue worldwide	1,014.5	1,153.1	1,195.0	100%	100%	100%

Generics versus brand-name pharmaceutical products

As discussed in section 1.2, pharmaceutical firms that invest in R&D, develop novel drugs, and use patents to protect their investments through regulatory exclusivity are referred to as “originator” firms. When the patent protection expires, generic drug companies copy the API and sell it under the generic name or under a new trademark. The market penetration rate for generic drugs varies across countries. By value of sales, the generic drug market is approximately 30 percent of the global pharmaceutical market, but the share varies widely by region and country. As Table 6 shows, in North America generics are about 25 percent of the market compared with nearly 60 percent in the Asia-Pacific region.

¹⁵ Calculations using data from Statista. Pharmaceutical Market Worldwide. Study ID 10642.

Table 6: Global market for generic pharmaceuticals, by region (billions U.S. dollars)¹⁶

Region	2018	2019	2020	Average
North America				
Total pharmaceutical market	511.0	531.9	553.0	532.0
Generic drug market	113.8	124.5	135.8	124.7
Generic share (%)	22.3%	23.4%	24.6%	23.4%
Europe				
Total pharmaceutical market	240.4	250.8	260.5	250.6
Generic drug market	64.5	68.6	72.8	68.6
Generic share (%)	26.8%	27.4%	27.9%	27.4%
Asia-Pacific				
Total pharmaceutical market	257.6	277.4	296.1	277.0
Generic drug market	140.6	155.5	171.8	156.0
Generic share (%)	54.6%	56.1%	58.0%	56.3%
China				
China - pharmaceutical market	118.7	130.2	140.7	129.9
China - generic drug market	96.8	105.7	115.1	105.9
China - Generic share (%)	81.6%	81.2%	81.8%	81.5%
India				
India - pharmaceutical market	36.4	41.1	46.8	41.4
India - generic drug market	26.4	31.1	36.5	31.3
India - Generic share (%)	72.5%	75.7%	78.0%	75.6%
Rest of the World				
Total pharmaceutical market	97.5	100.7	103.6	100.6
Generic drugs market	29.3	30.3	31.2	30.3
Generic share (%)	30.1%	30.1%	30.1%	30.1%
Global pharmaceutical market	1,106.50	1,160.80	1,213.20	1,160.17
Global generic drug market	348.20	378.90	411.60	379.57
Generic share (%)	31.5%	32.6%	33.9%	32.7%

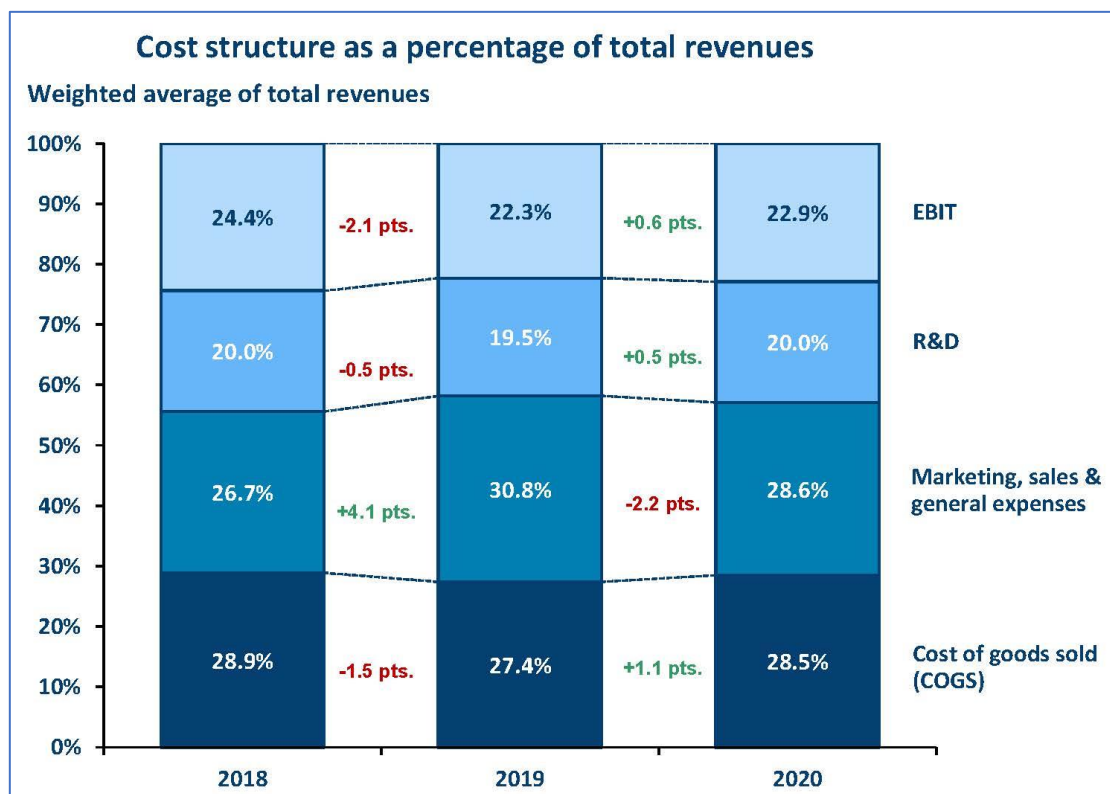
Profitability

A recent analysis of the top 20 pharmaceutical companies worldwide estimated their average profitability (earnings before interest and taxes, EBIT) at 23 percent of revenues in 2020. Average cost of goods sold (COGS) was 28.5 percent, operating expenses 28.6 percent, and R&D costs were 20 percent. See Figure 1 below.

The analysis was undertaken at Group level and focused on the largest companies. It is meant to provide insights into the average profitability and cost structure of the industry as a whole.

¹⁶ Data from BCC (June 2021). Global Markets for Generic Drugs. BCC Publishing Staff. Report Code PHM009J. Table 1. Page 13.

Figure 1: Cost structure as percentage of total revenues, 2018-2020¹⁷



2. The pharmaceutical global value chain

2.1. Overview

As described in section 1.3.3. of the UN TP Manual, value chain analysis, as developed by Michael Porter,¹⁸ describes the value-adding activities performed by a company in creating value for its customers; that is, all the activities involved in bringing a product from inception to final consumption separating them into primary and support activities.¹⁹

¹⁷ Smart Pharma (2022). Top 20 Pharma Companies – Performance and Strategy.

¹⁸ Porter, M. (1985). *Competitive Advantage: Creating and Sustaining Superior Performance*. New York: Free Press. Primary activities include all the direct activities, ranging from upstream purchasing and logistics to downstream distribution and final sales, (that is, the supply chain) involved in a particular product line. The firm also undertakes support activities (e.g., strategic management, regulatory affairs, human resources) that are also value creating but spread across the firm's product lines. Thus, Porter's value chain includes all supply chain and support activities that are revenue generating with respect to a particular product or product line.

¹⁹ Porter's value chain is most suitable for vertically integrated (upstream-downstream) production processes, such as in the pharmaceutical, agricultural, and capital-intensive industries. Other production models such as value shops and value networks are more common in industries such as consulting, banking, and e-commerce. See Stabell, C.B., and Fjeldstad, D.O. (May 1998). *Configuring Value for Competitive Advantage: On Chains, Shops, and Networks*. *Strategic Management Journal*.19.5.

The global value chain (GVC) of an MNE takes into account all of its activities on a worldwide basis.²⁰ GVC analysis can be expanded from examining a single MNE to taking into account all the activities, firms and countries, on a worldwide basis, that are involved in a particular industry such as apparel or automobiles.²¹ GVC analysis uses the value chain as the basic structure for describing and visualizing an MNE or an industry, but recognizes that the various production stages have become globalized and dispersed around the world.²²

This chapter explores the pharmaceutical GVC from a “big picture” perspective for the industry as a whole. It is important to keep in mind that this analysis provides a stylized overview of the pharmaceutical industry that cannot capture the many nuances and differences in how this GVC manifests itself in countries around the world. Chapter 3 discusses how these activities are organized within a typical multinational enterprise (MNE) in the pharmaceutical industry, in terms of value drivers and business models.

It is important to keep in mind that this stylized overview of activities is meant to provide an overview of the industry. For transfer pricing purposes, it will be critical to develop an understanding of the accurately delineated transaction, this includes identifying the economically significant characteristics of a transaction between related parties alongside the roles and responsibilities played of the parties to the transaction which is discussed in Chapter 4.²³

The GVC of the pharmaceutical industry encompasses the following core activities involved in the production of pharmaceutical drugs: research and development, primary and secondary manufacturing, marketing, and distribution. Since the pharmaceutical industry is heavily regulated at all of these stages, regulatory affairs can be considered to constitute an additional core activity for this industry. Lastly, there are various support and overhead activities that can also add value along the GVC (e.g., strategic management, support services). The following analysis focuses on these core activities, which are illustrated in Figure 3.

The GVCs for both small-molecule (chemical) and large-molecule (biological) pharmaceutical products generally follow the same basic steps.

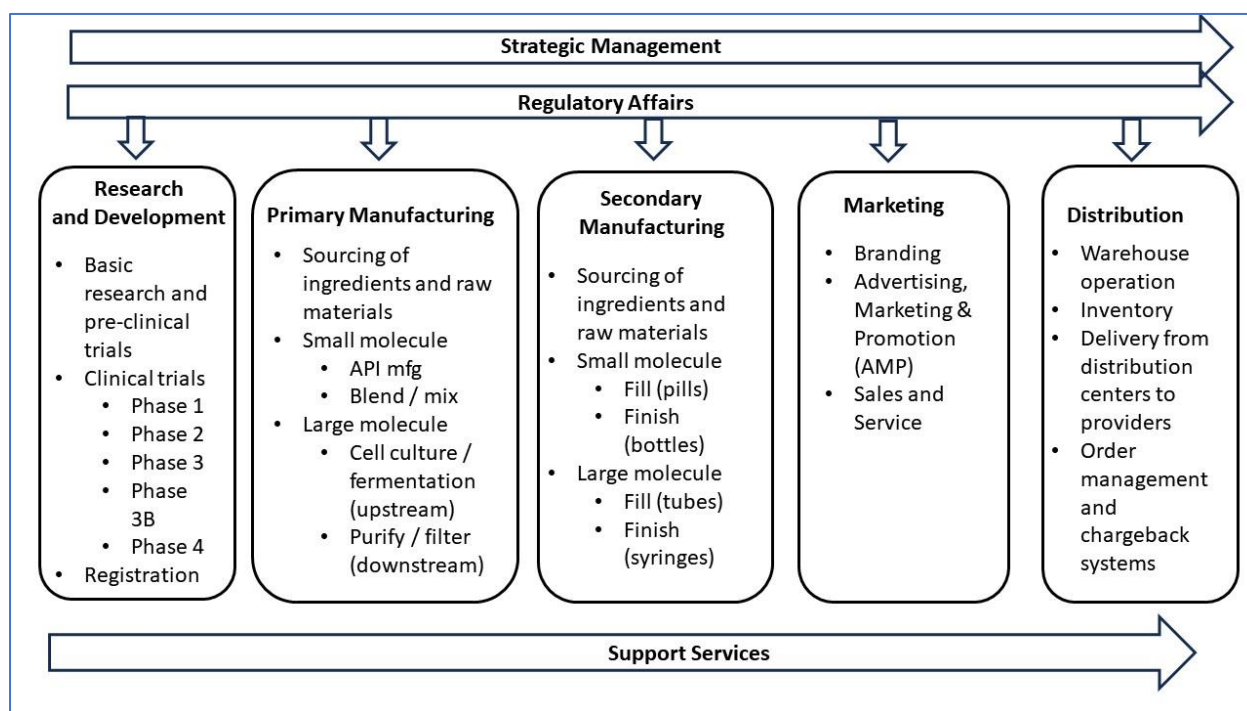
²⁰ See also Eden, L. (1998). *Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America*. University of Toronto Press. Chapter 3. *The Multinational Enterprise as an Integrated Business*. pp. 125-166.

²¹ Frederick, S. (2019). Global value chain mapping. In Ponte, S., Gereffi, G., and Raj-Reichert, G. (editors). *Handbook on Global Value Chains*. Edward Elgar Publishing. pp. 29-53.

²² Jones, L., Demirkaya, M., and Bethmann, E. (2019). *Global Value Chain Analysis: Concepts and Approaches*. *Journal of International Commerce and Economics*. Available from https://www.usitc.gov/journals/jice_home.htm.

²³ UN TP Manual, section 3.1ff.

