Interstitial Guidance on Transfer Pricing in the Pharmaceutical Industry

Foreword

The United Nations Committee of Experts on International Cooperation in Tax Matters ("the Committee") is globally recognized for its work in norm- and policy-shaping and for the guidance it provides in the area of international tax cooperation. It generates practical guidance for governments, tax administrators and taxpayers to help strengthen tax systems, with a view to mobilize financing for sustainable development.

Through its work, the Committee aims to prevent "double (or multiple) taxation" and "non-taxation" and assist countries to broaden their tax base, strengthen their tax administrations and to curb international tax evasion and avoidance. In all of its work, the Committee gives special focus to least developed countries and others in special situations, including small island states and landlocked countries.

The Committee is a subsidiary body of the UN's Economic and Social Council. It is comprised of twenty-five members nominated by Governments and acting in their expert capacity, drawn from the fields of tax policy and tax administration and selected to reflect an adequate equitable geographical distribution, representing different tax systems. The current membership was appointed by the Secretary-General, after notification was given to the Economic and Social Council, for a four-year term starting on 1 July 2021 and ending on 30 June 2025.

During its 23rd Session in 2021, the Committee decided to continue its work on transfer pricing given the relevance of intragroup trade and its potential impact on corporate income taxes. To this end, the Committee formed a Subcommittee on Transfer Pricing ("the Subcommittee").

The Committee mandated the Subcommittee to consider, report on and propose guidance on transfer pricing issues, on the basis:

- That it reflects article 9 of the United Nations Model Convention, and the arm's length principle embodied in it, and be consistent with relevant commentaries of the United Nations Model Convention;
- That the Subcommittee identify and consider the transfer pricing topics where guidance from the Committees was the most useful;
- That it reflects the realities for, and the needs of, developing countries, at their relevant stages of capacity development; and
- That it gives due consideration to relevant work in other forums, including the Inclusive Framework on Base Erosion and Profit Shifting, and may consult broadly.

During the 24th Session of the Committee, the Committee approved the Subcommittee's ambitious work plan, consisting of interstitial 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 Aspects of Agricultural Products
- Transfer Pricing in the Pharmaceutical Industry

- Dispute Avoidance and Bilateral Advance Pricing Agreement / Arrangement Programs

The guidance at hand is on "Transfer Pricing in the Pharmaceutical Industry".

The specific topics were chosen for their practical relevance and development focus, based on feedback from former participants of capacity development workshops in the area of transfer pricing.

By its 28th Session, the Committee had reviewed, refined, finalized and approved guidance on all of the above transfer pricing topics. It sought throughout to prepare products that assist all stakeholders, especially officials in developing countries, in dealing with the issues covered. The guidance products should also assist in making capacity development activities as practical, targeted and effective as possible.

The Subcommittee met productively on many occasions – predominantly virtually as well as in hybrid format in Vienna in 2023 and 2024. The generosity of the Austrian government and the Vienna University of Economics and Business is warmly acknowledged, as are the generous financial contributions from Denmark, the European Commission, India, Norway and Sweden to UN DESA's multi-donor project to provide strengthened substantive and logistical support to the work of the Committee, its subcommittees and related capacity development activities.

The Subcommittee is comprised of participants from tax administrations and policy-makers with wide and varied experience in dealing with transfer pricing, as well as from academia, international organizations and the private sector, including from multinational enterprises and advisers.

The participants of the Subcommittee and their countries (in the case of government officials) or current affiliations (in other cases) bearing in mind that membership is in a personal capacity, contributing to the guidance were the following: Ingela Willfors (Sweden, Co-Coordinator); Mathew Gbonjubola (Nigeria, Co-Coordinator); Matthew Andrew (Auckland University, New Zealand); Rajat Bansal (India); Melinda Brown (OECD); Rasmi Das (India); Barbara Dooley (Ireland); Lorraine Eden (Texas A&M University, USA); Mauro Faggion (European Commission); Björn Heidecke (Deloitte, Germany); Michael Kobetsky (Australian National University, Australia); Wazi Ligomeka (Malawi); Luis María Mendez (Argentina); Pande Oka Kusumawardani (Indonesia); Nana Mensah Otoo (Ghana); T.P. Ostwal (T.P. Ostwal & Associates LLP, India); El Hadramy Oubeid (Mauritania); Raffaele Petruzzi (WU Transfer Pricing Center, Institute for Austrian and International Tax Law, Vienna University of Economics and Business, Austria); Claudia Pimentel (Brazil); David Rüll (Germany); Jolanda Schenk (Shell, Netherlands); Ruchika Sharma (India); Stig Sollund (independent consultant, Norway); Trude Steinnes Sønvisen (Norway); José Troya González (CPA - Robalino, Ecuador); Monique van Herksen (Simmons & Simmons, Netherlands); Marcos Valadão (Getulio Vargas Foundation, Brazil); Yan Xiong (China). The early involvement of Carlos Perez-Gomez Serrano (KPMG, Mexico) and Anthony Munanda (ATAF) is also recognized.

The Subcommittee gratefully acknowledges the input of Philippe Paumier and Karl Wündisch who provided insightful comments on several drafts of this document, and thanks Ami Goldenstein, Marlinda Gianfrate, Sophie Roiret, Alan White, Kathrin Zoeller, and others who also provided helpful feedback.

The assistance of the Secretariat, including especially Ilka Ritter and Michael Lennard, assisted by Laura Burt, in this work is gratefully acknowledged.

Executive Summary

This guidance was prepared in response to the need, often expressed by developing countries, for practical guidance in applying the arm's length principle to the pharmaceutical industry. All tax administrations, but particularly those from developing countries, face resource and capacity constraints in a specialized area such as transfer pricing. These constraints make it important to ensure that the limited resources of tax administrations are targeted as efficiently and effectively as possible. In addition, given the importance of the pharmaceutical industry to all countries the goal of this guidance is to provide practical advice for tax authorities and to multinational enterprises (MNEs) in the pharmaceutical industry.

This guidance commences by describing the global value chain of the pharmaceutical industry, its value drivers and business models. The application of transfer pricing analysis to the pharmaceutical industry is the discussed. Practical issues relating to the delineation of the transaction and the comparability analysis are addressed. The document then provides several examples.

Two appendices provide additional context. A list of the abbreviations used in this guidance is attached as Appendix 1 and a glossary of key terms is attached as Appendix 2. Appendix 3 (forthcoming) lists potential questions that can be asked in a tax audit setting for a functional analysis in the pharmaceutical industry.

It should be noted that the analysis contained in this document may not reflect particularities present in all countries, but instead takes a systematic approach of describing the most pertinent features of the pharmaceutical industry and related transfer pricing issues.

It is important to highlight that the United Nations Practical Manual on Transfer Pricing for Developing Countries ("the UN TP Manual") in its most recent version is applicable to the pharmaceutical industry and the guidance provided in this document is based on, and should be read in conjunction with, the UN TP Manual.

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1. Introduction

1.1. The pharmaceutical industry

The pharmaceutical industry, which is part of the life sciences sector,[1] is dedicated to the discovery, development, manufacturing, marketing, distribution and sale of pharmaceutical products that are used for medical purposes in the treatment or the prevention of diseases. A pharmaceutical product (a drug or pharmaceutical material) is a chemical substance, based on an active pharmaceutical ingredient (API), which is designed to treat a disease or a 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 delivered products derived from living organisms (referred to as biological APIs). Nowadays, most large pharmaceutical companies use both chemical and biological technologies[4]; therefore, the term "pharmaceutical industry" used in this guidance includes both pharmaceutical and biotechnology firms.

In addition, companies in the pharmaceutical industry have been grouped historically in a separate category from firms in the diagnostics and medical device industries. Firms in these industries are closely related to, and strategic alliances are common with, pharmaceutical firms. Some of the largest pharmaceutical MNEs also have their own diagnostic and/or device divisions. However, products, value drivers and industry structures in the diagnostics and medical device industries are sufficiently different that they are not covered by this guidance.[5] [6]

[1] The life sciences sector encompasses a broad range of industries including pharmaceuticals, biotechnology, medical devices, contract research organizations (CROs) and contract manufacturing organizations (CMOs) that involve the scientific study of life. https://www.scilife.io/glossary/life-science

[2] For a recent overview of the pharmaceutical industry see Taylor, D. (2016). The Pharmaceutical Industry and the Future of Drug Development. Issues in Environmental Science and Technology, No. 41. In Hester, R. & Harrison, R. (eds.). Pharmaceuticals in the Environment. The Royal Society of Chemistry. Available from https://books.rsc.org/books/edited-volume/553/chapter/204949/The-Pharmaceutical-Industry-and-the-Future-of-Drug.

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

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

[5] On diagnostics, see Morel, C., et al. (2016) Ensuring Innovation in Diagnostics for Bacterial Infection. World Health Organization (WHO). See also Proffitt, A. (2023). Pharma-Diagnostics Lockstep: How Two Industries Can Work Together for Precision Medicine. Available from: https://www.bio-itworld.com/news/2023/03/07/pharma-diagnostics-lockstep-how-two-industries-can-work-together-for-precision-medicine.

[6] On medical devices see U.S. 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. Available from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/classification-products-drugs-and-devices-and-additional-product-classification-issues.

1.2. Segments in the pharmaceutical industry

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

1.2.1. Novel, generic, and orphan pharmaceutical products

i. Originator and generic drugs

The pharmaceutical industry consisted historically of two types of firms: originator companies and generic drug companies.[7] Originator firms conduct research and development (R&D) into new or novel API and seek patent protection for it. The API patent applies to any formulation of the drug (e.g., pill, cream, liquid) that includes the API.[8] The patent provides the firm with intellectual property rights (IP 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" or "branded" or "originator" drugs. The drugs 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 in practice depending on the length of time between the date when the patent was granted and the date of government authorization for the new pharmaceutical product. the authorization date depends on the number of years required to perform the clinical trials to develop and present the safe-assuring documentation needed for receiving the government authorization (see sections 3.1.1 and 4.2.2 discussing patents and business strategies related to patents).

When the patent protection expires for the originator drug, any firm (the "generic drug company") can copy the generic substance and sell a replica drug under the generic name or under a new trademark. The generic drug has the same API formula as the brand-name pharmaceutical product and is created to be the same also in terms of its product characteristics (e.g., dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use). Having the same product characteristics demonstrates *bioequivalence*, i.e., the generic and brand-name medicines are substitute

[7] Wündisch, Karl. International Transfer Pricing in the Ethical Pharmaceutical Industry. Amsterdam : IBFD Publications, c2003. Part 2, Chapter 2, 2.1.2. Competition from Generics, pp.36-39.

[8] Pharmaceutical firms can also apply for IPR protection via formulation patents, where the company takes an existing API and restructures or combines the API with other ingredients to create a new drug. See O'Brien, M. (2017). Types of pharmaceutical patents, O'Brien Patent Solutions. https://www.obrienpatents.com/types-pharmaceutical-patents/ .

products (they work in the same way and provide the same clinical benefits).[9]

It is important to note that pharmaceutical products may appear to be similar but "similarity can be deceptive."[10] Medicines are unique compounds and even when they have similar chemical compositions (i.e., they have *bioequivalence*) they may have very different uses or effects (i.e., different *bio-availabilities*). Both bioequivalence and bio-availability are important product characteristics that may affect the arm's length transfer price.

Originator companies face additional challenges that are not faced by their generic competitors, including:[11]

- The financial risks and cost involved to bring a new drug to market. On average, only one out of every 20 drugs that enter clinical testing will be approved for marketing, and it takes ten to 15 years to bring a new drug to market at a cost of up to 1.5 to 2 billion USD.[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 (see section 4.2.1 on price controls).
- The need to have several R&D projects in the "pipeline" simultaneously to ensure overall long-term profitability of the company in terms of the number of potentially approvable new drugs.
- The efforts and costs associated of complying with the regulatory requirements of multiple national government agencies and supranational organizations (see section 2.7 on regulatory affairs).

Because generic medicines do not have to undergo a repeat of the same clinical trials that are required of the original brand-name medicines in terms of demonstrating safety and effectiveness, the generic manufacturers do not have to incur the same up-front 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.

Once a generic product receives regulatory approval, the drug can enter the marketplace, creating competition between the originator drug and the generic. In addition, if multiple generic drugs are approved based on the same API, this can create additional competition leading to lower prices.[13] As a result, generic prices are typically much lower than the

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

[10] This section is drawn from Wündisch, K. (2003). International Transfer Pricing in the Ethical Pharmaceutical Industry. IBFD.

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

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

[12] Harrer, S., Shah, P., Antony, B., and Hu, J. (2019). Artificial Intelligence for Clinical Trial Design. Trends in Pharmacological Sciences, 40(8): 577-591. DOI: 10.1016/j.tips.2019.05.005.

[13] U.S. Food & Drug Administration. Generic Drugs Facts. Available from https://www.fda.gov/drugs/generic-

originator drug price.

