



A competition law approach to accessing insulin

A working paper

December 2022

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The year 2021 marked the centenary of the discovery of insulin. Considered one of the greatest medical achievements, the discovery of insulin has saved millions of lives. This milestone presents a timely opportunity to reflect on the opportunities and challenges on the path to achieving universal access to insulin.

Access to insulin and associated health technologies remains a challenge, with striking inequalities within and across countries. A failure to address these inequalities will be a significant factor in impeding progress towards achieving universal health coverage and related Sustainable Development Goals (SDGs).

Recognizing this challenge, the 74th World Health Assembly called for urgent, coordinated global action on diabetes. Concerted action is required on various fronts: from effective strategies for the prevention and control of diabetes, to the need for higher levels of treatment and care for people living with diabetes. The World Health Assembly Resolution WHA74.4 of May 2021 explicitly recognizes that diabetes prevention and control efforts are “hampered by, inter alia, lack of universal access to quality, safe, effective, affordable essential health services, medicines, diagnostics and health technologies”. In this context, the World Health Organization and governments are urged to take measures to increase access, including through the promotion of transparency in the markets for insulin and the convergence and harmonization of regulatory requirements for insulin.

The relationship between diabetes and health inequalities has also been negatively affected by the COVID-19 pandemic. Four out of five people living with diabetes are in low- and middle-income countries (LMICs), where already scarce resources are being directed towards managing the pandemic. In the current pandemic situation, people living with diabetes and other non-communicable diseases (NCDs) are at increased risk of their disease becoming more severe and also of death due to disruptions in essential healthcare and to COVID-19 itself. Even before the advent of COVID-19, health systems in LMICs faced challenges in accessing health technologies for both communicable and non-communicable diseases. The challenge now is to ensure that all efforts, both in pandemic response and in essential healthcare, are inclusive of all countries and peoples, consistent with the 2030 Agenda for Sustainable Development. ‘Connecting the Dots: Towards a more equitable, healthier and sustainable future: UNDP HIV and Health Strategy 2022–2025’ highlights the need to focus on building resilient health systems that reinforce efforts to promote inclusive governance for health, reduce inequalities, and leave no one behind.

As the global community and national governments step up efforts to respond to these concerns, UNDP seeks to make its contribution. Recognizing the need to address the multiple determinants of access to health technologies, UNDP has focused on access to insulin from the perspective of the global production and supply of insulin. The causes and barriers to insulin access are diverse. Limited competition in the production and supply, as well as high prices of insulin have shown to be key limitations to insulin access.

Guided by the recommendations of reports from the Global Commission on HIV and the Law in 2012 and the United Nations Secretary-General's High-Level Panel on Access to Medicines in 2016, UNDP has developed resources and provided technical support to LMICs on the use of competition law and policy as a tool to enhance access to health technologies.

This working paper proposes a competition law approach as one means for examining the challenge of promoting access to insulin. This is an area of policy and practice that could prove useful, although often underutilized, in efforts to promote access to health technologies. The working paper follows from previous work in this area. In 2014, UNDP published 'Using Competition Law to Promote Access and Health Technologies: A guidebook for low- and middle-income countries'. More recently in 2022, UNDP published a supplement, which updates the 2014 guidebook. Both publications are intended as guidance to competition and public health authorities in LMICs on the use of competition law to promote access to health technologies.

This working paper aims to bring attention to the relevance of competition law in addressing specific aspects of the insulin access challenge. It is important to note that it is not an attempt at drawing conclusions with respect to anti-competitive behaviours; rather, the goal is to provide practical guidance on the potential utility of competition law as a strategy to increase access to insulin.

We acknowledge with gratitude the inputs of the numerous experts and partners who have contributed to this work. We are also cognizant of the benefits of further exchange and feedback on the content, which is why this working paper aims to solicit inputs from as broad a range of stakeholders as possible.

We hope that this will stimulate further discussion and analysis on this important subject.

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a. Background and objectives

In 2021, when this working paper was being written, the world celebrated the 100th anniversary of the discovery of insulin, a discovery that changed the lives of millions of people around the world and won researchers F.G. Banting and J.J.R. Macleod the Nobel Prize. However, limited access to insulin by people living with diabetes is a substantial concern around the world. While comprehensive and global data on the access to insulin gap are not available, existing estimates suggest that there is a wide gap between the need for insulin and its availability for people with both type 1 and type 2 diabetes. At the macro level, procurement of insulin places a significant financial burden on public health systems.¹ Lack of access to insulin results in the death of those with type 1 diabetes and severely impairs good health in those with type 2 diabetes. The World Health Organization (WHO) estimates that in 2016, diabetes was the direct cause of 1.6 million deaths globally.² Estimates also suggest that in 2018, only half of the 63.3 million people globally with type 2 diabetes needing insulin had access. In addition, the lack of access is disproportionately distributed across regions, with some developing countries having the least access to insulin.³ The barriers to accessing insulin are diverse and often context-specific, but low competition in the supply and production of insulin and its high prices are key limitations in the insulin market.

Competition law is an important but often neglected legal and policy tool that countries and other stakeholders can use to protect consumer welfare and promote health and industrial and economic development. It aims to protect the integrity of markets to promote the efficient use of resources and encourage innovation in and access to health technologies.

1 “Based on cost estimates from a recent systematic review, it has been estimated that the direct annual cost of diabetes to the world is more than US\$827 billion.” World Health Organization, ‘Global Report on Diabetes’ Geneva, 2016, p. 14, [hereinafter ‘WHO Global Report 2016’], available at https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf.

2 World Health Organization, ‘Diabetes: Key Facts’, Geneva, 8 June 2020. Available at www.who.int/news-room/fact-sheets/detail/diabetes.

3 A recent paper using data from the International Diabetes Federation across 221 countries on the type 2 diabetes burden from 2018 to 2030 in a microsimulation exercise concluded that current levels of access to insulin are inadequate to meet the total global projected need, and noted that an increase in access to insulin would most benefit the African region. See Sanjay Basu, John S. Yudkin, Sylvia Kehlenbrink, Justine I. Davies, Sarah H. Wild, Kasia J. Lipska, Jeremy B. Sussman and David Beran, ‘Estimation of global insulin use for type 2 diabetes, 2018–30: a microsimulation analysis.’ *The Lancet Diabetes & Endocrinology* 7, no. 1 (2019), pp. 25–33 at 31 (hereafter Basu et al., ‘Estimation of global insulin use’). “We estimated global insulin use for type 2 diabetes by country and year, worldwide, from 2018 to 2030, identifying several important findings. First, current levels of insulin access are not only inadequate relative to projected need, but are disproportionately inadequate in the African, Asian, and Oceanic regions. The regions projected to increase insulin use most if access were improved were the African region in relative terms and the Asian region in absolute terms. The finding that Africa has the largest relative unmet insulin need also highlights the importance of availability and affordability improvements to the insulin market.”

See also David Beran, Zafar Mirza and Jicui Dong, ‘Access to insulin: applying the concept of security of supply to medicines.’ *Bulletin of the World Health Organization* 97, no. 5 (2019), pp. 358–364 at p.361. Available at <http://ncbi.nlm.nih.gov/pmc/articles/PMC6747032/>. (“Globally, one in two people with type 2 diabetes has access to the insulin they need, but in Africa this number is one in seven people.”)

In line with the United Nations Development Programme (UNDP) Strategic Plan,⁴ UNDP's HIV and Health Strategy⁵ focuses on three interconnected action areas: reducing inequalities and social exclusion that drive poor health; promoting effective and inclusive governance for health; and building resilient and sustainable health systems.

In 2014, UNDP published 'Using Competition Law to Promote Access to Health Technologies: A guidebook for low- and middle-income countries',⁶ aimed to support competition and public health authorities in low- and middle-income countries (LMICs) in understanding and using the tools of competition law to promote access to health technologies. In March 2022, UNDP published a Supplement to its 2014 'Guidebook on Using Competition Law', which includes recent cases and examples from a substantial number of countries, including LMICs, as well as recent market studies.⁷

The purpose of this paper is to place the 'access to insulin' issue, which affects global and national health systems and markets, in the context of competition law and policy, and to assess whether there may be reason for competition authorities, in cooperation with ministers of health and other relevant stakeholders, to explore sector inquiries or enforcement actions in the insulin market. This paper may also be useful to scholars working more widely on questions of access to medicines globally and within LMICs.

This paper does not make specific recommendations regarding the application of competition law to insulin manufacturers or products, but rather presents a framework for analysis that can serve as a starting point for further dialogue. The objective is not to draw a conclusion as to whether the insulin market globally or in any particular country is the object of anticompetitive abuse. Rather, the objective is to bring attention to how competition law and policy could be useful in addressing potential distortions in the insulin market, and whether further data collection and investigation should be pursued through the lens of 'competition law and policy'.

4 UNDP, 'Strategic Plan, 2022–2025', New York, 2021. Available at: <http://strategicplan.undp.org>.

5 UNDP, HIV, Health and Development, 'Connecting the Dots: Towards a More Equitable, Healthier and Sustainable Future: UNDP HIV and Health Strategy 2022-2025', New York, 2022. Available at: www.undp.org/publications/connecting-dots-towards-more-equitable-healthier-and-sustainable-future-undp-hiv-and.

6 UNDP, 'Using Competition Law to Promote Access to Health Technologies: A guidebook for low- and middle-income countries', New York, 2014. Available at: www.undp.org/publications/using-competition-law-promote-access-medicine.

7 Most of the doctrinal development in competition law has taken place in the United States and Europe, largely because these jurisdictions adopted legislation addressing anticompetitive practices, and pursued cases against these practices, significantly earlier than other jurisdictions, including LMICs. The 'practice gap' among jurisdictions is narrowing. UNDP, 'Using competition law to promote access to health technologies: A supplement to the Guidebook for low- and middle income countries', New York, 2022. Available at: www.undp.org/publications/using-competition-law-promote-access-health-technologies-supplement-guidebook-low-and.