Figure 3: The global value chain in the pharmaceutical Industry



Accordingly, the core activities that are explored in detail are:

- **Research and development (R&D):** Given the complexity of R&D in the pharmaceutical industry, the R&D stage is typically separated into (1) basic research and pre-clinical trials, (2) clinical trials, (3) registration, and (4) life cycle management studies (post approval clinical trials).
- **Primary manufacturing:** Production of the active pharmaceutical ingredient (API).
- **Secondary manufacturing:** Additional fill and finish stages to convert the API into a finished drug product.
- **Marketing:** The stage where the marketing strategy is designed and executed in light of scientific approval processes, regulations for market access, and price controls; includes detailing, advertising, marketing, and promotion (AMP) activities.
- **Distribution:** The stage where the finished drug product is distributed to customers, which are typically wholesalers, hospitals, clinics and retail pharmacies. Logistics can also involve complex upstream supply chains (from plants to country distributors).
- **Regulatory activities:** Pharmaceutical companies are highly regulated. These regulations impact a company's core activities ranging from regulations for clinical trials, the product approval and registration process, manufacturing, marketing, and distribution (see section 4.1 below for more details).²⁴

²⁴ Al-Worafi, Y.M. (2020). Drug Safety in Developing Countries. Academic Press.

2.2. Research and development

R&D: Basic research and pre-clinical trials

The basic research stage includes both the invention (research and discovery of new drugs) and incremental innovation (e.g., new dosages and delivery mechanisms for existing drugs). Basic research in the pharmaceutical industry is focused on drug discovery, which is the process by which new candidate medications are discovered. It is during this phase that patents are often filed, which grant pharmaceutical companies' exclusivity over product sales for a defined period of time. As these drug patents expire pharmaceutical companies need to develop new patentable drugs to maintain their revenue stream. Although most research and development for new products fails, R&D for new drugs is an essential aspect of the business model for large pharmaceutical companies.

Drug discovery is a lengthy, expensive, and difficult process with a low success rate.²⁵ In the pre-clinical development stage, new active compounds are tested under experimental conditions to gather information on the effects of the new drug.

At the clinical trials stage, potential new drugs are subjected to multiple rounds of clinical trials designed to test and establish their safety, efficacy, dosage and any adverse side effects. The reasons for clinical testing include: (1) preparation and submission of applications for regulatory approval and trials designed to test production processes for new vaccines and drugs; (2) testing of incremental innovations; (3) clinical testing of a new drug against existing rival drugs; and (4) additional safety monitoring after a drug has reached the market that a government may require to detect new side effects that were missed during earlier clinical trials.²⁶

While regulations and demands from regulatory authorities vary between countries, the following summarizes the clinical testing stages used by many regulatory authorities (cf. Figure 3):

- Phase 1: Testing of small groups of healthy volunteers to assess the safety of various dosage levels of a potential new vaccine or drug.
- Phase 2: Testing of larger numbers including individuals that have the medical condition that the vaccine or drug is designed to address. This phase focuses on the efficacy of the drug and potential side effects.
- Phase 3: Large numbers of volunteers in many locations engage in randomized trials to assess the effectiveness of the vaccine or drug.
- Phase 4: Post Marketing Studies. Additional studies that may be required by a regulatory agency or to test for side effects or new usages.

²⁵ Zirnstein, F., and Kaiser, P. (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In Petruzzi, R., Cottani, G., and Lang, M. (editors). *Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics*. Wolters Kluwer. Chapter 21.

²⁶ Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. *International Transfer Pricing Journal*. Section 3.1.

The clinical trials stage can take up to ten years. While this time frame was considerably shortened for the vaccine approval process during the COVID-19 pandemic, it is unclear if and how this will influence the time frame for other new drug approvals.

It will be important to correctly assess clinical trials for transfer pricing purposes. For example, in cases where local clinical trials are needed, it will have to be analyzed how this activity will be remunerated and if it constitutes a separate activity or is part of a larger activity (such as, for example, distribution services). In the analysis, the degree of knowledge needed to comply with local regulations will need to be taken into account alongside questions of decision-making, financing and approvals.

R&D statistics

In 2021, more than 6,000 drug products were in clinical trials involving humans (phases 1 through 4) with more than 5,500 new planned clinical trials.²⁷ The clinical trial phases absorb about 50 percent of R&D costs; the other half involve preclinical compound discovery and testing, and regulatory activities.

Business risks at the R&D stage of the pharmaceutical value chain is very high. Estimates put the composite success rate over all four phases of the so-called “R&D pipeline” for 2021 at 5% compared to a 2010-2021 average composite rate of 13.1%.²⁸ Success rates vary along the R&D pipeline, measured in terms of the success rate of graduating from one phase to at least the next phase. The success rates over the 2010-2021 period were: Phase 1 (56%), Phase 2 (38%), Phase 3 (67%) and Regulatory Submission (89%).

There are approximately 3,200 companies and more than 200 academic or research groups that are engaged in R&D activities in the global pharmaceutical industry. While a large number of research firms are headquartered in the United States (44%), Europe (25%), Japan (6%) and South Korea (4%)²⁹, the geography of firms is changing with an increasing number of China-headquartered firms entering the market increasing their market share from 2% ten years ago to 12% in 2022.

Emerging biopharma companies (EBPs), defined as pharma firms with less than \$500 million in sales and R&D spending of less than \$200 million per year, in 2021 accounted for a record 65% of the molecules in the R&D pipeline up from 50% in 2016 and 33% in 2001. Of the EBPs, 17% are headquartered in China compared to 20% in Europe and 46% in the USA. EBPs also hold different shares of the total national R&D pipeline, ranging from a high of 83% in China to 62% in the USA, 47% in Europe and a low of 22% in Japan.³⁰

²⁷ IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. p. 35. Available from <https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022>

²⁸ IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. Available from <https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022>

²⁹ IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. p. 22. Available from <https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022>.

³⁰ IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. p. 50. Available from <https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022>.

Registration

In order to be able to distribute drugs in a market, they have to be registered with the National Medicines Regulatory Authority (NMRA) of each country where the firm intends to market the new drug. This process is typically anticipated throughout the clinical trials with a companies' regulatory affairs staff determining and executing the regulatory filing strategy (how to build the dossier, country filing prioritization, etc.) by submitting dossiers to the various national regulatory authorities.

Once regulatory agency approval is provided, the company registers the product and applies for marketing authorization to market and sell the drug.

2.3. Primary (API) manufacturing

Pharmaceutical products are made from an active pharmaceutical ingredient (API) together with inactive ingredients (excipients) added to the API to produce a finished product.³¹ An API is “any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.”³² In short, an API is a bulk drug substance. The global market for APIs in 2020 was 173.3 billion USD.³³

The primary manufacturing stage involves the procurement of raw materials and excipients, and the manufacturing of the API. Pharmaceutical excipients are materials used in pharma production; they can be either natural (organic) or synthetic (inorganic). Natural excipients are substances derived from animals (e.g., gelatin, beeswax), plants (e.g., pectin, starch), or minerals (e.g., talc, paraffin). Synthetic excipients are organically derived (e.g., from petroleum or rocks) but are created through chemical manufacturing processes, which tend to make them more expensive than natural excipients.

Excipients are used in manufacturing and processing to protect and enhance the drug's stability, bioavailability, and product safety; assist in efficiency and delivery of the drug when used or consumed; and to product the integrity of the product during storage. The “ideal” excipient has the following characteristics: it is stable and reproducible, no undesired interactions, pharmacologically inert, desired functionality, and cost

³¹ BCC Research Staff (June 2019). Markets at a Glance: Pharmaceuticals. Report Code: PHM213A.

³² International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (November 2000). Topic Q7. Good Manufacturing Practice for Active Pharmaceutical Ingredients. Available from <https://www.ema.europa.eu/en/ich-q7-good-manufacturing-practice-active-pharmaceutical-ingredients-scientific-guideline>.

³³ BCC Publishing (January 2021). BCC Research Staff. Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B. p. 9.

effective.³⁴ In 2021, the global market for pharmaceutical excipients was \$8.29 billion USD, of which nearly 93 percent were organic excipients.³⁵

Chemistry and biology are at the “heart” of the primary manufacturing stage (see Figure 3).³⁶ Chemical (small molecule) drugs historically have been the “cornerstone of modern medicine” with less complex chemical structures, simpler manufacturing processes, and often administered orally.³⁷ The manufacturing process for creating a chemical API involves the procurement of chemical compounds, which are processed into intermediate materials that are further refined and purified into an API. These further processes normally include isolation, extraction, purification, milling, and packaging.³⁸ Once the API is manufactured, it is blended or mixed with other ingredients to make a bulk drug substance, or it is purified or filtered to create the bulk drug substance.

Biological (large molecule) drugs, on the other hand, are a relatively newer field of drugs and therapies are available primarily as intravenous injections. They are derived from naturally occurring sources, human, animal or micro-organisms and tend to have complex structures and manufacturing processes. The production of biological APIs typically involves cell culture/fermentation, followed by purifying and filtration. Large molecule drugs pose additional manufacturing challenges and risks and display greater fragility in storing and transporting them.³⁹

Both production processes typically involve the use of large-scale plants that can generate tens of millions of doses per year. The fixed costs of such plants are typically high due to the need to create and maintain hyper-clean rooms, acquire specialized capital equipment, and employ skilled personnel. Specialized inputs such as bioreactor bags, filters and cellular materials are also needed. The drug substance, once created, is combined with other pharmaceutical ingredients (e.g., excipients, adjuvants and preservatives) to formulate a drug product.

2.4. Secondary (pharma) manufacturing

Secondary manufacturing involves turning the bulk drug substance (the API) into one or more drug products; the typical secondary manufacturing stages are fill and finish. Raw materials and excipients are also needed at this stage. During the manufacturing

³⁴ For a detailed analysis of pharmaceutical excipients see Tcherpakov, M. (May 2021). Excipients in Pharmaceuticals: Global Markets to 2026. Report Code: PHM010. BBC Publishing. p. 13.

³⁵ Tcherpakov, M. (May 2021). Excipients in Pharmaceuticals: Global Markets to 2026. Report Code: PHM010. BBC Publishing. p. 17.

³⁶ Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal.

³⁷ USITC (2020). COVID-19 Related Goods: The U.S. Industry, Market, Trade, and Supply Chain Challenges. Publication number.5145. Available from <https://www.usitc.gov/publications/332/pub5145.pdf>

³⁸ BCC Publishing (January 2021). BCC Research Staff. Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B. p. 24.

³⁹ Deloitte (2015). Advanced Biopharmaceutical Manufacturing: An Evolution Underway. Deloitte Development LLC. p. 5.

process, the chemical API is combined with other ingredients and extruded as pills or capsules, which are then assembled in bottles that are labeled and packaged.

For biologic APIs, secondary production involves squirting doses into vials or syringes. At the finishing stage, the vials or syringes are capped with stoppers, labelled and packaged. These plants also require specialized assembly-line capital equipment (generating high fixed costs) and variable inputs such as vials, stoppers and packing and shipping costs. Some may also require cold storage to extend shelf life.

The location of the secondary manufacturing stage is typically dispersed across countries, partly due to government regulations that require local preparation and packaging, but also to take advantage of lower-cost locations. Tax policies have also been used to attract secondary manufacturing in the pharmaceutical industry to locate in developing countries.⁴⁰ In addition, toll manufacturing agreements between pharmaceutical MNEs and local firms can encourage dispersion of this stage of production. Some contract manufacturing organizations (CMOs) also offer fill-and-finish services to drug manufacturers. Pharmaceutical MNEs may choose to contract out secondary manufacturing if they do not have sufficient resources for their own in-house manufacturing facilities or if they prefer to focus on R&D and outsource the downstream activities.⁴¹

2.5. Marketing

Depending on a country's health care system, patients may obtain prescription pharmaceutical products at a hospital or medical clinic, or from retail pharmacies (some of which may operate as online business). In some countries, pharmaceutical companies, in addition to needing marketing authorization, will also need to ensure that their products are listed with insurance companies if they and/or a national regulatory body have agreed to cover certain medications under their insurance policies. Thus, prescribing behavior by physicians and cost coverage (payment either out-of-pocket by patients, full coverage through an insurance or a combination of both) are the primary drivers of demand for prescription pharmaceutical drugs.

Once a prescription drug has been approved and can be distributed, pharmaceutical companies must design and implement a market access/marketing strategy for the product. Marketing activities in the pharmaceutical industry range from sales activities through sales representatives to educational or scientific activities, such as industry-organized conferences and clinical studies.⁴² Direct marketing to consumers through advertisements and commercials is only permitted in the United States and New

⁴⁰ Eden, L. (1994). Puerto Rican Transfers and Section 936. 9 Tax Notes International 37.

⁴¹ BCC Research Staff (January 2021). Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B. BCC Publishing, p. 60.

⁴² Mulinari, S. (2016). Regulating Pharmaceutical Industry Marketing: Development, Enforcement, and Outcome of Marketing Rules. *Sociology Compass*. Available from [10.1111/soc4.12335](https://doi.org/10.1111/soc4.12335).

Zealand.⁴³

It is important to note that marketing strategies will vary between OTC drugs and prescription drugs. As noted in section 1.2., OTC products are typically sold in pharmacies, though some countries may also allow these products to be sold in drugstores, supermarkets or convenience stores.