One of the competitive risks faced by originator companies in the pharmaceutical industry, in addition to competition with generic drugs, is competition between patented drugs ("between-patent competition"). A patent provides the patent holder with a monopoly to exploit a drug, but it does not provide protection from other companies that produce drugs under other patents, which may have superior results or different treatments.The reduction in the present discounted value of a patent holder's return caused by competition between patented drugs can at least as large as within-patent competition.[14] For example, 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 hepatitis C market.[15]

ii. Orphan drugs

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

1.2.2. Over-the counter vs prescription drugs

Pharmaceutical products can also be segmented into categories depending on whether a medical professional is required to write a prescription for the medicine before purchase. A prescription drug is a pharmaceutical product that can only be supplied to a patient by the written prescription of an authorized health professional such as a physician or dentist.[18] Examples of prescription drugs typically include antibiotics and blood pressure tablets.

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, the drug must be supported with evidence including clinical trials to ensure the

drugs/generic-drug-facts.

[14]Lichtenberg, F.R. and Philipson, T.J. (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. https://doi.org/10.1016/j.healthpol.2019.05.009.

[15] Roediger, A., et al. (2019). Competition between on-patent medicines in Europe. Health Policy, 123(7): 652-660. https://doi.org/10.1016/j.healthpol.2019.05.009.

[16] See pages 21-23 in Taylor, D. (2016). The Pharmaceutical Industry and the Future of Drug Development. Issues in Environmental Science and Technology, No. 41. In Hester, R. & Harrison, R. (eds.). Pharmaceuticals in the Environment. The Royal Society of Chemistry. Available from https://books.rsc.org/books/edited-volume/553/chapter/204949/The-Pharmaceutical-Industry-and-the-Future-of-Drug.

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

[18] *See* Marathe, PA, et al. (2020). Over-the-counter medicines: Global perspective and Indian scenario. Journal of Postgraduate Medicine, 66(1): 28-34; and Chang, J., et al. (2016). Prescription to over-the-counter switches in the United States. Journal of Research in Pharmacy Practice, 5(3): 149-154.

efficacy of the drug. The government authority assesses the evidence provided to determine whether the drug will be registered. It is usually a requirement that the benefits of a drug proposed for registration outweigh the potential risks of using the drug.

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

Governmental regulations differ across countries on how OTC drugs can be accessed. OTC products are typically sold in pharmacies, although some countries may also allow (some of) these products to be sold in supermarkets or convenience stores. There are also countries that restrict sales of certain OTC products to customers who have spoken with an on-duty pharmacist. Other countries do not have this distinction, requiring only that OTC drugs must be bought in pharmacies. Particular drugs may be sold as prescription drug in one country and OTC in another country. Many OTC products may have been initially only available under prescription.

OTC products are much more readily available to consumers and are usually relatively affordable vis-à-vis prescription drugs. Marketing intangibles may be highly relevant for OTC products. Differences across countries in government regulations can also 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 of the pharmaceutical industry totaled 1.42 trillion US dollars; this includes both originator and generic pharmaceutical products, whether they require a prescription or are sold as OTC medicines.[20] While the United States has the largest share of revenues (43.7%) and five of the ten largest pharma MNEs are headquartered there, other countries' markets have also grown dramatically over the last decades. In 2022, China ranked second in terms of market revenues.[21]

[19] Poreds, P. (2022). A Short Note on Over-the-Counter Drugs. Journal of Basic and Clinical Pharmacy, 13(1): 123. https://www.jbclinpharm.org/articles/a-short-note-on-overthecounter-drugs-10292.html.

[20] Statista (2023). Global pharmaceutical industry - statistics & facts. Available from Global pharmaceutical industry - statistics & facts | Statista. See also https://www.zippia.com/advice/us-pharmaceutical-statistics/.

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

Figure 1: Pharmaceutical markets by revenues, Top 10 countries, 2022 (billions US dollars)[22]

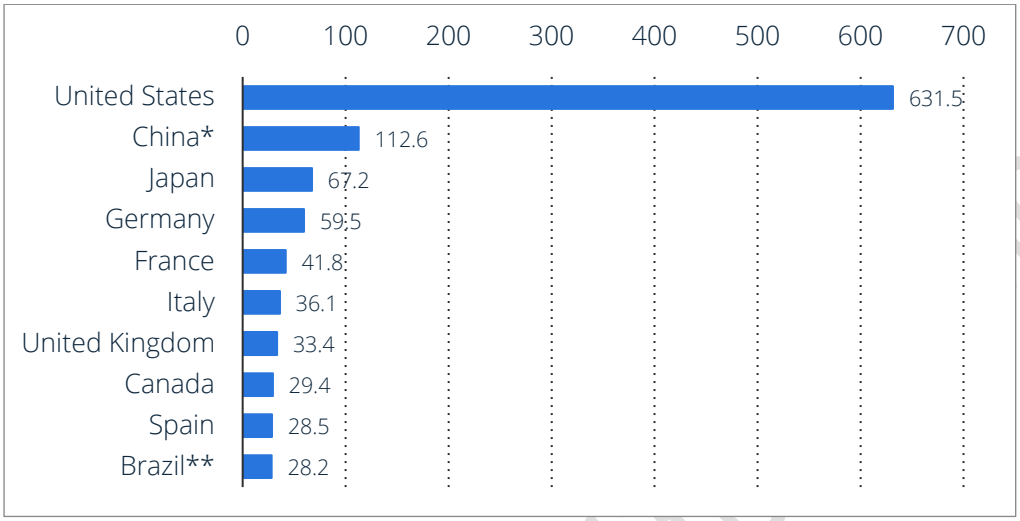


Table 1 provides data at the regional level on pharmaceutical markets in 2022. The largest market was North America (455.09 billion US dollars) followed by Asia (434.16 billion US dollars).

Table 1: Pharmaceutical markets by region, 2022 (billions US dollars)[23]

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

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

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

MENA (Region)	39.856
* Middle East	38.3
* North Africa	12.1
North America (Region)	455.093

1.3.2. Pharmaceutical exports and imports

Tables 2 and 3 provide publicly available data on the top 20 countries in terms of exports and imports of pharmaceutical products in 2021.[24] The trade balance is defined as exports minus imports, for both unfinished and finished products, so a negative trade balance means that imports exceed exports. Large exporting countries can also be large importing countries; for example, in 2021, the United States and Germany were in the top three countries for both exports and imports.

Table 2: Exports and imports of pharmaceutical products, Top 20 countries, 2021 (millions US dollars)

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

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

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

Table 3: Trade balances for pharmaceutical products, Top 20 countries, 2021

(millions US dollars)

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

1.3.3. Global revenues by market segments

Table 4 provides data on global revenues for the prescription and OTC segments of the pharmaceutical market for the years 2020, 2021, and 2022. Prescription drug sales were approximately 88 percent of global sales during this period; the remainder (12%) were sales of OTC medicines. Patent-protected prescription drugs represented about 77 percent of prescription drug sales, with the remainder split between generics (8%) and orphan (15%) prescription drugs.

Table 4: Sales of pharmaceutical products by market segment, 2020-2022[25]

(billions US dollars and % market)

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

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 under a new trademark. By value of sales, the generic drug market accounted for approximately 30 percent of the global pharmaceutical market during 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 (i.e., the generic share) was about 25 percent compared with nearly 60 percent in the Asia-Pacific region.

Table 5: Global market for generic pharmaceuticals, by region (billions US dollars)[26]

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%

[25] Calculations using data from Statista. Pharmaceutical Market Worldwide. Study ID 10642.

[26] BCC (2021). Global Markets for Generic Drugs. BCC Publishing Staff. Report Code PHM009J. Table 1. Page 13.

Asia-Pacific				
Total pharmaceutical market	257.6	277.4	296.1	277.0
Generic drug market	140.6	155.5	171.8	156.0
Generic share (%)	54.6%	56.1%	58.0%	56.3%
China				
China - pharmaceutical market	118.7	130.2	140.7	129.9
China - generic drug market	96.8	105.7	115.1	105.9
China - Generic share (%)	81.6%	81.2%	81.8%	81.5%
India				
India - pharmaceutical market	36.4	41.1	46.8	41.4
India - generic drug market	26.4	31.1	36.5	31.3
India - Generic share (%)	72.5%	75.7%	78.0%	75.6%
Rest of the World				
Total pharmaceutical market	97.5	100.7	103.6	100.6
Generic drugs market	29.3	30.3	31.2	30.3
Generic share (%)	30.1%	30.1%	30.1%	30.1%
Global pharmaceutical market	1,106.50	1,160.80	1,213.20	1,160.17
Global generic drug market	348.20	378.90	411.60	379.57
Generic share (%)	31.5%	32.6%	33.9%	32.7%

1.3.5. R&D statistics

There are approximately 3,200 companies and more than 200 academic or research groups that are engaged in R&D activities in the global pharmaceutical industry. While a large number of research firms are headquartered in the United States (44%), Europe (25%), Japan (6%) and South Korea (4%)[27], the geography of firms is changing with an increasing number of China-headquartered firms entering the market increasing their market share from two percent ten years ago to twelve percent in 2022.

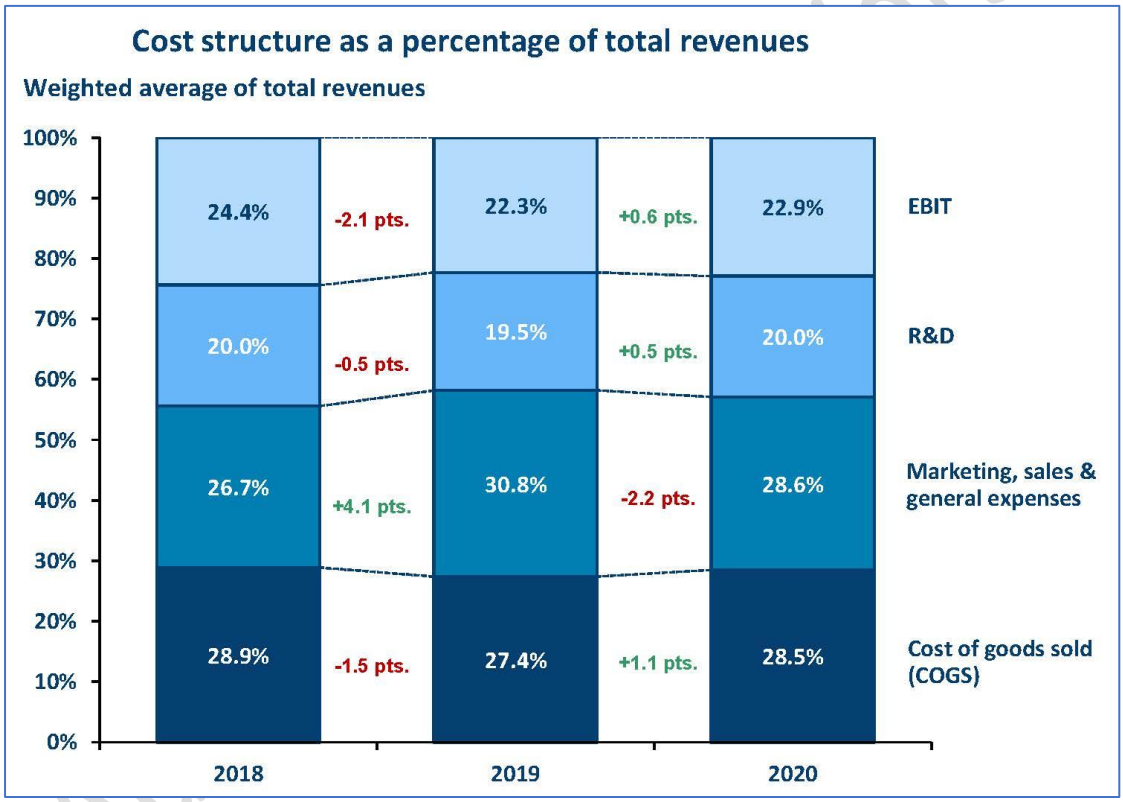
Emerging biopharma companies (EBPs), defined as pharma firms with less than 500 million US dollars in sales and R&D spending of less than 200 million US dollars per year, accounted for a record 65 percent of the molecules in the R&D pipeline in 2021, up from 50 percent in 2016 and 33 percent in 2001. Of the EBPs, 17 percent were headquartered in China compared to 20 percent in Europe and 46 percent in the USA. EBPs also hold different shares of the total national R&D pipeline, ranging from a high of 83 percent in China to 62 percent in the USA, 47 percent in Europe and a low of 22 percent in Japan.[28]

[27] IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. p. 22. Available from https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022.
[28] IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. p. 50. Available from https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022.

1.3.6. Industry profitability

A recent analysis of the top 20 pharmaceutical MNEs worldwide estimated their average profitability (earnings before interest and taxes (EBIT)) at 23 percent of revenues in 2020. Average cost of goods sold (COGS) was 28.5 percent, operating expenses 28.6 percent, and R&D costs were 20 percent. See Figure 2. The analysis was undertaken at the MNE group level and 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 percentage of total revenues, 2018-2020[29]



2. The pharmaceutical global value chain

2.1. Overview

As described in the UN TP Manual at section 1.3.3, value chain analysis, developed by Michael Porter,[30] describes the activities performed by a company, domestic or international, in

[29] Smart Pharma (2022). Top 20 Pharma Companies – Performance and Strategy.