This paper is based predominantly on secondary research and includes reference to a significant amount of publicly available research and data from the WHO, scholars, non-governmental organizations and interested agencies. Primary interviews and data have been used wherever possible to supplement existing information on or to cross-check market dynamics. The research conducted for this paper was not directed towards identifying anticompetitive conduct or agreements in a sufficiently specific way for direct use in a complaint filed by a competition authority. However, the analysis points to areas where such evidence might be sought in terms of exploring why certain types of conduct, including pricing behaviours, are observable, and whether they are potential motivation for further action, either in the form of sector inquiries or the opening of competition investigations that might lead to an enforcement action.

The paper begins with a description of insulin as a product and of the structure of the global supply market. It then elaborates competition law doctrines that may be relevant to assessing the insulin market and includes some data that may be useful in considering whether additional investigation and data-gathering are warranted. Finally, the paper provides model forms of evidentiary request that could be used in sector inquiries or enforcement procedures.

b. Insulin as a pharmaceutical product

A large number of individuals throughout the world require treatment with insulin for diabetes.⁸ For those with type 1 diabetes who lack the physical capacity to produce insulin, continuous access to insulin treatment is necessary to sustain their lives. For those with type 2 diabetes who may not produce sufficient insulin, or have resistance, the need for insulin treatment

8 According to the World Health Organization (WHO Global Report 2016, at p. 6):

“Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. This reflects an increase in associated risk factors such as being overweight or obese. Over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries. Diabetes caused 1.5 million deaths in 2012. Higher-than-optimal blood glucose caused an additional 2.2 million deaths, by increasing the risks of cardiovascular and other diseases. Forty-three percent of these 3.7 million deaths occur before the age of 70 years. The percentage of deaths attributable to high blood glucose or diabetes that occurs prior to age 70 is higher in low- and middle-income countries than in high-income countries. Because sophisticated laboratory tests are usually required to distinguish between type 1 diabetes, which requires insulin injections for survival, and type 2 diabetes (where the body cannot properly use the insulin it produces), separate global estimates of diabetes prevalence for type 1 and type 2 do not exist. The majority of people with diabetes are affected by type 2 diabetes. This used to occur nearly entirely among adults, but now occurs in children too.”

Regarding trends:

“By 2045, an estimated 629 million people will have diabetes. This constitutes a 48 percent increase over the 2017–2045 period.” Margaret Ewen, Huibert-Jan Joosse, David Beran and Richard Laing, ‘Insulin prices, availability and affordability in 13 low-income and middle-income countries’, *BMJ global health* 4, no. 3 (2019): e001410 [citing IDF Diabetes Atlas 7th edition, International Diabetes Federation, Brussels, 2015].

varies. For those who require insulin to treat type 2 diabetes, lack of access may lead to serious health complications, including death.⁹

Insulin is a hormone that is produced in the human body (and in various animal bodies). It aids the body in processing glucose or sugar.¹⁰ Insulin used in human treatment was initially obtained by extraction from animals (e.g. pigs). Today, insulin is a commonly produced biologic drug product.

Broadly speaking, there are two types of insulin. The first replicates ‘ordinary’ human insulin with no genomic variation. The second involves modification of the regular human genomic version and is referred to as ‘analogue’ (or ‘analog’) insulin. Both types of insulin (regular human and analogue) are biologic drug products because they are both made of organic material.¹¹ In this paper, the term ‘human insulin’ is used to refer to biologic products that replicate insulin as found in the human body, and ‘analogue insulin’ is used to refer to biologic products that incorporate insulin with genomic modification.¹²

9 “Diabetes of all types can lead to complications in many parts of the body and can increase the overall risk of dying prematurely. Possible complications include heart attack, stroke, kidney failure, leg amputation, vision loss and nerve damage. In pregnancy, poorly controlled diabetes increases the risk of fetal death and other complications.” WHO Global Report 2016, p.8. Approximately 63 million people worldwide require insulin to treat type 2 diabetes: Basu et al., ‘Estimation of global insulin use’.

10 Gisela Wilcox states:

“Insulin is the pivotal hormone regulating cellular energy supply and macronutrient balance, directing anabolic processes of the fed state. Insulin is essential for the intra-cellular transport of glucose into insulin-dependent tissues such as muscle and adipose tissue. Signaling abundance of exogenous energy, adipose tissue fat breakdown is suppressed, and its synthesis promoted. In muscle cells, glucose entry enables glycogen to be synthesised and stored, and for carbohydrates, rather than fatty acids (or amino acids) to be utilised as the immediately available energy source for muscle contraction. Insulin therefore promotes glycogen and lipid synthesis in muscle cells, while suppressing lipolysis and gluconeogenesis from muscle amino acids. In the presence of an adequate supply of amino acids, insulin is anabolic in muscle.”

Gisela Wilcox, ‘Insulin and insulin resistance’, *Clinical Biochemist Reviews* 26, no. 2 (2005), p. 26. Available at www.ncbi.nlm.nih.gov/pubmed/16278749.

11 Until recently, however, insulin was regulated as a small molecule chemical product by the US Food & Drug Administration. See discussion *infra* text at notes 134–135.

12 Because analogue insulin is used by humans, the term ‘human insulin’ may appear ambiguous, and some research papers refer always to ‘regular human insulin’ or ‘RHI’ when addressing insulin that has not been genetically modified.

Within the two broad categories, human and analogue, there are subtypes that define the speed at which the insulin initiates its therapeutic action, the time to maximum or peak effect, and the duration of the effect. Because various types of insulin work differently, people living with diabetes may be prescribed more than one type, and different types may come pre-mixed. Insulin presentations include vials, cartridges and pens. Box 1 explains the types of insulin in greater detail.¹³

Each of the types and subtypes of insulin has the same biological effect in the human body in assisting in the processing of glucose.

Insulin was traditionally administered by injection, usually self-administered by the person living with diabetes. There have been a number of advances in delivery technologies. Today, insulin may be delivered by a computerized pump device that administers small doses of rapid-acting insulin continuously and/or variable amounts of insulin when a meal is taken.¹⁴ In addition, insulin is today often packaged in injectable pen devices that are more portable for ease of use.

In 2021, long-acting insulin analogues and other therapies for diabetes were included in the WHO Model List of Essential Medicines.¹⁵ There is scientific debate regarding whether analogue insulin has any added benefits for diabetes treatment insofar as regular human insulin acts in the same way to process glucose, but with more limited variation in onset, peak effect and duration of therapeutic action.¹⁶ This is an important scientific question

13 See for detail, including correlation with brand names, Amanda Howard-Thompson, Muneeza Khan, Morgan Jones and Christa M. George, 'Type 2 diabetes mellitus: outpatient insulin management', *American Family Physician* 97, no. 1 (2018), pp. 29–37. Available at www.aafp.org/afp/2018/0101/p29.html#.

There are new analogue versions, 'ultra rapid-acting' and 'ultra long-acting', that have a longer or shorter duration. See also Lisa S. Rotenstein, Nina Ran, Joseph P. Shivers, Mark Yarchoan and Kelly L. Close, 'Opportunities and challenges for biosimilars: what's on the horizon in the global insulin market?', *Clinical Diabetes* 30, no. 4 (2012), pp. 138–150. Available at doi.org/10.2337/diaclin.30.4.138; Richard I.G. Holt, Clive Cockram, Allan Flyvbjerg and Barry J. Goldstein, (eds.), *Textbook of diabetes* (John Wiley & Sons, 2017).

14 See, for example, Howard Wolpert and Judy Shih, '28 New Technologies for Insulin Administration and Glucose Monitoring', *Textbook of Diabetes*, 4th edition (John Wiley & Sons, 2010) at p. 440; Rima B. Shah, Manhar Patel, David M. Maahs and Viral N. Shah, 'Insulin delivery methods: Past, present and future'. *International journal of pharmaceutical investigation* 6, no. 1 (2016), p. 1. Available at doi.org/10.4103/2230-973X.176456.

15 World Health Organization, 'WHO prioritizes access to diabetes and cancer treatments in new Essential Medicines Lists', October 2021. Available at www.who.int/news/item/01-10-2021-who-prioritizes-access-to-diabetes-and-cancer-treatments-in-new-essential-medicines-lists.

16 WHO Global Report 2016, *supra* note 1, at p. 6. See also the findings from a more recent Cochrane review of rapid-acting analogues online. Available at www.cochrane.org/CD013228/ENDOC_short-acting-insulin-analogues-versus-regular-human-insulin-type-2-diabetes-mellitus. For comparison of long-acting analogues and Neutral Protamine Hagedom (NPH) insulin in treating type 1 diabetes, see Bianca Hemmingsen, Bernd Richter and Maria-Inti Metzendorf, '(Ultra-)long-acting insulin analogues for people with type 1 diabetes mellitus', Cochrane review, 9 December 2019. Available at <https://doi.org/10.1002/14651858.CD013498>.

BOX 1. Types of insulin

Characteristics of insulin

Insulins are categorized by differences in:

- Onset (how quickly they act)
- Peak (how long it takes to achieve maximum impact)
- Duration (how long they last before they wear off)
- Concentration (units per ml)
- Route of delivery (whether they are injected under the skin or given intravenously).

Types of insulin

There are three main groups of insulins: fast-acting, intermediate-acting and long-acting insulin.

Fast-acting insulin

- is absorbed quickly from fat tissue (subcutaneous) into the bloodstream;
- is used to control the blood sugar during meals and snacks and to correct high blood sugars.

Includes:

- rapid-acting insulin analogues (e.g. Insulin Aspart, Insulin Lispro, Insulin Glulisine), which have an onset of action of 5 to 15 minutes, peak effect in 1 to 2 hours, a duration of action that lasts 4 to 6 hours. With all doses, large and small, the onset of action and the time to peak effect are similar. The duration of insulin action is, however, affected by the dose, so a few units may last 4 hours or less, while 25 or 30 units may last 5 to 6 hours;
- short-acting regular human insulin, which has an onset of action of 1/2 hour to 1 hour, peak effect in 2 to 4 hours, and duration of action of 6 to 8 hours. The larger the dose of regular human insulin, the faster the onset of action, but the longer the time to peak effect and the longer the duration of the effect.