In general, this stage of the global value chain is influenced by three factors; namely, (1) the patent protection period, (2) marketing regulations and (3) the fact that the recipient of the marketing strategy is often not the end-consumer of the product.

The patent protection period

New products are typically protected by patents, this holds especially true for prescription drugs. While the exact length of a patent varies between countries and products (see section 3.1. and 4.2. for further information on patents), the protection from direct competition it affords gives companies a defined timeframe during which to establish a product under recognizable trademark name and build up confidence and loyalty towards the product. This requires substantial marketing spending to rapidly gain market acceptance and requires actions to establish an environment that could allow the company to continue to successfully sell the product even after patent protection has lapsed.⁴⁴

Marketing regulations

The marketing activities undertaken by companies in the pharmaceutical industry are heavily regulated at the national (and supranational for the EU) level and may be enforced either through legal action or through an NMRA. This pertains to both prescription drugs and OTC drugs, though exact regulations may differ between the two categories. Regulations may limit the retail outlet, marketing channels used, the claims that can be made and the kind of supplementary information that may need to be provided. In addition to national regulations, many medical associations and hospitals or universities have professional or employee codes of conduct that cover interactions with the pharmaceutical industry.⁴⁵

Marketing strategy

Depending on the domestic regulations in place, pharmaceutical products that require a prescription are generally marketed to healthcare providers such as physicians, pharmacists and insurance organizations, which may be companies themselves or run by the government and may additionally be advertised to patients. This requires

⁴³ Ventola, C.L. (2011). Direct-to-Consumer Pharmaceutical Advertising: Therapeutic or Toxic? P & T : a peer-reviewed journal for formulary management 36(10).

⁴⁴ Zirnstein, F., and Kaiser, P. (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In Raffaele Petrucci, Giammarco Cottani and Michael Lang (editors). *Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics*. Wolters Kluwer, Chapter 21.

⁴⁵ Mulinari, S. (2016). Regulating Pharmaceutical Industry Marketing: Development, Enforcement, and Outcome of Marketing Rules. *Sociology Compass*. Available from [10.1111/soc4.12335](https://doi.org/10.1111/soc4.12335).

experience and expertise with the medical profession’s practices and knowledge on the regulatory requirements. Historically, an in-country marketing strategy required a large sales force; however, digitalization and increasing regulatory pressures may have decreased the importance of the number of “messengers” relative to the “message” (the value proposition and approval file).

OTC drugs are generally marketed to patients directly, though some OTC products may additionally be marketed to healthcare providers in order for them to recommend them to their patients.

2.6. Distribution

Once a new drug has been manufactured and packaged it has to be distributed to the point-of-sale in order for patients to be able to buy the products. In most countries, distribution of medication is facilitated through wholesalers – this applied to prescription and OTC drugs. These may operate as a “single channel wholesaler”, i.e., a wholesaler has the exclusive right to distribute medications from one pharmaceutical company within a certain region or country. Nevertheless, most countries encourage a multi-channel system in wholesaling, in which medications are distributed and supplied in parallel from different wholesalers.⁴⁶ In the latter case, wholesalers consolidate orders from multiple companies in their warehouse and packages products from several manufacturers that are destined for a particular point-of-sale into the same tote (container). Any products that are not sold or must be returned, together with the returned totes, are sent back to the distributor warehouse to be resold or disposed.⁴⁷

A graphic illustrating the typical flow of products, services, and funds for prescription drugs that are covered under insurance and purchased in a retail setting is illustrated in Figure 4 below.⁴⁸ In most countries, a pharmaceutical manufacturer sells its product to a wholesaler/distributor that supplies the product to health care providers (e.g., doctors, hospitals, medical clinics) and/or retail (including mail order) pharmacies. The purchasers dispense the medicines to patients, who take them as prescribed. In most countries, there are third-party payers (e.g., health insurers, employer health plans, and government programs) that provide insurance coverage to insured patients in return for insurance premiums; though patients will also typically make co-payments for the drugs purchased from pharmacies, hospitals, etc. The third-party payers also negotiate

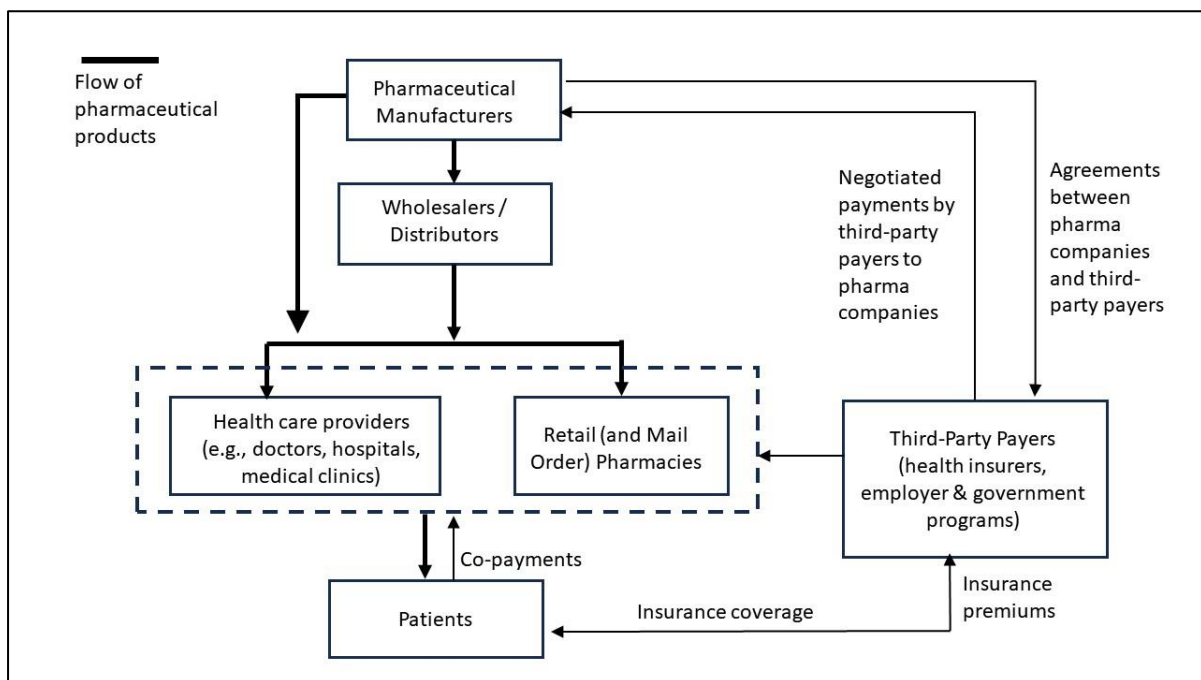
⁴⁶ Kanavos, P., Schurer, W., and Vogler, S. (2011). The pharmaceutical distribution chain in the European Union: structure and impact on pharmaceutical prices. European Commission, Brussels, Belgium

⁴⁷ On the complexities involved in pharmaceutical distribution see Augustine, N.R., Madhavan, G., and Nass, S.J. (editors) (2018). Making Medicines Affordable: A National Imperative. The National Academies Press. Chapter 2. Complexity in Action. Available from <http://nap.edu/24946>.

⁴⁸ Sood, N. et al. (2017). The Flow of Money Through the Pharmaceutical Distribution System. USC Leonard D. Schaeffer Center for Health Policy & Economic. Available from https://healthpolicy.usc.edu/wp-content/uploads/2017/06/The-Flow-of-Money-Through-the-Pharmaceutical-Distribution-System_Final_Spreadsheet.pdf. See also PharmaNewsIntelligence (March 2023). Fundamentals of the Pharmaceutical Supply Chain. Available from <https://pharmanewsintel.com/news/fundamentals-of-the-pharmaceutical-supply-chain>.

agreements with the pharmaceutical companies. The agreements may cover items such as which products are covered by a patient’s insurance plan, processing the prescription medicines through quality and utilization management checks, and managing formulary lists of covered medicines.

Figure 4: The typical distribution system for prescription pharmaceutical products⁴⁹



2.7. Regulatory affairs

All activities of the pharmaceutical industry are governed by a set of strict laws, regulations and policies that draw on the work and standards developed by the World Health Organization (WHO) but are specific to each country. The regulation takes place both on the demand and the supply side of the market.⁵⁰ On the supply side, there are a wide variety of government regulations in the pharmaceutical industry including:

⁴⁹ Variation of Figure 1 in Sood, N., Shih, T., Van Nuys, K., and Goldman, D. (2017). Flow of Money Through the Pharmaceutical Distribution System. Available from <https://healthpolicy.usc.edu/research/flow-of-money-through-the-pharmaceutical-distribution-system/>. For descriptions and graphics illustrating of other forms of pharmaceutical markets see National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient Access to Affordable Drug Therapies. Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.). (2017). Making Medicines Affordable: A National Imperative. National Academies Press (US). Chapter 2.

⁵⁰ Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal.

- Intellectual property rights (IPR) protection. In the pharmaceutical products this typically involves incentives to substitute generics and ensure innovation⁵¹
- Effectiveness and quality control by government agencies including safety monitoring of both R&D manufacturing and distribution practices
- Price controls and cost containment measures
- Regulation of marketing activities with respect to content and promotional channels and codes of conduct

On the demand side, government regulations typically separate “who selects” and “who pays” among four groups: patients, physicians, insurance companies, and pharmacies and hospitals.

NMRAs are tasked with monitoring the quality, safety and efficacy of drugs, and the accuracy of product information. This is done by ensuring that different elements of the global value chain are carried out according to specified standards. This includes parts of the R&D process / clinical trials, the procurement, manufacturing and distribution of drugs, as well as product promotion and advertising.⁵²

As all of these rules are specific to each jurisdiction, it is important to keep in mind that the below discussion focuses on general trends observed and cannot capture the many different rules and regulations as they manifest in countries around the world. In the following, the regulations applicable to the four general stages of the global value chain will be discussed: (1) Research and Development, (2) Manufacturing, (3) Marketing and (4) Distribution.⁵³

Research and Development

As described in section 2.2. the research and development process can be divided into basic research, pre-clinical trials and phase 1 through 4 trials. All of these phases have to adhere to what is commonly referred to as Good Clinical Research Practice (GCP). GCP is defined by the WHO as a process that incorporates established ethical and scientific quality standards for the design, conduct, recording and reporting of clinical research involving the participation of human subjects. Such a process intends to ensure the rights, safety and well-being of research subjects and the integrity of clinical research data.⁵⁴

⁵¹ See, for example, Eden, L. (1989). Pharmaceuticals in Canada: An Analysis of the Compulsory Licensing Debate. In Rugman, A.M. (editor) (1989). International Business in Canada: Strategies for Management. New York and Toronto: Prentice-Hall.

⁵² Maniadakis, N., Kourlaba, G., Shen, J., and Holtorf, A. (2017). Comprehensive taxonomy and worldwide trends in pharmaceutical policies in relation to country income status. BMC Health Services Research. 17. Available from <https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-017-2304-2>

⁵³ On government regulation and their influence on transfer pricing, see the UN TP Manual, sections 2.4.2.4, 3.4.5.3 and 3.4.5.15f.

⁵⁴ WHO (2015). Handbook for good clinical research practice (GCP): guidance for implementation. Available from [untitled \(who.int\)](#)

Manufacturing

Section 2.3 and 2.4 describe the typical manufacturing process of pharmaceutical products, commonly divided into primary and secondary manufacturing (see section 3.1. on batch manufacturing for an alternative approach). During manufacturing, companies commonly have to adhere to Good Manufacturing Practices (GMP). The WHO defines GMP as quality management that ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as required by the marketing authorization, clinical trial authorization or product specification. GMP is aimed primarily at diminishing the risks inherent in any pharmaceutical production from cross-contamination/mix-ups and false labelling.⁵⁵ This includes procedures for receipt of materials, production, packaging, labeling, quality control, release, storage and distribution.⁵⁶ In many countries, NMRAs will inspect equipment, facilities and manufacturing processes prior to approving a product.⁵⁷

Marketing

A relevant distinction is between prescription drugs and over-the-counter (non-prescription) medications as outlined in section 1.2. This distinction, which depends on national government regulations that determine which drugs require a physician's prescription, can influence how the product is marketed and distributed.