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

creating value for its customers. This includes all value-adding stages involved in bringing a product from inception to final consumption. Porter separated these stages into two types: primary and support activities.[31]

The value chain can be analyzed 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 (GVC) at both the individual firm (the MNE) and industry levels. At the MNE level, the GVC for the company takes into account all the activities of the entities in the MNE group on a worldwide basis.[32] At the industry level, the GVC takes into account all the activities, firms and countries, on a worldwide basis, that are involved in the pharmaceutical industry.[33]GVC analysis therefore uses the value chain as the basic structure for giving a general / stylized overview and visual that aims to describe an MNE or an industry, but recognizes that the various production stages have become globalized and dispersed around the world and that, in practice, the activities carried out by firms will vary in their intensity.[34]

This section explores the pharmaceutical GVC from the industry level and captures the value chain at a certain point in time. Section 3 discusses the pharmaceutical GVC 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. It is important to keep in mind that the country-level and firm-level GVC analyses provided in this guidance are stylized overviews of the pharmaceutical industry that cannot capture the many nuances and differences in how this GVC manifests itself 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 the economically significant characteristics of the controlled transactions together with the roles and responsibilities of the controlled entities involved in these transactions. This topic is discussed in section 4.[35]

2.2. The GVC of the pharmaceutical industry

The GVC of the pharmaceutical industry encompasses the following value-adding activities involved in the production and sale of pharmaceutical drugs: research and development, primary manufacturing, secondary manufacturing, and marketing and distribution. In addition to strategic management, since the pharmaceutical industry is typically heavily regulated at all stages of its GVC, regulatory affairs should also be seen as a core activity for

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

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

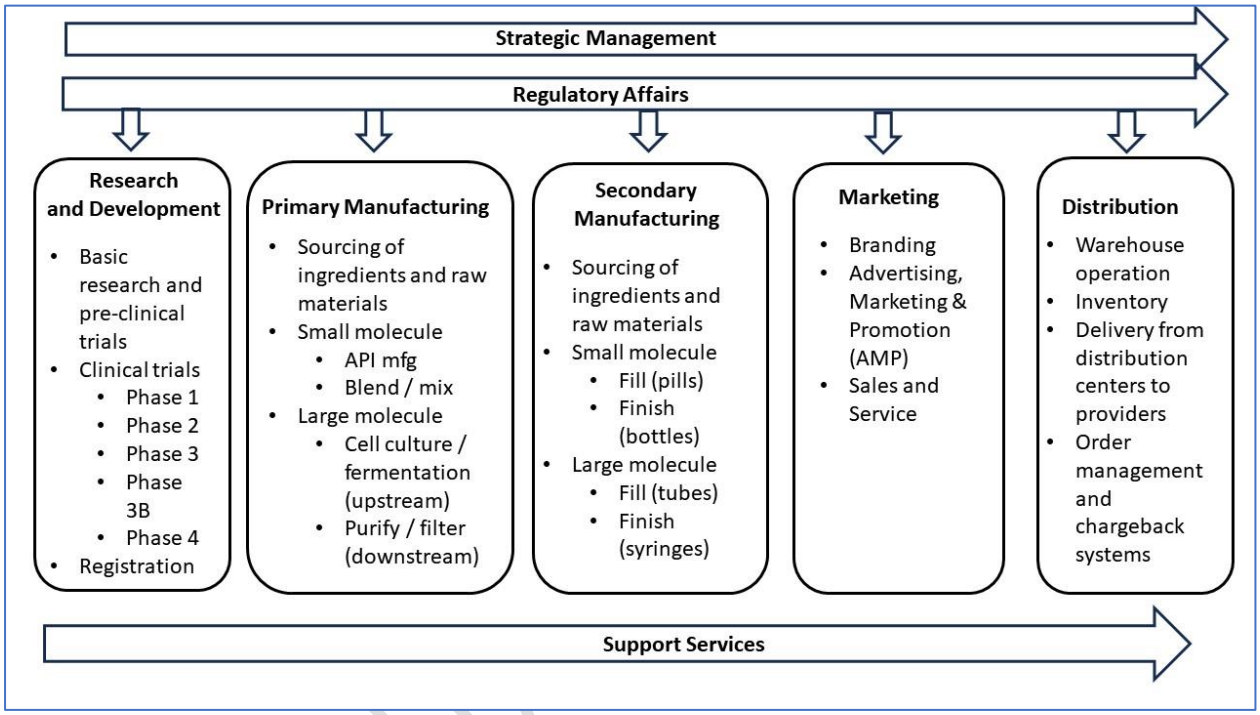
[33] Frederick, S. (2019). Global value chain mapping. In Ponte, S., Gereffi, G., and Raj-Reichert, G. (eds.). Handbook on Global Value Chains. Eduard Elgar Publishing. pp. 29-53.

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

[35] UN TP Manual, section 3.1ff.

this industry. Other value-adding activities in the pharma GVC include support services such as human resources, finance and control. The following analysis focuses on these value-adding activities, which are illustrated in Figure 3. The GVCs 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



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

- R&D: Given the complexity of R&D in the pharmaceutical industry, the R&D stage is typically separated into three substages: research, development and registration.
- 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 in light of scientific approval processes, regulations for market access, and price controls; includes detailing, advertising, marketing, and promotion (AMP) activities.
- Distribution: The stage where the finished drug product is transferred to wholesale distributors that handle the logistics and distribution to hospitals, clinics and retail pharmacies. Logistics can involve complex supply chains to ensure proper handling of drug products.
- Regulatory activities: Pharmaceutical companies are highly regulated. These regulations impact a company's core activities ranging from regulations for clinical trials, the product approval and registration process, manufacturing, marketing, and

distribution.[36]

2.3. Research and development

The R&D stage of the pharmaceutical GVC generally consists of three substages: research, development and registration.[37] A brief overview of each stage is provided below.

It is important to note that, from a business perspective, the R&D stage of the GVC for the pharmaceutical industry, especially for new drugs, is often highly complex and risky. The process of bringing a drug from discovery through testing in nonclinical models and ultimately in human trials, then through regulatory review to, commercialization, is an extremely complex and multifunctional process.[38]

2.3.1. Research

The research stage in the pharmaceutical industry 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 for new molecules for medicines to treat an ailment and also 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.

Drug discovery is a lengthy, expensive, and extremely extensive scientific based investment process with a low success rate.[39] In the pre-clinical stage, new active compounds are tested under experimental conditions to gather information on the effects of the potentially new drug. Depending on the specific national or regional regulations, pharmaceutical firms may also be required to submit an investigational new drug (IND) application to NMRA, requesting approval to move the proposed new drug to the clinical trials stage.[40] It is during this phase that pharmaceutical companies often file for patent protection for the API and the 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 to 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

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

[37] U.S. Food and Drug Administration. (2018). The Drug Development Process. https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process. See also IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. Available from https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022.

[38] Buckley, L.A., et al. (2020). Drug Development 101: A Primer. International Journal of Toxicology, 39(5): 379-396.

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

[40] Buckley, L.A., et al. (2020). Drug Development 101: A Primer. International Journal of Toxicology, 39(5): 379-396.

against existing rival drugs; and (4) additional safety monitoring after a drug has reached the market that a government may require to detect new side effects that were missed during earlier clinical trials.[41]

Figure 4 provides a general overview of the R&D process in the pharmaceutical industry, together with the estimated average number of years involved in each stage.[42] It should be noted, however, that the actual R&D process and time periods vary significantly across pharmaceuticals, firms and national or supranational authorities.

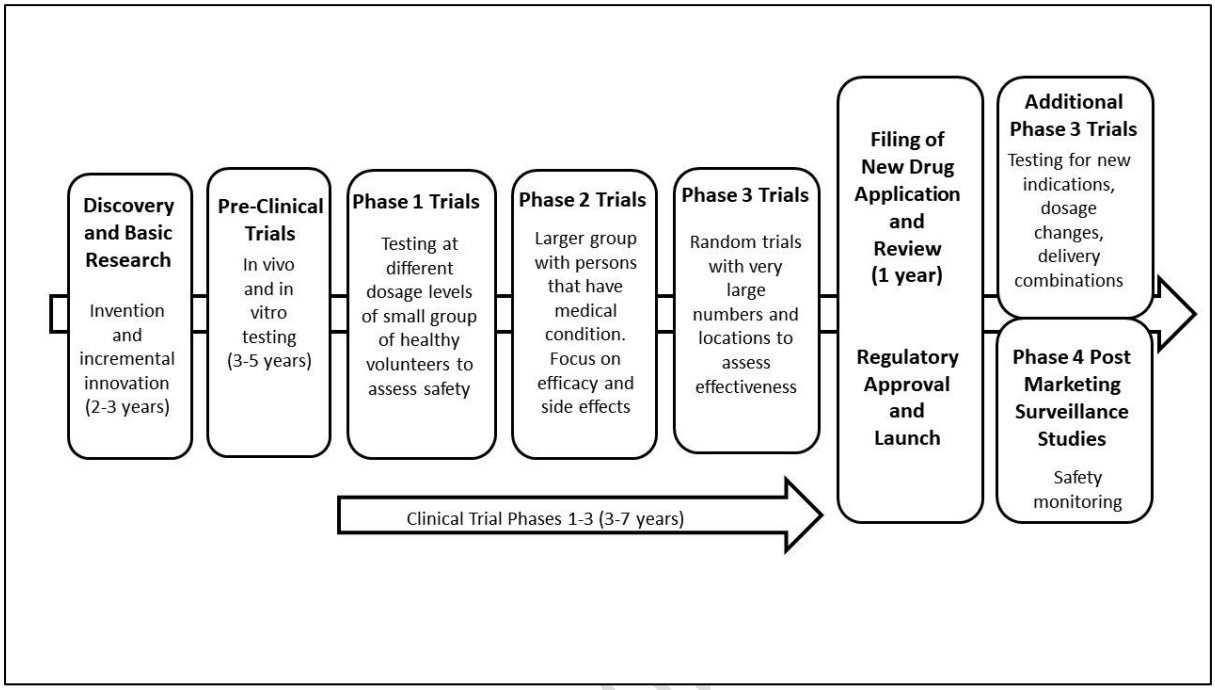
There are four clinical trial stages with stages 1 through 3 occurring prior to the filing and review of the new drug application with the NMRA and (if approved) the product launch. Additional phase 3 trials and phase 4 studies take place after a product launch. A short description of the four clinical trial stages is provided below.

- 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 that have the medical condition that the vaccine or drug is designed to address. This phase focuses on the efficacy of the drug and potential side effects.
- Phase 3: Large numbers of volunteers in many locations engage in randomized trials to assess the effectiveness of the vaccine or drug.
- Phase 4: Post Marketing Studies. Additional studies that may be required by the NMRA to test for side effects or new usages.

[41] Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal. Section 3.1.

[42] Figure adapted from Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal. The data on average years in each stage is from "Process of New Drug Development". Seikagaku Corporation. Available from https://www.seikagaku.co.jp/en/development/flow.html.

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.[43] Clinical trials phases 1 through 3 may take up to seven years.[44] 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 the time frame for other new drug approvals.

IQVIA estimates that the average composite success rate over all four phases of the so-called "R&D pipeline" (that is, phase 1, 2 and 3 clinical trials and regulatory submission) for the 2010-2021 period was 13.1 percent across all therapy areas. Success rates, measured in terms of the success rate of graduating from one phase to at least the next phase, varied across the R&D pipeline as follows: clinical trials (phase 1 (56%), phase 2 (38%) and phase 3 (67%)) and regulatory submission (89%).[45]

It will be 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 in that country may need to determine how this activity will be remunerated for transfer pricing purposes. One issue is whether the phase 4 trial constitutes a separate activity or is part of a larger activity such as marketing or distribution.

2.3.3. Registration

In order to be able to distribute drugs in a market, the API and pharmaceutical products made with the API will generally have to be registered with the NMRA or a supranational authority

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

[44] The data on average years in each stage is from "Process of New Drug Development". Seikagaku Corporation. Available at https://www.seikagaku.co.jp/en/development/flow.html.

[45] IQVIA Institute for Human Data Science (2022). Global Trends in R&D: Overview through 2021. Available from https://www.iqvia.com/insights/the-iqvia-institute/reports/global-trends-in-r-and-d-2022. The average composite success rate is measured by the product of the four success rates.

such as the European Medicines Agency (EMA) where the firm intends to market the new drug. Regulatory approval may be required at all three R&D stages (research, development and registration), depending on each national or regional regulations. Regulatory authorization typically starts at the clinical trials stage. In large multinationals, the company's regulatory affairs staff at the headquarter level may determine the MNE group's overall regulatory filing strategy (e.g., how to build the dossier, country filing prioritization, etc.). In the region- and country-level affiliates, teams of national registration experts prepare and submit dossiers to the various national regulatory authorities. Post-approval, the NMRA in one or more countries may also require additional drug safety monitoring and phase 4 clinical trials, which require additional 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 a marketing authorization to market and sell the drug. Approval is typically needed in each country where the firm intends to sell the pharmaceutical product. See section 2.7 for a discussion of regulatory affairs activities within the MNE group.

2.4. Manufacturing

The manufacturing stage of the pharmaceutical GVC consists of two substages: primary and secondary manufacturing, which are discussed below, together with the impact of technological change on both stages.

2.4.1. Primary (API) manufacturing

Primary manufacturing involves production of the API; secondary manufacturing is of 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.[46] 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."[47] In short, an API is a bulk drug substance. The global market for APIs in 2020 was 173.3 billion US dollars.[48]

The primary manufacturing stage of the pharmaceutical GVC 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).[49] 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

[46] BCC Research Staff (2019). Markets at a Glance: Pharmaceuticals. Report Code: PHM213A.

