United Nations

Transfer Pricing in the Pharmaceutical Industry

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Background and Acknowledgements

About the Committee

The United Nations Committee of Experts on International Cooperation in Tax Matters (the "Committee") comprises twenty-five members appointed by the Secretary-General, after notifying the Economic and Social Council, to serve in their personal capacity for a four-year term. Selected for their expertise in tax policy and administration, the members reflect diverse geographical regions and tax systems. The Committee is globally recognized for its normative and policy-shaping work and for the practical guidance it provides in tax policy and administration.

Committee Mission

The Committee develops tools and resources for governments, tax administrators, and taxpayers to help strengthen tax systems and mobilize financing for sustainable development, as well as strengthen international tax cooperation. The work aims to prevent double taxation and non-taxation while helping countries broaden their tax base, strengthen administration, and combat tax evasion and avoidance. The Committee places special emphasis on addressing the needs of least developed countries, small island developing States, and landlocked developing countries.

Committee Working Methods

The Committee meets twice annually—in spring (New York) and fall (Geneva). Between these sessions, Subcommittees work on specific topics under the Committee's oversight. These Subcommittees, whose participants also serve in their personal capacity, prepare proposals and draft guidance for review and approval by the Committee. This collaborative approach ensures thorough, multi-disciplinary and multi-stakeholder examination of complex tax issues, while maintaining the Committee's ultimate responsibility for all published guidance.

Transfer Pricing and the Sustainable Development Goals

At its Twenty-third Session in 2021, the Committee's 2021-2025 membership decided to establish a Subcommittee on Transfer Pricing, with a mandate to consider, report on and propose guidance on transfer pricing issues that:

— Reflects Article 9 of the United Nations Model Convention and the arm's length principle embodied in it, and is consistent with relevant commentaries of the Convention

- Identifies and considers transfer pricing topics where guidance from the Committees is most useful
- Reflects the realities and needs of developing countries at relevant stages of capacity development
- Gives due consideration to relevant work in other forums, such as the Inclusive Framework on Base Erosion and Profit Sharing (BEPS), including through broad consultation.

During its Twenty-fourth Session, the Committee approved the Subcommittee's ambitious workplan, consisting of guidance on the following topics:

- Transfer Pricing during the COVID-19 Economic Downturn
- Transfer Pricing Compliance Assurance—An End-to-End Toolkit
- Transfer Pricing of Carbon Offsets and Carbon Credits
- Transfer Pricing of Agricultural Products
- Transfer Pricing in the Pharmaceutical Industry
- Bilateral Advance Pricing Agreement/Arrangement Programmes—Frequently Asked Questions

This initiative served to develop guidance products to address priority challenges faced by developing countries in implementing effective transfer pricing regimes and make capacity development activities as practical, targeted and effective as possible. By strengthening their approach to transfer pricing, countries can reduce the risk of double taxation, thereby facilitating cross-border trade, fostering a more attractive investment climate, and increasing tax revenues. In turn, this can support greater domestic resource mobilization, enabling increased investment in achieving the Sustainable Development Goals (SDGs). The Subcommittee comprises a number of Committee members and other participants from tax administrations and policymakers with wide and varied experiences related to transfer pricing, as well as people from academia, international and regional organizations, and the private sector.

This Publication

This publication, "*Transfer Pricing in the Pharmaceutical Industry*", is part of a series of guidance products developed to strengthen transfer pricing capacities in developing countries. It provides practical advice to both tax authorities and multinational enterprises (MNEs) on applying the arm's length principle in the pharmaceutical industry, including an overview of the industry's global value chain, value drivers, and business models, as well as guidance on delineating transactions, conducting comparability analyses, and addressing key transfer pricing issues. This publication, reviewed, refined, and approved by the Committee during its Twenty-seventh and Twenty-eighth Session in October 2023 and March 2024 provides countries with guidance on transfer pricing practices, specifically tailored to the pharmaceutical industry.

Acknowledgements

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Disclaimer

Contents

Abbreviations

AMP	Advertising, Marketing and Promotion
API	Active Pharmaceutical Ingredient
COGS	Cost of Goods Sold
CUP Method	Comparable Uncontrolled Price Method
DAEMPE	Development, Acquisition, Enhancement, Maintenance, Protection and Exploitation
EBIT	Earnings Before Interest and Taxes
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
Incoterms	International Commercial Terms
MNE	Multinational Enterprise
NMRA	National Medicines Regulatory Authority
OPEX	Operating Expenses
OPM	Operating Profit Margin
PLI	Profit Level Indicator
RPM	Resale Price Method
R&D	Research and Development
TNMM	Transactional Net Margin Method
UN TP Manual	United Nations Practical Manual on Transfer Pricing for Developing Countries (2021)
WHO	World Health Organization

Executive Summary

This guidance was prepared in response to the need, often expressed by developing countries, for practical guidance on 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. These make it important to target the limited resources of tax administrations as efficiently and effectively as possible. Given the importance of the pharmaceutical industry to all countries, the goal of this guidance is to provide practical advice to both tax authorities and multinational enterprises (MNEs).

The guidance begins by describing the global value chain of the pharmaceutical industry, its value drivers and business models. It then discusses the application of transfer pricing analysis, addresses practical issues relating to the delineation of transactions and comparability analysis, and provides several examples.

Two appendices provide additional context. Appendix 1 presents a glossary of key terms. Appendix 2 lists potential questions that can be asked as part of a functional analysis during a tax audit in the pharmaceutical industry.

The analysis in this document may not reflect the particularities specific to all countries. It takes a systemic approach, describing the most pertinent general features of the pharmaceutical industry and related transfer pricing issues. The United Nations Practical Manual on Transfer Pricing for Developing Countries (UN TP Manual) applies to the pharmaceutical industry; the current guidance should be read in conjunction with the most recent version of the Manual. References in this document are to the 2021 edition.

1. Introduction

1.1. The Pharmaceutical Industry

The pharmaceutical industry, part of the life sciences sector,[1] is dedicated to the discovery, development, manufacturing, marketing, distribution and sale of pharmaceutical products used for medical purposes in the treatment or prevention of diseases. A pharmaceutical product (a drug or pharmaceutical material) is a chemical substance, based on an active pharmaceutical ingredient (API) designed to treat a disease or medical condition.[2]

Pharmaceuticals made with an API are normally separated into two broad categories corresponding to the API's characteristics as either chemical (small molecule) or biological (large molecule).[3] Historically, pharmaceutical companies delivered products based on chemical APIs, whereas biotechnology companies offered products derived from living organisms (referred to as biological APIs). Nowadays, most large pharmaceutical companies use both chemical and biological technologies.[4] In this guidance, the term "pharmaceutical industry" encompasses both pharmaceutical and biotechnology firms.

Companies in the pharmaceutical industry historically have been grouped separately from firms in the diagnostics and medical devices industries, although the latter are closely related to and have strategic alliances with pharmaceutical firms. Some of the largest pharmaceutical multinational enterprises (MNEs) also have their own diagnostic and/or device divisions. Products, value drivers and industry structures in the diagnostics and medical device industries are sufficiently different, however, and are not covered in this guidance.[5, 6]

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1 The life sciences sector encompasses a broad range of industries, including pharmaceuticals, biotechnology, medical devices, contract research organizations and contract manufacturing organizations that involve the scientific study of life. See more at the SciLife Life Science Glossary, available at: https://www.scilife.io/glossary/life-science.

2 For a recent overview of the pharmaceutical industry, see D. Taylor (2016). The Pharmaceutical Industry and the Future of Drug Development: Issues in Environmental Science and Technology. In R. Hester and R. Harrison, eds., Pharmaceuticals in the Environment, vol. 41. The Royal Society of Chemistry.

3 BCC Research Staff (2019). Markets at a Glance: Pharmaceuticals. Report code PHM213A.

4 T. Segal (2022). Biotech vs. Pharmaceuticals: What's the Difference? Investopedia.

5 On diagnostics, see C. Morel et al. (2016). Ensuring Innovation in Diagnostics for Bacterial Infection. World Health Organization. See also A. Proffit (2023). Pharma-Diagnostics Lockstep: How Two Industries Can Work Together for Precision Medicine. Bio-IT World.

6 On medical devices, see the United States Department of Health and Human Services (2017). Classification of Products as Drugs and Devices and Additional Product Classification Issues: Guidance for Industry and FDA Staff.

1.2. Segments in the Pharmaceutical Industry

The pharmaceutical industry can be categorized into different segments. One common classification depends on whether the manufacturer is the originator of a product (developed the API and the pharmaceutical product and obtained a patent) or provides a generic version (uses an existing API and formulation to create a generic drug). A second classification is based on whether a prescription from a medical professional (e.g., a doctor) is or is not needed to purchase the pharmaceutical product.

1.2.1. Novel, generic and orphan pharmaceutical products

Originator and generic drugs

The pharmaceutical industry consisted historically of two types of firms: originator and generic drug companies.[7] Originator firms conduct research and development (R&D) into new or novel APIs and seek patent protection accordingly. An API patent applies to any formulation of a drug (e.g., pill, cream, liquid) that includes the API.[8] The patent provides the firm with intellectual property rights over the use and sale of the API in any formulation for the life of the patent; competitors cannot offer generic versions until the patent has expired. The originator company can also attach a trademark to the originator product, which is then sold either directly by the patent owner or indirectly by one or more licensees under the trademark.

In short, originator companies discover new drugs to meet clinical needs; apply for patent protection; conduct multiple clinical trials to demonstrate efficacy and safety for human use; and either manufacture, market and sell the drugs themselves or license the API formula to other firms during the life of the patent. These products are referred to as "novel", "branded" or "originator" drugs. They are typically protected by product and/or process patents 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 the time between when the patent was granted and government authorization for the new pharmaceutical product. The authorization date depends on the number of years required to perform clinical trials to develop and present safety assurances needed to receive authorization (sections 3.1.1 and 4.2.2).

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 a new trademark. The generic drug has the same API formula as the brand name pharmaceutical product and is created to have the same product characteristics (e.g., dosage form, safety, strength, route of administration, quality, performance characteristics and intended use). Having the same characteristics

7 K. Wündisch (2003). International Transfer Pricing in the Ethical Pharmaceutical Industry. Amsterdam: IBFD Publications.

8 Pharmaceutical firms can also apply for intellectual property rights protection via formulation patents, where the company takes an existing API and restructures or combines it with other ingredients to create a new drug. See M. O'Brien (2017). Types of Pharmaceutical Patents. O'Brien Patent Solutions.

demonstrates bioequivalence, i.e., generic and brand name medicines are substitute products (they work the same way and provide the same clinical benefits).[9]

Pharmaceutical products may appear similar yet deceptively so.[10] Medicines are unique compounds. Even when they have similar chemical compositions (i.e., bioequivalence), they may have very different uses or effects (i.e., different bioavailabilities). Both bioequivalence and bioavailability are important product characteristics that may affect the arm's length transfer price.

Originator companies face challenges beyond those of their generic competitors, including:[11]

- The financial risks and costs involved in bringing a new drug to market. On average, only 1 of every 20 drugs that enter clinical testing will be approved for marketing, and it takes 10 to 15 years to bring a new drug to market at a cost of up to $2 billion.[12]
- Price controls and the buying power of third-party payers (e.g., public or private insurance, regulating bodies where applicable) seeking cost savings on their purchases (section 4.2.1).
- The need to have several R&D projects in the "pipeline" simultaneously to ensure the overall long-term profitability of the company in terms of the number of potentially approvable new drugs.
- The efforts and costs associated with complying with the regulatory requirements of multiple national government agencies and supranational organizations (section 2.7).

Because generic medicines do not have to undergo a repeat of the same clinical trials required for original brand name medicines, in terms of demonstrating safety and effectiveness, manufacturers of generics do not incur the same upfront R&D and regulatory costs and associated risks as originator firms. As a result, the cost structure of generic drug companies differs substantively from originator companies.

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9 United States Food and Drug Administration (n.d.). Generic Drugs: Questions & Answers.

10 This section is drawn from K. Wündisch, International Transfer Pricing in the Ethical Pharmaceutical Industry. Product characteristics include: size and dosage of the solid (e.g., tablet, capsule), semi-solid (cream, gel) or liquid (e.g., injectable, syrup); the transport system for the active substance (i.e., biologic virus, adenovirus); the size of molecules and proteins; the solution or salt and type of salt; the size of crystal particle form and isomer; the type, number and degree of impurities; the type, number and characteristics of diluents; inert excipients; viscosity, solubility and osmolality; color-coating and flavour agents; storage characteristics; remaining shelf-life and side-effect profile.

11 V. Kellogg (2020). ROI in Pharmaceutical R&D: How to Halt the Decline. In Challenges Facing Pharma and Biotech Companies, chapter 3. Report code PHM218A. BCC Publishing.

12 S. Harrer et al. (2019). Artificial Intelligence for Clinical Trial Design. Trends in Pharmacological Sciences 40(8): 577–591.

Once a generic product receives regulatory approval, the drug can enter the marketplace, creating competition with the originator drug. If multiple generic drugs are approved based on the same API, this can create further competition, leading to lower prices.[13] Generic prices are typically much lower than originator drug prices.

One risk faced by originator companies, in addition to competition from generic drugs, is competition between patented drugs. A patent provides the patent holder with a monopoly to exploit a drug but does not provide protection from other companies that produce drugs under other patents, which may have superior results or involve different treatments. The reduction in the present discounted value of a patent holder's return caused by competition between patented drugs can be at least as large as within-patent competition.[14] A recent study of between-patent competition in Europe found that intense competition significantly lowered the profitability and economic life of patented pharmaceuticals in the market for hepatitis C drugs.[15]

Orphan drugs

In addition to novel and generic drugs, a third category involves so-called "orphan drugs". These target rare diseases and disorders, where "rare" is defined as less than 200,000 patients.[16] Given the small potential market and the costs of developing an API and pharmaceutical product, fewer firms are willing to enter the orphan drug segment without additional financial support. Further, only a few consumers can bear the financial costs of purchasing these drugs. Some governments provide incentives to pharmaceutical firms to develop orphan drugs and may also cover some costs for patients.[17]

1.2.2. Over-the-counter and prescription drugs

Pharmaceutical products can be categorized based on whether a medical professional must write a prescription for the medicine before purchase. A prescription drug can only be supplied to a patient based on a written prescription by an authorized health professional, such as a physician or dentist.[18] Examples of prescription drugs typically include antibiotics and blood pressure tablets.

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13 United States Food and Drug Administration (n.d.). Generic Drugs Facts.

14 F. R. Lichtenberg and T. J. Philipson (2002). The Dual Effects of Intellectual Property Regulations: Within- and Between-Patent Competition in the U.S. Pharmaceuticals Industry. Journal of Law and Economics XLV (October): 643–672.

15 A. Roediger et al. (2019). Competition Between On-patent Medicines in Europe. Health Policy 123(7): 652–660.

16 See Taylor, The Pharmaceutical Industry and the Future of Drug Development

17 Countries that subsidize the development of orphan drugs include the Kingdom of the Netherlands, the United Kingdom and the United States. See J. P. Cohen and A. Felix (2014). Are Payers Treating Orphan Drugs Differently? Journal of Market Access and Health Policy.

18 See P. A. Marathe et al. (2020). Over-the-Counter Medicines: Global Perspective and Indian Scenario. Journal of Postgraduate Medicine 66(1): 28–34. See also J. Chang et al. (2016). Prescription to Over-the-Counter Switches in the United States. Journal of Research in Pharmacy Practice 5(3): 149–154.

In many countries, prescription drugs are registered with a national medicines regulatory authority (NMRA) and may have a specific registration number. For a prescription drug to be registered, it must be supported by evidence, including clinical trials to ensure its efficacy. The government authority assesses evidence to determine whether the drug will be registered. It is usually a requirement that the benefits of a drug proposed for registration outweigh its potential risks.

Over-the-counter drugs do not require a prescription from a medical professional.[19] They may be protected by patents but this is less likely compared to prescription drugs. Examples of over-the-counter drugs include, for example, low-dose pain medication.

Government regulations around accessing over-the-counter drugs differ across countries. Products are typically sold in pharmacies, although some countries may also allow some to be sold in supermarkets or convenience stores. Countries may restrict the sales of certain over-the-counter products to customers who have spoken with an on-duty pharmacist. Other countries do not have this stipulation, requiring only that such drugs must be bought in pharmacies. Particular drugs may be sold as prescription drugs in one country and over-the-counter drugs in another country. Many over-the-counter products were initially only available with a prescription.

Over-the-counter products are much more readily available to consumers and are usually relatively affordable compared to prescription drugs. Marketing intangibles may be highly relevant for the former. Differences in government regulations can encourage cross-border shopping and medical tourism.