As noted in section 2.6., in most countries, pharmaceutical sales are made indirectly through distributors to hospitals, pharmacies and other retail distribution outlets. In only a few countries (e.g., Japan) do pharmaceutical companies sell directly to physicians who then sell medicines to their patients. In most countries, however, physicians prescribe the medicines that are purchased by households, hospitals and government medical services. In fact, compared with many other industries, the pharmaceutical industry distributes its products to consumers through a very large and sophisticated customer base; that is, the medical profession.⁵⁸

Marketing in the pharmaceutical industry is therefore typically directed at physicians, using trained and educated company representatives that are usually recruited for a relatively short term. Detailing is a 1:1 marketing technique pharmaceutical companies use to educate physicians about the vendor's products, hoping the physician will prescribe the company's products more often.⁵⁹ Against the background of rising digital communication channels and specialty medicine development, there is a shift to real-

⁵⁵ WHO (2014). WHO good manufacturing practices for pharmaceutical products: Main principles. Available from [TRS 986 - Annex 2: WHO good manufacturing practices for pharmaceutical products: Main principles](#)

⁵⁶ Kaufman, B., and Novack, G.D. (2003). Compliance Issues in Manufacturing of Drugs. *The Ocular Surface*. Volume 1. Issue 2. Available from [https://doi.org/10.1016/S1542-0124\(12\)70131-3](https://doi.org/10.1016/S1542-0124(12)70131-3).

⁵⁷ Zirnstein, F., and Kaiser, P. (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In Petruzzi, R., Cottani, G., and Lang, M. (editors). *Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics*. Wolters Kluwer, Chapter 21.

⁵⁸ Collins, M., and Wundisch, K. (2004). Transfer pricing in the Ethical Pharmaceutical Industry. *International Bureau of Fiscal Documentation (IBFD)*. Section 2.4.

⁵⁹ Revo. How Medical Detailing Is Changing With Pharma Marketing Technology. Available from <https://revosuite.com/blog/how-medical-detailing-is-changing-with-pharma-marketing-technology>

time, data-driven marketing strategies making increased use of digital communication channels as well as key opinion leaders.⁶⁰ Marketing of pharmaceuticals is also heavily regulated in most countries, as explained in section 2.5. This encompasses rules on which marketing channels may be used as well as what claims can be made.⁶¹

Distribution

The distribution and storage of drugs is, as discussed in section 2.6., is an important activity in the global value chain of pharmaceutical companies. Substandard and / or falsified products are a significant threat to public health and safety. Consequently, it is important to ensure the quality and safety of drugs; to prevent the exposure to substandard and falsified products; and to ensure that the integrity of the distribution chain is maintained. Accordingly, most countries have established Good Distribution Practices (GDP) in line with recommendations by the WHO. Such regulation would, for example, generally cover the need for written procedures and clearly specified responsibilities, traceability requirements, systems for quality risk management including systems for managing returns, complaints and product re-calls.⁶²

⁶⁰ Somaiya, H. (2022). Omnichannel Is The Next Step In Pharmaceutical Marketing. Forbes. Available from [Omnichannel Is The Next Step In Pharmaceutical Marketing \(forbes.com\)](https://www.forbes.com)

⁶¹ Mulinari, S. (2016). Regulating Pharmaceutical Industry Marketing: Development, Enforcement, and Outcome of Marketing Rules. Sociology Compass. Available from [10.1111/soc4.12335](https://doi.org/10.1111/soc4.12335).

⁶² WHO (2020). Good storage and distribution practices for medical products. Available from [TRS 1025 - Annex 7: Good storage and distribution practices for medical products \(who.int\)](https://www.who.int)

3. Value drivers and business models in the pharmaceutical industry

In this chapter we examine the pharmaceutical global value chain through the perspective of an individual company in the industry. We cover three topics: value drivers, business models, and the role of developing countries within the pharmaceutical GVC.

3.1. Value drivers in the pharmaceutical industry

The pharmaceutical GVC is the most knowledge intensive of all GVCs. The *Global Value Chain Development Report 2021* estimated the knowledge intensity of pharmaceuticals and medical devices at 66.3 percent, compared with 17.4 percent for computers and electronics, 13.7 percent for information technology services, and 2.3 percent for food and beverages.⁶³ Thus, the key drivers of profits in the pharmaceutical industry are **knowledge-based assets**. Examples include:

- Innovative drugs will generally be protected by a **patent**. It is even possible that a drug is protected by several patents because of secondary patents covering, for example manufacturing know-how, or because the drug and / or the API is a combination of different chemical compounds each of which is covered by a patent. If patent protection is missing, generic manufacturers can compete, which has an impact on a company's revenues (see section 5.3.5.1. on patent cliffs). The value of the patent is influenced by the marketing authorization because the latter will determine if a product can be sold in a specific country.
- Marketing intangibles such as trademarks and customer lists. Products may be marketed under a specific **trademark**. The trademark without the patent and the required marketing authorization may have limited value since the product cannot be sold without authorization resulting from the successful R&D activities.
- Products generally have to undergo a rigorous testing process, and a NMRA has to issue a **marketing authorization** for companies to be able to sell the product in a specific geographical area and with specific indications according to the tests carried out. This process largely verifies and is thus dependent on the quality and efficacy of the underlying drug.
- **Patent, market authorization and marketing intangible combined**, can be of significantly valuable and it is common for a pharmaceutical product to be associated with more than one intangible at a time.

⁶³ Asian Development Bank (2021). Global Value Chain Development Report 2021: Beyond Production.

The interactions between each of these classes of intangible assets, as well as the parties that have performed the functions, borne the risks and incurred the costs associated with the DAEMPE functions in relation to the intangible assets, are relevant in the delineation of transactions between related parties in this industry.

Below we discuss some of these key drivers (1) patents, (2) marketing intangibles, (3) know-how and (4) the role played by technological change in this industry.⁶⁴

Patents

Technological knowledge, driven primarily by a firm's research and development (R&D) activities, has been widely perceived as the most important of the MNE's firm specific advantages and the key long-term value driver in the pharmaceutical industry.⁶⁵ R&D activities carry a high risk in view of the uncertainty of the outcome and will often involve large investments that may or may not lead to a new product. It is estimated that the average time a successful pharmaceutical product takes from R&D to market may be 12 to 15 years, with the economic cost of developing a successful compound (including opportunity costs and costs of failed products) being approximately 2 billion USD.⁶⁶

The firm's goal is generally to develop an innovative product that will be granted patent protection for a set time period during which the patent holder alone can decide which companies are allowed to use a specific formulation, manufacturing process or chemical compound. As a result, patents provide the patent holder with an opportunity to recoup the costs involved in developing the patented innovation and act as a reward for engaging in risky and lengthy R&D. The patent protection depends on the patent type, scope coverage and local availability of legal remedies which differs between countries and can last up to 20 years. See section 4.2. on a discussion on patent lifecycle management and patent cliffs.

How R&D costs and revenues are reported on a company's income statement therefore can have a substantial impact on its profitability (and thus corporate income taxes due) given that failed projects occur frequently and have large sums of sunk costs that – due to the asynchrony of R&D efforts and general accounting principles – cannot be spread

⁶⁴ For a discussion of intangibles including patents, trademarks and brands more generally, see Chapter 6 of the UN TP Manual.

⁶⁵ Eden, L. (1998). *Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America*. University of Toronto Press. p. 135.

⁶⁶ Siddiqui, Y.J. (2019). *Transfer Pricing and Value Creation in the Pharmaceutical Sector*. In Petruzzi/Tavares (Eds). *Transfer Pricing and Value Creation*. Several studies have estimated the R&D costs to bring a new medicine to market, with estimates ranging from 314 million to 2.8 billion U.S. dollars. For a review and new U.S. estimate (i.e., median capitalized R&D cost of nearly one billion US dollars) see Wouters, O.J., McKee, M., and Luyten, J. (2020). *Estimated Research and Development Investment Need to Bring a New Medicine to Market, 2009-2018*. JAMA. 323.9

out over time.⁶⁷

An alternative to costly and risky in-house development is the acquisition of smaller firms and their intellectual property by larger firms.⁶⁸ Most of the intangible-related costs on the balance sheets of pharmaceutical MNEs are acquisition-related costs. Once off patent, firms with small molecule drugs face competition from generics; those with biologics face competition from biosimilars.

Marketing intangibles

Marketing intangibles are created through marketing activities and may assist in the exploitation of a pharmaceutical product and may have important promotional value for pharmaceutical products (UN Manual, section 6.2.4). Marketing intangibles include trademarks, trade names, customer lists and customer relationships, and proprietary market and customer data that is used in marketing activities and in selling goods to customers.

In the pharmaceutical industry, as in most industries, there may be a combination of central and local marketing activities performed within an MNE group. Distributors belonging to a pharmaceutical MNE may perform marketing activities which reflect the activities performed by independent distributors. In some cases, distributors may perform marketing activities that are not performed by independent distributors. These activities may include the modifications of marketing material developed centrally for the group. Marketing by a distributor belonging to a pharmaceutical MNE in a specific market may result in the distributor incurring marketing expenses exceeding those incurred by comparable independent distributors. This may result in the distributor creating a valuable marketing intangible.

The UN TP Manual states that, depending on the facts and circumstances, the marketing activities of a distributor may result in the following results:

“a) The activities may lead to the creation of a local marketing intangible but not attract a return greater than the return of otherwise comparable uncontrolled distributors, for instance if the resulting intangible is not unique, despite the expenses incurred being greater than those of comparable uncontrolled distributors;

b) The activities may lead to the creation of a local marketing intangible (distinct from the foreign-owned brand) and attract a return greater than that of otherwise comparable uncontrolled distributors, for instance if the resulting intangible is unique and valuable;

⁶⁷ Zirnstein, F., and Kaiser, P. (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In Petruzzi, R., Cottani, G., and Lang, M. (editors). *Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics*. Wolters Kluwer. Chapter 21.

⁶⁸ Zirnstein, F., and Kaiser, P. (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In Petruzzi, R., Cottani, G., and Lang, M. (editors). *Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics*. Wolters Kluwer. Chapter 21.

c) The activities may not lead to the creation of a local marketing intangible and not attract a return greater than the return of otherwise comparable uncontrolled distributors, for instance if the additional value created is captured by the distributor through anticipated increased sales volumes; or

d) The activities may not lead to the creation of a local marketing intangible but attract a return greater than the return of otherwise comparable uncontrolled distributors, for instance if the distributor's marketing activities are a valuable contribution to the foreign-owned brand." (UN TP Manual, section 6.2.4.5)

Most pharmaceutical products will be protected by a trademark with regard to the drug's name, symbol or logo. The trademark owner can, as a result, exclude others from using the drug's name, symbol or logo. The trademarked drug may additionally be a brand in case the trademark carries social and commercial significance. In contrast to a patent, a trademark registration continues indefinitely.

As noted above, the marketing of a pharmaceutical product aims at establishing the trademark in a way as to continue to successfully sell the drug after patent protection has lapsed. This includes managing pricing and discounts strategically so as to maximize acceptance by the target population where competition is both "within patent" (competition between patented products) and patent versus generic products. Many companies execute a centralized portfolio management approach in this regard. Other marketing strategies may revolve around establishing generic or biosimilar products as a brand or investing heavily in the brand value of the parent company.

Know-how

While in the past pharmaceutical companies focused on protecting their products and an active compound, they now increasingly seek additional patent protection on know-how, for example with regards to its manufacturing process. This is especially relevant when production is scaled up from small batch production needed for clinical trials to producing at scale.

In terms of value creation, manufacturing know-how in the pharmaceutical and biotech sector is generally regarded as less important than and highly dependent on the R&D process and output, though its complexity can be underestimated with regard to biologics and biotech products.

Technological advancement

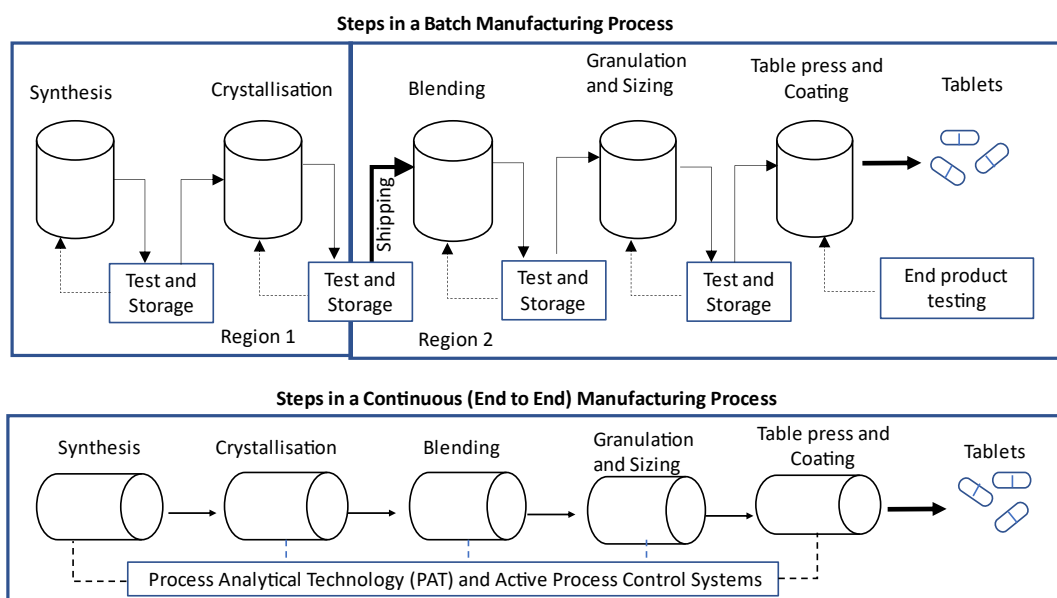
The pharmaceutical industry, as most other industries, is undergoing tremendous changes due to technological advancements. In the following, two of these changes are discussed; namely, (1) digitalization and (2) the shift from batch to continuous manufacturing.