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

[48] BCC Publishing (2021). BCC Research Staff. Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B. p. 9.

[49] BCC Publishing (2021). BCC Research Staff. Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B.

organically derived (e.g., from petroleum or rocks) but are created through chemical manufacturing processes, which tend to make them more expensive than natural excipients.

Excipients are used in manufacturing and processing to protect and enhance the drug's stability, bioavailability, and product safety; assist in efficiency and delivery of the drug when used or consumed; and to protect the integrity of the product during storage. The "ideal" excipient has the following characteristics: it is stable and reproducible, with no undesired interactions, pharmacologically inert, desired functionality, and cost effective.[50] In 2021, the global market for pharmaceutical excipients was 8.29 billion US dollars, about five percent of the global API market, of which nearly 93 percent were organic excipients.[51]

Chemistry and biology are at the "heart" of the primary manufacturing stage.[52] Chemical (small molecule) drugs historically have been the cornerstone of modern medicine with less complex chemical structures, simpler manufacturing processes, and often administered orally.[53] The manufacturing process for creating a chemical API involves the procurement of chemical compounds, which are processed into intermediate materials that are further refined and purified into an API. These further processes normally include isolation, extraction, purification, milling, and packaging.[54] Once the API is manufactured, it is blended or mixed with other ingredients to make a bulk drug substance, or it is purified or filtered to create the bulk drug substance.

Biological (large molecule) drugs, on the other hand, are a relatively newer field of drugs and therapies and available primarily as intravenous injections. They are derived from naturally occurring sources, human, animal or micro-organisms and tend to have complex structures and manufacturing processes. The production of biological APIs typically involves cell culture / fermentation, followed by purifying and filtration. Large molecule drugs pose additional manufacturing challenges and risks and display greater fragility and therewith considerable risks in storing and transporting them.[55]

Both production processes typically involve the use of 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 hyper-clean rooms, acquire specialized capital equipment, and employ skilled personnel. Specialized inputs such as bioreactor bags, filters and cellular materials are also needed. The drug substance, once created, is combined with other pharmaceutical ingredients (e.g., excipients, adjuvants and preservatives) to formulate a drug product.

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

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

[52] Paumier, P. (2022). Transfer Pricing in the Pharmaceutical Industry. International Transfer Pricing Journal.

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

[54] BCC Publishing (2021). BCC Research Staff. Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report Code: PHM200B. p. 24.

[55] Deloitte (2015). Advanced Biopharmaceutical Manufacturing: An Evolution Underway**.** Deloitte Development LLC. p. 5.

2.4.2. Secondary manufacturing

Secondary manufacturing involves turning the bulk drug substance (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 (FDFs).[56] Raw materials and excipients are also needed at this stage. The variety of FDFs includes, for example, liquids, gels, tablets, aerosol sprays, and topical ointments.

For drugs based on chemical APIs, in the secondary manufacturing stage the chemical API is typically combined with other ingredients and extruded as pills or capsules, which are then labeled and packaged. For drug products based on biologic APIs, secondary production typically 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.[57]

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 costs. Some may also require cold storage throughout the cold chain logistics process and also to extend shelf life.

2.4.3. Manufacturing and technological change

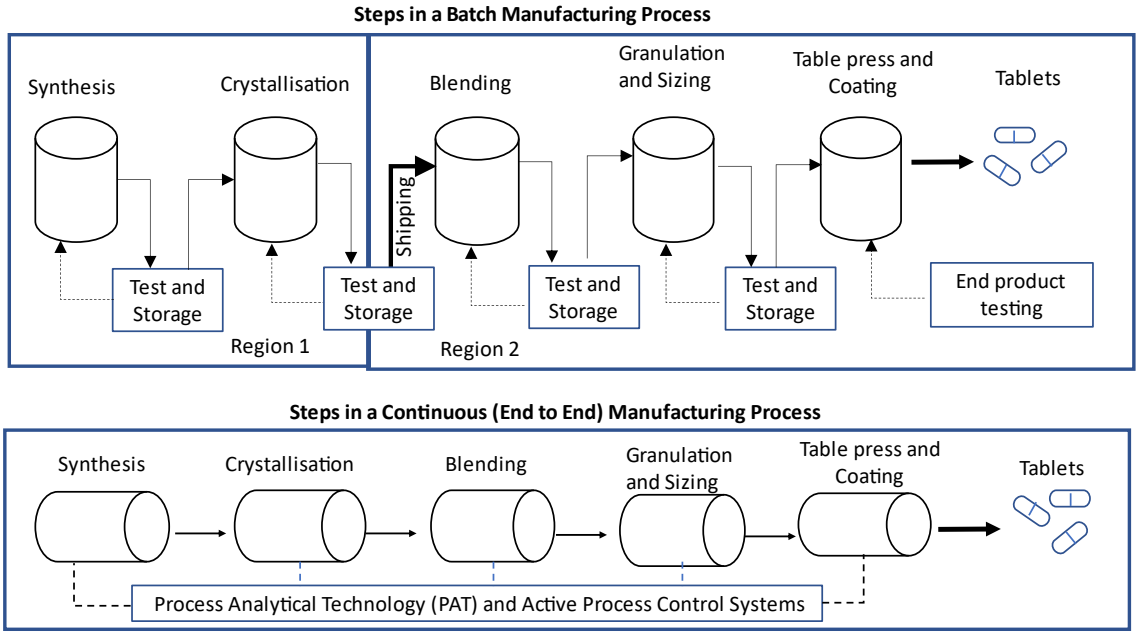
Digitalization is playing an important role in ongoing technological change in the pharmaceutical industry in terms of process technology as firms shift from batch to continuous manufacturing. Most pharmaceutical manufacturing is done by traditional batch manufacturing (BM) processes where raw materials are inputted at the beginning of the process and discharged as a finished product at the end in numbered batches.[58] This involves a number of processes (e.g., blending, granulation, drying) and may require work to be undertaken at different facilities. As a result, BM may suffer from lack of agility, flexibility and reliability, making it difficult for manufacturers to respond quickly to sudden changes in demand or adapt when certain inputs aren't available. BM generally results in the clear separation of the primary and secondary manufacturing stages into different plants and locations. Figure 5 illustrates the typical batch manufacturing process in the pharmaceutical industry.

[56] Shivdasani, Y., Kaygisiz, N.B., Berndt, E.R., and Conti, R.M. (2021). The geography of prescription pharmaceuticals supplied to the USA: levels, trends, and implications. Journal of Law and the Biosciences, doi:10.1093/jlb/lsaa085, https://pubmed.ncbi.nlm.nih.gov/33986950/, page 1.

[57] Janczura, M., Sip, S., and Cielecka-Piontek, J. (2022). The development of innovative dosage forms of the fixed-dose combination of active pharmaceutical ingredients. Pharmaceutics: 14(4): 834.

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

Figure 5: Batch versus continuous manufacturing in the pharmaceutical industry[59]



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

While the cost savings have been estimated at more than 30 percent, the pharmaceutical industry, however, has been slow to shift from batch to continuous manufacturing for a variety of technical, operational, economic and regulatory reasons.[60]

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

[59] Based on Hock, S.C., Siang, T.K. & Wah, C.L. (2021). Continuous manufacturing versus batch manufacturing: benefits, opportunities and challenges for manufacturers and regulators. Generics and Biosimilars Initiative Journal. Figure 2. Available from 10.5639/gabij.2021.1001.004.

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

2.5. Marketing

In this section, the role of marketing as part of the pharmaceutical industry's global value chain is discussed. See also section 3.1 on value drivers in the pharmaceutical industry including section 3.1.2 on marketing intangibles.

Marketing in the pharmaceutical global value chain is typically viewed as the combination of advertising, marketing and promotion (AMP) activities, which are used by a pharma company to promote the sale of its products, together with its downstream sales to wholesale distributors.

The World Health Organization (WHO) defines the promotion of pharmaceuticals as, informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs.[61] In this respect, activities in the pharmaceutical industry range from sales activities through sales representatives to educational or scientific activities, such as industry-organized conferences and clinical studies.[62]

Detailing is a key marketing technique that pharmaceutical companies use to educate physicians about the pharmaceutical products, hoping the physician will prescribe the company's products more often.[63] Detailing entails explaining the characteristics of different drugs in terms of their bio-equivalence and bio-availabilities through the use of skilled pharma representatives. This activity is enhanced through building long-term 1-on-1 relationships.[64] Information is communicated through in-person visits by pharma sales representatives to doctors and hospitals or, alternatively, via digital channels termed e-detailing.

It is important to note that marketing strategies will vary between OTC drugs and prescription drugs and are heavily regulated at the national (and supranational for the EU) level and may be enforced either through legal action or through a NMRA or a supranational agency such as the EMA for the European Union. Regulation pertains to both prescription drugs and OTC drugs, though exact regulations often differ between the two categories.[65] Regulations may limit the retail outlets, marketing channels used, the claims that can be made and the kind of supplementary information that may need to be provided. In addition to national regulations, many medical associations and hospitals or universities have professional or employee codes of conduct that cover interactions with the pharmaceutical industry.[66] For example, direct marketing to consumers through advertisements and commercials is only permitted in the

[61] World Health Organization (1988). Ethical criteria for medicinal drug promotion. Geneva: World Health Organization.

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

[63] Revo Suite (2024). How Medical Detailing Is Changing With Pharma Marketing Technology. Available from https://revosuite.com/blog/how-medical-detailing-is-changing-with-pharma-marketing-technology

[64] Ascher, J., Höglund, D., M'lika, A., Ostojic, I. & Vancauwenberghe, I. (2018). From product to customer experience: The new way to launch in pharma. McKinsey & Company. Available from https://www.mckinsey.com/industries/life-sciences/our-insights/from-product-to-customer-experience-the-new-way-to-launch-in-pharma#/

[65] See, for example, Chang, J., et al. (2016). Prescription to over-the-counter switches in the United States. Journal of Research in Pharmacy Practice, 5: 149-154.

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

United States and New Zealand.[67] Marketing in the pharmaceutical industry therefore requires not only expertise on the drugs and the medical profession's practices but also knowledge of the regulatory requirements.

Pharmaceutical products that require a prescription are generally marketed to healthcare providers, such as physicians, pharmacists and health insurance organizations (which may be independent companies or under the purview of the government);[68] the products may additionally be advertised to patients. OTC drugs are generally marketed to patients directly, though some OTC products may also be promoted to healthcare providers in order for them to recommend them to their patients.[69]

New products are typically protected by patents; this holds especially true for prescription drugs. In this respect, once a prescription drug has been authorized to be distributed, pharmaceutical companies design and execute a market access / marketing strategy for the product. While the exact length of a patent varies between countries and products (see sections 3.1.1 on the value driver patents), the protection from direct competition provided by a patent gives companies a defined timeframe during which to establish a product under a recognizable trademark name and to build up confidence and loyalty towards the product. 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;[70] although this may depend on the presence of price controls (see section 4.2.1 for a discussion on price controls and cost containment measurements).

Against the background of rising digital communication channels and specialty medicine development, there has been an ongoing shift to real-time, data-driven marketing strategies making increased use of digital communication channels as well as key opinion leaders.[71] In-country marketing strategy generally requires a large sales force for detailing purposes; however, digitalization and increasing regulatory pressures may be decreasing the number of "messengers" required to disseminate the "message." For example, a recent PwC study predicted that pharma sales forces and medical science liaisons were likely to be cut by ten to 15 percent due to digitalization of pharma MNEs' go-to-market strategy.[72]

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

[68] Wündisch, K. (2003). Transfer pricing in the Ethical Pharmaceutical Industry. International Bureau of Fiscal Documentation (IBFD). Part I, Chapter 2.4, p, 66-71.

[69] Chang, J., et al. (2016). Prescription to over-the-counter switches in the United States. Journal of Research in Pharmacy Practice, 5(3): 149-154.

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

[71] Somaiya, H. (2022). Omnichannel Is The Next Step In Pharmaceutical Marketing. Forbes. Available from Omnichannel Is The Next Step In Pharmaceutical Marketing (forbes.com)

[72] Solbach, T. et al. (2020). No going back: Pharma companies' route to a digitalized go-to-market model. Strategy & PwC, page 12. https://www.strategyand.pwc.com/de/en/industries/pharma-life-sciences/pharmas-route-to-digitization/pharmas-route-to-digitization.pdf

2.6. Distribution

Once a drug product is manufactured it has to be distributed to the point-of-sale in order for patients to be able to buy the product, taking into account its specific safety regulations and distribution particularities, such as the need for cold storage. See also section 2.7.4 for more details on regulatory affairs for distribution. In most countries, distribution of pharmaceuticals is facilitated through wholesalers and hospitals – this applies to both prescription and OTC drugs. Pharmaceutical manufacturers either sell their products in bulk form to wholesale distributors or set up their own wholly owned distributors. Distributors therefore are intermediaries between manufacturers and their customers (i.e., retailers and health care providers).[73] Distribution may be to a "single channel wholesaler", i.e., a wholesaler that has the exclusive right to distribute medications from one pharmaceutical company within a certain region or country. However, most countries encourage a multi-channel system in wholesaling, in which medications are distributed and supplied in parallel from different wholesalers.[74] In the latter case, wholesalers consolidate orders from multiple companies in their warehouse and package products from several manufacturers that are destined for a particular point-of-sale into the same tote (container). Any products that are not sold or must be returned are sent back to the distributor warehouse to be resold or disposed.[75]

A graphic illustrating the typical flow of products, services, and funds for prescription drugs that are covered under health insurance and purchased in a retail setting is provided in Figure 6.[76] In most countries, a pharmaceutical manufacturer sells its products to one or more wholesale distributors, which supply the products to health care providers (e.g., doctors, hospitals, medical clinics) and/or retail (including mail order) pharmacies. The purchasers dispense the pharmaceuticals to patients, who take them as prescribed.