1.3. Statistics on the Pharmaceutical Industry

1.3.1. Sales and market share

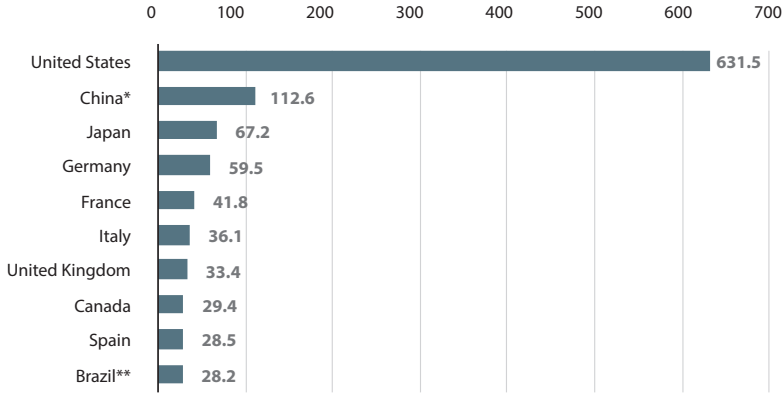
In 2021, worldwide revenues in the pharmaceutical industry totalled $1.42 trillion. This included both originator and generic pharmaceutical products, and those requiring a prescription and sold over the counter.[20] While the United States has the largest share of revenues (43.7 per cent) and 5 of the 10 largest pharmaceutical MNEs are headquartered there, markets in other countries have grown dramatically in recent decades. In 2022, China ranked second in terms of market revenues (figure 1).[21]

19 P. Poreds (2022). A Short Note on Over-the-Counter Drugs. Journal of Basic and Clinical Pharmacy 13(1): 123.

20 Statista (2023). Global Pharmaceutical Industry—Statistics & Facts.

21 Pharmanews Intelligence (2023). Comparing Global Pharmaceutical Markets: US, UK, and China. See also China Briefing (2022). How Big Is China's Biopharma Market?

Figure 1: Pharmaceutical markets by revenues, top 10 countries, 2022, billions of United States dollars



Source: IQVIA (2023). Revenues of Leading 10 National Pharmaceutical Markets Worldwide in 2022 (in Billions of US Dollars). Prices are reported at the ex-manufacturer level (price when sold from a manufacturer to a wholesaler or direct to pharmacies).
*Hospital market only.
**Pharmacy market only.

Table 1 provides data on regional pharmaceutical markets in 2022. The largest market was North America ($455.09 billion) followed by Asia ($434.16 billion).

Table 1: Pharmaceutical markets by region, 2022

Region	Billions of United States Dollars
Sub-Saharan Africa	20.7
* East and Central Africa	6.3
* West Africa	8.3
* Southern Africa	7.4
Asia	434.2
* North-East Asia	258.3
* South-East Asia	27.7
* South Asia	38.9

Europe	390.8
* Western Europe	290.1
* Emerging Europe	88.2
Latin America	66.3
Middle East and North Africa	40.0
* Middle East	38.3
* North Africa	12.1
North America	455.1

Sources: BMI (2023). Global Pharmaceuticals Report, Q3; BMI (2023). Sub-Saharan Africa Pharmaceuticals Report, Q3; BMI (2023). MENA Pharmaceuticals Report, Q3; BMI (2023). Latin America Pharmaceuticals Report, Q3; BMI (2023). Europe Pharmaceuticals Report, Q3; BMI (2023). Asia Pharmaceuticals Report, Q3.

1.3.2. Pharmaceutical exports and imports

Tables 2 and 3 provide publicly available data on the top 20 countries in terms of pharmaceutical exports and imports in 2021.[22] The trade balance is defined as exports minus imports, for both unfinished and finished products. A negative trade balance means that imports exceed exports. Large exporting countries can also be large importing countries; for example, in 2021, Germany and the United States were among the top three countries for both exports and imports.

Ireland, Switzerland and Germany had the largest positive trade balances (net exports). The largest negative trade balances (net imports) were in United States, Japan and the Russian Federation.

Table 2: Exports and imports of pharmaceutical products, top 20 countries, 2021 (millions of United States 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

22 OEC (2021). Which Countries Export Pharmaceutical Products? Available at: https://oec.world/en/visualize/tree_map/hs92/export/show/all/630/2021/.

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 (Kingdom of the)	35,585.56	9	United Kingdom	28,793.44
10	United Kingdom	24,800.78	10	Netherlands (Kingdom of the)	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	Russian Federation	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	Republic of Korea	9,428.77	19	Republic of Korea	9,743.98
20	Slovenia	8,402.58	20	Türkiye	7,356.04

Table 3: Trade balances for pharmaceutical products, top 20 countries, 2021 (millions of United States 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	Russian Federation	(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 (Kingdom of the)	8,574.33	8	Saudi Arabia	(5,583.18)
9	Italy	7,819.36	9	Türkiye	(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	Viet Nam	(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	Czech Republic	(3,187.54)

1.3.3. Global revenues by market segment

Table 4 provides data on global revenues for the prescription and over-the-counter segments of the pharmaceutical market from 2020 to 2022. Prescription drug sales were approximately 88 per cent of global sales during this period; the remainder (12 per cent) comprised sales of over-the-counter medicines. Patent-protected prescription drugs represented about 77 per cent of prescription drug sales, with the remainder split between generics (8 per cent) and orphan (15 per cent) prescription drugs.

1.3.4. 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 can copy the API and sell the product under the generic name or a new trademark. By value of sales, the generic drug market accounted for approximately 30 per cent of the global pharmaceutical market from 2018 to 2020, but the share varied widely by region and country. As Table 5 shows, in North America, the market penetration rate for generics was about 25 per cent compared with nearly 60 per cent in Asia-Pacific.

Table 4: Sales of pharmaceutical products by market segment, 2020–2022 (billions of United States dollars and percentage of total market)

	Billions of United States dollars			Percentage 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
Total over-the-counter pharmaceutical revenues worldwide	121.5	129.1	137.0	12.0	11.2	11.5
Total prescription and over-the-counter pharmaceutical revenues worldwide	1,014.5	1,153.1	1,195.0	100	100	100

Source: Calculations using data from Statista, Pharmaceutical Market Worldwide, Study ID 10642.

Table 5: Global market for generic pharmaceuticals by region, amount (billions of United States dollars) and share (percentage)

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				
Pharmaceutical market	$118.7	$130.2	$140.7	$129.9
Generic drug market	$96.8	$105.7	$115.1	$105.9
Generic share	81.6%	81.2%	81.8%	81.5%
India				
Pharmaceutical market	$36.4	$41.1	$46.8	$41.4
Generic drug market	$26.4	$31.1	$36.5	$31.3
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%

Source: BCC (2021). Global Markets for Generic Drugs, table 1, p. 13

1.3.5. Research and development statistics

Approximately 3,200 companies and more than 200 academic or research groups engage in R&D activities in the global pharmaceutical industry. While a large number of research firms are headquartered in the United States (44 per cent), Europe (25 per cent), Japan (6 per cent) and the Republic of Korea (4 per cent),[23] the geography is changing with an increasing number of firms headquartered in China. They increased their market share from 2 per cent ten years ago to 12 percent in 2022.

Emerging biopharma companies, defined as firms with less than $500 million in sales and R&D spending of less than $200 million per year, accounted for a record 65 per

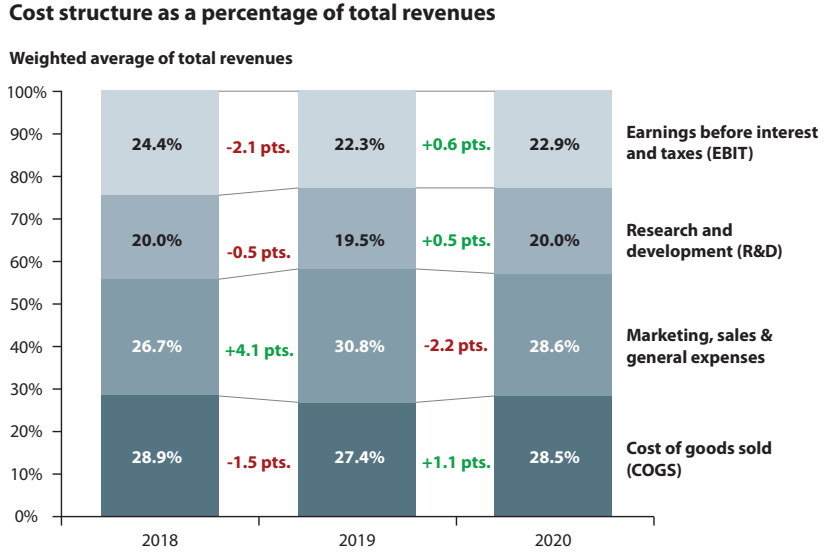
23 IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview Through 2021.

cent of the molecules in the R&D pipeline in 2021, up from 50 per cent in 2016 and 33 per cent in 2001. Of these firms, 17 per cent were headquartered in China, 20 per cent in Europe and 46 per cent in the United States. Their shares of the total national R&D pipeline ranged from a high of 83 per cent in China to 62 per cent in the United States, 47 per cent in Europe and 22 per cent in Japan.[24]

1.3.6. Industry profitability

A recent analysis of the top 20 pharmaceutical MNEs worldwide estimated that their average profitability (earnings before interest and taxes, EBIT) was 23 per cent of revenues in 2020. The average cost of goods sold (COGS) was 28.5 per cent, operating expenses (OPEX) were 28.6 per cent and R&D costs were 20 per cent (figure 2). The analysis, undertaken at the MNE group level, focused on the largest companies. It provides some insights into the average profitability and cost structure of the pharmaceutical industry as a whole.

Figure 2: Cost structure as a percentage of total revenues, 2018–2020



Source: Smart Pharma (2022). Top 20 Pharma Companies—Performance and Strategy.

24 Ibid.

2. The Pharmaceutical Global Value Chain

2.1. Overview

As described in the United Nations Practical Manual on Transfer Pricing for Developing Countries (UN TP Manual) in section 1.3.3, value chain analysis, developed by Michael Porter, describes activities performed by a company, domestic or international, to create value for its customers.[25] This includes all stages of value addition involved in bringing a product from inception to final consumption. Porter separated these stages into two types: primary and support activities.[26]

The value chain can be analysed at the firm or industry level and from a domestic or international perspective. In this guidance, the focus is on the pharmaceutical global value chain at both the individual firm and industry levels. At the MNE level, the global value chain for the company takes into account all activities of entities in the MNE group worldwide.[27] At the industry level, the global value chain entails all activities, firms and countries, on a worldwide basis, involved in the pharmaceutical industry.[28] Global value chain analysis uses the value chain to give a general or stylized overview and visual to describe an MNE or industry. It recognizes that various production stages have become globalized and dispersed around the world, and that, in practice, activities carried out by firms will vary in their intensity.[29]

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

26 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 C. B. Stabell and D. O. Fjeldstad (1998). Configuring Value for Competitive Advantage: On Chains, Shops, and Networks. Strategic Management Journal 19(5).

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

28 S. Frederick (2019). Global Value Chain Mapping. In S. Ponte, G. Gereffi and G. Raj-Reichert, eds., Handbook on Global Value Chains, pp. 29–53. Eduard Elgar Publishing.

29 L. Jones, M. Demirkaya and E. Bethmann (2019). Global Value Chain Analysis:

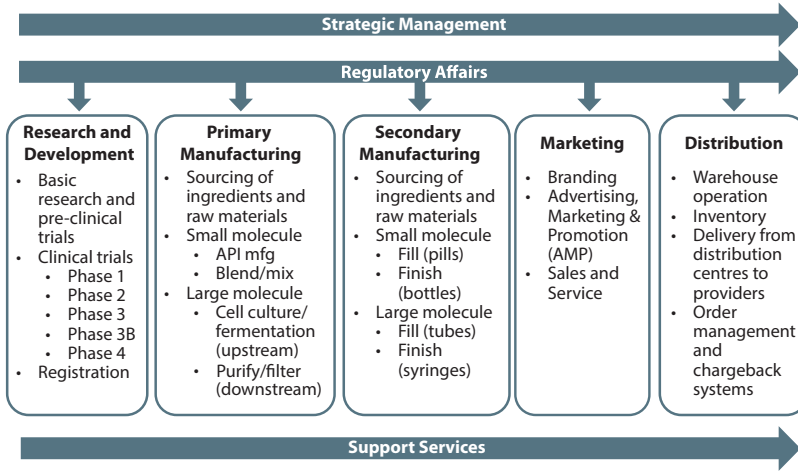
This section explores the pharmaceutical global value chain from the industry level and at a certain point in time. Section 3 discusses the global value chain from the firm level, explaining how activities are organized within a typical MNE in the pharmaceutical industry, in terms of value drivers and business models. As stylized overviews, country- and firm-level analyses in this guidance cannot capture the many nuances and differences in how a global value chain manifests in firms and countries around the world.

For transfer pricing purposes, it will be important to accurately delineate the controlled transactions under review. This includes identifying economically significant characteristics of the controlled transactions and the roles and responsibilities of the controlled entities involved in them. This topic is discussed in section 4.[30]

2.2. The Global Value Chain of the Pharmaceutical Industry

The global value chain of the pharmaceutical industry encompasses the following value adding activities in the production and sale of pharmaceutical drugs: R&D, primary manufacturing, secondary manufacturing, and marketing and distribution. In addition to strategic management, regulatory affairs are a core activity, since the pharmaceutical industry is typically heavily regulated at all stages. Other value-adding activities include support services such as human resources, finance and control. The following analysis focuses on activities illustrated in figure 3. The global value chains for both small-molecule (chemical) and large-molecule (biological) pharmaceutical products generally include the same stages.

Figure 3: The global value chain in the pharmaceutical industry



Concepts and Approaches. Journal of International Commerce and Economics.

30 See the UN TP Manual, section 3.1ff.

Core activities explored in detail are:

- **R&D**: Given the complexity of R&D in the pharmaceutical industry, this stage is typically separated into three substages: research, development and registration.[31]
- **Primary manufacturing**: Production of the API.
- **Secondary manufacturing**: Additional manufacturing (e.g., fill and finish) to convert the API into a finished drug product.
- **Marketing**: The stage where the marketing strategy is designed and executed based on scientific approval processes, regulations for market access and price controls; it includes advertising, marketing and promotion activities.
- **Distribution**: The stage where the finished drug product is transferred to wholesale distributors that handle logistics and distribution to hospitals, clinics and retail pharmacies. Logistics can involve complex supply chains to ensure proper handling of drug products.
- **Regulatory activities**: Since pharmaceutical companies are highly controlled, regulations impact core activities ranging from clinical trials to product approval and registration, manufacturing, marketing and distribution.[32]

2.3. Research and Development

From a business perspective, the R&D stage, especially for new drugs, is often highly complex and risky. It entails bringing a drug from discovery to testing in non-clinical models and ultimately human trials, and then to a regulatory review and commercialization.[33] A brief overview of each of the three substages follows.

2.3.1. Research

The research stage encompasses drug discovery (the process by which new candidate medications are discovered), pre-clinical trials and new drug applications to the regulatory authority. Both research on new molecules for medicines to treat an ailment and the discovery of substances or methods to diagnose a disorder are included. In addition, both the discovery of new drugs and incremental innovation (e.g., new dosages and delivery mechanisms for existing drugs) are included.

31 United States Food and Drug Administration (2018). The Drug Development Process. See also IQVIA Institute for Human Data Science, Global Trends in R&D.

32 Y. M. Al-Worafi (2020). Drug Safety in Developing Countries. London, UK: Academic Press.

33 L. A. Buckley et al. (2020). Drug Development 101: A Primer. International Journal of Toxicology 39(5): 379–396.

Drug discovery is a lengthy, expensive and extensive scientific-based investment process with a low success rate.[34] In the pre-clinical stage, new active compounds are tested under experimental conditions to gather information on the effects of the potential new drug. Depending on specific national or regional regulations, pharmaceutical firms may also be required to submit an investigational new drug application to the NMRA, requesting approval to move the proposed new drug to the clinical trials stage.[35] During this phase, pharmaceutical companies often file for patent protection for the API and potentially new drug products.

2.3.2. Development

In the development 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 diagnostics, 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 missed during earlier clinical trials.[36]

Figure 4 provides a general overview of the R&D process, together with the estimated average number of years involved in each stage.[37] Actual R&D processes and time periods, however, vary significantly across pharmaceuticals, firms, and national or supranational authorities.

There are four clinical trial stages. Phases 1 to 3 occur prior to the filing and review of the new drug application with the national medicines regulatory authority and (if approved) the product launch. Additional phase 3 trials and phase 4 studies take place after a product launch. A short description of the four clinical trial stages follows.

- **Phase 1**: Testing of small groups of volunteers to assess the safety of various dosage levels of a potential new vaccine or drug.
- **Phase 2**: Testing of larger numbers, including individuals with 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**: Randomized trials using large numbers of volunteers in many locations to assess the effectiveness of the vaccine or drug.

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34 F. Zirnstein and P. Kaiser (2022). Transfer Pricing in the Pharmaceutical and Life Sciences Sector. In R. Petruzzi, G. Cottani and M. Lang, eds., Fundamentals of Transfer Pricing: Industries, Regions, New Technologies, and Other Topics, chapter 21. Alphen aan den Rijn, the Netherlands: Wolters Kluwer.

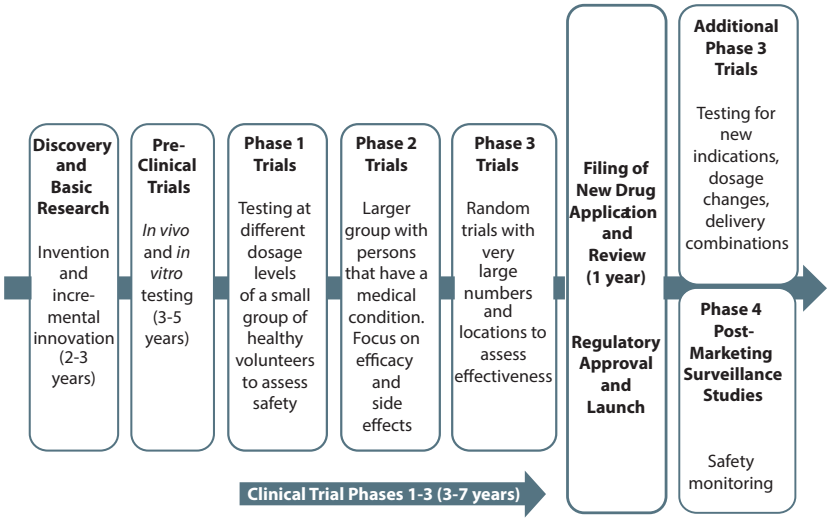
35 Buckley et al., Drug Development 101.