Digitalization is believed to transform the pharmaceutical industry in the coming years:

- Artificial intelligence (AI) and machine learning is projected to lead to massive changes in the R&D landscape with the potential for spurring innovations while saving costs.
- Blockchain technology is believed to transform the supply chain management of the pharmaceutical industry.
- Big data and analytics have the potential to improve patient healthcare as well as the operational efficiency of the manufacturing process.⁶⁹

Digitalization is playing an important role in ongoing technological change in the pharmaceutical industry in terms of process technology as firms shift from batch to continuous manufacturing. Most pharmaceutical manufacturing is done by traditional “batch” manufacturing (BM) processes where raw materials are inputted at the beginning of the process and discharged as a finished product at the end in numbered batches.⁷⁰ This involves a number of processes (e.g., blending, granulation, drying) and may require work to be undertaken at different facilities. As a result, BM may suffer from lack of agility, flexibility and reliability, making it difficult for manufacturers to respond quickly to sudden changes in demand or adapt when certain inputs aren’t available. BM generally results in the clear separation of the primary and secondary manufacturing stages into different plants and locations. Figure 5 illustrates the typical batch manufacturing process in the pharmaceutical industry.

Figure 5: Batch versus continuous manufacturing in the pharmaceutical industry⁷¹



⁶⁹ Siddiqui, Y.J. (2019). Transfer Pricing and Value Creation in the Pharmaceutical Sector. In Petruzzi/Tavares (Eds). Transfer Pricing and Value Creation.

⁷⁰ Brookings Institution (2015). Promoting Continuous Manufacturing in the Pharmaceutical Sector. Available from <https://www.brookings.edu/wp-content/uploads/2015/10/Continuous-manufacturing-discussion-guide.pdf>.

⁷¹ Authors’ drawing based on Hock, Siang and Wah (2021). Continuous manufacturing versus batch manufacturing: benefits, opportunities and challenges for manufacturers and regulators. Generics and Biosimilars Initiative Journal. Figure 2. Available from 10.5639/gabij.2021.1001.004.

Continuous manufacturing (CM) is the main alternative to batch processing as it integrates individual continuous unit operations with process analytical technology that monitors and controls the process parameters and material and quality attributes. See Figure 5. Manufacturing processes are streamlined by eliminating steps. CM, as a result, uses smaller scale equipment, less materials, and can be located in a single plant facility making it more agile and flexible than BM. The resulting value chain is shorter and takes less end-to-end time to complete. Companies are also able to perform both primary and secondary manufacturing stages in the same plant at the same location with no real distinction between primary and secondary manufacturing.

While the cost savings have been estimated at more than 30%, the pharmaceutical industry, however, has been slow to shift from batch to continuous manufacturing for a variety of technical, operational, economic and regulatory reasons.⁷²

The shift from batch to continuous manufacturing could have very significant effects as primary and secondary manufacturing can be consolidated in one location. The need to decentralize steps in the production process to lower cost is likely to be reduced, especially for small molecule drugs. As a result, some of the activities performed by MNEs in this industry in the manufacturing stages may be centralized closer to R&D plants.

As the digitalization of the industry progresses, this will have an impact on tax and transfer pricing matters. For example, questions on how to distinguish between “traditional” and AI-generated value creation in the R&D process will emerge along with the need for analysis which related party value should be attributed to. As regards data, questions of which related entity owns data generated, for example, based on stock levels or through patient’s use of healthcare apps will have to be analyzed closely for transfer pricing purposes.

3.2. Business models in the pharmaceutical industry

As noted in 1.3.2.1 of the UN TP Manual, in order to be able to perform a transfer pricing analysis, it is crucial to understand how the management of an MNE is organized and what framework exists for decision-making. In the following, integrated business models, decentralized business models and strategic alliances will be discussed in relation to the pharmaceutical industry.

⁷² For a discussion of these barriers and possible solutions see Hock, Siang and Wah (2021). Continuous manufacturing versus batch manufacturing: benefits, opportunities and challenges for manufacturers and regulators. *Generics and Biosimilars Initiative Journal*. Figure 2. Available from 10.5639/gabij.2021.1001.004. See also Brookings Institution (2015). *Promoting Continuous Manufacturing in the Pharmaceutical Sector*. Available from <https://www.brookings.edu/wp-content/uploads/2015/10/Continuous-manufacturing-discussion-guide.pdf>.

All companies, domestic and multinational, have an enterprise operating model⁷³ or business model⁷⁴ that defines the company's customer value proposition and is designed to create a long-run competitive advantage in an industry. These operating/business models essentially organize the firm's functions performed, assets used, and risks assumed along its value chain of getting products or services to market.

Firms choose their degree of vertical integration (how many stages of the value chain to keep in-house) and horizontal integration (how many plants or entities to have at any one stage in the value chain) based on factors such as transaction and governance costs, economies of scale and scope, government regulations, and the importance of local consumer tastes and incomes. For example, a firm's decision as to whether to centralize a function in one entity/location within the MNE group or to have multiple entities/locations performing the same activity depends on the tradeoff between the benefits from global integration (i.e., economies of scale and scope) relative to the need to be locally responsive or comply with domestic regulations to differences in customers and consumers across countries.⁷⁵

The range of possible operating/business models runs from a fully-integrated single business to a loosely-held holding company or conglomerate. In between are models consisting of closely- or loosely-related portfolio of businesses.⁷⁶ In large matrix organizations, such as many of the world's leading pharmaceutical multinationals, the MNE typically consists of multiple related businesses where the MNE's global operating model is based on a three-way matrix structure of products, geographies and functions.

Integrated business model

Starting in the late 1990s, the largest and most global MNEs in industries such as fast-moving consumer goods and pharmaceuticals – MNEs with global brands – began to adopt what is referred to as a “centralized business model” or “principal structure”.⁷⁷ To manage the complex matrix of products, geographies and functions associated with their global value chains and the associated risks, these global MNEs adopted a tiered and nested organizational design. In addition to the parent firm, there are one or more principals that function as entrepreneurial entities for each of the regions within the MNE network. The principals have oversight responsibility for MNE entities within that region (e.g., Asia, Latin America).

⁷³ Kates, A., Kesler, G., and DiMartino, M. (2021). *Networked, Scaled and Agile: A Design Strategy for Complex Organizations*. Kogan Page. Kesler, G., and Kates, A. (2007). *Bridging Organizational Design and Performance: Five Ways to Activate a Global Operating Model*. John Wiley & Sons.

⁷⁴ van Herksen, M. (2009). *Business Models*. In Bakker, A. (editor). *Transfer Pricing and Business Restructurings: Streamlining all the Way*. International Bureau of Fiscal Documentation. Chapter 2.

⁷⁵ Eden, L. (1998). *Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America*. University of Toronto Press. Chapter 3. *The Multinational Enterprise as an Integrated Business*.

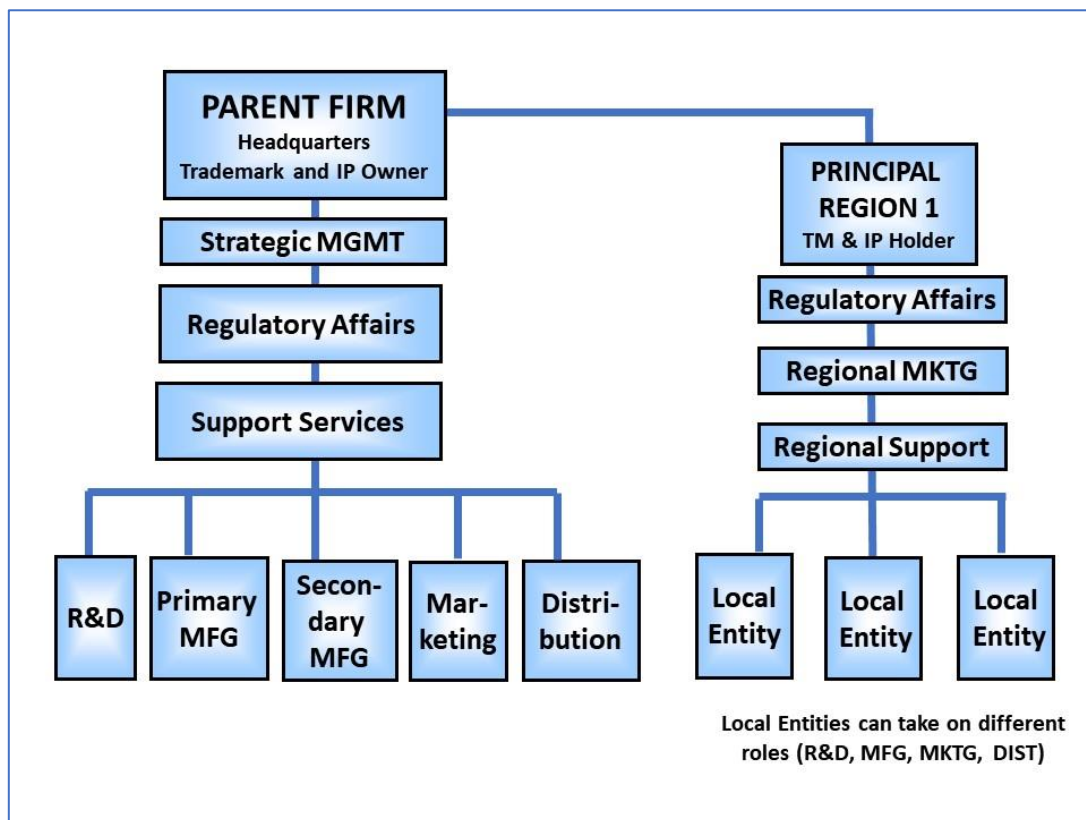
⁷⁶ Kates, A., Kesler, G., and DiMartino, M. (2021). *Networked, Scaled and Agile: A Design Strategy for Complex Organizations*. Kogan Page.

⁷⁷ van Herksen, M. (2009). *Business Models*. In Bakker, A. (editor). *Transfer Pricing and Business Restructurings: Streamlining all the Way*. International Bureau of Fiscal Documentation. Chapter 2.

In addition, the global MNE may set up centralized “hub structures” at the regional and /or global level, with responsibility for certain business functions such as information technology, human resource management, and international finance. Some functions, such as marketing, may involve multiple tiers: a centralized entity responsible for the marketing of the global brand(s), regional entities responsible for marketing of regional products, and local marketing teams within each country that are responsible for local products and fine tuning for local tastes and incomes.⁷⁸ For more information on centralized services within the MNE group see section 5.2.4. of the UN TP Manual.

Figure 6 provides an illustration of a typical operating model of a global MNE. The parent firm is the headquarters for the MNE group and the ultimate trademark and IP owner. Within the parent entity are departments and/or domestic affiliates responsible for strategic management, regulatory affairs, and support services, in addition to entities responsible for the primary activities in the MNE’s value chain (R&D, primary and secondary manufacturing, marketing, and distribution). The parent firm typically has one or more regional principals that are the IP and trademark holder in their region. Each principal has its own regulatory affairs, marketing, and support services functions, and owns and/or has responsibility for local entities within the region. The local entities may be distributors responsible for their own local markets but may also take on other roles such as clinical testing, secondary manufacturing, and local marketing.

Figure 6: The matrixed operating model of the typical pharmaceutical MNE



⁷⁸ Kates, A., Kesler, G., and DiMartino, M. (2021). Networked, Scaled and Agile: A Design Strategy for Complex Organizations. Kogan Page.

Decentralized business model

Some pharmaceutical MNEs are adopting an alternative business model consisting of a centralized portfolio management team (the parent firm) and a group of decentralized subsidiaries.⁷⁹ Each subsidiary specializes in a particular therapeutic area, product line and/or technologies while the parent firm provides centralized leadership to the group. This business model, referred to as a “decentralized” or “hub-and-spoke” model, is typically the result of acquisitions of existing biotech and/or pharmaceutical businesses, which remain mostly standalone in terms of their activities after acquisition.

Being commonly controlled by a parent firm, however, offers potential benefits such as greater focus, operational efficiency, fundraising, and risk mitigation when compared with a set of uncontrolled businesses. Management and financing activities are typically centralized permitting more flexible fundraising and pooling of risks.