Intermediate-acting insulin:

- is absorbed more slowly and lasts longer;
- is used to control the blood sugar overnight, while fasting and between meals;
- can be either purely human insulin or pre-mixed (human and analogue).

Includes:

- neutral protamine Hagedorn (NPH) human insulin, which has an onset of insulin effect of 1 to 2 hours, a peak effect of 4 to 6 hours, and duration of action of more than 12 hours;
- pre-mixed insulin, which is NPH pre-mixed with either human insulin or a rapid-acting insulin analogue. The insulin action profile is a combination of the short- and intermediate-acting insulins.

Long-acting insulin:

- is absorbed slowly, has a minimal peak effect, and a stable plateau effect that lasts most of the day;
- is used to control the blood sugar overnight, while fasting and between meals.

Includes:

- long-acting insulin analogues (Insulin Glargine, Insulin Detemir, Insulin Degludec), which have an onset of insulin effect in 1.5 to 2 hours. The insulin effect plateaus over the next few hours and is followed by a relatively flat duration of action that lasts 12 to 24 hours for insulin detemir and 24 hours for insulin glargine.

Source: Diabetes Education Online, Diabetes Teaching Center at the University of California, San Francisco, USA.¹⁷

17 Available at <https://dtc.ucsf.edu/learning-library/resource-materials>.

because human insulin is typically priced substantially lower than analogue insulin. In most developed country markets, analogue insulin is far more widely prescribed and used than regular human insulin.¹⁸ This paper does not take a position regarding the comparative merits of human and analogue insulin. There are advocacy groups led by people living with diabetes that do not consider human insulin an adequate substitute for analogue insulin. In their view, the availability of human insulin at lower prices does not adequately address the full spectrum of pricing and access issues needed for a comprehensive response to the needs of people living with diabetes.¹⁹

Although there may be some complexity involved for people living with diabetes switching between different insulin products, including between human and analogue, as different products are likely to have different effects on glucose levels, it is generally acceptable from a medical standpoint to switch between insulin products.²⁰ This is meaningful from a competition law standpoint in that significant changes in price should be expected to result in changes to insulin prescribing and usage patterns, recognizing that switching may entail costs both in financial and convenience terms for people living with diabetes.

BOX 2. Definition of 'biosimilar'

The term 'biosimilar' refers to a biological pharmaceutical that is considered by medicines regulatory authorities to be 'highly similar' to an approved reference biological pharmaceutical, with no clinically meaningful differences compared to the reference product. In the United States regulatory system, a distinction is drawn between 'biosimilars' and 'interchangeable' biosimilars, the latter meeting additional requirements that allow substitution of the interchangeable for the reference product without consulting the prescriber (e.g. substitution by the pharmacist).^{*} The term 'biosimilar' is defined by national (and regional) regulatory authorities according to specific criteria that may vary between jurisdictions.

^{*}U.S. Food & Drug Administration, 'Biological Product Definitions', <https://www.fda.gov/media/108557/download>; and European Medicines Agency and European Commission, 'Biosimilars in the EU', Brussels, 2019.

¹⁸ See, for example, for the United States, Judith A. Johnson, Congressional Research Service, 'Insulin Products and the Cost of Diabetes Treatment', *In Focus* 7-5700, 19 November 2018. Available at <https://fas.org/spp/crs/misc/IF11026.pdf>.

¹⁹ Interview with Elizabeth Pfeister, T1 International, 29 July 2020.

²⁰ See, for example, Amanda Howard-Thompson, Amanda, Muneeza Khan, Morgan Jones and Christa M. George, 'Type 2 diabetes mellitus: outpatient insulin management', *American Family Physician* 97, no. 1 (2018), pp. 29–37.

Recent estimates suggest that the global insulin market, which includes both human and analogue insulin, has been growing exponentially. Having reached an estimated US\$25.7 billion in sales in 2019, it is expected to register a compound annual growth rate of 4.19 percent between 2020 and 2025.²¹ A number of countries have seen their demand for insulin surge over the past two decades,²² indicating investment and expansion opportunities in the sector; however, these opportunities have mostly contributed to the expansion of three large pharmaceutical companies.

Currently, the global insulin supply market is perhaps one of the most concentrated segments within the pharmaceutical sector, dominated by three multinational companies: Eli Lilly (based in the United States), Novo Nordisk (based in Denmark) and Sanofi (based in France).²³ These companies are estimated to account for over 90 percent of the global insulin market by volume and value, and for all insulin supplied to the US market²⁴ and 88 percent of total market registrations.²⁵ The figures mark a steady rise in the market share of all three companies in an already concentrated market, up from 88.7 percent by value in 2012.²⁶

21 Mordor Intelligence, 'Human Insulin Drugs Market – Growth, Trends, COVID-19 Impact, and Forecasts 2021–2026', Hyderabad, 2020. Available at: www.mordorintelligence.com/industry-reports/insulin-market.

22 Basu et al., 'Estimation of global insulin use'.

23 David Beran, Margaret Ewen, Molly Lepeska and Richard Laing, 'Access to Insulin: Current Challenges and Constraints', Update March 2017, Health Action International, Amsterdam, 2017, at p. 6 [hereinafter Beran et al., 'Current Challenges']. "This report confirms from different data perspectives the dominance of Eli Lilly, Novo Nordisk, and Sanofi with regards to the global insulin market. Although other insulin manufacturers have been identified based on the data available, their size and market penetration seem to be low", p. 23. See also David Beran, R. O. Laing, W. Kaplan, R. Knox, A. Sharma, V. J. Wirtz, J. Frye and M. Ewen, 'A perspective on global access to insulin: a descriptive study of the market, trade flows and prices', *Diabetic medicine* 36, no. 6 (2019), pp. 726–733 (hereafter Beran et al., 'Trade Flows').

24 Congressional Research Service of the United States of America, 'Insulin Products and the Cost of Diabetes Treatment', Washington, DC, 19 November 2018. Available at: <https://fas.org/sgp/crs/misc/IF1026.pdf>. Previous studies attribute over 99 percent of the market by value to the top three companies (see, for example, Beran et al., 'Trade Flows', *supra* note 22, p. 726). In recent years, however, exports from local producers in India have increased to some extent (see Table 1 of this paper), although the exact split between what the Indian firms produce under contract manufacturing for the three large firms and what they sell under their own brands is not available.

25 William T. Cefalu, Daniel E. Dawes, Gina Gavlak, Dana Goldman, William H. Herman, Karen Van Nuys, Alvin C. Powers, Simeon I. Taylor and Alan L. Yatvin, 'Insulin access and affordability working group: conclusions and recommendations'. *Diabetes Care* 41, no. 6 (2018), pp. 1299–1311. Available at <https://care.diabetesjournals.org/content/41/6/1299>.

26 Veronika J. Wirtz, 'Insulin Market Profile', Health Action International, Amsterdam, 2016. Available at http://haiweb.org/wp-content/uploads/2016/04/ACCISS_Insulin-Market-Profile_FINAL.pdf. Knox presents the individual market shares by volume and in revenue terms globally, noting that the individual market shares by volume are: Novo Nordisk (52 percent), Sanofi (17 percent) and Eli Lilly (23 percent). Market shares by revenue are: Novo Nordisk (41 percent), Sanofi (32 percent) and Eli Lilly (23 percent). See Ryan Knox, 'Insulin insulated: barriers to competition and affordability in the United States insulin market', *Journal of Law and the Biosciences* (2020), pp. 1–25, at p. 9. Available at <https://doi.org/10.1093/jlb/l5aa061>.

These companies earn their predominant revenue from selling analogue insulin, but also produce and sell human insulin products.²⁷

The global insulin market and the increasing concentration are interesting for a number of reasons. The main reasons are the distribution of production activities and the sluggishness of change in the market structure. Increasing sales have led to the diversification of production, but the sector has not seen the entry of new companies despite a steady projection of growing global demand.²⁸ For instance, Novo Nordisk's production sites are now located in the United States, Brazil, China, Japan, Bangladesh and the Russian Federation; Eli Lilly produces in the United States, France, Italy, China and the Russian Federation; and Sanofi produces its insulin in Germany, Ireland and the Russian Federation.²⁹ At the same time, a small number of biosimilar insulin products are also being sold primarily in developed country markets.³⁰ In LMICs, biosimilar production of both human and analogue insulin is located in a few countries, notably, Bangladesh, China,³¹ El Salvador, Mexico, Poland and the United Arab Emirates, with some companies supplying to countries worldwide.

Data available from the United Nations Comtrade (UN Comtrade) database show the amount of insulin supplied worldwide from the countries where the top three companies have production facilities as well as other countries that have some capacity for local production. A recent study estimates that 174 countries imported insulin, as per the UN Comtrade database between 2000 and 2018, of which many exported insulin products at certain time periods but have not been able to sustain these exports.³² But over time, the difference in exports from local manufacturers operating independently and the steady rise in product registrations of the top three companies within LMIC markets where they sell their products

27 By the last quarter of 2019, Novo Nordisk had a market share (by volume) of 46 percent of the global diabetes market. See Novo Nordisk, 'Investor Presentation Third Quarter 2019', Bagsværd, Denmark, 2019, p. 20. Available at <https://investor.novonordisk.com/q3-2019-presentation>.

28 See Basu et al., 'Estimation of global insulin use'.

29 Beran et al., 'Trade Flows', *supra* note 23 at p. 728. Interview with Eskayef, Bangladesh, 24 August 2020. The list of independent insulin manufacturers worldwide shows that outside the top 3, only 15 other companies have more than one product registered in any territory worldwide, of which only 8 companies account for 2 percent or more of global market sales.

30 See, for example, Andrea Llano, Miles Fisher and Gerry McKay, 'Biosimilar insulin: the current landscape'. *Practical Diabetes* 34, no. 2 (2017), pp. 51–54. Available at www.practicaldiabetes.com/article/biosimilar-insulin-current-landscape.