36 P. Paumier (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal, section 3.1.

37 Figure adapted from ibid. The data on average years in each stage are from the Seikagaku Corporation's Process of New Drug Development. Available at: https://www.seikagaku.co.jp/en/development/flow.html.

— **Phase 4**: Post-marketing studies that may be required by the national medicines regulatory authority to test for side effects or new usages.

Figure 4: The research and development process in the pharmaceutical Industry



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.[38] Phases 1 through 3 may take up to seven years.[39] While this time frame was considerably shortened for the vaccine approval process during the COVID-19 pandemic, it is so far unclear if and how this will influence other new drug approvals.

IQVIA estimates that the average composite success rate over all four phases from 2010 to 2021 was 13.1 per cent across all therapy areas. Success rates, measured in terms of graduating from one phase to at least the next phase, varied as follows: phase 1 at 56 per cent, phase 2 at 38 per cent, phase 3 at 67 per cent and regulatory submission at 89 per cent.[40]

It is important to correctly assess clinical trials for transfer pricing purposes. For example, if phase 4 trials (post-marketing studies) are required in a particular country, the tax administration there may need to determine how this activity will be remunerated for transfer pricing purposes. One issue is whether the trial constitutes a separate activity or is part of a larger activity such as marketing or distribution.

38 IQVIA Institute for Human Data Science, Global Trends in R&D.

39 The data on average years in each stage are from the Seikagaku Corporation's Process of New Drug Development.

40 IQVIA Institute for Human Data Science, Global Trends in R&D.

2.3.3. Registration

To distribute drugs in a market, the API and pharmaceutical products made with it will generally have to be registered with the national medicines regulatory authority or a supranational authority, such as the European Medicines Agency (EMA), depending on where the firm intends to market the new drug. Regulatory approval may be required at all three R&D stages according to national or regional regulations. Regulatory authorization typically starts at the clinical trials stage. In large MNEs, the company's regulatory affairs staff at the headquarters level may determine the group's overall regulatory filing strategy (e.g., how to build the dossier, country filing prioritization, etc.). In regional and country-level subsidiaries, teams of national registration experts may prepare and submit dossiers to the various national regulatory authorities. Post-approval, the national medicines regulatory authority in one or more countries may also require additional drug safety monitoring and phase 4 clinical trials, which require work at the regional and/or national levels.

Once regulatory agency approval is provided, the company is generally required to register the product and apply for authorization to market and sell the drug. Approval is typically needed in each country where the firm intends to sell the pharmaceutical product (section 2.7).

2.4. Manufacturing

The manufacturing stage of the pharmaceutical global value chain consists of two substages: primary and secondary manufacturing. These are discussed below, along with the impact of technological change on both.

2.4.1. Primary manufacturing

Primary entails manufacturing production of the API; secondary manufacturing entails the drug product based on the API. Pharmaceutical products are made from an API together with inactive ingredients (excipients) added to the API to produce a finished product.[41] 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." [42] In short, an API is a bulk drug substance. The global market for APIs in 2020 was $173.3 billion.[43]

41 BCC Research Staff (2019). Markets at a Glance: Pharmaceuticals. Report code PHM213A.

42 International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (2000). Topic Q7: Good Manufacturing Practice for Active Pharmaceutical Ingredients.

43 BCC Research Staff (2021). Active Pharmaceutical Ingredients: Global Markets. Report code PHM200B.

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).[44] 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 that 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 safety; assist in the efficiency and delivery of the drug when used or consumed; and protect the integrity of the product during storage. The ideal excipient is stable and reproducible, with no undesired interactions; pharmacologically inert; suitable for the desired functionality; and cost-effective.[45] In 2021, the global market for pharmaceutical excipients was $8.29 billion, about 5 per cent of the global API market. Nearly 93 per cent of excipients were organic.[46]

Chemistry and biology are at the heart of the primary manufacturing stage.[47] Chemical (small molecule) drugs historically have been the cornerstone of modern medicine with less complex chemical structures and simpler manufacturing processes. They are often administered orally.[48] The manufacturing process to create 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 processes normally include isolation, extraction, purification, milling and packaging.[49] Once the API is manufactured, it is blended or mixed with other ingredients or purified or filtered to create the bulk drug substance.

Biological (large-molecule) drugs are a newer field of drugs and therapies available primarily as intravenous injections. They are derived from naturally occurring sources, human, animal or microorganisms, and tend to have complex structures and manufacturing processes. The production of biological APIs typically involves cell culture/fermentation, followed by purification and filtration. Large molecule drugs pose additional manufacturing challenges and risks. They have greater fragility, complicating storage and transportation.[50]

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44 Ibid.

45 For a detailed analysis of pharmaceutical excipients, see M. Tcherpakov (2021). Excipients in Pharmaceuticals: Global Markets to 2026. Report code PHM010. BBC Publishing.

46 Ibid.

47 Paumier, Transfer Pricing in the Pharmaceutical Industry.

48 United States International Trade Commission (2020). COVID-19 Related Goods: The U.S. Industry, Market, Trade, and Supply Chain Challenges. Publication number 5145.

49 BCC Research Staff, Active Pharmaceutical Ingredients: Global Markets.

50 Deloitte (2015). Advanced Biopharmaceutical Manufacturing: An Evolution Underway. Deloitte Development LLC.

Both production processes typically involve large-scale factories 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 hyperclean rooms, acquire specialized capital equipment and employ skilled personnel. Specialized inputs such as bioreactor bags, filters and cellular materials are also needed. Drug substances, once created, are combined with other pharmaceutical ingredients (e.g., excipients, adjuvants and preservatives) to formulate drug products.

2.4.2. Secondary manufacturing

Secondary manufacturing involves turning the API into one or more drug products. This stage is often referred to as "fill and finish" manufacturing because the API is converted into consumable formulations or final dosage forms.[51] Raw materials and excipients are also needed at this stage. The variety of final dosage forms includes, for example, liquids, gels, tablets, aerosol sprays and topical ointments.

For drugs based on chemical APIs, the secondary manufacturing stage typically involves combining the API with other ingredients and extruding the drug product as pills or capsules, which are then labelled and packaged. For drug products based on biological APIs, secondary production usually involves squirting doses into vials or syringes. At the finishing stage, the vials or syringes are capped with stoppers, labelled and packaged. The pharmaceutical industry is also actively involved in developing innovative dosage forms, using industry 4.0 technologies such as 3D printing, to create new fixed-dose combination drugs.[52]

Secondary production plants often require specialized assembly line capital equipment generating high fixed costs, and variable inputs such as vials, stoppers, and packing and shipping materials. Some may also require cold storage to sustain the cold chain logistics process and extend shelf life.

2.4.3. Manufacturing and technological change

Digitalization plays an important role in ongoing technological changes in the pharmaceutical industry as firms shift from batch to continuous manufacturing. Most pharmaceutical manufacturing is done by traditional batch manufacturing processes, where raw materials are input and discharged as a finished product at the end in numbered batches.[53] This involves a number of steps (e.g., blending, granulation and drying) and may require work at different facilities. As a result, batch manufacturing may suffer from a lack of agility, flexibility and reliability, making it difficult for manufacturers to respond quickly to sudden changes in demand or adapt when certain inputs are not available. Batch manufacturing generally results

51 Y. Shivdasani et al. (2021). The Geography of Prescription Pharmaceuticals Supplied to the USA: Levels, Trends, and Implications. Journal of Law and the Biosciences 8(1).

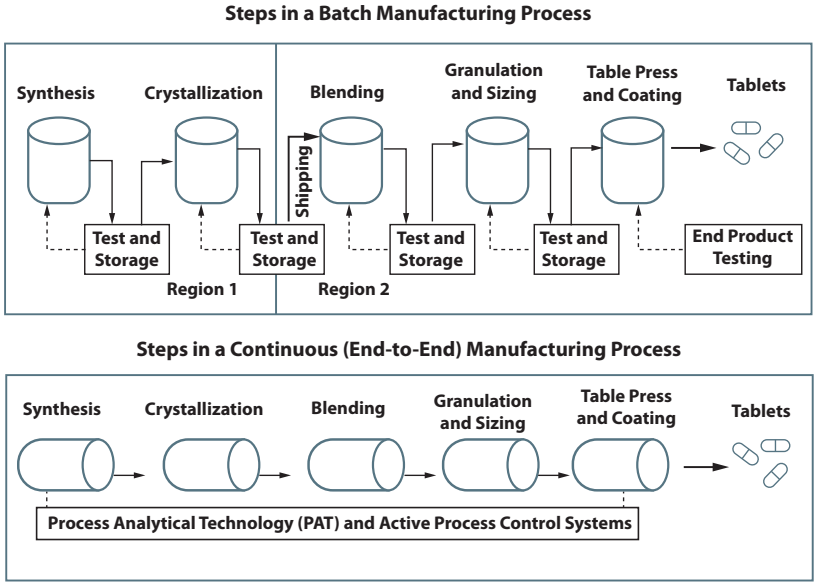
52 M. Janczura, S. Sip and J. Cielecka-Piontek (2022). The Development of Innovative Dosage Forms of the Fixed-Dose Combination of Active Pharmaceutical Ingredients. Pharmaceutics 14(4): 834.

53 Brookings Institution (2015). Promoting Continuous Manufacturing in the Pharmaceutical Sector.

in the clear separation of the primary and secondary manufacturing stages into different plants and locations.

Continuous manufacturing is the main alternative to batch processing. It integrates individual continuous unit operations with process analytical technology that monitors and controls process parameters and material and quality attributes. Manufacturing processes are streamlined by eliminating steps. As a result, continuous manufacturing uses smaller-scale equipment and fewer materials. It can be located in a single plant facility, making it more agile and flexible than batch manufacturing. 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 location with no real distinction between them. Figure 5 compares batch and continuous manufacturing processes. While cost savings in continuous manufacturing have been estimated at more than 30 per cent, the pharmaceutical industry has been slow to shift to it for a variety of technical, operational, economic and regulatory reasons.[54]

Figure 5: Batch and continuous manufacturing in the pharmaceutical Industry



Source: Based on S. C. Hock, T. K. Siang and C. L. Wah (2021). Continuous Manufacturing Versus Batch Manufacturing: Benefits, Opportunities and Challenges for Manufacturers and Regulators. Generics and Biosimilars Initiative Journal 10(1): 44–56, figure 2.

54 For a discussion of these barriers and possible solutions, see ibid. See also Brookings Institution, Promoting Continuous Manufacturing in the Pharmaceutical Sector.

The shift could have very significant effects as primary and secondary manufacturing could be consolidated in one location. The need to decentralize steps in the production process to lower costs would likely be reduced, especially for small molecule drugs. Some activities in manufacturing stages could be centralized closer to R&D plants.

2.5. Marketing

This section discusses the role of marketing as part of the pharmaceutical industry's global value chain (see also sections 3.1 and 3.1.2). Marketing in the pharmaceutical global value chain is typically viewed as the combination of advertising, marketing and promotional activities, which companies use to sell products, including downstream to wholesale distributors.

The World Health Organization (WHO) defines the promotion of pharmaceuticals as informational and persuasive activities by manufacturers and distributors that induce the prescription, supply, purchase and/or use of medicinal drugs.[55] Activities range from activities through sales representatives to educational or scientific initiatives such as industry-organized conferences and clinical studies.[56]

Detailing is a key marketing technique that pharmaceutical companies use to educate physicians about pharmaceutical products, hoping that products will be prescribed more often.[57] Skilled pharma representatives explain the characteristics of different drugs in terms of their bioequivalence and bioavailabilities. This activity is enhanced by building long-term relationships.[58] Information is communicated through in-person visits by pharma sales representatives to doctors and hospitals or via digital channels, termed e-detailing.

Marketing strategies vary between over-the-counter and prescription drugs, and are heavily regulated at the national level (and the supranational level for the European Union). Regulations may be enforced through legal action or a national medicines regulatory authority or supranational agency. Regulation pertains to both prescription and over-the-counter drugs, although exact regulations often differ between the two categories.[59] Regulations may limit retail outlets, marketing channels, claims that can be made and the kinds of supplementary information to be provided. In addition to national regulations, many medical associations and hospitals or universities have

55 WHO (World Health Organization) (1988). Ethical Criteria for Medicinal Drug Promotion. Geneva, Switzerland: WHO.

56 S. Mulinari (2016). Regulating Pharmaceutical Industry Marketing: Development, Enforcement, and Outcome of Marketing Rules. Sociology Compass.

57 Revo Suite (2024). How Medical Detailing Is Changing with Pharma Marketing Technology.

58 J. Ascher et al. (2018). From Product to Customer Experience: The New Way to Launch in Pharma. McKinsey & Company.

59 See, for example, Chang et al., Prescription to Over-the-Counter Switches in the United States.

professional or employee codes of conduct that cover interactions with the pharmaceutical industry.[60] For example, direct marketing to consumers through advertisements and commercials is only permitted in the United States and New Zealand.[61] Marketing in the pharmaceutical industry therefore requires not only expertise on drugs and medical practices but also knowledge of regulatory requirements.

Pharmaceutical products that require a prescription are generally marketed to healthcare providers, such as physicians, pharmacists and health insurance organizations that may be independent companies or under the purview of a government.[62] Products may additionally be advertised to patients. Over-the-counter drugs are generally marketed to patients directly, though some may also be promoted to healthcare providers to recommend to their patients.[63]

New products are typically protected by patents, especially prescription drugs. Once a prescription drug has been authorized for distribution, pharmaceutical companies then design and execute a market access/marketing strategy. While the exact length of a patent varies among countries and products (section 3.1.1), protection from direct competition by a patent gives companies a defined period in which to establish a product under a recognizable trademark name and build confidence and loyalty to it. Substantial marketing activities are needed to rapidly gain market acceptance. Successful marketing may enable a pharmaceutical company to continue to sell its products even after patent protection has lapsed,[64] although this may depend on the presence of price controls (section 4.2.1).

With increasing digital communications channels and specialty medicine development, there has been an ongoing shift to real-time, data-driven marketing strategies making increased use of digital channels as well as key opinion leaders.[65] In-country marketing strategies generally require a large sales force for detailing purposes. Digitalization and increasing regulatory pressures, however, may be decreasing the number of "messengers" required to disseminate the "message". A recent study predicted that pharma sales forces and medical science liaisons were likely to be cut by 10 to 15 per cent due to the digitalization of go-to-market strategies.[66]

60 Mulinari, Regulating Pharmaceutical Industry Marketing.

61 C. L. Ventola (2011). Direct-to-Consumer Pharmaceutical Advertising: Therapeutic or Toxic? P&T: A Peer-Reviewed Journal for Formulary Management 36(10).

62 K. Wündisch (2003). Transfer Pricing in the Ethical Pharmaceutical Industry. Amsterdam, the Netherlands: IBFD Publications.

63 Chang et al., Prescription to Over-the-Counter Switches in the United States.

64 Zirnstein and Kaiser, Transfer Pricing in the Pharmaceutical and Life Sciences Sector.

65 H. Somaiya (2022). Omnichannel Is the Next Step in Pharmaceutical Marketing. Forbes.

66 T. Solbach et al. (2020). No Going Back: Pharma Companies' Route to a Digitalized Go-to-Market Model. Strategy & PwC.

2.6. Distribution

Once a drug product is manufactured, it has to be distributed to the point-of-sale, taking into account specific safety regulations and distribution particularities, such as the need for cold storage (section 2.7.4). In most countries, distribution is facilitated through wholesalers and hospitals — this applies to both prescription and over-the-counter drugs. Pharmaceutical manufacturers either sell their products in bulk to wholesale distributors or set up their own wholly owned distributors. Distributors therefore are intermediaries between manufacturers and their customers (i.e., retailers and healthcare providers).[67] Distribution may be to a single-channel wholesaler with the exclusive right to distribute medications from one pharmaceutical company within a certain region or country. Most countries, however, encourage a multichannel system in which medications are distributed and supplied in parallel from different wholesalers.[68] In the latter case, wholesalers consolidate orders from multiple companies in their warehouses and package together products from several manufacturers that are destined for a particular point-of-sale. Any products that are not sold or must be returned are sent back to the distributor warehouse to be resold or disposed.[69]

Figure 6 illustrates the typical flow of products, services and funds for prescription drugs covered under health insurance and purchased in a retail setting.[70] In most countries, a pharmaceutical manufacturer sells its products to one or more wholesale distributors. They then supply the products to healthcare providers (e.g., doctors, hospitals, medical clinics) and/or retail (including mail order) pharmacies. The purchasers dispense the pharmaceuticals to patients to take them as prescribed.

In most countries, third-party payers (e.g., health insurers, employer health plans and government programmes) provide insurance coverage to patients in return for insurance premiums. Patients will typically make co-payments for drugs they purchase. Third-party payers may also negotiate agreements with pharmaceutical companies on which products are included in insurance plans, the processing of prescription medicines through quality and utilization management checks, and the management of formulary lists of covered medicines.