Strategic alliances

Strategic alliances among firms are common in most industries, including the pharmaceutical industry. In a strategic alliance, two or more firms cooperate at one or more stages along the value chain. The alliance may or may not involve equity ownership. Some examples in the pharmaceutical industry are the following:⁸⁰

- Joint venture: A common business model is for a pharmaceutical company to be the “discovery” firm and for it to align in an international joint venture with another company. The second firm commercializes and does the selling of the final product. A typical joint venture could involve a biotechnology firm that does not have access to a distribution network and so chooses to ally with a pharmaceutical firm.
- Co-marketing arrangement: One firm provides a non-exclusive license to the co-marketer allowing both the licensor and licensee firms to market the same product under different brand names.
- Co-promotion arrangement: Both firms promote the product under the same brand name.
- Contract R&D arrangement.

3.3. Typical location of GVC stages in the pharmaceutical industry

⁷⁹ Nover, A., Anderson, L., and Jacquet, P. (May 2022). The Hub-and-Spoke Model: An Emerging Biopharma Trend. LEK Consulting. Available from https://www.lek.com/sites/default/files/PDFs/2420_hub-spoke.pdf. See also Global Business Reports: US Pharmaceuticals & Biopharmaceuticals (2021). Hub and Spoke: A new model to cure disease. Available from <https://projects.gbreports.com/usa-pharma-biopharma-2021/hub-and-spoke>

⁸⁰ Collins, M., and Wundisch, K. (2004). Transfer pricing in the Ethical Pharmaceutical Industry. International Bureau of Fiscal Documentation (IBFD). Appendix Q: Strategic Alliances.

The typical location of GVC stages for a pharmaceutical MNE can be described as follows.

- An MNE's **core R&D activities** are typically centralized in (one of) the (regional) headquarter country/ies, with the exception of the clinical testing stage where national government regulations require (or subsidize) local testing for health and safety reasons and to encourage geographic decentralization. In general, these tests would be limited to late stage clinical trials (stages 3 and 4) or local mandatory studies. Contract R&D functions, i.e. research and development activities under the guidance and for the benefit of the parent company, is often carried out in countries that have science or R&D parks and that encourage the location of local R&D activities.
- Primary **manufacturing** of the API is often centralized in one or a limited numbers of countries taking into account cost efficiencies, government health-and-safety regulations, and distance to local markets. Secondary manufacturing of medicines from an (imported) API (i.e., the fill and finish / preparation and packaging stage) is also often decentralized for cost efficiency and government regulation reasons. In fact, downstream stages such as marketing is typically performed inside final markets.⁸¹
- The extent to which **marketing** activities for local (and possible regional) sales are carried out by a MNE's subsidiary depends on government regulations that determine whether and how advertising is restricted, and the role of generics versus brand-name pharmaceuticals. Factors such as the size and income level of the economy and the health profile and preferences of the population also influence the amount of spending that MNEs allocate to marketing in a specific jurisdiction. Downstream stages such as distribution, marketing and sales are typically performed inside final markets.⁸²
- Perhaps the most typical activity carried out by foreign affiliates of pharmaceutical MNEs are local **distributors**. The typical functions of a related party distributor in the pharmaceutical industry, together with possible questions to be asked by a tax administrator as part of a functional analysis, are outlined in Appendix 4.
- **Regulatory activities:** Negotiation with governments and/or health care providers on the products to be distributed (both to ensure marketing authorization and, if relevant, coverage by health insurance(s)) are typically

⁸¹ Eden, L. (1998). *Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America*. University of Toronto Press. p. 156.

⁸² Eden, L. (1998). *Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America*. University of Toronto Press. p. 156.

performed locally, though this ultimately depends on the size and income of the market and the degree of regulation of the pharmaceutical market. The product medical attributes are generally managed globally by the MNE, as products are validated by health agencies based on their efficacy.

4. Transfer pricing analysis

In this chapter we outline how the industry background provided can aid in conducting a transfer pricing analysis within the pharmaceutical industry.

4.1. Overview

It is necessary to carry out a detailed transfer pricing analysis starting with a comparability analysis. According to section 3.1 of the UN TP Manual, a comparability analysis includes two “distinct but related analytical processes”:

- Developing an understanding of the accurately delineated transaction, which includes:
 - Identifying the economically significant characteristics and circumstances of the controlled transaction, i.e. the transaction between associated enterprises; and
 - Identifying the respective roles and responsibilities of the parties to the controlled transaction, as part of a functional analysis.
- Comparing the prices and other conditions of the controlled transaction (established in the first step) with those prices and other conditions in uncontrolled transactions taking place under comparable circumstances; the latter transactions are referred to as “comparable uncontrolled transactions” or “comparables”.

The concept of comparability analysis is used in the selection of the most appropriate transfer pricing method and in applying that method to arrive at an arm’s length price or financial indicator (i.e., the arm’s length result).

4.2. Accurate delineation of the transaction

The first step in undertaking a transfer pricing analysis always involves the accurate delineation of the transaction.

The arm’s length price for a transaction between two or more associated enterprises must be based on the actual transaction between the parties. The examination of the controlled transaction involves analyzing the written contract, as a starting point, vis-à-

vis the conduct of the parties. If the conduct of the parties is inconsistent with the written contract, the conduct of the parties should be treated as the best evidence of the actual controlled transaction. In the case of multiple transactions, the transfer pricing professional must also decide whether the transactions should be evaluated separately or if they can be reasonably aggregated.

Accurately delineating transaction can be very complex in the pharmaceutical industry, as key activities in relation to specific risks may be fragmented between or amongst different entities with a multinational group and government regulations as outlined in section 2.7. are prevalent in the pharmaceutical industry. It will also be necessary to take into account the business models in the industry, as described in section 3.2, which are very complex and highly integrated. Similarly, contractual arrangements may be difficult to analyze due to their technical nature and language.⁸³

Industry and market context

The transfer price of a particular pharmaceutical product in a particular market depends on market conditions such as the level of competition (from other firms and substitute products) and the need for complementary products, income levels of buyers, and so on. Here we focus on aspects that are specific to the pharmaceutical industry, including (1) price controls and cost containment measures, (2) parallel imports, (3) business strategies in relation to patents and (3) the COVID-19 pandemic.

i. Price controls and cost containment measures

Some countries establish drug price controls, that is, they establish government rules that affect the market for certain pharmaceutical formulations through price regulation (e.g. imposing cap prices in certain medicines and controlling the volume to be sold). This is generally done to manage healthcare costs.⁸⁴

In several countries, a pharmaceutical insurance scheme may exist for certain prescribed pharmaceutical drugs in which a government subsidizes the cost drugs. These schemes are designed to meet health and economic outcomes. In some countries, patients may be restricted to generic prescription drugs. For example, in Australia for prescribed drugs registered under the Pharmaceutical Benefits Scheme, the customer is given the choice of choosing a cheaper generic drugs if an off-patent drug has been prescribed.

There are a variety of methods used for pricing regulation that affect margins and profits on pharmaceutical products. See Appendix 3 for a list and explanation of the most common pricing methods.

⁸³ Siddiqui, Y.J. (2019). Transfer Pricing and Value Creation in the Pharmaceutical Sector. In Petruzzi/Tavares (Eds). Transfer Pricing and Value Creation.

⁸⁴ On price controls, see the UN TP Manual, sections 2.4.2.4, 3.4.5.3, 3.4.5.15 and 16.

ii. Parallel imports of pharmaceutical products

Parallel trade⁸⁵ encourages the free movement of identical products between countries in order to encourage competition and reduce prices. Parallel imports refer to branded goods that are imported into a market and sold there without the trademark owner's consent in that market.⁸⁶ Parallel imports are manufactured under the brand's official license – destined or packaged for a particular jurisdiction. Parallel importing occurs when there is a material price difference for the same goods between jurisdictions. The goods are then imported into a different jurisdiction without the brand owner's consent.

An important concept in parallel imports is the concept of exhaustion of intellectual property rights (IPR exhaustion), which refers to the extent to which an intellectual property rights holder can control the distribution of its branded goods.⁸⁷ According to the concept of IPR exhaustion, once an IP rights holder sells a product to which its IP rights are attached, the IP rights are exhausted. This means that parallel imports are not counterfeit products as they are manufactured under the official license of the original owner.⁸⁸

Parallel importing may force an MNE's distribution subsidiary to compete with third parties selling identical pharmaceutical products at a lower price. In some countries, this may even be fostered through regulatory provisions that aim at containing health care costs. Since parallel imports are obtained from a foreign jurisdiction at a price that is lower than the corresponding prices in the destination jurisdiction, parallel importing usually results in decreasing revenues / margins for MNE's distribution subsidiaries.

Parallel imports raise important transfer pricing questions in respect of the remuneration of a MNE's distribution subsidiary.

Firstly, in case of a material impact from parallel imports on the subsidiary's remuneration, questions arise in how far this impact needs to be offset, for example through end-year adjustments, by the subsidiary's transaction partner. This will depend on the risk profile of the subsidiary, regulations in place and the transfer pricing methodology applied.

Secondly, the question arises if and to what extent the transactions of the third-party parallel importer can function as a comparable for a MNE's distribution subsidiary. An associated pharmaceutical distributor in a country where parallel imports are made available has no control over the amounts imported through the third-party parallel importer and the pricing thereof. The use of parallel imports as comparables for transfer pricing purposes will thus depend on the underlying facts in terms of comparability of functions carried out, assets used, and risks borne by the subsidiary vis-à-vis the parallel importer. Collins and Wundisch, for example, argue that "The fact that the prices of parallel imports are lower than those of a multinational group's own direct imports of

⁸⁵ Danzon, P.M. (1997). Trade and Price Differentials for Pharmaceuticals: Policy Options. UK Office of Health Economics, London.

⁸⁶ International Trademark Organization. Parallel Imports. See <https://www.inta.org/topics/parallel-imports/>

⁸⁷ International Trademark Organization. Parallel Imports. See <https://www.inta.org/topics/parallel-imports/>

⁸⁸ Kamuzora, F., and Issaias, A. (2018). Parallel Imports Remain A Grey Area For Ip Rights In East Africa. Bowmans. Available from <https://www.bowmanslaw.com/insights/intellectual-property/parallel-imports-remain-a-grey-area-for-ip-rights-in-east-africa/>

the same products into the country does not provide any particularly useful evidence about the arm's length quality of the group's transfer prices into that country. Such parallel imports are in any case a simple trade transaction of an arbitrageur at a different stage in the trading chain. The transfer prices into the country from which the parallel imports are derived, which may perhaps be thought to provide a basis for comparison at the same stage, will not be useful either since they will be geared (if they are arm's length prices themselves) to the market conditions prevailing in that country, and these will normally not be the same as those in the country of origin towards which the parallel trader is gearing his pricing."⁸⁹

Lastly, the question arises if and to what extent the marketing efforts of the distribution subsidiary also generate benefit for the parallel imports and should thus be considered when determining the distribution sub's remuneration. As the parallel imports were produced by the same MNE group, the parallel importer's sales are ultimately to the benefit of the group, though both the MNE group as well as the subsidiary cannot influence the occurrence of parallel imports and argue that its remuneration should only take into account the functions it carried out and the benefit it intended to create.

iii. Business strategies in relation to patents

In recent decades, two concepts around patents have gained some traction: "patent cliff" and "patent lifecycle management." The term "patent cliff" refers to the potential sharp drop in expected profits after the patent for a firm's product expires. Once the product is "off patent" and no longer protected from competition by the patent, the product faces more competition from existing branded products and from rival firms producing and selling generic products. The additional competition reduces the product's sales, market share, and profitability.⁹⁰ Patent cliffs therefore generally result in lower revenues for originator companies once the patent has expired. The size of the patent cliff varies across countries, depending on patent expiry dates, the degree of market penetration by generics, and customer loyalty to originator products.⁹¹

In developed economies, it is estimated that patent expiry typically leads to, on average, an 80 per cent market share loss for the formerly patented drug and a 20–30 per cent reduction of the drug's price, with a further price decrease with each additional generic entrant. In some cases, the price of the formerly patented drug decreases by up to 90 per cent once off-patent.⁹² This may be less the case in developing countries where off-patent branded drugs continue to dominate local markets.⁹³

⁸⁹ Collins, M., and Wundisch, K. (2004). Transfer Pricing in the Ethical Pharmaceutical Industry. International Bureau of Fiscal Documentation (IBFD). Section 2.1.1, par. 95.

⁹⁰ For evidence of the effects of the patent cliff in Kenya see Khalil, F. and Onyango, J.O. (2019). Effect of Patent Expiry on the Performance of Innovator and Multinational Pharmaceutical Companies in a Low Middle Income Country. *Frontiers in Medical Technology*. Available from 10.3389/fmedt.2022.783460.

⁹¹ Price differentials can range widely across countries, even within the European Union as documented in European Parliament (2011). Differences in Costs of and Access to Pharmaceutical Products in the EU. Directorate General for Internal Policies. Policy Department A: Economic and Scientific Policy.

⁹² Gurgula O. (2020). Strategic Patenting by Pharmaceutical Companies - Should Competition Law Intervene? *International Review of Intellectual Property and Competition Law*. 51(9).