31 China produces for Novo Nordisk and Eli Lilly but also has a number of local companies engaged in insulin production.

32 Abhishek Sharma and Warren Kaplan, 'Insulin imports fail to meet many countries' needs', *Science* 373, no. 6554 (2021), p. 494. Reasons for a lack of sustained exports could be numerous, including increased domestic demand, shifts from human to analog insulin, preference for certain brands and difficulties in sustaining production.

through distributors are both noteworthy indicators. Table 1 presents these trends between 2017 and 2019 for key exporters of insulin products worldwide.³³

TABLE 1. Total insulin exports (kg) from the top three companies and other local manufacturers, 2017–2019

Exports from Eli Lilly, Novo Nordisk and Sanofi country production sites				Exports from countries with local manufacturers*			
Country	Total global exports 2017 (kg)	Total global exports 2018 (kg)	Total global exports 2019 (kg)	Country	Total global exports 2017 (kg)	Total global exports 2018 (kg)	Total global exports 2019 (kg)
Brazil	268,746	465,019	904,271	Argentina	138,687	82,264	127,517
China	725,778	772,448	611,206	Bangladesh	32,434	45,068	58,744
France	959,761	1,033,995	947,589	Egypt	69,075	61,720	85,399
Germany	2,777,552	2,245,555	3,042,304	El Salvador	15,517	57	900
Italy	316,920	194,501	319,692	India	376,986	360,263	392,420
Russian Federation	604,116	362,484	579,456	Iran	207,413	45,283	39,044
USA	2,993,082	3,694,433	1,531,672	Mexico	250,927	293,330	278,710
				Poland	128,806	135,171	139,681
				United Arab Emirates	42,255	55,524	46,162

Source: Compiled from UN Comtrade database, accessed August 2021. For coverage and limitations, see UN Comtrade User Guide available at: <https://unstats.un.org/wiki/display/comtrade>.

Notes: The table only contains data on insulin products both packaged and not packaged for retail sales (Commodity codes: 300331 and 300431).

* China has local manufacturers of insulin but is also a major manufacturer for Novo Nordisk and Eli Lilly. Given that the database provides aggregate data only, China is presented in the left half of the table.

A number of other factors, including technological challenges related to the production of biosimilars, the difficulties of achieving economies of scale in production, and regulatory challenges, can account for the trends observed in the market. If the issue pertains to regulatory regimes, then pending regulatory changes in the United States and elsewhere and the recent expansion of the WHO pre-qualification programme to include insulin³⁴ can increase the number of biosimilar insulin products, although the timing and scale of those developments are uncertain.

33 Beran et al. note a total of 20 countries where insulin is produced, and use the United Nations Comtrade (UN Comtrade) data together with data from individual manufacturers available in IQVIA for comparison. Table 1 updates some of the data in Beran et al., ‘Trade Flows’, *supra* note 23, and more recently, Sharma and Kaplan, *supra* note 32, using UN Comtrade data only. The list of local production sites presented in the table is based on the updated list provided in Sharma and Kaplan, *supra* note 32.

34 World Health Organization, ‘WHO launches first-ever insulin prequalification programme to expand access to life-saving treatment for diabetes’, Geneva, 13 November 2019. Available at www.who.int/news-room/detail/13-11-2019-who-launches-first-ever-insulin-prequalification-programme-to-expand-access-to-life-saving-treatment-for-diabetes.

Because the global insulin market is mostly dominated by three multinational companies, it seems relevant to consider the factors that account for the dominance, and whether such market concentration has any real or potential adverse effects on product choice, pricing and competition. In theory, market concentration on its own is not a matter of concern for competition law, unless it leads to an excess amount of market power and the relevant effects on competition, allocation of resources, and social welfare, the latter measured in this case by its impact on access to medicines in different markets.³⁵

There are indications that in the global insulin market, the market power of Novo Nordisk, Eli Lilly and Sanofi is increasing in varying degrees, such as in their growing market shares, which could affect product choice, pricing strategies, procurement or absence thereof, and other market dynamics.

To begin with, the growth of these companies appears to be accompanied by a concomitant expansion of analogue insulin products, which are increasingly gaining ground, not just in the high-income markets, but also in LMICs.³⁶ Markets for insulin, especially in LMICs, are split between private (out-of-pocket) and public (government-procured).³⁷ In public procurement processes, there has been a surge in analogue insulin in government procurement,³⁸ which remains paradoxical given that analogue insulin continues to cost substantially more than human insulin,³⁹ and healthcare budgets in a number of developing countries have

35 Jan De Loecker, Jan Eeckhout and Gabriel Unger *The Rise of Market Power and the Macroeconomic Implications* (2018). Available at: www.janeeckhout.com/wp-content/uploads/RMP.pdf; John Van Reenen and Christina Patterson, 'The rise of star firms has been better for investors than for employees'. *Harvard Business Review* (2017).

36 On the growth of these companies and their products worldwide, a study of international trade and pricing of insulin using detailed trade data for 186 importing countries between 1995 and 2013 that emerged from 12,000 observations, Helble and Aizawa conclude that international trade increased substantially during this period: Matthias Helble and Toshiaki Aizawa, 'International trade and determinants of price differentials of insulin medicine', *Health policy and planning* 32, no. 1 (2017), pp. 1–10. On the increasing use of analogue insulin, see David Beran, Margaret Ewen and Richard Laing, 'Constraints and challenges in access to insulin: a global perspective'. *The Lancet Diabetes & Endocrinology* 4, no. 3 (2016), pp. 275–285. Figure 1 shows the greater penetration of analogue insulin in upper middle-income, lower middle-income and low-income markets.

37 Although many upper middle-income countries have made significant strides in providing government/prepaid healthcare financing, there are still many countries like India where this is not the case.

38 Several analyses of national essential medicines lists note that most countries now list analogue and human insulin together, including those in LMICs (Wirtz 2016, *supra* note 26).

39 See, for example, Jing Lou, Nazleen F. Khan and Thomas Manetti, 'Implementation of a Health Plan Program for Switching From Analogue to Human Insulin and Glycemic Control Among Medicare Beneficiaries With Type 2 Diabetes', *JAMA*. 2019; 321(4):374–384. 10.1001/jama.2018.21364. The authors present the results of a study between 2014 and 2016 in four states in the United States, suggesting that, for many patients with type 2 diabetes, using human insulins may result in clinical outcomes that are similar to those using insulin analogues. The study also showed a more than 50 percent reduction in total insulin costs for the insurer. See also, Elizabeth Bashoff, 'Human Insulin may be a Low-Cost Option for Some People with Diabetes', Harvard Health Blog, 6 June 2019. Available at www.health.harvard.edu/blog/human-insulin-may-be-a-lower-cost-option-for-some-people-with-diabetes-2019060316747.

struggled to cope with the increasing share of insulin purchases as a share of total public procurement expenses.⁴⁰ Systematic data on trade of insulin as a commodity in recent years are difficult to obtain. Two studies using data up to 2013 conclude that international trade decreased substantially during this period, and 35 countries/territories had no insulin purchases at all despite the proliferation of new insulin products at the global level.⁴¹

Prima facie, the expansion of analogue insulin in public procurement, given the price difference between analogue and human insulin, remains difficult to explain fully. This, coupled with the fact that between 2004 and 2013, 62 countries worldwide bought insulin from only one source country,⁴² points to a significant amount of market power among a few companies to set the price and impact procurement choices in the public sector. This raises questions on product choice and competition. Does the concentration of supply in a few companies contribute to the rise of analogue insulin on a global scale? Is this power helping companies influence choices for procurement in a wide range of countries, thus helping to expand their market reach and influence in product baskets, and thereby leading to rising prices with lower access? Relatedly, given that biosimilar insulin products made by different manufacturers can be considered homogeneous goods,⁴³ does product selection criteria leading to the ascendancy of analogue insulin have a relationship with the exclusion of competition, specifically by increasing barriers to entry for new companies in those product markets? If not, what could account for the fact that despite rising demand and constrained budgets, governments often choose analogue insulin over cheaper human insulin products?

Answering these questions requires taking note of a number of market peculiarities in the insulin market. First, out-of-pocket expenses tend to comprise a large share of purchases in many countries, mostly LMICs, but also in some high-income countries such as the United States.⁴⁴

40 Ibid. The authors note that insulin procurement already occupied large shares of budgets in African countries in the early 2000s, which were struggling to balance the rising demand for insulin with other healthcare priorities such as HIV. See also Beran et al., 'Current Challenges', *supra* note 22, p. 16 for the ranges in government procurement prices in different LMICs.

41 Helble and Aizawa, *supra* note 35, p. 7. Beran et al., 'Trade Flows', *supra* note 23' p. 728.

42 Beran et al, Trade Flows, *supra* note 23.

43 See, for example, Andrea C. Tricco, Huda M. Ashoor, Jesmin Antony, Joseph Beyene, Areti Angeliki Veroniki, Wanrudee Isaranuwachai, Alana Harrington et al. "Safety, effectiveness, and cost effectiveness of long acting versus intermediate acting insulin for patients with type 1 diabetes: systematic review and network meta-analysis." *BMJ* 349 (2014).

44 Available studies on the topic also note that: (i) the unavailability of insulin in the public sector often forces individuals to buy insulin from private outlets (see, for example, Beran et al., 'Current Challenges', *supra* note 22); and (ii) data, where available, show that private-sector prices are significantly higher (see Beran et al., 'Trade Flows', *supra* note 22 at p. 279, for a comparison of public- and private-sector prices in select LMICs for a year's supply of insulin [13 doses], showing that it can range between US\$50 and US\$250).

Although there are no multi-country surveys that adequately capture the ways in which this impacts insulin access, the T1 International Survey of 2018 (the largest international survey driven by or of people living with diabetes) contains responses from 1,425 participants worldwide, of whom around 45 percent (631) are from the United States and the rest from 89 other countries. The survey results show that 13.1 percent of the respondents, many of whom from LMICs, had no coverage at all for the costs and that the prices of insulin heavily affected choice and living standards of patients that paid for it privately.⁴⁵

Second, while insulin pens have been a milestone in insulin delivery, there are some aspects of the pens market that might require more attention.