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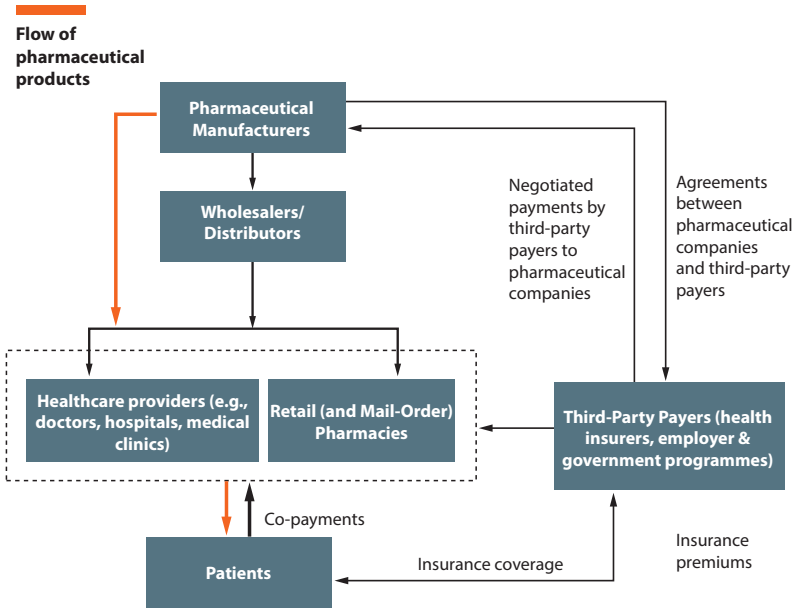
67 M. C. Dabora, N. Turaga and K. A. Schulman (2017). Financing and Distribution of Pharmaceuticals in the United States. Journal of the American Medical Association 318(1): 21–22. Congressional Budget Office (2007). Prescription Drug Pricing in the Private Sector.

68 P. Kanavos, W. Schurer and S. Vogler (2011). The Pharmaceutical Distribution Chain in the European Union: Structure and Impact on Pharmaceutical Prices. Brussels: European Commission.

69 On the complexities involved in pharmaceutical distribution, see N. R. Augustine, G. Madhavan and S. J. Nass, eds. (2018). Complexity in Action. In Making Medicines Affordable: A National Imperative, chapter 2. Washington, DC: National Academies Press.

70 N. Sood et al. (2017). The Flow of Money Through the Pharmaceutical Distribution System. Leonard D. Schaeffer Center for Health Policy & Economic, University of Southern California. See also Pharma News Intelligence (2023). Fundamentals of the Pharmaceutical Supply Chain.

Figure 6: The typical distribution system for prescription pharmaceutical products



Source: Adapted from N. Sood et al. (2017). The Flow of Money Through the Pharmaceutical Distribution System, figure 1. Leonard D. Schaeffer Center for Health Policy & Economic, University of Southern California.

2.7. Regulatory Affairs

All activities of the pharmaceutical industry are governed by strict laws, regulations and policies that draw on WHO standards but are specific to each country. Regulation takes place both on the demand and supply side of the market.[71]

On the supply side, a wide variety of government regulations includes:

- Intellectual property rights protection, which in pharmaceutical products typically involves incentives to ensure innovation[72]
- Effectiveness and quality control regulation 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, promotional channels and codes of conduct

71 Paumier, Transfer Pricing in the Pharmaceutical Industry.

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

On the demand side, government regulations typically separate the selection of pharmaceuticals from who pays for pharmaceutical products. There are at least five possible groups: patients, physicians, insurance companies, pharmacies and hospitals, as illustrated in figure 6.

On the supply side, national medicines regulatory authorities are tasked with monitoring the quality, safety and efficacy of drugs, as well as the accuracy of product information, which is done by ensuring that different elements of the global value chain operate according to specified standards. This includes parts of the R&D process and clinical trials; the procurement, manufacturing and distribution of drugs; and product promotion and advertising.[73] The following subsections discuss government regulations applicable to the four general stages of the global value chain: R&D, manufacturing, marketing and distribution.[74]

Regulatory policies on the demand and supply sides of pharmaceutical markets vary widely across countries.[75] Rules are specific to each jurisdiction. The discussion below focuses on general trends without attempting to capture the many different rules and regulations as they manifest in countries around the world.

2.7.1. Regulatory affairs and research and development

Each stage of the R&D process (section 2.3) must adhere to good clinical research practices. The WHO defines a good clinical research practice 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.[76] The process is intended to ensure the rights, safety and well-being of research subjects and the integrity of clinical research data.

2.7.2. Regulatory affairs and manufacturing

Manufacturing pharmaceutical products is commonly divided into primary and secondary manufacturing (section 2.4). Companies are expected to adhere to good manufacturing practices, defined by WHO as quality management that ensures that products are consistently produced and controlled according to the quality standards appropriate for their intended use and as required by the marketing

73 N. Maniadakis et al. (2017). Comprehensive Taxonomy and Worldwide Trends in Pharmaceutical Policies in Relation to Country Income Status. BMC Health Services Research 17.

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

75 See, for example, M. Berger et al. (2023). Exploring the Effectiveness of Demand-Side Retail Pharmaceutical Expenditure Reforms: Cross-Country Evidence from Weighted-Average Least Squares Estimation. International Journal of Health Economics and Management 23: 149–172. See also C. Rémuzat et al. (2017). Supply-side and Demand-Side Policies for Biosimilars: An Overview in 10 European Member States. Journal of Market Access and Health Policy 5(1): 1–16.

76 WHO (World Health Organization) (2015). Handbook for Good Clinical Research Practice (GCP): Guidance for Implementation.

authorization, clinical trial authorization or product specification.[77] This approach is aimed primarily at diminishing the risks inherent in any pharmaceutical production from cross-contamination/mix-ups and false labelling. It includes procedures for the receipt of materials, production, packaging, labelling, quality control, release, storage and distribution.[78]

In many countries, national medicines regulatory authorities will inspect equipment, facilities and manufacturing processes prior to approving a product.[79] In addition, many countries have a legal requirement that every pharmaceutical manufacturer must employ a highly skilled scientist, who can certify that the company applies good manufacturing practices and that its medicine batches meet pharmaceutical quality systems standards.[80]

2.7.3. Regulatory affairs and marketing

The marketing of pharmaceuticals is heavily regulated in most countries (section 2.5). This encompasses rules on which marketing channels may be used and which claims can be made.[81] There are key regulatory differences between prescription drugs and over-the-counter medications. Government regulations that determine which drugs require a physician's prescription can influence how drugs are marketed and distributed.[82]

In most countries, pharmaceutical sales occur indirectly through wholesale 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, physicians prescribe medicines that are purchased by households, hospitals and government medical services.

Depending on a country's healthcare system, patients may obtain prescription pharmaceutical products at a hospital or medical clinic or from retail pharmacies (some of which may operate as online businesses). In some countries, pharmaceutical MNEs, in addition to needing marketing authorization, must also ensure that their products are listed with health insurance companies if they and/or a national medicines regulatory authority have agreed to cover certain medications under insurance policies. Prescribing behaviour by physicians and cost coverage (out-of-pocket payments by

77 WHO (World Health Organization) (2014). WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles.

78 B. Kaufman and G. D. Novack (2003). Compliance Issues in Manufacturing of Drugs. The Ocular Surface 1(2).

79 Zirnstein and Kaiser, Transfer Pricing in the Pharmaceutical and Life Sciences Sector.

80 See the Royal Society of Chemistry on Qualified Person in the Pharmaceutical Industry, available at: https://www.rsc.org/careers/cpd/practising-scientists/qp-pharmaceutical/.

81 Mulinari, Regulating Pharmaceutical Industry Marketing. See also T. L. Alves, J. Lexchin and B. Mintzes (2019). Medicines Information and the Regulation of the Promotion of Pharmaceuticals. Science and Engineering Ethics 25: 1167–1192.

82 Chang et al., Prescription to Over-the-Counter Switches in the United States.

patients, full coverage through insurance or a combination of both) are therefore primary drivers of demand for prescription drugs.

2.7.4. Regulatory affairs and distribution

The distribution and storage of drugs is an important activity in the global value chain of pharmaceutical companies (section 2.6). Substandard and/or falsified products are a significant threat to public health and safety. Upholding the quality and safety of drugs helps to prevent exposure to substandard and falsified products, and maintain the integrity of the distribution chain. Most countries have established good distribution practices in line with WHO recommendations. Regulations generally cover the need for written procedures and clearly specified responsibilities; traceability requirements; and systems for quality risk management, including managing returns, complaints and product recalls.[83]

83 WHO (World Health Organization) (2020). Good Storage and Distribution Practices for Medical Products.

3. Value Drivers and Business Models in the Pharmaceutical Industry

This section discusses value drivers and business models.

3.1. Value Drivers in the Pharmaceutical Industry

Of all global value chains, the one for pharmaceuticals is the most knowledge-intensive. The Global Value Chain Development Report 2021 estimated the knowledge intensity of pharmaceuticals and medical devices at 66.3 per cent, compared to 17.4 per cent for computers and electronics, 13.7 per cent for information technology services and 2.3 per cent for food and beverages.[84] Key drivers of profits in the pharmaceutical industry are knowledge-based. In performing a transfer pricing analysis, it is important to consider interactions among intangible assets, as well as the parties that have undertaken functions, borne risks, and incurred costs related to the development, acquisition, enhancement, maintenance, protection, and exploitation (DAEMPE) of those assets.

Some major profit drivers are R&D and patents, marketing intangibles, marketing authorization, know-how and digitalization. Their importance varies among countries and depends on the specific transaction under review during a transfer pricing analysis.

3.1.1. Research and development and patents

Technological knowledge, driven primarily by a firm's R&D activities, is widely perceived as the most important of the specific advantages of an MNE and the key long-term value driver in the pharmaceutical industry.[85] R&D activities carry a high risk given the uncertainty of the potential outcome and large investments that may or may not lead to a new product. The average time for a successful pharmaceutical product to move from R&D to market may be 10 to 15 years, with the economic cost of developing a successful compound (including opportunity costs and the costs of failed products) reaching up to $2 billion.[86]

Innovative drugs are generally protected by one or more patents. Protection by several patents is possible where secondary patents cover, for example, manufacturing know-how, or where the drug and/or API combine different chemical compounds, each of which is covered by a patent.

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

85 G. Vallat (2020). Application of the DEMPE Concept in the Pharmaceutical Industry. International Transfer Pricing Journal 27(3).

86 S. Harrer et al. (2019). Artificial Intelligence for Clinical Trial Design. Trends in Pharmacological Sciences 40(8): 577–591.

If patent protection is missing, generic manufacturers can enter the industry and compete with existing suppliers, diminishing the original company's revenues. The value of the patent may also be affected by the need for a marketing authorization that will determine if a product can be sold in a specific country.

A firm's goal is generally to develop an innovative product that will be granted patent protection for a set 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 costs involved in developing an innovation and realize a reward for engaging in risky and lengthy R&D. Patent protection depends on the patent type, the scope of coverage and the national availability of legal remedies, which differ among countries and can last up to 20 years. Once a patent ends, firms with chemical drugs face competition from generics; those with biological drugs can expect competition from biosimilars (section 4.2.2).

How R&D costs and revenues are reported on a company's income statement can have a substantial impact on profitability and thus corporate financial exposure, risk profile and income taxes. Failed projects occur frequently and have large sunk costs that, due to the asynchrony of R&D costs incurred and accounting principles, cannot be spread out over time.[87]

An alternative to costly and risky in-house development is for larger firms to acquire smaller firms and their intellectual property.[88]

3.1.2. Marketing intangibles

Marketing intangibles can have important value for pharmaceutical products.[89] Potential marketing intangibles may include, for example, trademarks or trade names, brands, or customer lists, relationships and proprietary data. For a more detailed discussion of marketing intangibles, see section 6.2.4 of the UN TP Manual.

From a transfer pricing perspective, an important question is whether national marketing activities generate a national marketing intangible distinct from the foreign-owned brand and yield a return greater than otherwise comparable uncontrolled distributors (section 6.2.4.5 of the UN TP Manual). In analysing any intangible, it is important to determine if it is unique and valuable (section 6.2.4.3 of the UN TP Manual). Some intangibles, notably customer lists and relationships, and proprietary market and customer data, are not subject to intellectual property rights law and cannot be registered; however, this is not a necessary condition for an item to be characterized as an intangible for transfer pricing purposes (section 6.2.2.4 of the UN TP Manual). It is also common for a pharmaceutical product to be associated with more than one intangible asset at a time.

87 Zirnstein and Kaiser, Transfer Pricing in the Pharmaceutical and Life Sciences Sector.

88 Ibid.

89 C. Roberge (2013). Transfer Pricing in the Pharmaceutical Industry: The Remuneration of Marketing Intangibles. International Transfer Pricing Journal 20(4).

This discussion is not intended to be exhaustive or offer a complete list of elements that may constitute local marketing intangibles in the pharmaceutical industry. Tax administrations and taxpayers should analyse the specific facts and circumstances, taking into account their knowledge of the domestic pharmaceutical industry and keeping in mind domestic legislation as well as relevant guidance on transfer pricing.

i. Trademark/trade name

Most pharmaceutical products will be protected by a trademark on the drug's name, symbol or logo. The trademark owner can, as a result, exclude others or negotiate a license agreement using the drug's name, symbol or logo. The trademarked drug may additionally be a brand where the trademark carries social and commercial significance. In contrast to a patent, a trademark may — if regularly prolonged — continue indefinitely.

Marketing a pharmaceutical product aims at establishing the trademark so that sales continue after patent protection has lapsed. This includes managing pricing and discounts strategically to further acceptance by the population where competition occurs among patented products and between patented and generic products.

The trademark without the patent and the required marketing authorization may have limited value since the product cannot be sold without authorization resulting from successful R&D activities.

Instead of focusing on the trademark, alternative marketing strategies revolve around establishing generic or biosimilar products as a brand or investing heavily in the brand value of the originator company.

ii. Brand/global brands

Brands can generate market share, increase customer loyalty, offer the potential for higher profit margins and guard against competitive attacks.[90] Branding can help to create a unique and valuable marketing intangible. This is not present in otherwise comparable uncontrolled transactions. It can generate a significant premium for the product (section 6.2.4.3 of the UN TP Manual).

Pharmaceutical MNEs use advertising, marketing and promotion activities to establish brand awareness and product loyalty. Given the high costs of bringing a drug through the R&D and regulatory processes, branding is critically important to drive value and generate sales. Some branded drug products become so-called blockbuster drugs that are globally recognized as best-in-class solutions to particular diseases or conditions. Global sales of the leading blockbuster drug reached $37.8 billion in 2022.[91]

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90 J-B. Steenkamp (2014). How Global Brands Create Firm Value: The 4V Model. International Marketing Review 31(1): 5–29

91 S. J. Haakonsson (2009). The Changing Governance Structures of the Global Pharmaceutical Value Chain. Competition and Change 13(1): 75–95. For a list of the top 20 blockbuster drugs in 2022, see D. Chandel, V. Xie and V. Kovacevic (2023). Top 20 Drugs in 2023, by 2022 Sales Statistics.

Branding can create an important competitive advantage for national or regional pharmaceutical companies by building brand awareness, loyalty and perceptions of quality.[92] In India, creating brand awareness of national generic drugs has been a major value driver in the country's pharmaceutical industry.[93] Perceived quality correlates positively to present market value and expected future potential.[94]

iii. Customer lists, relationships and proprietary data

A pharmaceutical product that requires a prescription will generally be marketed to healthcare providers, such as physicians, pharmacists and health insurance organizations. This often entails the development of a customer list. In performing the marketing function, the sales force carries out the detailing function described in section 2.5, and may additionally develop relationships with physicians, hospitals, pharmacists and health insurance organizations. In performing marketing activities, proprietary market data such as sales figures, customer demographics, therapy preferences and market research may also be generated.

3.1.3. Marketing authorization

To market and sell pharmaceutical drugs in most countries, firms must generally register and receive approval from the national medicines regulatory authority.[95] In the registration process, the firm provides information about a given drug and where it was manufactured. The regulatory authority evaluates the firm's data and scientific evidence on the drug's effects, based on a rigorous testing process, and decides whether to grant permission to market and sell the drug in that country. Once marketing approval has been received, the product can be manufactured and sold.

Retaining market authorization in a particular country often requires specific follow-up activities such as phase 3B clinical trials and phase 4 marketing surveillance surveys (sections 2.3.2 and 2.3.3).

A marketing authorization is based on the quality and efficacy of the underlying drug and the quality of the regulatory file in line with national regulations. It also creates a barrier to entry for competitors that do not have one.

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92 S. K. Panchal, B. M. Khan and S. Ramesh (2012). Importance of Brand Loyalty Brand Awareness and Perceived Quality Parameters in Building Brand Equity in the Indian Pharmaceutical Industry. Journal of Medical Marketing: Device, Diagnostic and Pharmaceutical Marketing 12 (March).

93 S. Nath Sanyal, S. K. Datta and A. K. Banerjee (2013). Conceptualizations of Branding: Strategy Based on the Indian Pharma Sector. International Journal of Pharmaceutical and Healthcare Marketing 7(2): 175–198.

94 S. Nath Sanyal and S. K. Datta (2011). The Effect of Perceived Quality on Brand Equity: An Empirical Study on Generic Drugs. Asia Pacific Journal of Marketing and Logistics 23(5): 604–625.

95 European Medicines Agency, marketing authorization. Available at: https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation.