⁹³ Khalil, K., and Onyango, J.O., (2022) Effect of Patent Expiry on the Performance of Innovator Multinational Pharmaceutical Companies in a Low Middle Income Country. *Frontiers in Medical Technology*. 4:783460. Available from doi: 10.3389/fmedt.2022.783460.

The currently anticipated patent cliff encompasses drugs with annual revenues of more than 200 billion USD that are going off-patent through 2030.⁹⁴ In many developing countries patent cliffs are estimated to be much less pronounced.

Patent lifecycle management refers to the practice of extending patent protection by filing secondary product patents on a new formulation (changes in tablet forms, dosage amount, etc.) and methods of use, or new process patent on manufacturing techniques related to mass production of the drug or other processes.⁹⁵ Viewed from a barrier to entry perspective, attempts to extend patent life can be viewed as “ever-greening”, that is, “exploiting loopholes” in patent laws and regulatory processes by “filing disguised or artful patents” on previously patented inventions just before the original pharmaceutical product goes off patent.⁹⁶ Examples include obtaining additional patents for different attributes of drug development (e.g., delivery profiles, methods of manufacture, formulations, and packaging) before the original patent expires, switching to over-the-counter status, setting up an in-house generic unit, and releasing a successor drug with a different brand name and minor changes (“brand migration”).

iv. COVID-19 global pandemic

As in other industries, pharmaceutical companies have been faced with disruptions in their business models caused by the global pandemic including through value chain disruptions, delayed regulatory responses/approvals, and slowdowns for some patient procedures (e.g., non-emergency surgeries and infusion therapies). On the other hand, parts of the pharmaceutical industry were a clear “winner” of the pandemic. Reference is made to the proposed guidance on transfer pricing during the COVID-19 economic downturn.⁹⁷

4.3. Choosing a transfer pricing method (exemplary)

As noted in section 3.1.8 of the UN TP Manual, the most appropriate transfer pricing method can be selected based on delineating the transaction while being aware of the industry and market context of the transaction. This should be done bearing in mind the available data.

Using a transfer pricing method is the mechanism by which the prices or results of the controlled transaction are compared to the prices or results of comparable uncontrolled

⁹⁴ Garnder, J. (2023). Big pharma’s looming threat: a patent cliff of ‘tectonic magnitude’. Biopharma Dive. Available from [Big pharma’s looming threat: a patent cliff of ‘tectonic magnitude’ | BioPharma Dive](#)

⁹⁵ Lee, Y., and Fong, E.A. (2020) Patent lifecycle management strategies in open innovation projects. Drug Discovery Today. 25.10. Available from <https://doi.org/10.1016/j.drudis.2020.06.019>.

⁹⁶ This practice is also referred to as “evergreening” and innovation or patent harvesting. See Kumar, A. and Nanda, A. (2017) Ever-greening in pharmaceuticals: Strategies, consequences and provisions for prevention in USA, EU, India and other countries. Pharmaceutical Regulatory Affairs, 6:1. Available from DOI: 10.4172/2167-7689.1000185

⁹⁷ See ANNEX A to E/C.18/2023/CRP.26

transactions. In this way, the application of transfer pricing methods helps assure that transactions conform to the arm's length principle.

In the following, the method selection for transactions involving tangible goods will be discussed. Within a pharmaceutical MNE, transfer pricing for tangible products may take different forms. This might involve the sale of active ingredients from a primary manufacturing member of a multinational group to another group member for secondary formulation into finished products. This may also involve the sale of the secondary formulation to another group member for packaging and labelling and / or the sale of pharmaceutical products to third parties, such as wholesalers.

One method that could be used for these types of transactions are, in principle, the Comparable Uncontrolled Price (CUP) Method, which compares the price charged in a controlled transaction to the price charged for property or services transferred in a comparable uncontrolled transaction in comparable circumstances. CUPs may be based on either "internal" comparable transactions or on "external" comparable transactions (see section 4.2. of the UN TP Manual).

For transactions involving goods, product comparability should be closely examined (see section 4.2.2.3 of the UN TP Manual). For tangible products, it will be the physical features, quality, reliability, availability and volume of supply that will be important to consider. A key product comparability distinction is the prescription and OTC category of drugs considered in section 1.2. In certain situations, for off-patent drugs there may be a strong product similarity between the drugs and generics, if the trade names for the off-patent drugs are not valuable.

Pharmaceutical products may also appear to be similar but "similarity can be deceptive."⁹⁸ It is important to recognize that medicines are unique compounds and even when they have similar chemical compositions (i.e., they have bioequivalence) they may have very different uses or effects (i.e., different bio-availabilities). To determine product comparability, the transfer pricing professional must take into account both bioequivalence and bio-availability characteristics (i.e., "similar" medicines with "similar" effects) and to make adjustments for their differences.

Examples of product characteristics that should be considered in assessing comparability of controlled transactions of pharmaceutical products with uncontrolled transactions include the following (non-exhaustive) list of characteristics:

- size and dosage of the solid (e.g. tablet, capsule), semi-solid (cream, gel), or liquid (e.g. injectable, syrup)
- transport system for the active substance (i.e. biologic virus, adenovirus)
- size of molecules and proteins
- solution or salt and type of salt
- size of crystal particle form and isomer

⁹⁸ This section (including the product characteristics list) is drawn from Collins, M., and Wundisch, K. (2004). *Transfer Pricing in the Ethical Pharmaceutical Industry*. International Bureau of Fiscal Documentation (IBFD). Part 6. Section 2.2.1. General. paragraph 337.

- type, number, and degree of impurities
- type, number, and characteristics of diluents
- inert excipients
- viscosity, solubility, and osmolality
- color-coating and flavour agents
- storage characteristics
- remaining shelf-life
- side-effect profile

As a result, the product comparability requirements needed to reliably apply the CUP method are often not fulfilled, even before contractual terms and economic conditions are analyzed. In practice, this means that the CUP method for physical goods transactions in the pharmaceutical industry is limited to situations in which an independent enterprise buys physical products that are identical or very similar to those bought by an associated company granted that contractual terms and economic conditions are similar and / or adjustment can be performed.

Depending on the nature of the functions carried out, the risks borne, and the assets used by the associated enterprise involved in the transfer of goods, the Resale Price Method may be a suitable transfer pricing method.

The Resale Price Method (RPM) is one of the traditional transaction methods and analyzes the price of a product that a related sales company charges to an unrelated customer (i.e. the resale price) to determine an arm's length gross margin, which the sales company retains to cover its sales, general and administrative (SG&A) expenses, and still make an appropriate profit. The appropriate profit level is based on the functions it performs, the assets it uses and the risks it assumes. The remainder of the product's price is regarded as the arm's length price for the intragroup transactions between the sales company and a related company. As the method is based on arm's length gross profits rather than directly determining arm's length prices (as with the CUP Method) the RPM requires less direct transactional (product) comparability than the CUP Method (see section 4.3 of the UN TP Manual).

Alternatively, if the function carried out can be described as constituting simple manufacturing or assembling functions (see section 4.4 of the UN TP Manual), the Cost Plus Method (CPM) may be used. The CPM begins with the costs incurred and seeks to apply an appropriate cost plus mark-up to the cost, to calculate an appropriate gross profit in light of the functions performed, risks assumed, assets used or contributed and market conditions. The method evaluates the arm's length nature of an intragroup charge by reference to the gross profit mark-up on costs earned by independent suppliers of tangible property or services in comparable uncontrolled transactions. That is, it compares the gross profit mark-up earned by the tested party for manufacturing the product or for providing the service to the gross profit mark-ups earned by comparable companies engaged in comparable transactions.

4.4. Performing a functional analysis

As noted above, taxpayers need to undertake a thorough functional analysis as a cornerstone of their transfer pricing analysis. Its purpose is to gain an understanding of the operations of an enterprise in connection with its transactions with associated enterprises. The functional analysis examines the respective roles of the parties to the controlled transaction under examination. The roles undertaken by each of the associated enterprises will affect the determination of an arm's length remuneration for the controlled transaction since compensation in transactions between two independent enterprises will usually reflect the functions that each enterprise performs, taking into account assets employed and risks assumed.

To perform a transfer pricing analysis, tax authorities and practitioners perform an analysis of the functions, assets and risks of commonly controlled entities as outlined in section 3.4.4. of the UN TP Manual. Table 3 below list the possible functions performed, assets utilized and risks assumed by a local entity in a particular tax jurisdiction, depending on its location within the MNE global value chain and the roles and responsibilities assumed by the entity within the multinational group.

Table 3: FAR Analysis (Functions, Assets and Risks) of the Controlled Taxpayer

Functions	Assets	Risks
Corporate strategy formulation	Intangible assets	Collection risk
Distribution and sales activities	• Brand names	Country/regional risk
Finance, accounting, treasury and legal	• Logos	Entrepreneurial risk
General management functions	• Patents and licensing rights	Financial risk
Human resource management	• Product registration, market authorization and regulatory approvals	General business risk
Intragroup services (e.g., legal, accounting, information technology)	• Technical knowhow	Market risk
Inventory management	• Trademarks and tradenames	Product risk
Manufacturing, production, assembly, and process engineering	• Trade secrets	Reputation risk
Market development	Tangible assets	
Market intelligence on technological developments	• Land, buildings and warehouses	
Marketing, advertising and promotion (AMP) activities	• Natural resources	

Post-sale activities including supply of replacements	• Office equipment	
Product design and engineering	• Vehicles	
Product development	Other (soft) assets	
Purchasing, materials management and other procurement activities	• Customer lists	
Quality control	• Goodwill	
Research and development activities	• Workforce in place	
Technical assistance	• Distribution network	
Testing and quality controls		
Transportation, warehousing and inventory		

In terms of assets, the core value drivers in the pharmaceutical industry are, as described in section 3.1., are (1) patents, (2) marketing intangibles and (3) know-how.

In terms of risks, an entrepreneurial entity in an MNE group would be expected to take on both upside and downside strategic risks related to its core activities within the group; a limited risk entity would typically take on few risks. These may include: ⁹⁹

- R&D success and portfolio regeneration;
- manufacturing quality standards;
- continuity of supply: supply shortages and other disruptions risks;
- integration and success of acquisitions and alliances;
- managerial and operational efficiency;
- market competition: patent protection and generic/biosimilar entries;
- pricing and reimbursement policies/cost containment measures;
- credit and foreign exchange risk;
- reputational risks;
- regulatory risks;
- product liability risks.

5. Transfer pricing examples in the pharmaceutical industry

⁹⁹ Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. *International Transfer Pricing Journal*. On pharmaceutical risks along the supply chain see also Jaberidoost, M., Nikfar, S., Abdollahiasl, A., and Dinarvand, R. (2013). Pharmaceutical supply chain risks: a systematic review. *DARU Journal of Pharmaceutical Sciences*. Available from <http://www.daruips.com/content/21/1/6>

6. Appendix 1: List of Abbreviations

AI	Artificial intelligence
AMP	Advertising, marketing and promotion activities
API	Active pharmaceutical ingredient
ATC	Anatomical therapeutic chemical classification
BM	Batch manufacturing
CM	Continuous manufacturing
COGS	Cost of goods sold
CUP	Comparable uncontrolled price
DIST	Distribution activities
EBIT	Earnings before interest and taxes
EBP	Emerging biopharma companies
ERP	External reference pricing
EU	European Union
FAR	Functions, assets, and risks analysis
GCP	Good clinical research practice
GDP	Good distribution practice
GMP	Good manufacturing practice
GVC	Global value chain
HTA	Health technology assessment
ICO	[International commercial operations agreement]
IPR	Intellectual property rights
IRP	Internal reference pricing
MEA	Managed entity arrangements
MFG	Manufacturing activities
MKTG	Marketing activities
MNE	Multinational enterprise
NMRA	National medicines regulatory authority
OPM	Operating profit margin
OTC	Over the counter (non-prescription) medication
PBM	Pharmacy benefit management company
PLI	Profit level indicator
R&D	Research and development
RPM	Resale price method
TNMM	Transactional net margin method
UN	United Nations
UN TP Manual	United Nations Practical Manual on Transfer Pricing for Developing Countries (2021)
VAT	Value added tax
WHO	World Health Organization

7. Appendix 2: Glossary of Pharmaceutical Terms

Active pharmaceutical ingredient	Any substance or mixture of substances that is part of a drug (medicinal) product, intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure and function of the body. ¹⁰⁰
Adjuvants	An ingredient in a medicine that increases or modifies the activity of the other ingredients. Adjuvants are often included in vaccines to enhance the body's immune response. ¹⁰¹
Bio-availability	Bioavailability is a subcategory of absorption and is the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when a medication is administered intravenously, its bioavailability is 100 percent. However, when a medication is administered via other routes (such as orally), its bioavailability generally decreases due to incomplete absorption and first-pass metabolism. Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration. ¹⁰²
Bioequivalence	Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and their bio-availabilities, in terms of rate (Cmax and tmax) and extent of absorption (area under the curve), after administration of the same molar dose under the same conditions, are similar to such a degree that their effects can be expected to be essentially the same. ¹⁰³
Biologics	A category of products regulated by [relevant regulatory bodies] including vaccines, blood and blood components, allergenic compounds, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. ¹⁰⁴