For instance, pens first introduced in the 1980s by the three companies⁴⁶ have been constantly updated to provide new versions of next-generation pens, including smart pens and, most recently, connected pens.⁴⁷ Some of these pens, at a closer glance, seem to thrive on product differentiation of a kind that is not health-related, but technology-driven.⁴⁸ Once again, detailed studies of how the market structure for insulin is influenced by product coupling with insulin pens are not available, but current trends raise a number of questions. To what extent are insulin pens a hindrance for the entry of competition in the insulin market? Is product coupling of pens and specific analogue insulin products in any way linked to the rise of analogue insulin and the resistance to switch to newer alternatives among consumers?

45 T1 International, 'Cost and rationing of insulin and diabetes supplies: Findings from the 2018 T1 International survey'. Available at www.t1international.com/media/assets/file/T1International_Report_-_Costs_and_Rationing_of_Insulin__Diabetes_Supplies__2.pdf. Study responses from high-income respondents showed a much higher percentage of coverage of all costs (32.4 percent). The only exception to this was in the United States, where the survey shows that only 6.5 percent of the respondents had coverage of all costs. A 2020 survey by T1 International has recently been published. This survey covers a total of 1,080 participants from 64 different countries, but the sample size is largely skewed towards respondents from the United States. To be able to draw insightful comparisons that are geographically diverse and based on country income levels, most of the downstream analyses of the 2020 survey have focused on the five most represented countries, namely the United States, Ghana, Canada, the Philippines and the United Kingdom. See Elizabeth Pfeister et al., 'Costs and Underuse of Insulin and Diabetes Supplies: Findings from the 2020 T1 International Cross-Sectional Web-based Survey', *Diabetes Research and Clinical Practice* 179 (2021), pp. 1–9.

46 First generation pens introduced by the companies in the 1990s include the Novopen (Novo Nordisk), AllStar (Sanofi), and prefilled pens, such as FlexPen, FlexTouch (Novo Nordisk), Humalog Pen, Kwikpen (Eli Lilly) and SoloSTAR (Sanofi).

47 Kesavadev, Saboo and Krishna (2020) trace the development of the pens market in three stages: the first generation pens versus the second generation pens (smart pens with memory functions in the market since 2007), and the more recent connected pens, which are in the market with new features that include more than just memory functions. See Jothydev Kesavadev, Banshi Saboo, Meera B. Krishna and Gopika Krishnan, 'Evolution of Insulin Delivery Devices: From Syringes, Pens, and Pumps to DIY Artificial Pancreas', *Diabetes Ther* no. 11 (2020). pp. 1251–1269.

48 For instance, the InPen system is a Bluetooth-enabled wireless insulin pen with a smartphone interface and a bolus advisor. Kesavadev, Saboo and Krishna, *supra* note 47, p. 1255.

These questions remain important given the difficulties of producing medical devices that could match new insulin products for generic companies, and the fact that pens pose additional hindrances in supplying a mixture of insulins to consumers.⁴⁹

Third, there is some anecdotal evidence suggesting that countries with mixed sourcing of insulin (i.e. countries that opted to source insulin not just from the three companies, but remained open to other generic companies) had higher levels of insulin availability in both the public and private sectors. Data on the availability of insulin in the private and public sectors in select sub-Saharan African countries⁵⁰ considered in conjunction with the most recently available data on insulin sourcing,⁵¹ suggest that the countries that have a higher level of insulin availability in the public sector, such as Mauritius and Mozambique, sourced it from companies other than the top three. This link between insulin availability and how it is sourced raises questions regarding procurement choices.⁵²

49 Ibid, p. 1256.

50 David Beran, Maria Lazo-Porras, Camille M. Mba and Jean Claude Mbanya, 'A Global Perspective on the Issue of Access to Insulin', *Diabetologica* (2021), issue 64, no. 5, pp. 954–962, doi: 10.1007/s00125-020-05375-2.

51 Sharma and Kaplan, *supra* note 32.

52 On this point, see also IQVIA Institute, 'Understanding Insulin Market Dynamics in Low and Middle Income Countries: Producers, Supply and Costs', August 2021. Available at: www.iqvia.com/insights/the-iqvia-institute/reports/understanding-insulin-market-dynamics-in-low-and-middle-income-countries. Among the many findings, the report highlights how, despite some emerging diversity in supply, an overwhelming 19 LMICs of the sample considered in the report were still dependent on the three largest companies for a significant share (>95 percent) of their insulin supplies.

Competition law is directed towards maintaining competitive markets and protecting the interests of consumers. It may be enforced through government action by way of investigation and civil and/or criminal prosecution by competition authorities. Competition law may also be enforced by private actors in civil actions brought before competent administrative authorities or courts. Competition investigations can be opened by competition authorities on their own initiative and may also be initiated based on information provided by the public.

Competition law enforcement actions are often terminated through some form of settlement, which may include the payment of monetary fines and/or the imposition of injunction and/or other equitable relief. A successful competition law prosecution in the courts may result in the award of damages, a compulsory licence, an injunction and other equitable relief. Criminal competition prosecution may result in fines and imprisonment for culpable individuals.

a. National and international aspects

As with most legislative and regulatory schemes, competition law is typically adopted and implemented within the territory of each individual country, and competition authorities typically focus their enforcement inquiries and prosecutions on activities taking place within a national territory. There are some competition rules embodied within international agreements, such as multilateral, regional and bilateral trade agreements. In addition, there are a significant number of agreements among countries directed towards facilitating cooperation among national competition authorities. The European Union is a legally integrated regional entity that maintains a regional competition enforcement authority and related judicial institutions and processes, as well as national competition authorities and related judicial institutions and processes.

Important for this discussion is that anticompetitive behaviours may take place across national territories or jurisdictions. For example, a multinational company with offices in Country A may, from that office, direct anticompetitive activities in Country B, and the activities directed from Country A may have a direct and substantial effect in Country B. Also, two or more actors may engage in anticompetitive conduct involving several countries, whose activities may affect several national markets.

b. Types of standards: ‘per se’ and ‘rule of reason’

Competition authorities and courts approach potential anticompetitive conduct under two standards. Some types of conduct or agreement are anticompetitive on their face, i.e. illegal per se. These types of conduct or agreement are unlawful once their existence is demonstrated. They may not be defended on grounds of offsetting pro-competitive effects.

For other types of conduct or agreement, competition law balances the potential anticompetitive effects against the potential pro-competitive effects, and only if the anticompetitive effects outweigh the pro-competitive effects is the conduct considered unlawful. This balancing test is generally referred to as the ‘rule of reason’.

For the competition authority, it is substantially easier to prosecute a case involving conduct that is illegal *per se* because it is not necessary to undertake an economic analysis, including market definition, which may be complex. For example, it is illegal for two or more horizontal competitors to fix the price of their product regardless of whether their conduct can be demonstrated to have an impact on a market or whether that impact is pro-competitive or anticompetitive.

C. Types of anticompetitive arrangements or practices

Competition law typically addresses two primary types of anticompetitive arrangements or practices.

i. Horizontal and vertical restraints

The first involves combinations in restraint of trade, or anticompetitive agreements between undertakings. For example, Section 1 of the US Sherman Act⁵³ and Article 101 of the Treaty on the Functioning of the European Union (TFEU)⁵⁴ address this type of anticompetitive behaviour.

Anticompetitive combinations or agreements between undertakings may be categorized as ‘horizontal’ or ‘vertical’. ‘Horizontal’ restraints involve two or more independent competitive companies, and ‘vertical’ restraints or practices take place within a supply chain from the manufacturer to the end-user.⁵⁵ Horizontal restraints include conduct such as price-fixing, output restraints and geographical allocation of territories. Vertical restraints include conduct such as abusive licensing conditions, product-tying arrangements and restraints on parallel trade.

53 Section 1 of the US Sherman Act provides: "Every contract, combination in the form of trust or otherwise, or conspiracy, in restraint of trade or commerce among the several States, or with foreign nations, is declared to be illegal."

54 Article 101 of the TFEU prohibits "all agreements between undertakings, decisions by associations of undertakings and concerted practices which may affect trade between Member States and which have as their object or effect the prevention, restriction or distortion of competition within the internal market."

55 There is not always a neat distinction between horizontal and vertical arrangements. A horizontal arrangement usually involves competitors or potential competitors at the same/similar level of the supply chain (e.g. producers). Companies in a vertical distribution chain may technically be independent of each other but tied together by some form of distribution arrangement.

ii. Monopolization or abuse of dominant position

The second primary type of anticompetitive conduct involves monopolization or abuse of dominant position. For example, Section 2 of the US Sherman Act⁵⁶ and Article 102 of the TFEU⁵⁷ address this type of behaviour. A monopoly or dominant position may be abused to the detriment of competitors and/or consumer welfare.⁵⁸

Antitrust/competition law in the United States and the European Union does not make it unlawful to achieve a monopoly position or dominant position on the market, provided that such a position is acquired without engaging in abusive conduct. Competition authorities and courts recognize that a company may achieve monopoly power by virtue of successful legitimate business practices, network effects or good fortune. Similarly, competition law does not prevent a company from maintaining a dominant position or monopoly provided that it does so without engaging in abusive conduct.

A monopoly or dominant position on the market generally means that the monopolist has the power to raise prices over competitive prices for an extended period without inducing market entry by competitors. A monopoly or dominant position is understood in the context of the ‘relevant market’, which can be defined in terms of product, geography and other factors. For example, an originator pharmaceutical company may own a patent on a drug that allows it to preclude other parties from making the same or a substantially similar drug. But whether the originator pharmaceutical company has monopoly power with respect to that drug will depend on the extent to which there are substitutable products that can be used by people living with a medical condition, thereby reducing the pricing and exclusionary power of the patent owner.⁵⁹ Market definition for pharmaceutical products often depends on the anatomical therapeutic chemical (ATC) level⁶⁰ at which the market is assessed.