3.1.4. Know-how

While pharmaceutical companies in the past focused on protecting an API and its products, they now increasingly seek additional patent protections on related know-how, such as that related to manufacturing processes. This is especially relevant when production is scaled up from small batches needed for clinical trials. Manufacturing know-how has been called the most difficult asset to evaluate, due to its slippery and ambiguous nature. As a result, know-how is often protected by trade secrets rather than process patents.[96]

3.1.5. Digitalization

In the coming years, digitalization is expected to transform the pharmaceutical industry in the following ways:[97]

- Pharmaceutical manufacturing is expected to shift from batch to continuous manufacturing, affecting plant locations (section 2.4.3).
- Artificial intelligence and machine learning are projected to lead to massive changes in the R&D landscape with the potential for spurring innovations while saving costs.
- Blockchain technology may transform the supply chain management of the pharmaceutical industry.
- Big data and analytics could improve patient healthcare and the operational efficiency of the manufacturing process.

As digitalization progresses, it will have an impact on tax and transfer pricing matters. For example, questions on how to distinguish between "traditional" and artificial intelligence-generated value creation in R&D will emerge, along with the need for analysis on how to allocate the created value between or among related parties. In terms of data, questions of which related entity owns data generated, for example, based on stock levels or through the use of healthcare apps by patients, may also have to be closely analysed for transfer pricing purposes.

3.2. Business Models in the Pharmaceutical Industry

3.2.1. Organizational structures

As noted in section 1.3.2.1 of the UN TP Manual, to perform a transfer pricing analysis, it is crucial to understand the management and organizational structure of an MNE. The organizational structure may or may not be fully aligned with the legal

96 R. M. Visconti. (2013). Evaluating Know-How for Transfer Price Benchmarking. Journal of Finance and Accounting 1(1): 27–38.

97 Y. J. Siddiqui (2019). Transfer Pricing and Value Creation in the Pharmaceutical Sector. In R. Petruzzi and R.J.S. Tavares, eds., Transfer Pricing and Value Creation. See also G. Hole, A. S. Hole and I. McFalone-Shaw (2021). Digitalization in Pharmaceutical Industry: What to Focus on Under the Digital Implementation Process? International Journal of Pharmaceuticals X(3): 10095.

structure. For example, one legal entity may house employees assigned to different management teams or operational divisions. Alternatively, a management team or division may employ individuals or use assets housed in different legal entities.

Some MNEs may be organized into a functional structure, where each entity in the group is staffed with employees responsible for a particular function (e.g., R&D, manufacturing, distribution). Other firms may be organized by product lines where each entity is responsible for all the stages along the value chain for a particular product line (e.g., motorcycles, cars and trucks). A third common structure is by geography, either by country or region. Matrix structures, which are organized by product line and geography, are perhaps the most common organizational structure for large MNEs. For more details, see section 1.3.2 of the UN TP Manual.

In large matrix organizations, such as many of the world's leading pharmaceutical multinationals, the MNE typically consists of multiple related businesses and the global operating model is based on a three-way matrix structure of products, geographies and functions.

3.2.2. Business models

All companies, national and multinational, have an enterprise operating model[98] or business model[99] 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 the value chain of providing products or services to the 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 being able to respond to national or regional consumer tastes and incomes. For example, the choice to centralize a function in one entity or location within the MNE group or to have multiple entities or locations performing the same activity will be affected by the trade-off between the cost savings of global integration relative to the benefits of being nationally responsive to differences across countries in, for example, consumers, markets and regulations.[100]

Today, MNEs use many types of business models; see the discussion in sections 1.3.3.11 through 1.3.3.17 of the UN TP Manual. The range of possible operating/

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

99 M. van Herksen (2009). Business Models. In A. Bakker, ed., Transfer Pricing and Business Restructurings: Streamlining All the Way, chapter 2. International Bureau of Fiscal Documentation.

100 Eden, Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America.

business models runs from a centralized one to a loosely held holding company or conglomerate. In between, there are models consisting of closely or loosely related portfolios of businesses.[101] The type of business model may have implications for the form of related party transactions. For example, an MNE with a centralized business model is likely to have one or more entities providing centralized intragroup services (see the UN TP Manual, section 5.2.4).

i. Centralized business model

Starting in the late 1990s, the largest and most global MNEs in industries such as fast-moving consumer goods and pharmaceuticals began to adopt a "centralized business model" or "principal structure".[102] To manage the complex matrix of products, geographies and functions associated with their global value chains and related risks, these MNEs adopted a tiered and nested organizational design. In addition to the parent firm, one or more "principals" function as entrepreneurial entities for each geographical region within the MNE network. The principals have oversight responsibility for entities within that region.

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 marketing the global brand(s), regional entities responsible for marketing regional products, and national marketing teams overseeing national products and fine-tuning for national needs and incomes.[103] For more information on centralized services within the MNE group, see section 5.2.4 of the UN TP Manual.

Figure 7 provides a simple illustration of an MNE with a centralized business model in the pharmaceutical industry. The parent firm is the headquarters for the MNE group and the ultimate trademark and intellectual property owner.

Within the parent entity are departments and/or national affiliates responsible for strategic management, regulatory affairs and support services, in addition to entities that carry out primary activities in the value chain (R&D, primary and secondary manufacturing, marketing and distribution). The parent firm may have one or more regional principals with responsibility for the intellectual property and trademarks in their region. Each principal has its own regulatory affairs, marketing and support services functions, and owns and/or has responsibility for national entities within the region. The national entities may be distributors responsible for their own markets but may also take on other roles such as

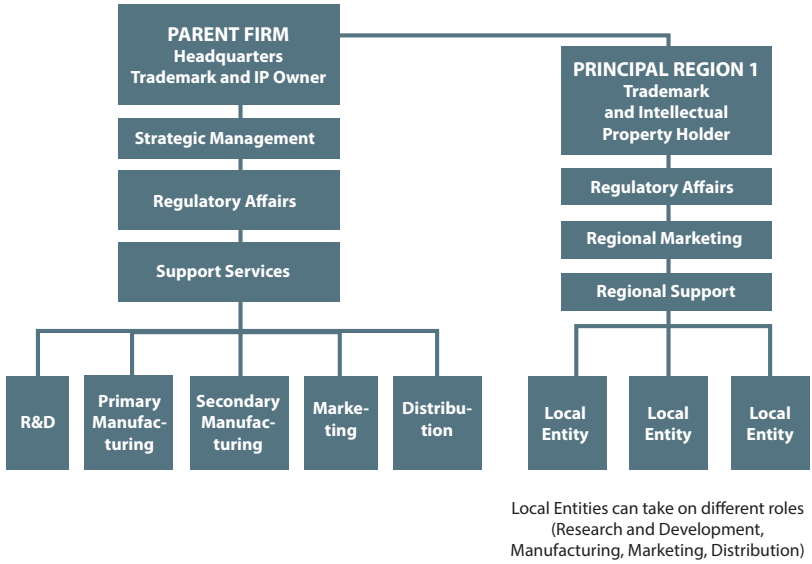
101 Kates, Kesler and DiMartino, Networked, Scaled and Agile: A Design Strategy for Complex Organizations.

102 van Herksen, Business Models. See also Y. Hervé and L. Eden (2023). Shapley Value in Dispute Resolution: Lessons in Transfer Pricing from a Life Sciences MNE. Tax Notes International 112 (6 November): 753–768.

103 Kates, Kesler and DiMartino, Networked, Scaled and Agile: A Design Strategy for Complex Organizations.

clinical testing, secondary manufacturing, and national or regional marketing.[104] As discussed above, a highly stylized business model is described here. It is essential to understand and analyse the organizational structures in each MNE group.

Figure 7: Example of a pharmaceutical multinational enterprise with a centralized business model



ii. 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.[105] Each subsidiary specializes in a particular therapeutic class, 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, may result from the acquisition of independent biotech and/or pharmaceutical businesses, which remain mostly stand-alone in terms of their activities after acquisition.

104 On the business models of MNEs in the life sciences industry, see also Hervé and Eden, Shapley Value in Dispute Resolution: Lessons in Transfer Pricing from a Life Sciences MNE. It is important to note that this discussion is of highly stylized business models, which may not fully reflect the real-life complexities of a large pharmaceutical MNE operating across borders.

105 A. Nover, L. Anderson and P. Jacquet (2022). The Hub-and-Spoke Model: An Emerging Biopharma Trend. LEK Consulting. See also Global Business Reports: US Pharmaceuticals & Biopharmaceuticals (2021). Hub and Spoke: A New Model to Cure Disease.

Being commonly controlled by a risk-bearing parent firm, however, offers potential benefits, such as greater focus, operational efficiency, financing and risk mitigation compared to a set of uncontrolled businesses. Management and financing activities as well as transfer pricing and taxation may be managed centrally, permitting more flexible financing and the pooling of risks and resources.

iii. Strategic alliances

Strategic alliances among firms are common in most industries, including pharmaceuticals. 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:[106]

- A joint venture: A common business model is for a pharmaceutical company to be the "discovery" firm and to align with another company in an international joint venture. The partner firm commercializes and sells the final product. A typical joint venture might involve a biotechnology firm that does not have access to a distribution network and so chooses to ally with a pharmaceutical firm.
- A 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-development agreements: Both firms jointly engage in one or more R&D projects at the development stage (e.g., clinical testing).
- A co-promotion arrangement: Both firms promote the product under the same brand name.
- A contract R&D arrangement for manufacturing, license and supply agreements.

3.2.3. Business models and location decisions

The basic R&D and pre-clinical testing activities of an MNE historically have been centralized in the country of the headquarters or one or more countries with regional headquarters.[107] Clinical testing stages may take place in several strategic locations, reflecting the need to test drugs on populations with different demographic characteristics and/or domestic health and safety requirements. Contract R&D activities, which are carried out under the guidance and for the benefit of the parent company,

106 Wündisch, Transfer Pricing in the Ethical Pharmaceutical Industry, appendix Q.

107 See the historical overview provided in Shivdasani et al. The Geography of Prescription Pharmaceuticals Supplied to the USA. See also C. Baxerres and M. Cassier (2022). Introduction: Pharmaceutical Markets in the Global South: Shaped by History and Multiple Regulations. In C. Baxerres and M. Cassier, eds., Understanding Drugs Markets: An Analysis of Medicines, Regulations and Pharmaceutical Systems in the Global South. Routledge. See also M. Cassier (2022). A New Geography of Pharmaceuticals: Trajectories of Artemisinin-Based Medicines. In Baxerres and Cassier, eds., Understanding Drugs Markets, chapter 5.

often take place in countries that have science or R&D parks and that encourage local R&D activities.

The location of the secondary manufacturing stage is typically dispersed across countries, partly due to government regulations that require national or regional preparation and packaging but also to take advantage of lower-cost locations. Tax policies have been used to attract secondary manufacturing in the pharmaceutical industry.[108] This stage may also be outsourced to third parties through contract manufacturing, for example where pharmaceutical MNEs lack sufficient resources for in-house manufacturing facilities or prefer to focus on R&D and outsource downstream activities.[109]

National and/or regional responsiveness, including being close to the customer, and adapting to national and regional markets and tastes, can be important factors driving the decentralization of marketing activities. Pharmaceutical MNEs are increasingly organized around their customers and pay more attention to national/regional responsiveness, which increases, for example, the need for and roles of national/regional medical liaisons.[110]

The type and extent of marketing activities carried out in a specific country depend on several factors. For example, whether the MNE has a centralized or decentralized business model can affect marketing activities in a particular country, as can government regulations. Factors such as the size and income level of an economy and the health profile and preferences of the population determine spending allocated to marketing in a specific jurisdiction. This is also the case for other downstream stages such as distribution, where national/regional responsiveness creates pressures to shift activities to market jurisdictions.[111]

In terms of regulatory activities, negotiations with governments and/or healthcare providers on products to be distributed, both to ensure marketing authorization and, if relevant, coverage by health insurance, are typically performed nationally and or regionally. This ultimately depends on the size, resources and degree of regulation of the pharmaceutical market. The medical attributes of products are generally managed globally by the MNE, as products are validated by health agencies based on their efficacy and safety.

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

109 BCC Research Staff (2021). Active Pharmaceutical Ingredients: Global Markets. BCC Publishing. Marketing strategies will vary between over-the-counter and prescription drugs. As noted in section 1.2., the former are typically sold in pharmacies, though some countries may also allow these products to be sold in drugstores, supermarkets or convenience stores.

110 J. Ascher et al. (2018). From Product to Customer Experience: The New Way to Launch in Pharma. McKinsey & Company.

111 Eden, Taxing Multinationals: Transfer Pricing and Corporate Income Taxation in North America.

A key issue for both MNEs and government health authorities, as identified by WHO, is the shortage of healthcare workers worldwide and the imbalance between needs and supplies. Recent surveys of pharmaceutical education and links with the health needs of populations and national priorities illustrate disparities in the presence of skilled healthcare workers across countries.[112]

112 WHO (World Health Organization). (2016). Global Strategy on Human Resources for Health: Workforce 2030. Geneva. See also A. Etukakpan et al. (2023). Transforming Pharmaceutical Education: A Needs-Based Global Assessment for Policy Development. Exploratory Research in Clinical and Social Pharmacy 9 (February): 100234. See also N. Konduri et al. (2017). Individual Capacity Building Approaches in a Global Pharmaceuticals System Strengthening Program: A Selected Review. Journal of Pharmaceutical Policy and Practice 10: 16.

4. Transfer Pricing Analysis

4.1. Overview

The industry background provided in this guidance can aid in conducting a transfer pricing analysis within the pharmaceutical industry, starting with a comparability analysis. Section 3.1 of the UN TP Manual describes a comparability analysis as including 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
  - 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 the prices and other conditions in uncontrolled transactions taking place under comparable circumstances; the latter are referred to as "comparable uncontrolled transactions" or "comparables"

Comparability analysis is used in selecting the most appropriate transfer pricing method and 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 involves the accurate delineation of the transaction, which entails defining a transaction (or group of transactions) between two or more commonly controlled entities (typically, affiliates in an MNE group). Defining and accurately delineating the relevant transaction(s) frames the scope of the transfer pricing analysis and the application of the arm's length principle, since the arm's length price for a transaction between two or more associated enterprises must be based on the actual transaction (or transactions) between the related parties.

The examination of the controlled transaction involves analysing the written contract, as a starting point, as well as the conduct of the parties and other relevant factors. 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. For multiple transactions, the transfer pricing professional must also decide whether the transactions should be evaluated separately or can be reasonably aggregated.

Accurately delineating transactions can be very complex in the pharmaceutical industry, as key activities in relation to economically significant risks may be fragmented across different entities within a multinational group. A regulatory structure affecting all stages of the global value chain requires tax auditors to have detailed knowledge of the industry and to consider the business model of the taxpayer (section 3.2), which is often very complicated and highly integrated. Contractual arrangements may be difficult to analyse due to their technical nature and language.[113]

4.2.1. Industry and market context

The transfer price of a particular pharmaceutical product in a given market is affected by market conditions, such as the level of competition (from other firms and substitute products); the need for complementary products; the income levels of buyers and so on. This section focuses on aspects specific to the pharmaceutical industry, including price controls and cost containment measures, parallel imports and business strategies in relation to patents.

i. Price controls and cost containment measures

Some countries establish drug price controls or government rules that regulate the prices of certain pharmaceutical formulations.[114] These may entail, for example, imposing a cap on prices of certain medicines and/or controlling the volume to be sold. Price controls are generally used to manage national healthcare costs.[115]

In some countries, insurance may exist for certain prescribed pharmaceutical drugs, or 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 cheaper generic drugs if an off-patent drug has been prescribed.

In performing a transfer pricing analysis, price controls will need to be examined on a case-by-case basis.

ii. Parallel imports of pharmaceutical products

Parallel imports refer to branded goods brought into a market and sold there without the trademark owner's consent.[116] Parallel imports originate as genuine products manufactured under the official license of the original trademark owner and destined for a particular jurisdiction.[117] Parallel importing occurs when there is a

113 Siddiqui, Transfer Pricing and Value Creation in the Pharmaceutical Sector.

114 Price ceilings may not affect the markets in general and their volumes in particular if the ceilings are higher than the market equilibrium price; in such cases, the price ceilings are non-binding.

115 On price controls, see the UN TP Manual, sections 2.4.2.4, 3.4.5.3, 3.4.5.15 and 3.4.5.16.

116 See the International Trademark Organization on Parallel Imports, available at https://www.inta.org/topics/parallel-imports/.

117 F. Kamuzora and A. Issaias (2018). Parallel Imports Remain a Grey Area for IP Rights in East Africa. Bowmans.

material price difference for the same product between two jurisdictions. The price difference encourages additional purchases in the first jurisdiction that are destined for sale in the second jurisdiction.

An important concept for parallel imports is the exhaustion of intellectual property rights, which refers to the extent to which a rights holder can control the distribution of trademarked goods.[118] According to the concept of intellectual property rights exhaustion, once a rights holder sells a product to which its rights are attached, those rights are exhausted.

Parallel importing may force the distribution subsidiary of an MNE in the second country to compete in its market with third parties selling the identical pharmaceutical product at a lower price. In some countries, parallel imports may even be fostered through regulatory provisions aimed at containing healthcare costs. Parallel trade regulations[119] encourage the free movement of identical products among countries to encourage competition and reduce prices. Since parallel imports are obtained from a foreign jurisdiction at a price lower than the corresponding prices in the destination jurisdiction, parallel importing usually results in decreasing revenues/margins for the distribution subsidiaries of the MNE.