In most countries, there are third-party payers (e.g., health insurers, employer health plans, and government programs) that provide insurance coverage to insured patients in return for insurance premiums. Patients will also typically make co-payments for the drugs they purchase from pharmacies, hospitals, etc. The third-party payers may also negotiate agreements with the pharmaceutical companies, where the agreements cover which products are included in a patient's insurance plan, processing the prescription medicines through quality and utilization management checks, and managing formulary lists of covered

[73] Dabora, M.C., Turaga, N., and Schulman, K.A. (2017) Financing and distribution of pharmaceuticals in the United States, JAMA, 318(1): 21-22; Congressional Budget Office. (2007). Prescription Drug Pricing in the Private Sector. Available from https://www.cbo.gov/sites/default/files/110th-congress-2007-2008/reports/01-03-prescriptiondrug.pdf.

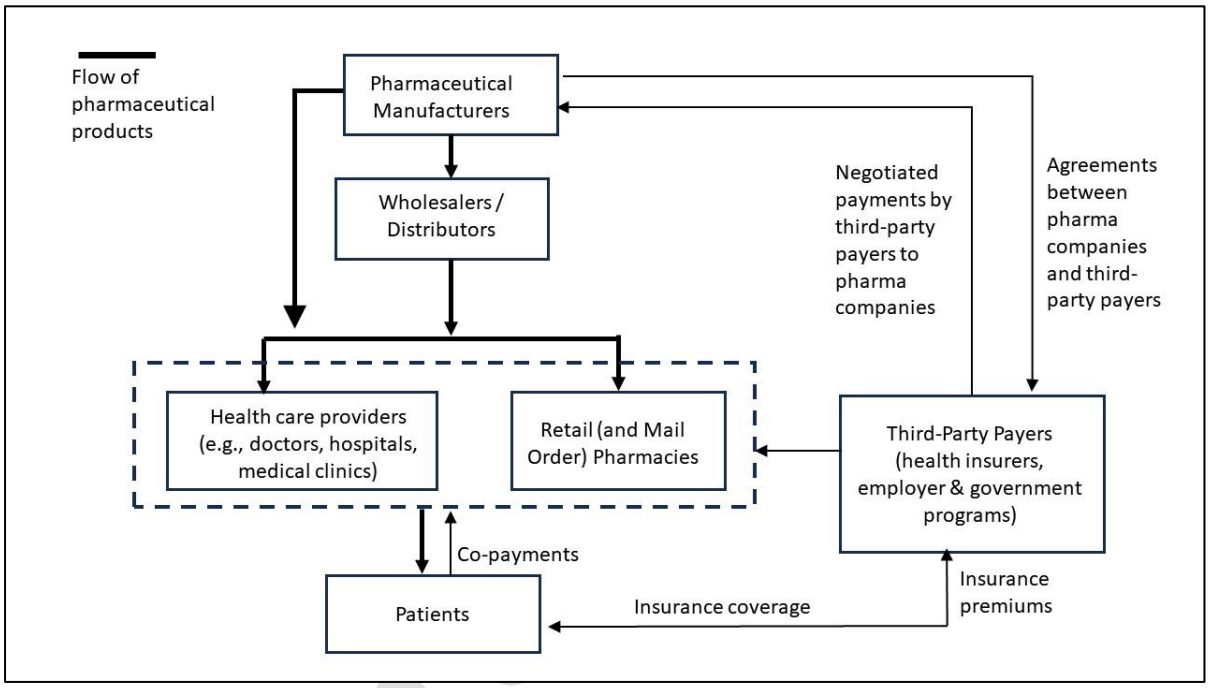
[74] Kanavos, P., Schurer, W., and Vogler, S. (2011). The pharmaceutical distribution chain in the European Union: structure and impact on pharmaceutical prices. European Commission, Brussels, Belgium

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

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

medicines.

Figure 6: The typical distribution system for prescription pharmaceutical products [77]



2.7. Regulatory affairs

All activities of the pharmaceutical industry are governed by a set of strict laws, regulations and policies that draw on the work and standards developed by the WHO but are specific to each country.

Regulation of the pharmaceutical industry takes place both on the demand and the supply side of the market.[78] On the supply side, there are a wide variety of government regulations including:

- Intellectual property rights protection, which in pharmaceutical products typically involves incentives to ensure innovation[79]
- Effectiveness and quality control regulation by government agencies including safety monitoring of both R&D manufacturing and distribution practices

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

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

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

- Price controls and cost containment measures
- Regulation of marketing activities with respect to content, promotional channels and codes of conduct

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, NMRAs are tasked with monitoring the quality, safety and efficacy of drugs, and the accuracy of product information, which is done by ensuring that different elements of the global value chain are carried out according to specified standards. This includes parts of the R&D process / clinical trials; the procurement, manufacturing and distribution of drugs, as well as product promotion and advertising.[80] In the following subsections, government regulations applicable to the four general stages of the global value chain are discussed: (1) R&D, (2) manufacturing, (3) marketing and (4) distribution.[81]

Regulatory policies on the demand and supply sides of pharmaceutical markets vary widely across countries.[82] As the rules are specific to each jurisdiction, it is important to keep in mind that the discussion below focuses on general trends observed and cannot capture the many different rules and regulations as they manifest in countries around the world.

2.7.1. Regulatory affairs: Research and development

As described in section 2.3, the research and development process can be divided into different stages, each of which must adhere to what is commonly referred to as Good Clinical Research Practice (GCP). GCP is defined by the WHO as a process that incorporates established ethical and scientific quality standards for the design, conduct, recording and reporting of clinical research involving the participation of human subjects.[83] GCP 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: Manufacturing

Section 2.4 describes the typical manufacturing process of pharmaceutical products, commonly divided into primary and secondary manufacturing. During manufacturing, companies are expected to adhere to Good Manufacturing Practices (GMP). The WHO defines GMP as quality management that ensures that products are consistently produced and controlled according to the quality standards appropriate to their intended use and as

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

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

[82] See, for example, Berger, M., 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; and Rémuzat, C. 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.

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

required by the marketing authorization, clinical trial authorization or product specification.[84] GMP is aimed primarily at diminishing the risks inherent in any pharmaceutical production from cross-contamination/mix-ups and false labelling. GMP includes procedures for receipt of materials, production, packaging, labeling, quality control, release, storage and distribution.[85]

In many countries, NMRAs will inspect equipment, facilities and manufacturing processes prior to approving a product.[86] In addition, many countries have a legal requirement that every pharmaceutical manufacturer must employ a highly skilled scientist, who can certify that the company's medicine batches meet GMP and Pharmaceutical Quality Systems (PQS) standards.[87]

2.7.3. Regulatory affairs: Marketing

Marketing of pharmaceuticals is heavily regulated in most countries, as explained in section 2.5. This encompasses rules on which marketing channels may be used as well as what claims can be made.[88] There are key regulatory differences between prescription drugs and OTC medications. Government regulations that determine which drugs require a physician's prescription can influence how the drug is marketed and distributed.[89]

In most countries, pharmaceutical sales are made 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 the medicines that are purchased by households, hospitals and government medical services.

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

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

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

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

[87] https://www.rsc.org/careers/cpd/practising-scientists/qp-pharmaceutical/.

[88] Mulinari, S. (2016). Regulating Pharmaceutical Industry Marketing: Development, Enforcement, and Outcome of Marketing Rules. Sociology Compass. Available from 10.1111/soc4.12335. See also Alves, T.L, Lexchin, J., & Mintzes, B. (2019). Medicines Information and the Regulation of the Promotion of Pharmaceuticals. Science and Engineering Ethics, 25: 1167-1192.

[89] Chang, J., et al. (2016). Prescription to over-the-counter switches in the United States. Journal of Research in Pharmacy Practice, 5(3): 149-154.

2.7.4. Regulatory affairs: Distribution

The distribution and storage of drugs is, as discussed in section 2.6, is an important activity in the global value chain of pharmaceutical companies. Substandard and/or falsified products are a significant threat to public health and safety. Consequently, it is important to ensure the quality and safety of drugs, to prevent the exposure to substandard and falsified products, and to ensure that the integrity of the distribution chain is maintained. Accordingly, most countries have established Good Distribution Practices (GDP) in line with recommendations by the WHO. Such regulations generally cover the need for written procedures and clearly specified responsibilities, traceability requirements, systems for quality risk management including systems for managing returns, complaints and product re-calls.[90]

3. Value drivers and business models in the pharmaceutical industry

In this section value drivers and business models are discussed.

3.1. Value drivers in the pharmaceutical industry

The pharmaceutical GVC is the most knowledge intensive of all GVCs. The *Global Value Chain Development Report 2021* estimated the knowledge intensity of pharmaceuticals and medical devices at 66.3 percent, compared with 17.4 percent for computers and electronics, 13.7 percent for information technology services, and 2.3 percent for food and beverages.[91] Thus, the key drivers of profits in the pharmaceutical industry are knowledge-based. In performing a transfer pricing analysis, the interaction between these classes of intangible assets, as well as the parties that have performed the functions, borne the risks and incurred the costs associated with the DAEMPE (development, acquisition, enhancement, maintenance, protection and exploitation) of functions in relation to the intangible assets, are relevant.

Below some of these key drivers are discussed: (1) R&D and patents, (2) marketing intangibles, (3) marketing authorization and (4) know-how and (5) digitalization.

The importance of these key drivers will vary between countries and will depend on the specific transaction that is under review during a transfer pricing analysis.

3.1.1. Value driver: R&D and patents

Technological knowledge, driven primarily by a firm's R&D activities, has been widely perceived as the most important of the MNE's firm specific advantages and the key long-term value driver in the pharmaceutical industry.[92] R&D activities carry a high risk in view of the uncertainty of the potential outcome and will often involve large investments that may or may not lead to a new product. It is estimated that the average time a successful pharmaceutical product takes from R&D to market may be ten to 15 years, with the economic cost of developing a successful compound (including opportunity costs and costs of failed

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

[91] Asian Development Bank (2021). Global Value Chain Development Report 2021: Beyond Production.

[92] Vallat, G. (2020). Application of the DEMPE concept in the pharmaceutical industry. International Transfer Pricing Journal, 27.3.

products) of up to 1.5 to 2 billion USD.[93]

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

If patent protection is missing, generic manufacturers can enter the industry and compete with existing suppliers, which has an impact on a company's revenues. The value of the patent can be affected also by the need for a marketing authorization because the latter will determine if a product can enter and be sold in a specific country.

The firm's goal is generally to develop an innovative product that will be granted patent protection for a set time period during which the patent holder alone can decide which companies are allowed to use a specific formulation, manufacturing process or chemical compound. As a result, patents provide the patent holder with an opportunity to recoup the costs involved in developing the patented innovation and act as a reward for engaging in risky and lengthy R&D. The patent protection depends on the patent type, scope coverage and national availability of legal remedies, which differs between countries and can last up to 20 years. Once off patent, firms with small molecule drugs face competition from generics; those with biologics face competition from biosimilars. See also section 4.2.2 for a discussion on patent lifecycle management and patent cliffs.

How R&D costs and revenues are reported on a company's income statement therefore can have a substantial impact on its profitability (and thus corporate financial exposure, risk profile and income taxes) given that failed projects occur frequently and have large sums of sunk costs that – due to the asynchrony of R&D costs incurred and accounting principles – cannot be spread out over time.[94]

An alternative to costly and risky in-house development is the acquisition of smaller firms and their intellectual property by larger firms.[95]

3.1.2. Value driver: Marketing intangibles

Marketing intangibles can have important value for pharmaceutical products.[96] Potential marketing intangibles can include, for example, (1) trademarks / trade names, (2) brands / global brands, and (3) customer lists, relationships and proprietary data. For a more detailed discussion of marketing intangibles, see the UN TP Manual at section 6.2.4.

From a transfer pricing perspective, an important question is whether national marketing activities may generate a national marketing intangible that is distinct from the foreign-

[93] Harrer, S., Shah, P., Antony, B., and Hu, J. (2019). Artificial Intelligence for Clinical Trial Design. Trends in Pharmacological Sciences, 40(8): 577-591. DOI: 10.1016/j.tips.2019.05.005.

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

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

[96] Roberge, C. (2013). Transfer pricing in the pharmaceutical industry: The remuneration of marketing intangibles. International Transfer Pricing Journal, 20.4

owned brand and generates a return greater than otherwise comparable uncontrolled distributors (section 6.2.4.5 of the UN TP Manual). In analyzing any intangible, it is important to determine if the intangible 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 (see. 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.

It should be noted that 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 are directed to analyze the specific facts and circumstances closely 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 with regard to 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 in case the trademark carries social and commercial significance. In contrast to a patent, a trademark may – if regularly prolonged – continue indefinitely.