56 Section 2 of the US Sherman Act provides: “Every person who shall monopolize, or attempt to monopolize, or combine or conspire with any other person or persons, to monopolize any part of the trade or commerce among the several States, or with foreign nations, shall be deemed guilty of a felony.”

57 Article 102 of the TFEU states: “Any abuse by one or more undertakings of a dominant position within the internal market or in a substantial part of it shall be prohibited as incompatible with the internal market in so far as it may affect trade between Member States.”

58 ‘Monopoly’ and ‘dominant position’ are essentially synonymous. ‘Monopoly’ is the term generally used in the United States, and ‘dominant position’ is the term generally used in the European Union.

59 With respect to geography, a hospital may be the only medical services provider within a 100-mile radius. If the radius is expanded to 250 miles, there may be four hospitals. Whether there is a monopoly may depend on the distance people living with diabetes are typically willing to travel to obtain medical services.

60 In the ATC classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five different levels. See World Health Organization, ‘ATC/DDD Toolkit’. Available at www.who.int/toolkits/atc-ddd-toolkit#:~:text=In%20the%20Anatomical%20Therapeutic%20Chemical,groups%20at%20five%20different%20levels.

Markets may also be defined in terms of the type of purchaser. There may be different markets for government procurement and out-of-pocket individual purchasing in the same geographic territory. In the case of the insulin market, evidence suggests that it is not just price and quality that define the markets; the expertise and practices of the dominant suppliers in marketing and tendering, especially within government schemes, may add to disadvantages for the competitive suppliers.⁶¹

It is possible that several companies collectively dominate a market. This situation is referred to by economists as an ‘oligopoly’. Article 102 of the TFEU refers to “[a]ny abuse by one or more undertakings of a dominant position”. This allows for a finding that several companies collectively occupy a dominant position.⁶² Section 2 of the US Sherman Act refers to: “[e]very person who shall monopolize, or attempt to monopolize, or combine or conspire with any other person or persons, to monopolize”. The language of the Sherman Act likewise leaves open the possibility that more than one person or company may combine to dominate a market.⁶³

d. Potential horizontal restraints

Competition law addresses both ‘agreements between undertakings’ or contracts in restraint of trade, and ‘abuse of dominant position’ or monopoly. The types of evidence needed to demonstrate improper conduct are different depending on which form of conduct is addressed. In terms of agreements between undertakings, competition authorities investigating an individual national insulin market would be seeking evidence that companies have engaged or are engaging in some form of ‘horizontal collusion’ to maintain prices above what they would be in a competitive market.

61 Personal interviews, firms in Bangladesh. See also: Deborah Cohen, ‘The prickly problem of access to insulin’, *BMJ* 343 (2011), p. d5782.

62 See, generally, Nicolas Petit, ‘The oligopoly problem in EU competition law’, In *Handbook on European Competition Law*, I. Liannos and D. Geradin (eds.), Edward Elgar Publishing, Cheltenham, UK, 2013. Available at <http://ssrn.com/abstract=1999829>.

63 The term ‘monopoly’ may be understood in common vernacular to refer to the position of a single (i.e. ‘mono’) enterprise or supplier. The question of multi-firm dominance of a market is the subject of jurisprudential debate within the United States, but there is support among leading commentators for findings of dominance by two or more firms: William J. Robinson and Ashley M. Koley, ‘Antitrust enforcement against oligopolies’, *Antitrust Law Daily*, Oct 2019 (Wolters Kluwer), citing Areeda and Hovenkamp on ‘shared monopoly’; and see Richard A. Posner, ‘Oligopoly and the Antitrust Laws: A Suggested Approach’, *21 Stan. L. Rev.* 1562, no. 10.2307 (1969), p. 12275231562. The US Supreme Court historically has interpreted the language of the Sherman Act in a way that allows it to address the modern economy within the limitations of the Act’s late 19th century drafting.

i. Price and availability

Analogue insulin is sold in vials⁶⁴ or in prefilled pens, which can often be more convenient than syringes for the user, and are available in two forms: disposable and reusable which needs replacement of cartridges and needles. Eli Lilly, Sanofi and Novo Nordisk are the three largest manufacturers of pens: Eli Lilly manufactures the KwikPen for Humalog, Humalog Mix 50/50 and Humalog Mix 75/25; Sanofi manufactures the SoloSTAR for Lantus and Apidra; and Novo Nordisk manufactures the FlexPen for Novolog and Novolog Mix 70/30, as well as the FlexTouch for Levemir.⁶⁵ Each of these pens generally has a capacity of 300 units, or 3 millilitres (ml) of insulin.⁶⁶

The user price of a vial of analogue insulin in the United States is today approximately US\$300,⁶⁷ and people living with diabetes may require between one and six vials per month. Insulin pens are in general more expensive than vials, and price comparisons between vials and pens show that while a vial with 1,000 units, or 10 ml, can range between US\$22 and US\$200, a box of pens with 1,500 units, or 15 ml, can cost roughly around US\$330.⁶⁸ Hence, the price of insulin treatment in the United States may run from US\$3,600 to US\$21,600 per year. The United States accounts for only 15 percent by volume of the global insulin market yet generates almost half of the pharmaceutical industry's insulin revenue.

64 Insulin is generally supplied by vial, and a standard measurement is 10 ml, 100-UL/ml. "Insulin is measured in International Units (units); most insulin is U-100, which means that 100 units of insulin are equal to 1 ml." See Dr Claire Wladis, 'Insulin'. Available at www.cwladis.com/math104/insulin.php.

65 Michele Pisano, 'Overview of insulin and non-insulin delivery devices in the treatment of diabetes', *Pharmacy and Therapeutics* 39, no. 12 (2014), pp. 866–873. In addition, a number of studies find that switching from vials to pens led to better adherence of insurance regimes among people living with diabetes, and reduced healthcare and hospitalization costs of up to US\$1,748 per person. See, for example, David Cobden, Won Chan Lee, Sanjeev Balu, Ashish V. Joshi and Chris L. Pashos, 'Health outcomes and economic impact of therapy conversion to a biphasic insulin analog pen among privately insured patients with type 2 diabetes mellitus', *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 27, no. 7 (2007), pp. 948–962. But on the whole, healthcare outcomes are usually decided by a number of other factors, such as the age of people living with diabetes and co-morbidities they exhibit, and other studies have cautioned against drawing conclusions without considering these factors: Tina K. Thethi, 'Comparing insulin vials to pens –comparison of charges, not healthcare benefits', *J Med Econ* 16, No. 10 (2013), pp. 1228–1230.

66 In general, the pens hold 300 units (3 ml) of insulin and deliver 60 to 80 units per dose in 1-unit increments. But the FlexPen and the KwikPen deliver up to 60 units per dose, and the SoloSTAR and the FlexTouch deliver up to 80 units per dose. See Pisano, *supra* note 65, p. 867.

67 See, for example, Joyce Frieden, 'Senators Probe 'Enormous' Insulin Price Spikes', *Medpage Today*, 8 May 2018; Bram Sable-Smith, 'How Much Difference Will Eli Lilly's Half-Price Insulin Make?', *Kaiser Health News*, 12 March 2019.

68 Pisano, *supra* note 65, p. 868.

Note that regular human insulin is recently available from some distributors for less than US\$25,⁶⁹ making the annual cost between US\$300 and US\$1,800. Mylan (USA) and Biocon (India) just recently announced that the US Food & Drug Administration (FDA) had approved their New Drug Application for insulin glargine injection, which is now expected to be available in vial and pre-filled pen presentations at a much-reduced price compared with the originator products in the US market. Mylan intends to offer it at a wholesale cost of US\$147.98 per package of five 3 ml pens and US\$98.65 per 10 ml vial, making it the cheapest brand of insulin glargine currently available in the United States. To what extent this will change the market dynamics in the short term will perhaps depend on the distribution networks. Approval as a biosimilar is pending in the United States, further to a recent change in the regulatory approval pathway for insulin.⁷⁰ Moreover, the further step of approval as an ‘interchangeable’ is a predicate to allowing pharmacists to substitute the biosimilar for Lantus without specific physician approval.⁷¹

Insulin prices vary widely in different markets outside the United States,⁷² and lack of access to insulin is a serious public health problem affecting many LMICs.⁷³ The principal impact is on the individuals who are unable to afford the product, or who face financial hardship based on lack of affordability. The lack of government purchases of insulin in several countries, affecting access to those who need it most, is largely a by-product of increasing prices of insulin combined with inadequate public budget resources, especially for analogue formulations when compared to human insulin.⁷⁴ The cost of analogue insulin has increased over by 1,000 percent compared to its initial price in the 1990s.⁷⁵ And yet, the trend of

69 See, for example, Julia Belluz, ‘Walmart’s \$25 insulin can’t fix the diabetes drug price crisis’, *Vox*, 11 April 2019. Available at www.vox.com/science-and-health/2019/4/10/18302238/insulin-walmart-relio.

70 PRNewswire, ‘Mylan and Biocon Announce U.S. FDA Approval of Semglree™ (insulin glargine injection)’, 11 June 2020. Available at www.wfmz.com/news/pr_newswire/pr_newswire_health/mylan-and-biocon-announce-u-s-fda-approval-of-semglee-tm-insulin-glargine-injection/article_33d71fco-eeb4-5026-af14-4dbcda4cb2ee.html.

71 See *infra* notes 133–134. US State pharmacy and medical regulation may require additional modification to allow for ‘interchangeable’-based substitution.

72 Beran et al., ‘Trade Flows’, *supra* note 23, pp. 728–729; Beran et al., ‘Current Challenges’, *supra* note 23, pp. 13–22.

73 *Ibid.*, at p. 8. See also Ewen et al., *supra* note 8; Douglas Ball, Margaret Ewen, Richard Laing and David Beran, ‘Insulin price components: case studies in six low/middle-income countries’, *BMJ Global Health* 4, no. 5 (2019): e001705. Available at doi: 10.1136/bmjgh-2019-001705; Abhishek Sharma and Warren A. Kaplan, ‘Challenges constraining access to insulin in the private-sector market of Delhi, India’, *BMJ Global Health* 1, no. 3 (2016). Available at doi: 10.1136/bmjgh-2016-000112.