Parallel imports raise important transfer pricing issues related to the remuneration of distribution subsidiaries. A first issue is whether and to what extent the transactions of the third-party parallel importer can function as comparable transactions for the controlled transactions of the distribution subsidiary. An associated pharmaceutical distributor in a country where parallel imports are made available has no control over the quantities or volumes 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 underlying facts and circumstances in terms of the comparability of functions carried out, assets used and risks borne by the subsidiary vis-à-vis the parallel importer.

A second issue arises in cases of a material impact from parallel imports on the subsidiary's remuneration. In this case, there is a question as to which entity should assume the market risk (that is, the lost profits from parallel imports) and to what extent any potential impact needs to be accounted for in the remuneration of the subsidiary under the arm's length principle. This will depend, for example, on the risk profile of the distribution subsidiary and the contracts and regulations in place.

Lastly, the question arises as to whether and to what extent the marketing efforts of the distribution subsidiary also generate benefit for the parallel imports. As the parallel imports were produced by the same MNE group, the parallel importer's sales are ultimately to the benefit of the group. This fact alone, however, should not lead to a transfer pricing adjustment for the distribution entity. Instead, the actual transaction(s) need to be first delineated and then priced using an appropriate transfer pricing method.

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118 See the International Trademark Organization on Parallel Imports.

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

iii. COVID-19 pandemic

As in other industries, pharmaceutical companies have faced disruptions in their business models (positive and negative) caused by the COVID-19 pandemic, including value chain interruptions, stalled regulatory responses/approvals, and slowdowns in some patient procedures such as non-emergency surgeries and infusion therapies.[120] The pandemic also brought about an unprecedented level of collaboration between the pharmaceutical industry and governments.[121] For more details, see the guidance on transfer pricing during the COVID-19 economic downturn.[122]

4.2.2. Business strategies

The transfer price of a particular pharmaceutical product in a given market is affected by the firm's business strategies, especially patent and marketing strategies.

i. Business strategies for patents

In recent decades, two concepts around patents have gained traction: the "patent cliff" and "patent life cycle management."[123] The "patent cliff" refers to the potential sharp drop in expected profits after a patent for a firm's product expires. Once the product is "off patent", it faces more competition from existing branded products and from rival firms producing and selling generics or biosimilars. The additional competition reduces sales, market share and profitability. Patent cliffs generally result in lower revenues for originator companies. The effect varies across countries, depending on patent expiry dates, the degree and speed of market penetration by generics, and the extent of customer loyalty to originator products.[124]

In developed economies, patent expiry typically leads to an 80 per cent market share loss for the formerly patented drug and a 20 to 30 per cent reduction in the drug's price, with a further price decrease with each additional generic entrant. In some

120 On the pharmaceutical industry during COVID-19, see IQVIA Institute (2023). Global Use of Medicines 2023: Outlook to 2027. For the application of GAAP (generally accepted accounting principles) and IFRS (international financial reporting standards) to the pharmaceutical industry during COVID-19, see Deloitte (2023). Life Sciences Industry Accounting Guide.

121 L. C. Druedahl, T. Minssen and W. N. Price (2021). Collaboration in Times of Crisis: A Study on COVID-19 Vaccine R&D Partnerships. Vaccine 39(42).

122 United Nations (2025). Transfer Pricing During the COVID-19 Economic Downturn. New York, NY: United Nations.

123 For evidence of the effects of the patent cliff in Kenya, see F. Khalil and J. O. Onyango (2019). Effect of Patent Expiry on the Performance of Innovator and Multinational Pharmaceutical Companies in a Low Middle Income Country. Frontiers in Medical Technology 4: 783460.

124 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.

cases, the price of the formerly patented drug decreases by up to 90 per cent.[125] The fall in prices may be less severe in developing countries where off-patent branded drugs may continue to dominate local markets.[126]

Patent life cycle management refers to extending patent protection by filing secondary product patents on a new formulation (changes in tablet forms, dosage amount, etc.) or a new method of use, or new process patents on manufacturing techniques.[127] Viewed from the perspective of barriers to entry, attempts to extend patent life can be viewed as evergreening or 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.[128]

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").

ii. Business strategies in relation to marketing intangibles

In the pharmaceutical industry, as in most industries, a combination of marketing activities may be performed within an MNE group. Entities in the group may conduct marketing activities that reflect those performed by independent entities. They may also perform marketing activities not performed by independent entities, such as modifications of marketing material developed centrally for the group. Marketing by an entity belonging to a pharmaceutical MNE in a specific country may result in incurring marketing expenses. Depending on the success of the marketing activity, it may generate a valuable marketing intangible.

Section 6.2.4.5 of the UN TP Manual states that, depending on the facts and circumstances, the marketing activities of a distributor may have 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;

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

126 Khalil and Onyango, Effect of Patent Expiry on the Performance of Innovator Multinational Pharmaceutical Companies in a Low Middle Income Country.

127 Y. Lee and E. A. Fong (2020) Patent Lifecycle Management Strategies in Open Innovation Projects. Drug Discovery Today 25(10).

128 This practice is also referred to as evergreening and innovation or patent harvesting. See A. Kumar and A. Nanda (2017). Ever-greening in Pharmaceuticals: Strategies, Consequences and Provisions for Prevention in USA, EU, India and Other Countries. Pharmaceutical Regulatory Affairs 6:1.

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;

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.

4.3. Performing a Functional Analysis

As noted above, taxpayers need to undertake a thorough functional analysis as a cornerstone of their transfer pricing analysis. The 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 as well as the assets employed and risks assumed by each entity. This will affect the arm's length remuneration for the controlled transaction, since compensation for transactions between two independent enterprises will usually reflect the functions that each performs, taking into account assets employed and risks assumed.

The following examples look at the possible functions performed, assets utilized and risks assumed of a controlled entity in a particular tax jurisdiction. These depend on the entity's location within the MNE global value chain and its roles and responsibilities within the multinational group.

Functions that the controlled taxpayer may perform include:

- Corporate strategy formulation
- Distribution and sales activities
- Finance, accounting, treasury and legal
- General management functions
- Human resources management
- Intragroup services (e.g., legal, accounting, information technology)
- Inventory management
- Manufacturing, production, assembly and process engineering
- Market development
- Market intelligence on technological developments
- Marketing, advertising and promotion activities

- Post-sale activities including the supply of replacements
- Product design and engineering
- Product development
- Purchasing, materials management and other procurement activities
- Quality control
- Research and development activities
- Technical assistance
- Testing and quality controls
- Transportation, warehousing and inventory

In terms of assets, the core value drivers in the pharmaceutical industry are R&D and patents, marketing intangibles, marketing authorization, know-how and digitalization (section 3.1). Assets and other complementary factors that may be owned or controlled by the controlled taxpayer include:

- Intangible assets
  - Brand, including trademarks, trade names, and logos
  - Customer lists and relationships
  - Patents and licensing rights
  - Product registration, market authorization and regulatory approvals
  - Proprietary market data
  - Technical know-how
  - Trade secrets
- Tangible assets
  - Land, buildings and warehouses
  - Property, plants and equipment
  - Natural resources
  - Office equipment
  - Vehicles
- Other/complementary factors
  - Distribution network
  - Goodwill
  - Workforce in place[129]

129 While workforce in place is not an intangible asset in the UN TP Manual, the existence of a qualified and skilled workforce is likely to be an important complementary factor that can positively affect the profitability of the pharmaceutical industry in a particular country. See the UN TP Manual, sections 6.2.5.14 through 6.2.5.19.

In terms of risks for the controlled taxpayer, an entity in an MNE group that assumes economically significant risks (often an entrepreneur) would be expected to take on both upside and downside consequences of those risks. Possible risks include:[130]

- Bad debt risk
- Disruptions in supply continuity, supply shortages
- Country/regional risk
- Credit and foreign exchange risk
- Financial risk
- Integration and success of acquisitions and alliances
- Managerial and operational efficiency
- Manufacturing quality standards
- Market competition in terms of patent protection and generic/biosimilar entries
- Market risk
- Changes in pricing and reimbursement policies, cost-containment measures
- Product liability risk
- R&D success
- Regulatory risk
- Reputation risk
- Purchasing, materials management and other procurement activities
- Quality control
- Research and development activities
- Technical assistance
- Testing and quality controls
- Transportation, warehousing and inventory

130 Paumier, Transfer Pricing in the Pharmaceutical Industry. See also M. Jaberidoost et al. (2013). Pharmaceutical Supply Chain Risks: A Systematic Review. DARU Journal of Pharmaceutical Sciences.

5. Transfer Pricing Examples

5.1. Example 1: When the Comparable Uncontrolled Price Method May Not Be the Most Appropriate

5.1.1. Overview

Company A (resident in Country X) is a vertically integrated pharmaceutical firm that engages in R&D and manufactures a prescription drug that it distributes under the trademark DAY as well as under a generic trade name. It operates around the world through wholly owned subsidiaries and independent distributors.

Company B (resident in Country Y) is a wholly owned subsidiary of Company A. The patent for DAY in Country Y expired two years ago so the product is off patent. Company B has a non-exclusive contract with Company A to import DAY in finished form and to market and sell it to pharmaceutical wholesalers in Country Y. Company B operates in the main cities of Country Y, where the government does not regulate prices for prescription drugs.

Company A also sells the drug under a non-exclusive contract to independent pharmaceutical distributors in Country Y that distribute it to drug wholesalers in rural centres. The independent distributors do not have the right to use the trademark DAY, so they sell the product under a generic trade name.

Company B performs a transfer pricing analysis to determine whether the generic drugs may be used as comparables for DAY. The transfer pricing question at issue is the appropriate transfer price that Company B should pay Company A for its purchases of DAY.

5.1.2. Facts

Company B pays Company A $20 per pack of DAY; each pack contains 25 30-milligram tablets. The price paid by the independent distributors to Company A for the unbranded identical drug is $5 per pack; the pack size and tablet strength are the same.

The product sold by Company A to Company B and to the uncontrolled distributors in Country Y has the same chemical properties (e.g., API, chemical composition, efficacy).

The independent distributors and Company B have similar sales volumes in Country Y. They use the same currency to purchase Company A's products.

5.1.3. Determination of the transfer price

Company B conducts a transfer pricing analysis to accurately delineate the transaction and determine the most appropriate transfer pricing method. Both bioequivalence

and bioavailability are important product characteristics that may affect the arm's length transfer price (section 1.2.1). The firm concludes that DAY and its generic competitors have the same chemical compositions (i.e., the same bioequivalencies) and the same uses or effects (i.e., the same bioavailabilities).

Company B also concludes, however, that there are material differences between the controlled and uncontrolled transactions:

— The DAY trademark is valuable. It has high name recognition with physicians and patients and stands for an effective product that is efficient and safe. As such, physicians and patients are willing to pay a premium price for the trademarked product. The uncontrolled purchasers cannot use this trademark and must sell their product under a generic label.

Company B concludes that the transactions between Company A and the unrelated distributors cannot be used as internal comparables under the Comparable Uncontrolled Price (CUP) Method to determine an arm's length transfer price for DAY. While the API is identical for DAY and the drug sold to the independent distributors, the valuable trademark is a key difference. Company B finds that reliable adjustments cannot be made to account for such differences. It concludes that the CUP Method is not the most appropriate transfer pricing method for DAY.

5.2. Example 2: Application of the Transactional Net Margin Method to a Distributor Using a Porfolio Pricing Strategy

5.2.1. Overview

PAR Co., resident in Country X, is the parent firm of the East Group, which manufactures non-prescription pharmaceutical products. East Group's product range includes products for headaches, pain relief and anti-inflammation. The East Group sells its products through wholly owned distributors, which distribute to pharmacies and hospitals for over-the-counter sales.

PAR Co. has a wholly owned subsidiary, DIST Co., that is resident in Country Y, where it distributes East Group's products. DIST Co. imports five pharmaceutical products (products A through E) in finished form from other affiliates in the group and sells them to pharmacies and hospitals in Country Y. DIST Co. is responsible for promoting the five products in Country Y and also packages some of them.

The tax authorities in Country Y have commenced a review of Dist Co.'s transfer prices for the five pharmaceutical products purchased from other affiliates in the East Group.

5.2.2. Facts

Under the intercompany agreement, DIST Co. distributes five products (products A through E) to pharmacies and hospitals in Country Y. Some products are highly profitable; others are not. During the tax years in question, DIST Co.'s operating profit margin (OPM) was 8.1 per cent. Table 7 provides profit and loss data for the five products.

As the table shows, DIST Co. earns 13.7 per cent and 26.7 per cent operating margins on products A and B, respectively, and negative margins on products C, D and E.

Product E is not successful in Country Y (operating profit margin of -33.9 per cent) even though DIST Co. has incurred significant marketing costs ($3,200) for the product. The product, however, is profitable for the East Group in other countries. A financial forecast predicts that product E could be profitable in subsequent years.

Table 7: DIST Co.'s gross and net profit margins, by product line
(United States dollars)

Product	Net sales	Cost of goods sold (COGS)	Operating expenses (OE)	Earning before interest and taxes (EBIT)	Operating profit margin, percentage
A	90,000	45,000	32,700	12,300	13.7
B	1,500	300	800	400	26.7
C	2,400	1,200	1,600	(400)	-16.7
D	12,000	7,010	7,000	(2,010)	-16.8
E	4,000	2,155	3,200	(1,355)	-33.9
Total	109,900	5,665	45,300	8,935	8.1

5.2.3. Delineation of the transaction and selection of the transfer pricing method

DIST Co. hires an independent transfer pricing adviser to conduct a transfer pricing analysis for its products due to the upcoming transfer pricing audit. The adviser looks at intercompany contracts and prepares a functions, assets and risks analysis, concluding that the distributor performs two functions in addition to importing and distributing pharmaceutical products in Country Y:

- Some products are packaged by DIST Co. before the sale
- DIST Co. is responsible for promoting products

The tax adviser investigates whether DIST Co.'s marketing and promotion activities may be generating local marketing intangibles that should be considered. The adviser finds that the marketing department in Company A prepares promotional materials and one employee in Company B adapts and distributes them to the national market. The adviser concludes that there is insufficient evidence of local marketing intangibles.

The adviser finds that accurate delineation of the transaction, based on the contract terms, the conduct of the parties and all other economically significant characteristics, would consider Company B a full-fledged distributor that sells a range of pharmaceutical drugs purchased from Company A. The CUP Method cannot be applied as there are no internal or external comparables.

DIST Co. performs primarily marketing and distribution functions, except for packaging, which the adviser views as a routine activity. The adviser considers whether the Resale Price Method (RPM) using the ratio of gross profit to sales could be an appropriate transfer pricing method and looks for other distributors that perform comparable functions and assume comparable risks.

Two independent pharmaceutical distributors, BLUE Co. and GREEN Co., are listed on the stock exchange in Country Y. As a result, their EBIT and sales data are publicly available. GREEN Co. distributes products to relieve headaches and reduce inflammation. BLUE Co. distributes weight-loss products, anti-allergy tablets and vitamin tablets.

The adviser concludes that both companies are sufficiently similar to DIST Co. as distributors and operate in the same market under sufficiently similar conditions. Publicly available financial information on BLUE Co. and GREEN Co. is limited, however. For example, information on either firm's gross profit or operating expenses is not available, making it impossible to calculate the gross profit margins. The adviser concludes that the RPM cannot be applied.

Noting that DIST Co. is the simpler of the two related parties and does not own any unique and valuable intangibles, the adviser concludes that the most appropriate transfer pricing method is the Transactional Net Margin Method (TNMM), and that the appropriate profit level indicator (PLI) is the operating profit margin (OPM), using the EBIT-to-sales ratio.

5.2.4. Application of the Transactional Net Margin Method

The transfer pricing adviser compares the operating profit margins of DIST Co. with those of the unrelated distributors. GREEN Co.'s operating profit margin is 6.5 per cent and BLUE Co.'s is 8.5 per cent. Since DIST Co.'s overall operating profit margin is 8.1 per cent, the adviser finds that this is overall at arm's length. The adviser notes the following points to support this conclusion.

While it is preferable to determine the profit level indicator by transaction or product line, no such information is available for the unrelated parties GREEN Co. and BLUE Co. Therefore, it is appropriate to aggregate DIST Co.'s five product lines and determine its appropriate profit level indicator accordingly. Moreover, the product-line breakdown for DIST Co. is based on a simple apportionment of overheads and other indirect costs, making it difficult to determine product level profits with a high degree of accuracy.

DIST Co. submits the transfer pricing study prepared by its adviser to the tax authority in Country Y. The tax authority investigates whether DIST Co. is engaged in additional activities over and above packaging, such as manufacturing. It concludes that the only additional function is packaging, which does not require separate remuneration. After studying the report, the tax authority agrees with the accurate delineation of the transaction, and that the TNMM is the most appropriate method and the operating margin the appropriate profit level indicator. The tax auditor also accepts the conclusion of the company's adviser that DIST Co.'s overall EBIT of 8.1 per cent on its product portfolio is arm's length.

5.3. Example 3: Transfer Pricing Involving a Possible Local Marketing Intagible

5.3.1. Overview

PAR Co. is the parent firm of the West Group, a pharmaceutical multinational that produces a well-known drug for treating ulcerative colitis under the trade name CURE. CURE is manufactured by PAR Co., which owns the intangibles (e.g., the trademark, patents and intangible property from clinical trials) as well as the API. PAR Co. has developed a proprietary formulation that can deliver the same medication as its competitors but in small tablets, whereas its competitors' products are sold in granular or large tablet formulations. Moreover, CURE can be taken once a day whereas other products must be taken twice a day.