The marketing of a pharmaceutical product aims at establishing the trademark in a way as to continue to successfully sell the drug after patent protection has lapsed. This includes managing pricing and discounts strategically so as to continue acceptance by the population where competition is both "within patent" (competition between patented products) and patent versus 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.

There are also alternative marketing strategies that instead of focusing on the trademark revolves 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, amplify channel power, offer the potential for higher profit margins, and guard against competitive attacks.[97] Branding can help create a unique and valuable marketing intangible; unique in that the intangible is not present in otherwise comparable uncontrolled transactions, and valuable in that branding can generate a significant expected premium value for the branded product (see section 6.2.4.3 of the UN TP Manual).

Pharmaceutical MNEs use AMP activities to establish brand awareness and product loyalty. Given the high costs of bringing a drug through the R&D and regulatory processes, branding

[97] Steenkamp, J-B. (2014). How global brands create firm value: the 4V model. International Marketing Review, 31.1: 5-29.

is a critically important value driver for pharma MNEs that helps generate the sales needed to cover the R&D and regulatory costs. Some branded drug products become so-called "blockbuster drugs" that are globally recognized as best-in-class solutions for particular diseases and conditions. For example, global sales of the #1 blockbuster drug in 2022 were 37. 8 billion US dollars.[98]

Branding can create an important competitive advantage for national or regional pharmaceutical companies by building brand awareness, loyalty and perceptions of quality.[99] For example, creating brand awareness for national branded generic drugs has been shown to be an important value driver in the Indian pharmaceutical industry.[100] Perceived quality has been shown to be positively related to brand equity in terms of present market value and expected future potential.[101]

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, which often entails the development of a customer list. In performing the marketing function, the sales force in carrying out the detailing function as described in section 2.5 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 additionally be generated.

3.1.3. Value driver: Marketing authorization

In order to market and sell pharmaceutical drugs in most countries, firms must generally register and receive approval from the country's NMRA.[102] In the registration process, the firm provides information about the drug and where it was manufactured. The regulatory authority evaluates the firm's data and scientific evidence on the drug's effects and decides whether to grant permission for the drug to be marketed and sold in that country. Drug products must undergo a rigorous testing process, and a NMRA has to issue a market authorization for companies to be able to sell the product in a specific country or region and to sell the drug with specific indications according to the tests that were carried out by the firm. Once marketing approval has been received the product can be manufactured and sold in that country.

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[98] Haakonsson, S.J. (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 Chandel, D. Xie, V. & Kovacevic, V. (2023). Top 20 drugs in 2023, by 2022 sales statistics. Available from https://xtalks.com/top-20-drugs-in-2023-by-2022-sales-statistics-3645/

[99] Panchal, S.K., Khan, B.M. & Ramesh, S. (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). Available from http://mmj.sagepub.com/content/12/2/81

[100] Nath Sanyal, S., Datta, S.K., and Banerjee, A.K. (2013). Conceptualizations of branding: strategy based on the Indian pharma sector. International Journal of Pharmaceutical and Healthcare Marketing, 7.2: 175-198.

[101] Nath Sanyal, S., and Datta, S.K. (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.

[102] European Medicines Agency. Marketing authorization. Available at: https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation.

Oftentimes, in order to retain a market authorization in a particular country, specific follow-up activities have to be undertaken such as phase 3B clinical trials and phase 4 marketing surveillance surveys (see section 2.3.2 and 2.3.3).

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

3.1.4. Value driver: Know-how

While in the past pharmaceutical companies focused on protecting an API and its products, pharma MNEs now increasingly seek additional patent protection on the related know-how, for example, with regards to manufacturing processes. This is especially relevant when production is scaled up from small batch production needed for clinical trials to producing at scale. 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.[103]

3.1.5. Value driver: Digitalization

In the coming years, digitalization is expected to transform the pharmaceutical industry in the following ways: [104]

- As discussed in section 2.4.3, pharmaceutical manufacturing is expected to shift from batch to continuous manufacturing, affecting plant location
- Artificial intelligence (AI) 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 is believed to transform the supply chain management of the pharmaceutical industry.
- Big data and analytics have the potential to improve patient healthcare as well as the operational efficiency of the manufacturing process.

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

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

[104] Siddiqui, Y.J. (2019). Transfer Pricing and Value Creation in the Pharmaceutical Sector. In Petruzzi/Tavares (Eds). Transfer Pricing and Value Creation. See also Hole, G., Hole, A.S., and McFalone-Shaw, I. (2021). Digitalization in pharmaceutical industry: What to focus on under the digital implementation process? International Journal of Pharmaceuticals: X.3: 10095.

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

Some MNEs may be organized into a functional structure, where each entity in the MNE group is staffed with employees that are responsible for a particular function (e.g., R&D, manufacturing, distribution). Other MNEs 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 by 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 the UN TP Manual section 1.3.2 on Management and Organizational Structures.

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

3.2.2. Business models

All companies, national and multinational, have an enterprise operating model[105] or business model[106] that defines the company's customer value proposition and is designed to create a long-run competitive advantage in an industry. These operating/business models essentially organize the firm's functions performed, assets used, and risks assumed along its value chain of 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 national or regional consumer tastes and incomes. For example, the choice as to whether to centralize a function in one entity/location within the MNE group or to have multiple entities/locations performing the same activity 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. [107]

There are many types of possible business models used by today's MNEs; see the discussion

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

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

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

of business models in the UN TP Manual sections 1.3.3.11 through 1.3.3.17. The range of possible operating/business models runs from a centralized business model to a loosely-held holding company or conglomerate. In between are models consisting of closely- or loosely-related portfolio of businesses.[108] The type of business model may have implications for the form of the related party transaction. For example, an MNE with a centralized business model is likely to have one or more entities providing centralized intragroup services (see 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 – MNEs with global brands – began to adopt what is referred to as a "centralized business model" or "principal structure".[109] To manage the complex matrix of products, geographies and functions associated with their global value chains and the associated risks, these MNEs adopted a tiered and nested organizational design. In addition to the parent firm, there are one or more "principals" that function as entrepreneurial entities for each of the regions within the MNE network. The principals have oversight responsibility for MNE entities within that region (e.g., Europe, Africa, Asia, Australia-New Zealand, Latin America).

In addition, the global MNE may set up centralized "hub structures" at the regional and /or global level, with responsibility for certain business functions such as information technology, human resource management, and international finance. Some functions, such as marketing, may involve multiple tiers: a centralized entity responsible for the marketing of the global brand(s), regional entities responsible for marketing of regional products, and national marketing teams within each country that are responsible for national products and fine-tuning for national needs and incomes.[110] 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 IP owner. Within the parent entity are departments and/or national affiliates responsible for strategic management, regulatory affairs, and support services, in addition to entities responsible for the primary activities in the MNE's value chain (R&D, primary and secondary manufacturing, marketing, and distribution). The parent firm may have one or more regional principals with responsibility for the IP 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 clinical testing, secondary manufacturing, and national or regional

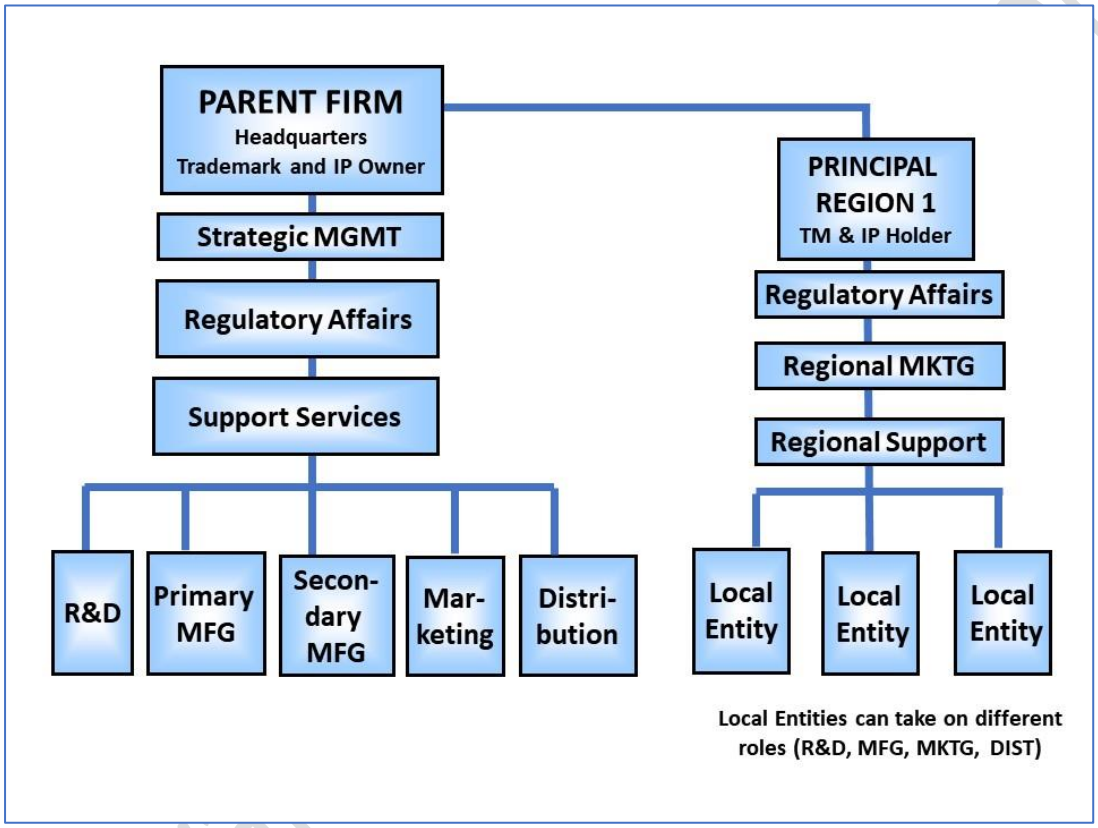
[108] Kates, A., Kesler, G., and DiMartino, M. (2021). Networked, Scaled and Agile: A Design Strategy for Complex Organizations. Kogan Page.

[109] van Herksen, M. (2009). Business Models. In Bakker, A. (editor). Transfer Pricing and Business Restructurings: Streamlining all the Way. International Bureau of Fiscal Documentation. Chapter 2. See also Hervé, Y. and Eden, L. (2023). Shapley Value in Dispute Resolution: Lessons in Transfer Pricing from a Life Sciences MNE. Tax Notes International, 112 (November 6): 753-768.

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

marketing. [111] As discussed above, it is important to understand that a highly stylized business model is described here. It will be essential to understand and analyze the organizational structures in a particular MNE group.

Figure 7: Example of a pharmaceutical MNE 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.[112] 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 acquisitions of independent biotech and/or pharmaceutical businesses, which remain

[111] On business models of MNEs in the life sciences industry see also Hervé, Y., and Eden, L. (2023). Shapley Value in dispute resolution: Lessons in transfer pricing from a life sciences MNE. *Tax Notes International*, 112(6): 753-768. It is also important to note that this discussion is of highly stylized business models, which may not fully reflect the real-life complexities of the reality of a large pharmaceutical MNE operating across borders.

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

mostly stand-alone in terms of their activities after acquisition.

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

iii. Strategic alliances

Strategic alliances among firms are common in most industries, including the pharmaceutical industry. In a strategic alliance, two or more firms cooperate at one or more stages along the value chain. The alliance may or may not involve equity ownership. Some examples in the pharmaceutical industry are the following:[113]

- Joint venture: A common business model is for a pharmaceutical company to be the "discovery" firm and for it to align in an international joint venture with another company. This partner firm commercializes and does the selling of the final product. A typical joint venture could involve a biotechnology firm that does not have access to a distribution network and so chooses to ally with a pharmaceutical firm.
- Co-marketing arrangement: One firm provides a non-exclusive license to the co-marketer allowing both the licensor and licensee firms to market the same product under different brand names.
- Co-development agreements: Both firms jointly engage in one or more R&D projects at the development stage (e.g., clinical testing).
- Co-promotion arrangement: Both firms promote the product under the same brand name.
- Contract R&D arrangement, contract manufacturing, license and supply agreements.

3.2.3. Business models and location decisions

An MNE's basic research and development and pre-clinical testing activities historically have been centralized in the headquarter country or one or more of the regional headquarter countries.[114] Clinical testing stages may take place in several strategic locations reflecting the need for drugs to be tested on populations with different demographic characteristics and / or domestic health and safety requirements. Contract R&D, i.e. research and development activities under the guidance and for the benefit of the parent company, is often carried out in countries that have science or R&D parks and that encourage the location of local R&D

[113] Wündisch, K. (2003). Transfer pricing in the Ethical Pharmaceutical Industry. International Bureau of Fiscal Documentation (IBFD). Appendix Q: Strategic Alliances, p. 289-294.

[114] See the historical overview provided in Shivdasani et al. (2021) and the introductory chapter by Baxerres, C. & Cassier, M. Introduction: Pharmaceutical markets in the Global South: Shaped by history and multiple regulations, in Baxerres, C., and Cassier, M. (eds.) (2022). Understanding Drugs Markets: An Analysis of Medicines, Regulations and Pharmaceutical Systems in the Global South, Routledge. https://www.taylorfrancis.com/books/oa-edit/10.4324/9780429329517/understanding-drugs-markets-carine-baxerres-maurice-cassier. See also Chapter 5, "A new geography of pharmaceuticals: Trajectories of artemisinin-based medicines" by Cassier, M., pp. 117-135.