74 See Beran et al., *supra* note 23 on how it affects different markets within and outside the United States.

75 T1 International, *supra* note 45, p. 2 (it is unclear if the estimates are adjusted for inflation).

increasingly using analogue insulin products, as observed in developed countries, is spreading on a global scale.⁷⁶

Although some reviews suggest that the dominant companies maintain high prices in high-income countries and offer lower prices in most LMICs,⁷⁷ existing evidence on the availability and pricing of insulin in these countries shows that a preference for analogue insulin can stretch public-sector budgets in many countries to purchase insulin even in the presence of some form of tiered pricing.⁷⁸ In this context, given the lack of scientific consensus or agreement on the advantages of analogue insulin over human insulin, the question remains as to why national procurement agencies prioritize analogue insulin despite budget constraints, as also highlighted earlier in this working paper.

The T1 International 2018 survey, the largest diabetes survey of out-of-pocket insulin access, covering 90 countries, concludes that even for the same insulin product, there is a wide range of prices across the world that does not necessarily correspond to purchasing power.⁷⁹ Figure 1 shows how the prices of pre-mixed analogue insulin can vary across markets, with high prices in countries with the poorest people. These price differentials persist across all categories of insulin products, including tests strips. For instance, the prices of brand test strips can vary from US\$13 per pack in Australia to US\$25 per pack in Ghana and US\$84 in

76 Cefalu et al., *supra* note 25. See also Yaser T. Bazargani, Anthonius de Boer, Hubert G.M. Leufkens and Aukje K. Mantel-Teeuwisse, 'Selection of essential medicines for diabetes in low- and middle-income countries: a survey of 32 national essential medicines lists', *PLoS one* 9, no. 9 (2014), p. e106072, who conduct a study of national essential medicines lists (NEMs) in 32 countries and note (on p. 4):

"Half of the countries included at least one recombinant human insulin in their NEML while one third (none of the low-income countries) had exclusively chosen recombinant human insulin(s). Half of the countries which incorporated solely recombinant human insulin(s) were from the region of the Americas. However, it is important to mention that 14 countries (44%) had not specified the source of insulin in their NEML. Six countries (19%) had selected insulin analogues as essential medicines, all of which were amongst the upper middle-income countries and predominantly from the region of the Americas (4 out of 6 countries)." Wirtz, *supra* note 25, at p. 43, compares human and analogue insulin in NEMs in 100 LMICs, and notes that: "Of the 100 countries in the LMIC study, 16 percent (n=16) listed analogue insulin as part of their NEML with WHO EMRO countries having the highest numbers of rapid and long-acting insulin. The higher prevalence of diabetes and the relative wealth of the countries in comparison to other regions may explain the higher percentage.

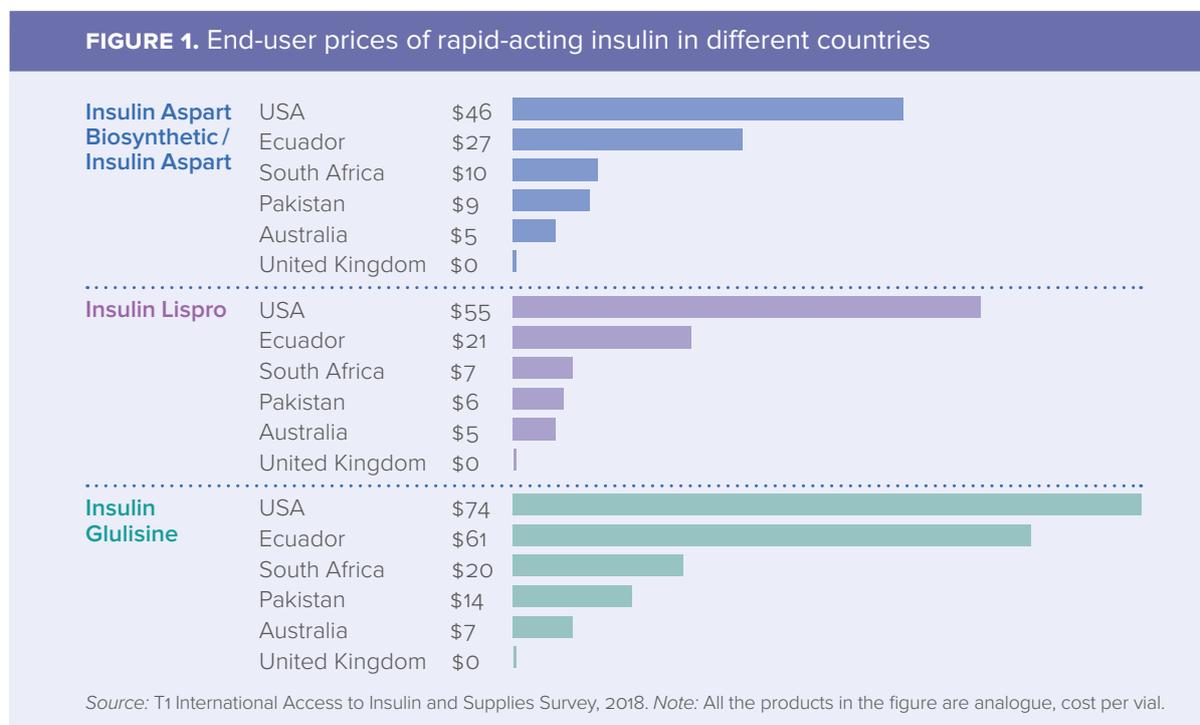
Among the countries with analogue insulin, Colombia, Saudi Arabia, Mexico and Ghana list more than one of each type, suggesting that these countries are less selective in listing analogue."

77 Hans V. Hogerzeil and Sterre Recourt, 'The importance of insulin donations for children in 43 low-and middle-income countries', *Journal of Public Health Policy* 40, no. 2 (2019), pp. 253–263. Available at doi: 10.1057/s41271-018-00159-w.

78 See Wirtz, *supra* note 26 at p. 81, who notes that: "it is surprising to see that lower-middle income countries such as Ghana list all types of analogue insulin given their limited healthcare resources." Also see Wirtz *supra* note 26, at p.43, discussed above in footnote 73. This point was also confirmed by interviews conducted for this study with international procurement officials.

79 The T1 International survey covered 1,425 participants in total, of which 631 (44.3 percent) were residents of the United States, and the remaining 804 were from 89 other countries, including selected LMICs split across parts of Asia, Africa and Latin America (the 2020 update covers only 64 countries). See, also, Cefalu et al., *supra* note 25, who note the same. Available at www.t1international.com/access-survey18.

South Africa, highlighting the lack of any correlation between pricing and purchasing power in question.⁸⁰ Moreover, despite a rise of biosimilar insulin supplies from several companies outside the United States and Europe, there does not appear to be a meaningful supply of lower-cost biosimilar analogue insulin on markets in LMICs.⁸¹



Government procurement prices are also still highly variable across countries. Previously, studies found that different purchasing policies at the central level within countries can lead to varying prices of insulin.⁸² A 2016 survey conducted in 13 LMICs found that governments were paying highly variable prices for the same insulin, e.g. US\$1.45 (Ethiopia) to US\$24.72 (China) for 1,000 IU NPH human insulin. Even identical products had variable procurement prices. For example, 1,000 IU Lantus (glargine) cost US\$21.56 (Indonesia) to US\$106.52 (China).⁸³ Explaining price differences can be complex, with several factors contributing to price increases in markets including retail chains, the presence of tiered pricing by pharmaceutical companies that may or may not be linked with the income levels of countries, and other supply chain inefficiencies, among others.

80 See T1 International, *supra* note 45.

81 See Baren et al., ‘Current Challenges’, *supra* note 23, p. 23.

82 “Mozambique purchases insulin by international tender at US\$4.50 (€3.95) per 10ml vial of 100IU insulin compared to US\$4.62 (€4.07) in Zambia. Zambia also purchases through national tender at US\$8.00 (€7.02) and US\$10.05 (€8.82) per vial.” David Beran, ‘Access to insulin in developing countries’, *Essential Drug Monitor* 34 (2005), pp. 27–28.

83 Ball et al., *supra* note 73.

There are some positive developments relating to affordability and access. The Indian biotech firm Biocon announced in September 2019 that it would supply regular human insulin at less than US\$0.10 per day (or about US\$36.50 per year) in LMICs, stating that these countries constitute 80 percent of the global diabetes burden. This amounted to a 50 percent reduction from previous prices.⁸⁴ How far this will alleviate the current insulin access barriers will depend on a large number of factors, including the penetration of, and demand for, analogue products. Whether Biocon/Mylan's new insulin product, insulin glargine injection, which is currently approved in 40 countries worldwide, will make a difference in expanding competition and lowering prices globally, and to what extent, remains to be seen.⁸⁵ Eli Lilly's biosimilar glargine has also been introduced. Sustainable and price-lowering access strategies usually require competition among several suppliers.

ii. Potential vertical restraints, supply chains and price differentials

Because of the continued lack of access to, and the persistence of price differentials for, various insulin products in countries that do not correspond to any 'ability to pay' parameters, a more thorough review of marketing practices, supply chain mark-ups, health system dynamics and procurement mechanisms that could account for these effects both in the public and private sectors is called for.⁸⁶

Typically, insulin manufacturers set the price for wholesalers, which then distribute along the retail chain when the product is sold in the private sector. Duties, taxes, mark-ups and other supply chain costs can affect the price of insulin by the time it reaches end-users, also in the public sector.⁸⁷ Relatedly, who sets protocol standards for treatment within countries, leading to prescription of some products over others, also remains an open issue. Another issue is how the supply chains are organized, how much is allocated to the sales force that markets the drugs, and in what ways this influences market shares and market segmentation.⁸⁸

84 Ayan Pramanik, 'Biocon to reduce insulin prices to \$0.10 per day', *The Economic Times* (India), 26 September 2019.

85 GaBI Online, 'Biocon/Mylan launch first insulin glargine biosimilar in Australia', 11 October 2019. Available at www.gabionline.net/Biosimilars/News/Biocon-Mylan-launch-first-insulin-glargine-biosimilar-in-Australia.