DIST Co. (resident in Country Y) is a wholly owned subsidiary of the West Group that distributes CURE to wholesalers that supply hospitals and pharmacies in Country Y. The number of these wholesalers is limited, and they have non-exclusive relationships with pharmaceutical manufacturers. Over time, DIST Co. has been able to forge an effective relationship with them.

Activities undertaken by DIST Co. in Country Y include advertising, marketing and promotion. DIST Co. has a dedicated sales force that visits and promotes CURE with physicians who specialize in treating ulcerative colitis. Over time, the sales force has done research and collected data on specific patient and physician preferences that are highly relevant for marketing and sales.[131] While physicians tend to prefer granular formulations, for example, DIST Co.'s sales force has learned that patients prefer small tablets and taking the medication once a day rather than twice a day. Further, patients taking small tablets once a day are much more likely to adhere to the treatment, leading to a higher treatment success rate with CURE compared to competitors' products. DIST Co.'s sales force has shared its research with Country Y's physicians and developed an in-house marketing policy that stresses its findings. Success in persuading physicians that CURE is preferable to competing products has resulted in a growing market share for CURE in Country Y.

The tax administration in Country X is preparing to audit DIST Co. and wants to ascertain whether DIST Co. may be the owner of a local marketing intangible.

5.3.2. Analysis

In determining whether the marketing activities of DIST Co. created a local marketing intangible, the tax authority should consider several factors.

The first task is to accurately delineate the controlled transactions, including by examining the contract, conduct of the parties and other economically significant facts.

If DIST Co. is and has always operated by merely following detailed orders from other members of the group, then the accurate delineation would be that DIST Co. is

131 G. J. Buckley and L. O. Gostin, eds. (2013). Countering the Problem of Falsified and Substandard Drugs. Washington, DC: National Academies Press.

providing advertising, marketing and promotion services. To the extent that a local marketing intangible has been created, important DAEMPE functions are being performed elsewhere, not by DIST Co.

In contrast, if DIST Co. develops a strategy based on its own expertise and experience in Country Y, then the accurate delineation would be that to the extent an intangible has been created, DIST Co. is performing the important DAEMPE functions. The transfer pricing method and ultimately the arm's length outcome should reflect the DAEMPE functions.

An issue for consideration is whether the activities of DIST Co. have led to the creation of an intangible that is separate and distinct from, or tied to, the foreign-owned brand (UN TP Manual, section 6.2.4.4). It may be argued that the activities of its local sales force have created a valuable local marketing intangible that has aided in the commercial exploitation of the foreign-owned brand CURE in Country Y. This local intangible includes customer lists, close relationships with physicians and wholesalers, and proprietary market and customer data (UN TP Manual, section 6.2.4.1). The intangibles created have contributed substantially to the success of DIST Co. Another issue is whether these marketing intangibles are subject to intellectual property rights law (UN TP Manual, section 6.2.2.4).

Assuming a local marketing intangible has been created in Country Y, the next step is to determine which entities performed and controlled the important DAEMPE functions.

This example is not intended to be exhaustive or to offer a complete list of elements that may or may not constitute local marketing intangibles in the pharmaceutical industry. Tax administrations should analyse specific facts and circumstances, taking into account their knowledge of the domestic pharmaceutical industry and keeping in mind domestic legislation as well as relevant guidance on transfer pricing (UN TP Manual, section 6.2).

5.4. Example 4: Transfer Pricing of a Contract Research and Development Arrangement

5.4.1. Overview

Test Co., resident in Country Z, is a wholly owned subsidiary of the South Group. Test Co. is a contract R&D service provider that leases a laboratory in Country Z. It has staff qualified to carry out pharmaceutical R&D and expertise in the clinical testing of pharmaceutical products for safety purposes.

While Test Co.'s staff is qualified to undertake clinical testing, it does not make strategic and tactical decisions on the direction of R&D as it lacks the necessary qualifications, expertise, and managerial and technical skills. Test Co. uses state-of-the-art technology and protocols for its R&D work that are based on WHO guidelines.

Test Co. works exclusively for its parent firm, PAR Co., which is resident in Country X. Test Co. is treated for transfer pricing purposes as a service provider and

is compensated with reference to the Cost Plus Method with a 10 per cent mark-up over total costs.

The tax authority in Country Z audits Test Co. The question is whether it should be treated as a service provider and, if so, what is the appropriate transfer pricing method and transfer price for services provided to PAR Co.

5.4.2. Facts

PAR Co. and Test Co. have a written agreement that is updated annually. The contract is detailed and provides for remunerating Test Co. for its R&D work on an arm's length basis. Any intellectual property arising from Test Co.'s work is owned by PAR Co. under the contract.

Test Co. carries out its work as directed by the Head of R&D of Par. Co. who provides weekly instructions.

5.4.3. Selection of the most appropriate transfer pricing method

After a careful examination of the facts, the accurate delineation of the transaction is that Test Co. is an R&D service provider to the South Group.

As Test Co. works exclusively for PAR Co., there are no internal comparables to use in applying the CUP Method. Country X, however, has five independent companies carrying out R&D for the chemical and farming industries. These companies are listed on the stock exchange, making their financial information publicly available. They are considered comparable to Test Co. on the basis of a comparability analysis.

The auditor concludes that the TNMM is the most appropriate method. The appropriate profit level indicator should be net cost plus or operating profit divided by total costs.

6. Appendices

Appendix 1: 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.[132]
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.[133]
Bioavailability	A subcategory of absorption and 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 per cent. 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.[134]
Bioequivalence	Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and their bioavailabilities, in terms of the rate 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.[135]

132 G. J. Buckley and L. O. Gostin, eds. (2013). Countering the Problem of Falsified and Substandard Drugs. Washington, DC: National Academies Press.

133 European Medicines Agency. Glossary of Regulatory Terms. Available at: https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A.

134 Buckley and L. O. Gostin, eds., Countering the Problem of Falsified and Substandard Drugs.

135 WHO (World Health Organization), Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control), Glossary, available at: https://extranet.who.int/pqweb/content/glossary.

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.[136]
Biosimilar	A drug similar to a biological reference product and manufactured by a company other than the originator. Regulatory approval of biosimilars is technically possible following patent expiry of the reference product.[137]
Bulk product	Any pharmaceutical product that has completed all processing stages up to, but not including, final packaging.[138]
Clinical trial	A formal study carried out according to a prospectively defined protocol that is intended to discover or verify the safety and effectiveness of procedures or interventions in humans.[139]
Excipient	A pharmacologically inactive substance used along with the active pharmaceutical ingredients in the formulation of a medication.[140]
Generic pharmaceutical drug	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.[141]
Good clinical research practice	A standard for clinical studies that encompasses the design, conduct, monitoring, termination, audit, analysis, reporting and documentation of the studies, and that ensures they are scientifically and ethically sound and that the clinical properties of the pharmaceutical product (diagnostic, therapeutic or prophylactic) under investigation are properly documented.[142]

136 Nass, Madhavan and Augustine, eds., Making Medicines Affordable, appendix C.

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

138 WHO (World Health Organization), Prequalification of Medical Products.

139 Nass, Madhavan and Augustine, eds., Making Medicines Affordable, appendix C.

140 Buckley and L. O. Gostin, eds., Countering the Problem of Falsified and Substandard Drugs, appendix A. European Medicines Agency, Glossary of Regulatory Terms.

141 Ibid.

142 WHO (World Health Organization), Prequalification of Medical Products.

<table>
<tr><td>Good manufacturing practice</td><td>The part of quality assurance that ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.[143]</td></tr>
<tr><td>Industry classifications</td><td>National statistical agencies organize the pharmaceutical industry into separate industry groups based on the activity in which they are primarily engaged. For example, the North American Industry Classification System (NAICS) code organizes the pharmaceutical industry into five groups based on the similarity of their processes:[144]

<table>
<tr><td colspan="2">NAICS codes for pharmaceutical companies</td></tr>
<tr><td>236210</td><td>Pharmaceutical manufacturing plant construction</td></tr>
<tr><td>325199</td><td>Enzyme proteins (i.e., basic synthetic chemicals), except pharmaceutical use, manufacturing</td></tr>
<tr><td>325411</td><td>Enzyme proteins (i.e., basic synthetic chemicals), pharmaceutical use, manufacturing</td></tr>
<tr><td>325412</td><td>Pharmaceutical preparations (e.g., capsules, liniments, ointments, tablets) manufacturing; sodium chloride pharmaceutical preparations manufacturing</td></tr>
<tr><td>424210</td><td>Pharmaceuticals merchant wholesalers; radioactive pharmaceutical isotopes merchant wholesalers; specialty-line pharmaceuticals merchant wholesalers</td></tr>
<tr><td colspan="2">Source: United States Census Bureau, Introduction to NAICS, available at: https://www.census.gov/naics/?input=pharmaceutical&year=2022.</td></tr>
</table></td></tr>
<tr><td>Intermediate</td><td>A material produced during the processing of an active pharmaceutical ingredient that undergoes further molecular change or purification before it becomes an API.[145]</td></tr>
</table>

143 Ibid.

144 United States International Trade Commission, Covid-19 Related Goods: The U.S. Industry, Market, Trade and Supply Chain Challenges? Page 136.

145 WHO, Prequalification of Medical Products.

Marketing authorization	Also referred to as product licence or registration certificate. A legal document issued by the competent medicines regulatory authority authorizes the marketing or free distribution of a medical product in the respective country after evaluation of safety, efficacy and quality.[146]
National medicines regulatory authority	Responsible for the registration of and other regulatory activities concerning medical products, such as medicines, vaccines, blood products and medical devices.[147]
Over-the-counter drug	Medicine that does not require a prescription to be sold to patients. Also known as non-prescription medicines.[148]
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.[149]
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 ingredients, formulation, mode of action, etc., giving the patent holder the sole right to sell the drug while the patent is in effect.[150]
Pharmacy benefit management	Entails developing and administering drug-benefit plans for employers and health insurers.[151]
Phase 1 clinical trial	A clinical study where a new medicine is given to humans for the first time, usually healthy volunteers. It looks at the ways the body responds to the medicine, and its main effects and side effects.[152]
Phase 2 clinical trial	A clinical study conducted after phase I to evaluate a medicine's effects on a particular condition and determine its common short-term side effects.[153]

146 Ibid.

147 WHO (World Health Organization) (2014). Guidelines on Submission of Documentation for a Multisource (Generic) Finished Pharmaceutical Product: Quality Part. WHO Technical Report Series, No. 986, annex 6.

148 Fitch Solutions, Latin America Pharmaceuticals Report Q2 2023.

149 Buckley and Gostin, eds., Countering the Problem of Falsified and Substandard Drugs, appendix A.

150 Fitch Solutions, Latin America Pharmaceuticals Report Q2 2023.

151 Nass, Madhavan and Augustine, eds., Making Medicines Affordable, appendix C: Glossary.

152 European Medicines Agency, Glossary of Regulatory Terms.

153 Ibid.

Phase 3 clinical trial	A clinical study usually conducted with a large group of patients to gather information about a medicine's efficacy and safety and evaluate its benefits and risks.[154]
Phase 4 clinical trial	A clinical study that takes place after the authorization of a medicine.[155]
Prescription drugs	Patented and generic medicines regulated by legislation that require a physician's prescription before they can be sold to a patient.[156]

154 Ibid.

155 Ibid.

156 Fitch Solutions, Latin America Pharmaceuticals Report Q2 2023.

Appendix 2: Transfer Pricing Questionnaire for the Pharmaceutical Industry

Appendix 2 provides potential questions for a tax administration to ask during a transfer pricing analysis of a controlled transaction within a multinational group in the pharmaceutical industry. The questions may be used in a functions, assets and risks analysis of the controlled entity and its related-party transactions. The questions are designed to ascertain facts and circumstances pertinent to the controlled transactions, asking for information that has not already been provided by the taxpayer (e.g., through transfer pricing schedules or documentation). The focus is on the main steps of the value chain: R&D, processing, supply chain management, and sales and marketing.

Some questions are quite detailed, and should be tailored to specific transactions, taxpayers and tax audits. A number of questions may be more appropriately answered by a local subsidiary in the MNE group; others may only be answered by the parent firm, depending on which entity or entities are being analysed, and whether the tax administration has jurisdiction to obtain the information. The entity under review may not be able to provide information relating to other entities, either because it does not have it or is not authorized to provide it. In that case, other avenues (e.g., requests for an exchange of information under a treaty) may be available to collect the relevant information.

Assessing the relevance of, and responses to, each question listed below calls for considering which entity or entities in the MNE group under review are involved in a particular function/transaction/activity and in what capacity, and which entity bears the costs and assumes the risks. While the term "entity" is used, information from multiple entities in the MNE group may be relevant for the controlled entity under review. The questions should be directed to an entity under review when it performs a particular function. When questions are asked in a "how" or "what" format, they also seek information on whether the entity under review undertakes that function.

Not all questions are suitable for all entities, cases and situations. In particular, the questions cannot meet the needs and fit the specifics of each country (including, importantly, the particular requirements of domestic transfer pricing, income tax and administrative tax law and regulations). Instead, the purpose is to provide options and considerations (and perhaps inspiration) for tax administrations, especially in developing countries. They can then tailor their questions to their priorities, requirements and constraints.

More information on transfer pricing risk assessments and audits can be found in Transfer Pricing Compliance Assurance: An End-to-End Toolkit.[157]

157 United Nations (2025). Transfer Pricing Compliance—An End-to-End Toolkit. New York, NY: United Nations.

The questions in this Appendix are grouped according to the main activities in the pharmaceutical global value chain, as follows: general information questions (section 1), R&D (section 2), primary and secondary manufacturing (section 3), marketing and sales (section 4), supply chain management (section 5), and registration and regulatory affairs (section 6). Section 7 provides questions on risks and section 8 provides a non-exhaustive list of other documents that may be requested from the taxpayer to assist in the transfer pricing analysis.

1. General Information Questions

1. Please outline the overall business strategy of the MNE group and the role of the controlled entity under review.
2. Please provide an overview of the main products sold, in both value and volume, in the country of the entity under review.
3. What are the intangible assets, including major brands, of the MNE group and which entities in the group own them?
4. Have there been any recent acquisitions made by the MNE group (assets or companies) and, if yes, do these acquisitions have an impact on the entity under review?
5. Has there been any recent business restructuring within the MNE group and if yes, does the restructuring have an impact on the entity under review?
6. Please provide an overview of the global value chain for the MNE group.
7. Has the controlled entity under review obtained a tax credit in the country of the entity under review? If so, what criteria have to be met to obtain this credit?

2. R&D

The following questions may be appropriate for the controlled entity under review if it performs one or more of the following R&D activities: general R&D, drug discovery, clinical testing and/or pre-clinical testing. Other situations where these questions may be relevant for the controlled entity include where the taxpayer contributes to R&D expenses incurred by an associated enterprise (via a cost sharing agreement or otherwise) and/or pays a royalty to an associated enterprise for the use of intellectual property resulting from R&D activities. Note that questions related to the registration of R&D, including clinical trials, are included in section 6 below.

2.1. General R&D

1. Please outline R&D activities relevant for the entity under review including steps such as the search for opportunities/drug discovery, pre-clinical testing, clinical studies and/or registration.
2. How long is the product development stage for the main products resulting from these R&D activities?

3. What is the strategic direction for these relevant R&D activities (i.e., what R&D strategy is being employed)?
4. How is the MNE group's R&D strategy determined? Does the entity under review play a role in this process?
5. Please provide an overview of R&D costs at the global level, broken down into internal vs. external R&D expenses for the period under review. Does the MNE group have a global business development department that analyzes and negotiates third-party agreements with regard to licenses, co-development and commercialization?

2.2. Drug discovery

6. Assuming the R&D activities of the entity under review include drug discovery, with a stage gate process (i.e., the development process with different approval stages), please explain how the stage gate process works in practice, including approval workflow and governance.
7. Is there an R&D executive team that oversees or is responsible for these drug discovery activities and, if yes, in which entity are the team members located?
8. With respect to relevant drug discovery activities, in what capacity is the R&D undertaken, for example, as a contract R&D service provider?
9. How is the budget for these activities determined and approved? Does the budget process take place at the local level, foreign (global) level or both?
10. With respect to drug discovery activities, how are costs managed: by project, by functional area, or globally?
11. Which entity manages day-to-day R&D-related laboratory operations? Are these activities undertaken as a service provider or by the R&D entity itself?
12. How are the operational R&D activities financed?
13. Which entity owns patents resulting from these R&D activities?
14. Which entity owns the product know-how used in and resulting from the R&D process?
15. Which entity owns the brands under which generic drugs resulting from the R&D activities are sold?
16. What is the process for handling patent protection in the MNE group? What is the process for handling patent infringement claims? Is the entity under review involved with these processes? If so, which entity bears the costs in relation to patent protection or patent infringement claims?
17. How are the results of R&D projects in which the entity under review participates shared among the entities in the MNE group?

18. Does the entity under review collaborate with health practitioners, customers, universities and/or other stakeholders in improving current drug formulations and/or developing new drug formulations/products?
19. Does the entity under review use data analytics to identify (potential) drug candidates or customers for the drugs that result from the R&D activities? If yes, please explain how data analytics are being used.
20. Does the entity under review participate in the development of these analytic tools?
21. Which data are used to run these analytic tools? Which entity is responsible for collating/collecting the data and which entity has ownership over the data?
22. Are there technology platforms that are shared between different R&D areas (for example, therapeutic areas or business units)?