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 also been used to attract secondary manufacturing in the pharmaceutical industry t.[115] This stage may also be outsourced to third parties in the form of contract manufacturing, for example in case pharmaceutical MNEs do not have sufficient resources for in-house manufacturing facilities or if they prefer to focus on R&D and outsource the downstream activities.[116]

In terms of marketing activities, in the pharmaceutical industry the importance of national and/or regional responsiveness (e.g., the need to be close to the customer and to adapt to national and regional markets and tastes) are important factors driving decentralization of marketing activities. Pharma MNEs are increasingly being organized around their customers and paying more attention to national/regional responsiveness, which increases for example, the need for and roles of national/regional medical liaisons.[117]

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 the marketing activities performed in a particular country. Government regulations can also affect the manner in which marketing activities are carried out. Factors such as the size and income level of the economy and the health profile and preferences of the population also influence the amount of spending that is 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. [118]

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

A key issue, identified by the WHO, for both MNEs and government health authorities, is the shortage of healthcare workers worldwide, and the imbalance between needs and supplies. Recent surveys of the status of pharmaceutical education, and its linkage with the health needs of the population and with the national priorities, illustrate the disparities across

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

[116] BCC Research Staff (2021). Active Pharmaceutical Ingredients: Global Markets. Staff Report. Report It is important to note that marketing strategies will vary between OTC drugs and prescription drugs. As noted in section 1.2., OTC products are typically sold in pharmacies, though some countries may also allow these products to be sold in drugstores, supermarkets or convenience stores.
Code: PHM200B. BCC Publishing. p. 60.

[117] Ascher, J., Höglund, D., M'lika, A., Ostojic, I. & Vancauwenberghe, I. (2018). From product to customer experience: The new way to launch in pharma. McKinsey & Company. https://www.mckinsey.com/industries/life-sciences/our-insights/from-product-to-customer-experience-the-new-way-to-launch-in-pharma#/.

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

countries in terms of skilled healthcare workers.[119]

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

- Developing an understanding of the accurately delineated transaction, which includes:
    - Identifying the economically significant characteristics and circumstances of the controlled transaction, i.e. the transaction between associated enterprises; and
    - Identifying the respective roles and responsibilities of the parties to the controlled transaction, as part of a functional analysis.

- Comparing the prices and other conditions of the controlled transaction (established in the first step) with those prices and other conditions in uncontrolled transactions taking place under comparable circumstances; the latter transactions are referred to as "comparable uncontrolled transactions" or "comparables".

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

4.2. Accurate delineation of the transaction

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

[119] World Health Organization (WHO). (2016.) Global Strategy on Human Resources for Health: Workforce 2030. Geneva, CH. See also Etukakpan, A., et al. (2023). Transforming pharmaceutical education: A needs-based global assessment for policy development. Exploratory Research in Clinical and Social Pharmacy, 9 (February), 100234. http://dx.doi.org/10.1016/j.rcsop.2023.100234, and Konduri, N., Rauscher, M., Wang, S-C. J. & Malpica-Llano-T. (2017). Individual capacity building approaches in a global pharmaceuticals system strengthening program: a selected review. Journal of Pharmaceutical Policy and Practice 10:16, DOI 10.1186/s40545-017-0104-z.

The examination of the controlled transaction involves analyzing 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. In the case of multiple transactions, the transfer pricing professional must also decide whether the transactions should be evaluated separately or if they can be reasonably aggregated.

Accurately delineating transactions can be very complex in the pharmaceutical industry, as key activities in relation to economically significant risks may be fragmented between or amongst different entities within a multinational group. The complex regulatory structure that affects all stages of the pharmaceutical GVC also requires tax auditors to have detailed knowledge in the pharmaceutical industry. It will also be necessary to take into account the business model used by the taxpayer, as described in section 3.2, which in this industry is often very complex and highly integrated. Similarly, contractual arrangements may be difficult to analyze due to their technical nature and language.[120]

4.2.1. Industry and market context

The transfer price of a particular pharmaceutical product in a particular 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. The focus in this section is on aspects that are specific to the pharmaceutical industry, including (1) price controls and cost containment measures, (2) parallel imports, and (3) business strategies in relation to patents.

i. Price controls and cost containment measures

Some countries establish drug price controls, that is, there are government rules that affect the market[121] for certain pharmaceutical formulations through price regulation (e.g. imposing a cap on prices of certain medicines and/or controlling the volume to be sold). This is generally done to manage national healthcare costs.[122]

In some countries, an insurance may exist for certain prescribed pharmaceutical drugs. In some countries, patients may be restricted to generic prescription drugs. For example, in Australia for prescribed drugs registered under the Pharmaceutical Benefits Scheme, the customer is given the choice of choosing cheaper generic drugs if an off-patent drug has been prescribed.

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

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

[121] 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.

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

ii. Parallel imports of pharmaceutical products

Parallel imports refer to branded goods that are imported into a market and sold there without the trademark owner's consent in that market.[123] Parallel imports originate as genuine products that were manufactured under the official license of the original trademark owner and destined for a particular jurisdiction. [124] Parallel importing occurs when there is a material price difference for the same product between two jurisdictions and the price difference encourages additional purchases in the first jurisdiction that are destined for sale in the second jurisdiction.

An important concept in the literature on parallel imports is that of exhaustion of intellectual property rights ("IPR exhaustion"), which refers to the extent to which an IPR holder can control the distribution of its trademarked goods. [125] According to the concept of IPR exhaustion, once an IPR holder sells a product to which its IP rights are attached, the IP rights are exhausted.

Parallel importing may force an MNE's distribution subsidiary 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 that aim at containing health care costs. Parallel trade regulations[126] encourage the free movement of identical products between countries in order to encourage competition and reduce prices. Since parallel imports are obtained from a foreign jurisdiction at a price that is lower than the corresponding prices in the destination jurisdiction, parallel importing usually results in decreasing revenues / margins for MNE's distribution subsidiaries

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

First, the issue arises as to whether and to what extent the transactions of the third-party parallel importer can function as comparable transactions for the controlled transactions of the MNE's distribution subsidiary. An associated pharmaceutical distributor in a country where parallel imports are made available has no control over the quantities/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 the underlying facts and circumstances in terms of comparability of functions carried out, assets used, and risks borne by the subsidiary vis-à-vis the parallel importer.

Second, in case of a material impact from parallel imports on the subsidiary's remuneration, the question arises 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 on, for example, the risk profile of the distribution subsidiary and the contracts and regulations in

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[123] International Trademark Organization. Parallel Imports. See https://www.inta.org/topics/parallel-imports/

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

[125] International Trademark Organization. Parallel Imports. See https://www.inta.org/topics/parallel-imports/

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

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. However, this fact alone 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.

iii. COVID-19 global pandemic

As in other industries, pharmaceutical companies have been faced with disruptions in their business models (positive and negative) caused by the global pandemic including through value chain disruptions, regulatory responses/approvals, and slowdowns for some patient procedures (e.g., non-emergency surgeries and infusion therapies).[127] The COVID-19 pandemic also brought about an unprecedented level of collaboration between the pharmaceutical industry and governments.[128] Reference is made to the guidance on transfer pricing during the COVID-19 economic downturn.[129]

4.2.2. Business strategies

The transfer price of a particular pharmaceutical product in a particular market is also affected by the firm's business strategies, in particular, (1) its patent and (2) marketing strategies.

i. Business strategies in relation to patents

In recent decades, two concepts around patents have gained traction: "patent cliff" and "patent lifecycle management."[130] The term "patent cliff" refers to the potential sharp drop in expected profits after the patent for a firm's product expires. Once the product is "off patent" and no longer protected from competition by the patent, the product faces more competition from existing branded products and from rival firms producing and selling generics or biosimilars. The additional competition reduces the product's sales, market share, and profitability. Patent cliffs therefore generally result in lower revenues for originator companies once the patent has expired. The size of the patent cliff varies across countries, depending on patent expiry dates, the degree and rapidity of market penetration by generics, and the extent of customer loyalty to originator products.[131]

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[127] On the pharmaceutical industry during COVID-19, see IQVIA Institute (2023). Global Use of Medicines 2023: Outlook to 2027. Available at: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/the-global-use-of-medicines-2023. For application of GAAP and IFRS accounting standards to the pharmaceutical industry during COVID-19, see Deloitte. (2023). Life Sciences Industry Accounting Guide. Available from https://www2.deloitte.com/content/dam/Deloitte/us/Documents/audit/us-2023-life-sciences-industry-accounting-guide.pdf.

[128] Druedahl, L.C., Minssen, T. & Price, W.N. (2021). Collaboration in times of crisis: A study on COVID-19 vaccine R&D partnerships. Vaccine, 39(42).

[129] UN (2024). Interstitial Guidance on Transfer Pricing During the COVID-19 Economic Downturn. Available from Transfer Pricing During COVID-19 Economic Downturn .pdf (un.org)

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

[131] Price differentials can range widely across countries, even within the European Union as documented in

In developed economies, it is estimated that patent expiry typically leads to, on average, an 80 percent market share loss for the formerly patented drug and a 20 to 30 percent reduction of the drug's price, with a further price decrease with each additional generic entrant. In some cases, the price of the formerly patented drug decreases by up to 90 percent once off-patent.[132] The decrease in drug prices may be less severe in developing countries where off-patent branded drugs may continue to dominate local markets.[133]

Patent lifecycle management refers to the practice of extending patent protection by filing secondary product patents on a new formulation (changes in tablet forms, dosage amount, etc.), a new method of use, or new process patents on manufacturing techniques.[134] Viewed from a barrier to entry perspective, attempts to extend patent life can be viewed as "ever-greening", 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.[135]

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, there may be a combination of marketing activities performed within an MNE group. Entities belonging to a pharmaceutical MNE may perform marketing activities which reflect the activities performed by independent entities. In some cases, these dependent entities may perform marketing activities that are not performed by independent entities. These activities may include the 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 how successful the marketing activity is, this may result in the creation in that country of (valuable) marketing intangible.

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

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.

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

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

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

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

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

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

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

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

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. Its purpose is to gain an understanding of the operations of an enterprise in connection with its transactions with associated enterprises. The functional analysis examines the respective roles of the parties to the controlled transaction under examination, as well as the assets employed and the risks assumed by each entity. This will affect the arm's length remuneration for the controlled transaction since compensation in transactions between two independent enterprises will usually reflect the functions that each enterprise performs, taking into account assets employed and risks assumed.

Below are examples of the possible functions that may be performed, assets utilized and risks assumed by a controlled entity in a particular tax jurisdiction, which depend, for example, on the entity's location within the MNE global value chain and the roles and responsibilities assumed by the entity within the multinational group.

Functions that may performed by the controlled taxpayer include:

- Corporate strategy formulation
- Distribution and sales activities
- Finance, accounting, treasury and legal
- General management functions
- Human resource 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 (AMP) activities
- Post-sale activities including 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, as described in section 3.1, are (1) R&D and patents, (2) marketing intangibles, (3) marketing authorization, (4) know-how and (5) digitalization. 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, plant and equipment
  - Natural resources
  - Office equipment
  - Vehicles
- Other / complementary factors
  - Distribution network
  - Goodwill
  - Workforce in place[136]

In terms of risks that may be assumed by the controlled taxpayer, an entity in an MNE group that assumes the economically significant risks (often an "entrepreneur") would be expected to take on both upside and downside consequences of those risks. Possible risks that may be assumed by the taxpayer include: [137]

- Bad debt risk
- Continuity of supply, supply shortages and other disruptions risks

[136] 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 pharmaceutical industry in a particular country. See paragraphs 6.2.5.14 through 6.2.5.19 in the UN TP Manual.

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

- 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

5. Transfer pricing examples

5.1. Example 1: When the CUP method may not be the most appropriate method

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 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. In Country Y the prices for prescription drugs are not regulated by the government.

Company A also sells the drug under non-exclusive contract to independent pharmaceutical distributors in Country Y that distribute the product to drug wholesalers in rural centers in Country Y. 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

The price that Company B pays to Company A to buy DAY is US dollar 20 per pack; each pack contains 25 thirty-milligram tablets. The price paid by the independent distributors to Company A for the unbranded identical drug is US dollar five per pack; the pack size and tablet strength are the same as purchased by Company B.

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 volume of sales to the independent distributors in Country Y is similar to the volume of

sales to Company B. The independent distributors and Company B both 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. As section 1.2.1 notes, both bioequivalence and bio-availability are important product characteristics that may affect the arm's length transfer price. The firm concludes that the product DAY and its generic competitors have the chemical compositions (i.e., the same bioequivalencies) and the same uses or effects (i.e., the same bio-availabilities).

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

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

5.2. Example 2: Application of TNMM to a distributor using a portfolio 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 products to pharmacies and hospitals for over-the-counter sale.

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

The tax authorities in Country Y have commenced a review of DIST Co's transfer prices. The question at issue is the transfer pricing of imports by DIST Co of the five pharmaceutical products A through E that are purchased from other affiliates in the East Group.

5.2.2. Facts

Under the intercompany agreement, DIST Co distributes five consumer 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) is 8.1%. Table 7 provides DIST Co's profit and loss data for the five products during the relevant tax years.