¹⁰⁰ Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013). Board on Global Health. Institute of Medicine. Buckley GJ, Gostin LO (editors). Countering the Problem of Falsified and Substandard Drugs. Washington (DC). National Academies Press (US). Appendix A: Glossary. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK202530/> doi: 10.17226/18272

¹⁰¹ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹⁰² Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013). Board on Global Health. Institute of Medicine. Buckley GJ, Gostin LO (editors). Countering the Problem of Falsified and Substandard Drugs. Washington (DC). National Academies Press (US). Appendix A: Glossary. Available from <https://www.ncbi.nlm.nih.gov/books/NBK202530/> doi: 10.17226/18272

¹⁰³ World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

¹⁰⁴ Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.) (2017). National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient

Biosimilar	A drug that is similar to a biological reference product, and which is manufactured by a company other than the originator. Regulatory approval of biosimilars is technically possible following patent expiry of the reference product. ¹⁰⁵
Bulk product	Any pharmaceutical product that has completed all processing stages up to, but not including, final packaging. ¹⁰⁶
Clinical trial	Formal study carried out according to a prospectively defined protocol that is intended to discover or verify the safety and the effectiveness of procedures or interventions in humans. ¹⁰⁷
Excipient	A pharmacologically inactive substance used along with the active pharmaceutical ingredients in the formulation of a medication. ¹⁰⁸
Generic pharmaceutical drug	A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorized. Its authorization is based on efficacy and safety data from studies on the authorized medicine. A company can only market a generic medicine once the exclusivity period for the original medicine has expired. ¹⁰⁹
Good clinical research practice	A standard for clinical studies which encompasses the design, conduct, monitoring, termination, audit, analysis, reporting and documentation of the studies and which ensures that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical product (diagnostic, therapeutic or prophylactic) under investigation are properly documented. ¹¹⁰
Good manufacturing practice	That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards

Access to Affordable Drug Therapies. Making Medicines Affordable: A National Imperative. National Academies Press (US). Appendix C: Glossary.

¹⁰⁵ Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.

¹⁰⁶ World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

¹⁰⁷ Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.) (2017). National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient Access to Affordable Drug Therapies. Making Medicines Affordable: A National Imperative. National Academies Press (US). Appendix C: Glossary.

¹⁰⁸ Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013). Board on Global Health. Institute of Medicine. Buckley GJ, Gostin LO (editors). Countering the Problem of Falsified and Substandard Drugs. Washington (DC). National Academies Press (US). Appendix A: Glossary. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK202530/> doi: 10.17226/18272

¹⁰⁸ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹⁰⁹ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹¹⁰ World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

	appropriate to their intended use and as required by the marketing authorization. ¹¹¹
Intermediates	An intermediate can be a material produced during steps of the processing of an active pharmaceutical ingredient that undergoes further molecular change or purification before it becomes an API. ¹¹²
Marketing authorization	Also referred to as product licence or registration certificate. A legal document issued by the competent medicines regulatory authority that authorizes the marketing or free distribution of a medical product in the respective country after evaluation of safety, efficacy and quality. ¹¹³
National medicines regulatory authority	The national authority responsible for the registration of and other regulatory activities concerning medical products, such as medicines, vaccines, blood products and medical devices. ¹¹⁴
Over-the-counter drug	Medicine that does not require a prescription to be sold to patients. Also known as non-prescription medicines. ¹¹⁵
Patent	A set of exclusive rights granted to an inventor or assignee for a limited period of time in exchange for the public disclosure of the invention. ¹¹⁶
Patented drug	An innovative medicine granted intellectual property protection by a patent office. The patent may encompass a wide range of claims, such as active ingredient, formulation, mode of action, etc., giving the patent holder the sole right to sell the drug while the patent is in effect. ¹¹⁷
Pharmacy benefit management	Develop and administer drug-benefit plans for employers and health insurers. ¹¹⁸
Phase 1 clinical trial	A type of clinical study where a new medicine is given to humans for the first time, usually in healthy volunteers. It looks

¹¹¹ World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

¹¹² World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

¹¹³ World Health Organization. WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Glossary. Available from <https://extranet.who.int/pqweb/content/glossary>

¹¹⁴ World Health Organization (2014). WHO Technical Report Series, No. 986. Annex 6. Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part.

¹¹⁵ Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.

¹¹⁶ Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013). Board on Global Health. Institute of Medicine. Buckley GJ, Gostin LO (editors). Countering the Problem of Falsified and Substandard Drugs. Washington (DC). National Academies Press (US). Appendix A: Glossary. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK202530/> doi: 10.17226/18272

¹¹⁷ Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.

¹¹⁸ Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.) (2017). National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient Access to Affordable Drug Therapies. Making Medicines Affordable: A National Imperative. National Academies Press (US). Appendix C: Glossary.

	at the way the medicine is dealt with by the body, its main effects and main side effects. ¹¹⁹
Phase 2 clinical trial	A type of clinical study conducted after phase I studies to evaluate a medicine's effects in a particular condition and to determine its common short-term side effects. ¹²⁰
Phase 3 clinical trial	A type of clinical study usually conducted in a large group of patients to gather information about a medicine's efficacy and safety, to allow its benefits and risks to be evaluated. ¹²¹
Phase 4 clinical trial	A type of clinical study that takes place after the authorization of a medicine. ¹²²
Prescription drugs	Patented and generic medicines regulated by legislation that requires a physician's prescription before they can be sold to a patient. ¹²³

¹¹⁹ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹²⁰ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹²¹ European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹²² European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A

¹²³ Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.

Reference pricing: Also known as benchmark pricing. Refers to the approach of understanding the appropriateness of prices of medicines based on selected benchmark prices, either from other jurisdictions (e.g. countries or other administrative regions) or a group of comparable medicines in the same system/formulary. Reference pricing can be stratified into external and internal reference pricing:

- External reference pricing (ERP; also known as international reference pricing) refers to the practice of using the price of a pharmaceutical product (generally ex-manufacturer price, or other common point within the distribution chain) in one or several countries to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country. Reference may be made to single-source or multisource supply products.
- Internal reference pricing (IRP; also known as domestic reference pricing). The practice of using the prices of identical medicines (ATC 5 level) or similar products (ATC 4 level) or even with therapeutic equivalent treatment (not necessarily a medicine) in a country in order to derive a benchmark or reference price for the purposes of setting or negotiating the price or reimbursement of the product in a given country.

Value-based pricing: Countries set prices for new medicines and/or decide on reimbursement based on the therapeutic value the medicines confer, usually assessed through health technology assessment (HTA).

Cost-plus pricing: Pricing policy that takes into account production costs, promotional expenses, research and development, administration costs, overheads, and a profit mark-up to determine a price.

Setting price and mark-up thresholds across the pharmaceutical supply and distribution chain: Setting price threshold means specifying maximum prices, also referred to as price caps or price ceilings, or specifying a maximum mark-up percentage. A mark-up represents the additional charges and costs that are applied to the price of a commodity in order to cover overhead costs, distribution charges, and profit. In the context of the pharmaceutical supply chain. Policies might involve regulation of wholesale and retail mark-ups as well as pharmaceutical remuneration.

Promoting price transparency: The sharing, disclosure and dissemination of information related to medicine prices to the public and relevant parties to ensure accountability. Full price transparency includes the publication of medicine prices at all price types (e.g. ex-factory prices, pharmacy retail prices), the disclosure of the net transaction prices of medicines between the suppliers (e.g. manufacturers,

¹²⁴ Shortened version of Table 1 in Tordrup, D. van den Ham, H.A., Glanville, J. and Mantel-Teeuwisse, A.K. (2020). Systematic reviews of ten pharmaceutical pricing policies – a research protocol. *Journal of Pharmaceutical Policy and Practice*, 13, 22. Available from <https://doi.org/10.1186/s40545-020-00228-0>

service providers) and the payers/purchasers (governments, patients), the sharing and publication of the contents of pricing arrangements, such as risk-sharing schemes and other managed-entry agreements, including the actual pricing and input factors that determine a medicines prices (e.g. production costs, R&D costs, added therapeutic value).

Price discounts for single source pharmaceuticals: Single source pharmaceuticals are pharmaceutical products supplied by a company that holds the patent rights, exclusive marketing rights, or supply agreements in a specific jurisdiction. A price discount is a price reduction granted to specified purchasers under specific conditions prior to purchase. Price discounts could include a rebate (payment made to the purchaser after the transaction has occurred) or a reduced price if the firm meets certain pre-agreed terms and conditions as specified in managed-entry agreements (MEAs) negotiated as market-entry conditions. MEA discounts can be classified as financial based (e.g. flat discounts, price-volume agreements, capping) or performance based (e.g. risk-sharing agreement, coverage with evidence development).

Promoting the use of quality assured generic and biosimilar medicines: Strategies directed at patients, prescribers or pharmacists to encourage the use of generic or similar biological medicines.

Competitive pricing based on tendering and negotiation: An approach that determines prices through tendering or negotiation among suppliers of medicines that are identical or comparable in chemical composition, pharmacological mechanisms and therapeutic use, taking into account factors such as quality, supply conditions. Tendering is any formal and competitive procurement procedure through which tenders (offers) are requested, received and evaluated for the procurement of goods, works or services, and as a consequence of which an award is made to the tenderer whose tender/ offer is the most advantageous. Negotiation refers to “discussion aimed at reaching an agreement”.

Pooled procurement: Pooled procurement refers to the arrangement where financial and non-financial resources are combined across various purchasing authorities to create a single entity for purchasing health products (e.g. medicines) on behalf of the individual purchasing authorities.

Tax exemptions or tax reductions for pharmaceuticals: There are two main categories of tax: direct taxes levied on the income of individuals and corporations, and indirect taxes that are added to the prices of goods and services. In developing countries, indirect taxes on international trade (e.g., customs duties) or on the purchase of goods and services (e.g., VAT), are major sources of government revenue. Policies relevant to pharmaceutical products might involve the reduction of taxes on medicines or the exemption of medicines from taxes, particularly sales taxes.

9. Appendix 4: Typical Functions of a Distributor in the Pharmaceutical Industry

The table below describes typical functions of a distribution entity in the pharmaceutical industry including indicative questions that tax authorities could ask during a transfer pricing audit.

Typical functions	Explanation and indicative questions that could be asked during audit activity by the tax authorities
Development of the global marketing strategy	<p>Refers to the development of a long-term plan that details the company's goals, the needs the company wants to address and its distinct competitive advantage.</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Which entity decides on the market strategy to follow or which market segments to target? • Which entity defines the company's competitive advantage and how it is pursued?
Development of the national marketing strategy	<p>Refers to the development of a medium to long-term plan that details the company's goals in a specific market (in which the company under audit operates), which needs the company wants to address and what its distinct competitive advantage is vis-à-vis national competitors.</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Which entity decides on the national market strategy to follow or which market segments to target? How far is this aligned with the MNE group's global strategy? • Which entity defines the company's competitive advantage and how it is pursued in the national market?
Development of the national distribution strategy	<p>The national distribution / sales strategy refers to the type of products that are distributed in a specific market and through what type of outlets (pharmacies, hospitals, in case of over-the-counter products also drugstores).</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Which entity decides on which products to distribute and in which packaging sizes? • How much is this strategy built and dependent on local market knowledge? • Who decides which distribution outlets are pursued?
Development of the product portfolio	<p>The product portfolio is an important part of a company's strategy and entails questions regarding the type of pharmaceutical product, packaging size, etc..</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Which entity decides on which products to distribute and in which packaging sizes?

Typical functions	Explanation and indicative questions that could be asked during audit activity by the tax authorities
Implementation of sales measures	<p>This activity refers to the actual conduct of the training events, sponsoring, and congress presence as well as to the production of the sales materials (product packaging, flyers, homepage, newsletter, etc.). In case these activities are not carried out by employees of the company under audit, this activity also covers the managing / contracting / supervising of any third parties.</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Who carries out the sales activities and / or supervises them? • Who produces sales materials used during sales activities?
Field sales force	<p>This refers to field staff that is in charge of distributing products, for example by regularly visiting hospitals or physician's offices in their distribution area.</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Who is the employer of field sales staff? Who do field sales staff report to? • Who trains the field sales staff and supervises them?
Securing market access / health insurance coverage for products	<p>This activity refers to interactions with public organizations regulating prescription medication as well as discussions with representatives from health insurances or associations of health insurances (depending on domestic health insurance regulations).</p> <p>Questions to be asked during audit:</p> <ul style="list-style-type: none"> • Who is the point of contact for public organizations regulating prescription medication?