2.3. Preclinical and Clinical Testing

23. Please describe the approval process for preclinical and clinical testing, as it affects the entity under review, and the bodies involved in the decision-making process.
24. What is the process for determining the required preclinical and clinical tests?
25. Please describe in detail the process for conducting preclinical and clinical tests, noting the role played by the entity under review. If any third party is engaged in the process, describe how it is on-boarded and the activities that it performs.
26. For relevant preclinical and clinical trials please provide available information on the proportionate share of internal and external costs.
27. Are the relevant preclinical and clinical tests undertaken by the developer of the intellectual property, a contract service provider and/or another entity?
28. How are the relevant preclinical and clinical testing protocols designed and approved?
29. If preclinical and clinical tests are regulated, which entity is responsible for compliance with the applicable regulations (e.g., animal welfare regulations and ethical standards)?
30. How are the preclinical and clinical testing facilities maintained and who decides on investments in the facility?
31. How are external testing facilities selected, and by which entity?
32. How are the resources (e.g., labor, financial) allocated for preclinical and clinical testing and which entity is responsible for these resources?
33. How are the relevant preclinical and clinical testing teams managed?
34. Are there safety protocols in place and which entity sets these protocols?

35. How are the relevant clinical and preclinical testing budgets managed?
36. Which entity bears the relevant costs and expenses of preclinical and clinical testing?

3. Manufacturing

The following questions may be appropriate in cases where the entity under review performs manufacturing/production planning/sourcing functions in the country where audited, contributes to expenses incurred by an associated enterprise (via a cost sharing agreement or otherwise) related to the above efforts, and/or pays for these functions rendered by an associated enterprise.

3.1. Production planning

1. Please explain the production planning process, including with respect to production volumes, relevant for the business of the entity under review.
2. What is the policy on back-up manufacturing sites for major products that are relevant for the entity under review?
3. How does the MNE group forecast demand for relevant pharmaceutical products? Is the local entity involved in the forecast?
4. Which entity manages the overall regional or local production process, including the selection of manufacturing sites, outsourcing decisions and facilities relevant for the entity under review?
5. Which entity determines the budget for production facilities? How is the budget for production facilities allocated?

3.2. Manufacturing Technology/Know-How

6. Does the entity under review require any licenses or proprietary technology for the drug manufacturing process? Are they off-the-shelf or tailor-made? If yes, which entities obtain and/or utilize them?
7. Is there a process development department relevant for the entityunder review? Which entity is primarily responsible for the management of product process development?
8. How are quality standards managed within the MNE group? Which department or entity is responsible for good manufacturing practices that would impact the entity under review?
9. Are there any manufacturing-related patents or know-how that are developed internally, or acquired from external sources, which are used during the manufacturing process by the entity under review?
10. At what stage of the drug production process are manufacturing-related patents or know-how utilized, and which entity develops or acquires them? Please describe the uniqueness of the relevant technologies and/or software involved.

11. Are there any further special skills needed for the production process?
12. Which entities provide the financial resources/funding to invest in manufacturing technology used by the entity under review?

3.3. Primary manufacturing

13. Please explain the steps involved in the drug manufacturing process and provide an overview of the various stages from raw materials to final product.
14. Does the MNE group differentiate between primary and secondary processing in pharmaceutical production? Primary processing typically involves production of the active pharmaceutical ingredient (API), while secondary processing typically involves the packaging ("fill and finish") manufacturing stages.
15. Please describe the process for management of day-to-day production operations for the entity under review.
16. How are standards for drug testing purposes developed, and which entities are involved?
17. Please provide an explanation of the quality control and safety processes in drug manufacturing, including the entities responsible.
18. How are quality control tests conducted?
19. How is the cost effectiveness of production processes evaluated?
20. If and to the extent that manufacturing activities that take place in the country where the entity under review is located are subject to environmental regulations, what entity is responsible for compliance with environmental regulations with respect to primary manufacturing?
21. If there are outsourced primary (API) manufacturing activities pertinent to the functions or business of the entity under review, please provide what share of the production in primary (API) manufacturing is outsourced and to what entity.
22. Does the MNE group engage in third-party sales of active ingredients or substances to third parties? If so, how is the pricing for such products determined?

3.4. Secondary manufacturing

23. What are the steps involved in the drug formulation process (for example, blending, granulation, tablet pressing) relevant for the entity under review, and which entities are responsible for these processes?
24. Please describe any additional processing steps such as tablet coating, encapsulation, or sterile filling, and indicate the entities responsible for these processes.
25. How does the MNE group handle the production of drug packaging, labeling, and printing, and which entities are involved in these activities as far as relevant for the entity under review?

26. Which entity decides on the packaging design?
27. Which entity manages day-to-day packaging operations?
28. Is labeling required for pharmaceutical products? If so, how is the alignment with legal standards ensured for the entity under review?
29. Which entity is in charge of product traceability and what specific initiatives are taken to ensure product traceability in line with the prevailing regulations?

3.5. Sourcing

30. What are the key raw materials, supplies and inputs required for the drug manufacturing process by the entity under review?
31. What is the structure of the sourcing process? Please indicate the entities involved, including those involved in price negotiations, supplier selection and contracting.
32. Is the entity working with any third-party wholesalers? If yes, which entity manages the contracts with third-party wholesalers?
33. Are there any hedging or foreign exchange procedures in place to manage risks related to sourcing and price fluctuations, and which entity is involved in these activities?
34. Please describe the factors that can affect sourcing prices, such as time, volume and quality relevant for the entity under review.
35. Does the MNE group have a trading strategy for sourcing, and if so, what does it cover?
36. What are the most important suppliers, especially for raw materials? Please list them for the country under review. Did the suppliers change within the last three to five years?

4. Marketing and Sales

The following questions may be appropriate in cases where the entity under review performs marketing and/or sales activities, does so in relation to sales in the country where audited, and/or pays for these functions rendered by an associated enterprise.

4.1. Marketing

1. Please provide a description and organization chart of the marketing function for the entity under review.
2. Please explain the role of the marketing department at all stages of the product life cycle, i.e., during pre-launch, launch, patent phase, after-patent phase. How early in the development process does the marketing function of the entity under review get involved?
3. Please indicate the reporting lines of the leader of the marketing department (full or dotted line reporting, local and/or to a regional or global organization).

4. How is the budget of the marketing organization managed in budget discussions and what are the main clusters of spending relevant for the entity under review?
5. Please explain the factors that are important for entering and competing in the market. How difficult is it for new competitors or new drugs to enter the market?
6. Please explain the market research process (including market segmentation).
7. Which entities bear the costs of market research?
8. Which entity selects and contracts the market research agencies relevant for the entity under review?
9. Which entity is managing communication, including the contracting of external research studies to be used for marketing conducted by or relevant for the entity under review?
10. How is participation in, and contribution to the costs of, global, regional, and local congresses—relevant to the entity under review—organized and managed?
11. Does the local entity receive any input from any other entity in the MNE group on the conduct of its advertising, marketing and promotion (AMP) activities? If yes, please describe the nature of these inputs and the mode of delivering these inputs.
12. Are the local marketing campaigns based on material prepared by global or regional teams?
13. Please provide an example of the customization of such campaigns to your country.
14. Would such customization require the approval of a global or regional organization? If yes, please provide examples of such guidance.
15. Are there campaigns based on corporate identity towards the public in which the entity under review participates? If yes, how is the material prepared and which entity bears the costs of such campaigns?
16. Provide the market share figures of the top 5 products sold by the entity under review for the period under review. In addition, provide the same market share data at the MNE level and for comparable countries in terms of market size and regulatory environments.
17. Please provide marketing plans for the entity under review for the top 5 products. On average, how often and by whom are changes made to this marketing plan?
18. If the entity under review performs local clinical development functions, please explain the interactions with the marketing department before and after regulatory approval.
19. Please explain the interactions and differences in the functional roles of the marketing and medical affairs departments in the entity under review.

4.2. Marketing Intangibles

20. Which entity conducts the advertising, marketing and promotion activities that are relevant for the entity under review?
21. Which entity is responsible for financing advertising, marketing and promotion expenses that may create marketing intangibles?
22. Please describe the key marketing intangibles deployed for selling the products in the market(s) relevant for the entity under review.
23. How are each of these intangibles developed/acquired/enhanced/maintained/protected/exploited (DAEMPE)? Describe the role of each entity participating in the DAEMPE process.
24. Please explain the relevance of brands/trademarks/tradenames for the business of the entity under review. Are any of the entity's products viewed as global brands? As local brands?
25. Please explain the brand spending process, relevant to the entity under review, in terms of information gathering, strategy direction, visual identity and brand-strategy implementation.
26. Does the inter-company agreement between the entity under review and the parent have any stipulations with respect to incurring local marketing and promotion expenses?

4.3. Sales

27. Please describe a typical sales process relevant for the country or market of the entity under review.
28. Please outline the structure of the sales force relevant for the entity under review. How does the sales force cover the local market—by regions within a country, by product line, by customer group (e.g., physicians, pharmacists, hospitals), or a combination of these approaches?
29. Please describe the composition and nature of the sales force (e.g., years of experience, educational qualifications, salaries, etc.).
30. Which entity is the employer of the sales force?
31. To which entity does the sales force report? Which entity supervises the sales force?
32. What training does sales staff receive with regard to the product, and which entity provides this training? Is the training mainly global, regional or national? Which entity prepares the training material for such trainings?
33. Which entity is managing communication including external research studies to be used during the sales process?
34. Please describe the process for establishing and maintaining relationships with key opinion leaders (e.g., in scientific and medical fields) and/or governmental bodies relevant for the entity under review; for example, to communicate the importance of a particular product or to

buy the product over competing alternatives through the life cycle of the product.

35. How does the local sales force respond to technical questions that health care professionals (e.g., physicians, pharmacists) might raise with respect to the marketed products?
36. Please provide a sample of the information package provided to health care professionals (for a given product or franchise) relevant for the country or market of the entity under review. Which department prepared the communication package and in which entity is this department located?
37. Are there any digital tools used by the sales force for preparing their visits or for interacting with health care professionals? If so, which entity developed these data tools?
38. How are the sales channels of OTC/prescription drugs defined'?
39. What are the target customer groups (e.g., doctors/pharmacies/hospitals) that are relevant for the entity under review?
40. Please indicate the number of clients (e.g., wholesalers, hospitals, pharmacies, if applicable) in the relevant territory of the entity under review.
41. Please indicate the role of data analytics and business intelligence in market segmentation relevant for the country or market of the entity under review. If available, is that data produced and processed locally or is it handled by a different entity?
42. Do key accounts exist? If yes, how were they acquired and how are they managed on a day-to-day basis?
43. Do master/framework agreements exist with customers relevant for the entity under review? If yes, please provide an overview and indicate if the terms of such agreements are defined locally or by a global or regional organization
44. Does the MNE group have a published price list?
45. Please describe the process for setting of prices of drugs sold locally. What inputs into the price-setting process, if any, are provided by the local entity?
46. Does the MNE group provide any guidance for sales and pricing for third parties relevant for the entity under review?
47. Please describe the budget process regarding sales and selling prices. How often are volumes and selling prices reviewed with regional or global management?
48. If applicable, please describe the escalation process regarding net selling price evolutions outside the budget review relevant for the entity under review.
49. Are any local price regulations applicable for the entity under review? Are mandatory rebate systems in place?

50. Please describe the process for conducting negotiations with the National Medicine Regulatory Authority (NMRA) or similar regulatory body with respect to price regulations relevant for the entity under review.
51. What is the role of Health Economics and Outcomes Research in putting together the file for engagement with either regulatory bodies or insurance organizations? Is the content of the file significantly amended locally or mainly globally prepared and locally amended?
52. Does the entity under review participate in tenders? If so, how is the process managed and what is the share of tenders in annual sales?
53. Are such tenders usually made on a portfolio of products?
54. Would a significant reallocation of resources (e.g., sales force and marketing, outside the budget process) from one product to another, or from one franchise to another, be subject to a decision by a regional or global department of the MNE group? If so, please describe the process. Please indicate where the department is located in the MNE group.

5. Supply Chain Management

The following questions may be appropriate in cases where the entity under review engages in warehousing and/or logistics, does so in relation to sales in the country where audited, and/or pays for these functions rendered by an associated enterprise.

5.1. General

1. Does the MNE group have a policy regarding supply chain management that is relevant for the entity under review?
2. Please describe the ordering, warehousing, distribution and transportation process.
3. Which entity manages day-to-day order fulfillment operations with respect to the entity under review?
4. Is special know-how required for warehousing and logistics?
5. Are there service level agreements with the supply chain function in place? If so, please provide them.

5.2. Warehousing

6. Are in-house or third-party warehouses used for storing pharmaceutical products and if yes, at which points in the supply chain, for the country or market of the entity under review?
7. In case of third-party warehouses, which entity identifies, selects and contracts the warehouse providers?
8. How is inventory management handled, and which entities have this responsibility?

5.3. Logistics

9. How is the logistics function (i.e., shipping companies, transport companies) for pharmaceutical products organized?
10. Which entity ensures timely delivery of pharmaceutical products and takes responsibility for any delays?
11. Please explain the methods of physical transport of pharmaceutical products destined for distribution, marketing and sale in the region or country of the entity under review.
12. Are there any differences between transport as it relates to products that originate within the MNE group and with external suppliers and customers?
13. Which entity bears the costs associated with the logistics function as it relates to products destined for distribution, marketing and sales in the region or country of the entity under review?
14. Please explain the process for negotiating the INCO-Terms for the logistics function as it relates to products destined for distribution, marketing and sales in the region or country of the entity under review.
15. What is the strategy for mitigating supply chain disruptions as it relates to products destined for distribution, marketing and sales in the region or country of the entity under review?

6. Registration and Regulatory Affairs

The following questions may be appropriate in cases where the entity under review engages in registration and/or regulatory affairs, does so in relation to sales in the country where audited, and/or pays for these functions purported to have been rendered by associated enterprises.

1. What registrations with respect to R&D (including clinical trials) are needed in the country or market of the entity under review?
2. Are there any local/sub-national requirements and/or is there a NMRA that needs to approve these R&D stages?
3. Please explain what is the contribution of the local entity in meeting registration/regulatory requirements? Are there any documents that are provided by the Group when preparing the local regulatory dossier?
4. Please explain the involvement of global regulatory and global medical affairs in the preparation of the regulatory dossier.
5. In seeking regulatory approval, is any reliance placed upon the granting (or otherwise) of regulatory approval to the MNE group by another national or supranational body, for example, by the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA)?
6. Which entity is responsible for registering drug patents within the MNE group? With which regulatory body (e.g., NMRA or patent offices) are these registrations made?

7. How are changes in government regulations that are relevant for the entity under review monitored and managed?
8. Is there a local regulatory affairs department in your country, and what is its role?
9. What are the escalation processes in place regarding regulatory affairs relevant for the entity under review?
10. How are resources (e.g., labor, financial) managed and allocated for regulatory affairs?
11. How is the accuracy of regulatory documents ensured, e.g., is there oversight from another entity in the MNE group?
12. How are communications between the entity under review and the NMRA and other regulatory bodies managed?
13. How does the MNE group deal with specific technical questions or challenges that NMRA or other regulatory bodies might raise and that are relevant for the entity under review?
14. Which entity is responsible for negotiations with insurance providers (public or private) to ensure (partial) reimbursement of the price of pharmaceuticals?
15. How is the regulatory affairs budget managed by the local entity? How is it managed within the MNE group?
16. What costs were borne over the past three-to-five years to obtain drug approvals and by which entity?

7. Risks

The following questions may be appropriate in cases where the entity under review assumes or is assigned risks, does so in relation to sales in the country where audited, and/or pays for these functions rendered by an associated enterprise.

1. What is the overall risk management strategy of the entity under review, i.e., in terms of identifying, assessing, responding to, and monitoring risks?
2. Are there any agreements in place that are relevant for the entity under review that require or guarantee a certain production volume? Which entity bears the cost of production failures or over-production?
3. Are there relevant social and environmental standards that need to be fulfilled, and which entity is responsible for managing them?
4. Are there relevant supply chain, logistics, and transport risks and which entity manages them?
5. Are there relevant pricing, financial and foreign exchange risks and which entity manages them?
6. Are there relevant risks of obsolescence or faulty products and which entity manages them? Is there a return policy in place? Are the costs managed locally and/or borne locally?

7. Are there any insurance policies in place to cover these risks for the entity under review, and which entity covers the insurance costs?
8. Who bears the risk and/or costs in relation to lawsuits about products?
9. Are there other measures taken to manage and mitigate risks relevant for the entity under review?

8. General Documents

The following non-exhaustive list of documents may be requested from the taxpayer to further assess its functional and risk profile. These should only be requested if relevant for the entity under review and information has not already been provided.

1. Intercompany contracts, including intercompany financial arrangements such as loans, corporate guarantees, etc.
2. Relevant group agreements covering the sale of products/services to third parties that are also sold to group companies
3. Advance Pricing Agreements/Arrangements and cost sharing arrangements
4. Registered trademarks
5. List of patented drugs including expected and actual revenue
6. Financial data including balance sheet and profit-and-loss statements
7. Organizational charts
8. Internal guidelines (for example, on production, quality, sales)
9. Operational manuals containing detailed procedures and processes for various business functions
10. Annual marketing and R&D spending details
11. Group risk policy/internal risk reporting
12. Job descriptions of key personnel, their reporting lines, and any performance measurement mechanisms in place (including key performance indicators)
13. External or internal brand valuations
14. Forecasts for the product pipeline
15. Press releases

UN Tax Committee

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