Table 7: DIST Co's gross and net profit margins, by product line ($'000)

Product	Net Sales	COGS	Operating Expense (OE)	EBIT (Operating Profit)	Operating Profit Margin (OPM)
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%

As the table shows, DIST Co earns 13.7% and 26.7% 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 (OPM of -33.9%) even though DIST Co has incurred significant marketing costs (OE $3,200) for the product. Product E, however, is profitable for the East Group in other countries. A financial forecast predicts that product E is expected to be more profitable in subsequent years.

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

An independent transfer pricing adviser is hired by DIST Co to conduct a transfer pricing analysis for its consumer products due to the upcoming transfer pricing audit. The advisor begins by looking at the intercompany contracts and preparing a FAR (functions, assets, and risks) analysis of DIST Co. The advisor concludes 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 in Country Y.
- DIST Co is responsible for promoting the products in Country Y.

The tax advisor investigates whether DIST Co's marketing and promotion activities may be generating local marketing intangibles that should be taken into account. The advisor finds that the promotion materials are prepared by the marketing department in Company A and one employee at Company B is responsible for adapting and distributing these materials for the national market. The advisor concludes there is insufficient evidence of local marketing intangibles.

The advisor concludes that the accurate delineation of the transaction based on the contract terms, the conduct of the parties and all other economically significant characteristics is that Company B is a fully fledged distributor that sells a range of pharmaceutical drugs purchased

from Company A.

The advisor concludes that the comparable uncontrolled price (CUP) method cannot be applied as they are no internal or external comparables.

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

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 anti-inflammatory products. BLUE Co distributes weight loss products, anti-allergy tablets and vitamin tablets.

The transfer pricing advisor concludes that GREEN Co and BLUE Co are sufficiently similar distributors to DIST Co and operate in the same market (Country Y) under sufficiently similar conditions to DIST Co. However, the publicly available financial information on BLUE Co and GREEN Co's business operations is limited. For example, information on either firm's gross profit or operating expenses is not available. Thus, the advisor cannot calculate the gross profit margins of the unrelated distributors. The advisor therefore concludes that the Resale Price Method cannot be applied.

The advisor therefore decides to consider the transactional net margin method (TNMM). The advisor notes that DIST Co is the simpler of the two related parties and does not own any unique and valuable intangibles. As a result, the advisor concludes that the most appropriate transfer pricing method is the 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 TNMM

The transfer pricing advisor therefore compares the operating profit margins of DIST Co with those of the unrelated distributors. GREEN Co's OPM is 6.5% and BLUE Co's OPM is 8.5%. Since DIST Co's overall OPM is 8.1%, the transfer pricing advisor finds that DIST Co's OPM overall is arm's length. The advisor also notes the following points in supporting this conclusion.

While it is preferable to determine the profit level indicator by transaction or by 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 at the aggregated level. Moreover, the product-line breakdown for DIST is also 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 advisor 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. The tax authority in Country Y concludes that the only additional function is packaging, which does not require separate remuneration. After studying the report, the tax authority in Country Y agrees with the accurate delineation

of the transaction and that the TNMM is the most appropriate method and operating margin (OM) is the appropriate profit level indicator. The tax auditor also accepts the conclusion of the company's advisor that DIST Co's overall EBIT of 8.1% on its product portfolio is arm's length.

5.3. Example 3: Transfer pricing involving a possible local marketing intangible

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 active pharmaceutical ingredient (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 its competitors' 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 wholesaler distributors that supply hospitals and pharmacies in Country Y. In Country Y, there are a limited number of wholesalers that sell to hospitals and pharmacies, and they have non-exclusive relationships with the pharmaceutical manufacturers. Over time, DIST Co has been able to forge an effective relationship with these local wholesalers.

The activities undertaken by DIST Co in Country Y include advertising, marketing and promotion (AMP) activities. DIST Co has a dedicated sales force that visits and promotes CURE with physicians that specialize in treating ulcerative colitis. Over time, DIST Co's sales force has done research and collected data on specific patient and physician preferences in Country Y; this data is highly relevant for the marketing and sale of CURE in country Y.[138] While physicians tend to prefer granular formulations for treatment of ulcerative colitis, DIST Co's sales force has learned that (1) patients prefer small tablets to granular or large tablet formulations; (2) patients prefer to take the medication once a day rather than twice a day; (3) patients taking small tablets once a day are much most likely to adhere to the treatment than if they take other formulations and (4) as a result, the treatment success rate with CURE is higher than with the competitors' products. DIST Co's sales force has shared its research with Country Y's physicians and has developed an in-house marketing policy that stresses these four points. DIST Co has been successful in persuading physicians that CURE is preferable to competing products, which 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.

[138] MacKenzie-Smith, L., Marchi, P., Thorne, H., Timeus, S., Young, R. & Le Calvé, P. (2018). Patient preference and physician perceptions of patient preference for oral pharmaceutical formulations: Results from a real-life survey", Inflammatory Intestinal Diseases, 2018, 3(1), pp. 43-51. Available from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266025/.

5.3.2. Analysis

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

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

If DIST is and has always operated by merely following detailed orders from other members of the group then the accurate delineation would be that DIST is providing an advertising, marketing and promotion services. To the extent that a local marketing intangible has been created, the important DAEMPE functions are being performed elsewhere, not in DIST.

In contrast, if DIST develops the 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, it may be that DIST is performing the important DAEMPE functions and the TPM and ultimately the AL outcome should reflect the DAEMPE conclusion.

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, from the foreign-owned brand (cf. 6.2.4.4 UN TP Manual). In the DIST Co case, 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 (cf. 6.2.4.1 UN TP Manual). The intangibles created have contributed substantially to the success of DIST Co.

Another issue for consideration is whether these marketing intangibles may not be subject to intellectual property rights (IPR) law (cf. 6.2.2.4 UN TP Manual).

Lastly, 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.

It should be noted that the above 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 are directed to analyze the specific facts and circumstances closely taking into account their knowledge of the domestic pharmaceutical industry and keeping in mind domestic legislation as well as relevant guidance on transfer pricing, such as section 6.2 of the UN TP Manual.

5.4. Example 4: Transfer pricing of a contract R&D 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, has staff qualified to carry out pharmaceutical R&D and expertise in clinical testing of pharmaceutical products for safety purposes.

While Test Co's staff are qualified to undertake clinical testing, they do not make strategic and tactical decisions on the direction of R&D as they do not have the necessary qualifications,

expertise as well as managerial and technical skills required to do so. 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 (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% markup over total costs.

The tax authority in Country Z audits Test Co. The question at issue is whether Test Co should be treated as a service provider and, if so, what is the appropriate transfer pricing method and transfer price for the services provided by Test Co 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 that Test Co is to be remunerated 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 on its R&D work as directed by PAR Co. Test Co receives weekly directions from the Head of R&D at PAR Co.

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 be used in applying the CUP Method. However, in Country X there are five independent R&D companies carrying on R&D in the chemical industry and farming industry. The independent companies are listed on the stock exchange in Country X making their financial information publicly available. The independent service providers are considered to be comparable to Test Co on the basis of a comparability analysis.

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

6. Appendix 1: List of abbreviations

AI	Artificial intelligence
AMP	Advertising, marketing and promotion activities
API	Active pharmaceutical ingredient
BM	Batch manufacturing
CM	Continuous manufacturing
COGS	Cost of goods sold
CUP	Comparable uncontrolled price
DAEMPE	Development, Acquisition, Enhancement, Maintenance, Protection and Exploitation of intangibles
EBIT	Earnings before interest and taxes
EBP	Emerging biopharma companies
EU	European Union
FAR	Functions, assets, and risks analysis
FDF	Final dosage form
GCP	Good clinical research practice
GDP	Good distribution practice
GMP	Good manufacturing practice
GVC	Global value chain
HTA	Health technology assessment
IND	Investigational new drug
IP	Intellectual property
MNE	Multinational enterprise
NMRA	National medicines regulatory authority
OPM	Operating profit margin
OTC	Over the counter (non-prescription) medication
PLI	Profit level indicator
PQS	Pharmaceutical Quality Systems
R&D	Research and development
RPM	Resale price method
TNMM	Transactional net margin method
UN	United Nations
UN TP Manual	United Nations Practical Manual on Transfer Pricing for Developing Countries (2021)
VAT	Value added tax
WHO	World Health Organization

7. Appendix 2: Glossary of pharmaceutical terms

Active pharmaceutical ingredient	Any substance or mixture of substances that is part of a drug (medicinal) product, intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure and function of the body.[139]
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.[140]
Bio-availability	Bioavailability is a subcategory of absorption and is the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when a medication is administered intravenously, its bioavailability is 100 percent. However, when a medication is administered via other routes (such as orally), its bioavailability generally decreases due to incomplete absorption and first-pass metabolism. Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration.[141]
Bioequivalence	Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or pharmaceutical alternatives, and their bio-availabilities, in terms of 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.[142]
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.[143]

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

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

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

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

[143] Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.) (2017). National Academies of Sciences, Engineering, and

Biosimilar	A drug that is similar to a biological reference product, and which is manufactured by a company other than the originator. Regulatory approval of biosimilars is technically possible following patent expiry of the reference product.[144]
Bulk product	Any pharmaceutical product that has completed all processing stages up to, but not including, final packaging.[145]
Clinical trial	Formal study carried out according to a prospectively defined protocol that is intended to discover or verify the safety and the effectiveness of procedures or interventions in humans.[146]
Excipient	A pharmacologically inactive substance used along with the active pharmaceutical ingredients in the formulation of a medication.[147]
Generic pharmaceutical drug	A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorized. Its authorization is based on efficacy and safety data from studies on the authorized medicine. A company can only market a generic medicine once the exclusivity period for the original medicine has expired.[148]
Good clinical research practice	A standard for clinical studies which encompasses the design, conduct, monitoring, termination, audit, analysis, reporting and documentation of the studies and which ensures that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical product (diagnostic, therapeutic or prophylactic) under investigation are properly documented.[149]
Good manufacturing practice	That part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing

Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient Access to Affordable Drug Therapies. Making Medicines Affordable: A National Imperative. National Academies Press (US). Appendix C: Glossary.

[144] Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.

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

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

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

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

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

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

<table>
<tr><td></td><td>authorization.[150]</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 in their processes:[151]

<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 : https://www.census.gov/naics/?input=pharmaceutical&year=2022</td></tr></table></td></tr>
<tr><td>Intermediates</td><td>An intermediate can be a material produced during steps of the processing of an active pharmaceutical ingredient that undergoes further molecular change or purification before it becomes an API.[152]</td></tr>
<tr><td>Marketing authorization</td><td>Also referred to as product licence or registration certificate. A legal document issued by the competent medicines regulatory authority that authorizes the marketing or free distribution of a medical product in the respective country after evaluation of safety, efficacy and quality.[153]</td></tr>
<tr><td>National medicines regulatory authority</td><td>The national authority responsible for the registration of and other regulatory activities concerning medical products, such as medicines, vaccines, blood products and medical devices.[154]</td></tr>
<tr><td>Over-the-counter</td><td>Medicine that does not require a prescription to be sold to patients.</td></tr>
</table>

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

[151] USITC, page 136.

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

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

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

drug	Also known as non- prescription medicines. [155]
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.[156]
Patented drug	An innovative medicine granted intellectual property protection by a patent office. The patent may encompass a wide range of claims, such as active ingredient, formulation, mode of action, etc., giving the patent holder the sole right to sell the drug while the patent is in effect.[157]
Pharmacy benefit management	Develop and administer drug-benefit plans for employers and health insurers.[158]
Phase 1 clinical trial	A type of clinical study where a new medicine is given to humans for the first time, usually in healthy volunteers. It looks at the way the medicine is dealt with by the body, its main effects and main side effects.[159]
Phase 2 clinical trial	A type of clinical study conducted after phase I studies to evaluate a medicine's effects in a particular condition and to determine its common short-term side effects.[160]
Phase 3 clinical trial	A type of clinical study usually conducted in a large group of patients to gather information about a medicine's efficacy and safety, to allow its benefits and risks to be evaluated.[161]
Phase 4 clinical trial	A type of clinical study that takes place after the authorization of a medicine.[162]
Prescription drugs	Patented and generic medicines regulated by legislation that requires a physician's prescription before they can be sold to a patient.[163]

[155] Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.
[156] Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013). Board on Global Health. Institute of Medicine. Buckley GJ, Gostin LO (editors). Countering the Problem of Falsified and Substandard Drugs. Washington (DC). National Academies Press (US). Appendix A: Glossary. Available from: https://www.ncbi.nlm.nih.gov/books/NBK202530/ doi: 10.17226/18272
[157] Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.
[158] Nass, S. J., Madhavan, G., & Augustine, N. R. (Eds.) (2017). National Academies of Sciences, Engineering, and Medicine. Health and Medicine Division. Board on Health Care Services. Committee on Ensuring Patient Access to Affordable Drug Therapies. Making Medicines Affordable: A National Imperative. National Academies Press (US). Appendix C: Glossary.
[159] European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A
[160] European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A
[161] European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A
[162] European Medicines Agency. Glossary of regulatory terms. Available from https://www.ema.europa.eu/en/about-us/about-website/glossary/name_az/A
[163] Fitch Solutions. Latin America Pharmaceuticals Report Q2 2023. Pharmaceuticals Glossary.