86 See the study on the impact of increased prices of insulin prices in the US market on cost-related underuse: Darby Herkert, Pavithra Vijayakumar, Jing Luo, Jeremy I. Schwartz, Tracy L. Rabin, Eunice DeFilippo and Kasia J. Lipska, 'Cost-related insulin underuse among patients with diabetes', *JAMA Internal Medicine* 179, no. 1 (2019), pp. 112–114.

87 Beran et al., 'Current Challenges', *supra* note 23.

88 The spending ratios of Eli Lilly on its insulin product portfolio captured in a recent Staff Report prepared for Senators Charles E. Grassley and Ron Wyden, Chairman and Ranking Member of the US Senate Finance Committee, underscores this point. The evidence shows that the company's research and development (R&D) spending was a fraction of the money it spent on marketing the drugs. According to the report, Eli Lilly reported spending nearly US\$1.5 billion on sales and marketing expenses on the drugs, as opposed to the roughly US\$450 million it spent on R&D between 2014 and 2018. See US Senate Finance Committee, 'Insulin: Examining the Factors Driving the Rising Cost of a Century Old Drug', Staff Report, Washington, DC, 14 January 2021, pp. 16–18 (hereinafter 'Senate Staff Insulin Report'). Available at [www.finance.senate.gov/imo/media/doc/Grassley-Wyden%20Insulin%20Report%20\(FINAL%201\).pdf](http://www.finance.senate.gov/imo/media/doc/Grassley-Wyden%20Insulin%20Report%20(FINAL%201).pdf).

At the macro level, procurement of insulin places a significant financial burden on the global public health system.⁸⁹ This could at least partially account for why it is undersupplied in the public healthcare system. Other structural factors affecting pricing and access include:

- the manner in which drugs are procured and financed for the national health system;
- the characteristics of the drug reimbursement scheme;
- the extent to which individuals purchase and pay for insulin ‘out-of-pocket’;
- the manufacturer’s selling price plus the number of intermediaries between the manufacturer and the end-user and their mark-ups;
- the presence or absence of tariffs, quotas or other trade measures imposed at the border;
- the characteristics of the intellectual property system, including the extent to which insulin products and related delivery devices are patented and what strategies exist to re-examine and potentially clear out improperly granted patents;
- the rules governing the health regulatory authority and the regulatory processes involved in placing insulin products on the market;
- the system for the granting and maintenance of regulatory market exclusivity;
- the behaviour of insulin prescribers, typically physicians;
- advertising and promotion activities of insulin suppliers;
- cold chain and storage costs.

Although the discussion in Section 2d (i) on price and availability shows that there are varying prices of insulin in both the public and private sectors across countries, systematic evidence on the nature of supply-side barriers affecting the pricing of insulin in different countries is not available.

Some recent studies using WHO/HAI methodology⁹⁰ shed light on the availability, price differentials and health system barriers to access to insulin in different contexts. A 2018 study of the availability of insulin products across 99 pharmacies in Zambia using the WHO/HAI methodology concludes that not only were most prices of the products higher than their international reference prices, but also the products were not adequately available either in the public or private sectors.⁹¹ A 2016 study with the same methodology conducted in the

89 WHO Global Report 2016, *supra* note 1, p. 14: “Based on cost estimates from a recent systematic review, it has been estimated that the direct annual cost of diabetes to the world is more than US\$827 billion.”

90 The WHO and Health Action International (HAI) developed a standard methodology for examining price components through the use of case studies in 2008, which offer a comparable basis across countries/regions: WHO/HAI, ‘Measuring medicine prices, availability, affordability and price components’, WHO/PSM/PAR/2008.3, Geneva, 2008.

91 Andrea Hannah Kaiser, Lindsey Hehman, Birger Carl Forsberg, Warren Mukelabai Simangolwa and Jesper Sundewall, ‘Availability, prices and affordability of essential medicines for treatment of diabetes and hypertension in private pharmacies in Zambia’, *PLOS One* 14, no. 12 (2019). Available at <https://doi.org/10.1371/journal.pone.0226169>.

Hubei province of China covered 30 public-sector outlets and 30 private pharmacies and found that the mean availability was highest, by 90 percent higher in some cases, in public hospitals for pre-mixed human insulin. In primary care institutions and private pharmacies, the mean availability ranged from 10 percent to 33 percent, and, on the whole, the median prices of all insulin types were 1.36 to 2.59 times higher than Australian Pharmaceutical Benefit Scheme prices in all three segments of healthcare for both human and analogue insulins. The study also found that some people living with diabetes pay 4 to 16 days of wages to purchase a month's treatment depending on the insulin type and whether they accessed the public or private sector. Most importantly, the study found the largest component of the user price to be the manufacturers' selling price, which accounted for about 60 percent of the total.⁹² Another 2018 study using the same methodology in Nepal found that the mean availability of two types of human insulins listed on the 2011 Nepal Essential Medicines List were only 14.3 percent and 42.9 percent, respectively, in the private-sector and public-sector pharmacies surveyed by the authors. The study also found that the median user prices of human insulin cartridges, analogue insulin cartridges and pens were, respectively, 2.1, 4.6 and 5.3 times that of human insulin vials.⁹³

A recent six-country study (Rio de Janeiro province of Brazil, Hubei and Shaanxi provinces of China, Ghana, Haryana state in India, Indonesia and Uganda), also using the WHO/HAI methodology, specifically investigated the role of mark-ups in LMICs⁹⁴ and concluded that, on the whole, cumulative mark-ups can account for between 8.7 percent and 565.8 percent, of which the part of the price paid by the person living with diabetes that was directly attributable to the manufacturer's selling price varied between 15 percent and 92 percent.⁹⁵ A number of country-specific factors, such as taxes along the supply chain, tariffs, and a lack of competitive public procurements and price regulation, were found to play a significant role in the lack of transparency of insulin prices throughout the supply chain.⁹⁶

92 Chenxi Liu, Xinping Zhang, Chaojie Liu, Margaret Ewen, Zinan Zhang and Guoqin Liu, 'Insulin prices, availability and affordability: a cross-sectional survey of pharmacies in Hubei Province, China', *BMC Health Services Research* 17, no. 1 (2017), p. 597. Available at doi: 10.1186/s12913-017-2553-0.

93 Abhishek Sharma, Parash Mani Bhandari, Dipika Neupane, Warren A. Kaplan and Shiva Raj Mishra, 'Challenges constraining insulin access in Nepal—a country with no local insulin production', *International Health* 10, no. 3 (2018), pp. 182–190. Available at doi: 10.1093/inthealth/ihy012.

94 Ball et al., *supra* note 73, p. 5.

95 *Ibid.*

96 See also Beran et al., 'Current Challenges', *supra* note 23.

iii. Price-fixing

As introduced earlier, there are various potential types of anticompetitive conduct that may explain the availability and pricing features of the global insulin market and its various submarkets (e.g. national markets).

The first type of horizontal collusion might involve an agreement to fix prices at a particular level or to establish a fixed ‘baseline’ price below which the companies agree not to sell. This might be evidenced by written documents and/or oral testimony regarding an explicit agreement to cooperate with respect to price-setting. Price-fixing among horizontal competitors is generally considered a per se violation of competition law because potential pro-competitive effects do not overcome the nearly certain adverse effects on the market or people living with diabetes.

As with other types of potentially anticompetitive behaviour, a price-fixing scheme might involve more than a single country. For example, potential competitors might agree that Company X will charge a higher price in Country A and allow Company Y to undercut its price in Country A, whereas Company Y will charge a higher price in Country B and allow Company X to undercut its price in Country B. In this manner, the two conspiring companies would each be able to secure a higher than competitive market price in the respective countries.

An important related question is whether price-fixing can be inferred from parallel pricing behaviours, such as circumstances where a price increase by Company A is followed by equivalent price increases by Companies B and C.⁹⁷ Unlike price decreases, which if met might simply signal the necessity to meet price competition, parallel price increases may not be ‘naturally sensible’ because companies maintaining lower prices presumably would gain market share against a competitor company that raised prices. Jurisprudence differs in national jurisdictions as to whether and under which circumstances parallel pricing behaviour may represent horizontal anticompetitive conduct without express evidence of collusion.⁹⁸

97 ‘Parallel pricing’ is sometimes also referred to as ‘shadow pricing’. Shadow pricing behaviour involving Sanofi and Novo Nordisk in the US market is described in detail in the recent Staff Report prepared for Senators Charles E. Grassley and Ron Wyden, Chair and Ranking Member of the US Senate Finance Committee, respectively. See Senate Staff Insulin Report, *supra* note 85. This Staff Report does not address competition law issues specifically. See also discussion and citations in the US Federal Trade Commission’s response regarding excessive pricing actions: Federal Trade Commission, ‘Report on Standalone Section 5 to Address High Pharmaceutical Drug and Biologic Prices’; and ‘Statement of Commissioners Rohit Chopra and Rebecca Kelly Slaughter, Federal Trade Commission Report on the Use of Section 5 to Address Off-Patent Pharmaceutical Price Spikes’, 24 June 2019.

98 See majority, concurring and dissenting opinions in *E.I. Du Pont De Nemours & Co. v. Federal Trade Commission*, 729 F.2d 128 (2d Cir. 1984).

Novo Nordisk products are registered in 111 countries, Sanofi products in 101 countries, and Eli Lilly products in 94 countries.⁹⁹ Most other companies produce and sell in a few countries only. A problematic pricing arrangement between several independent companies may be indicated not only by prices¹⁰⁰ that appear to rise in tandem, but also in the timing of the introduction of new products.

iv. Output restraints

A second type of horizontal collusion might involve an agreement among companies to supply a limited quantity of insulin product to the market. An output restraint has a similar effect to price-fixing because, assuming the number of individuals needing insulin (i.e. demand) is constant, the price for a smaller quantity of available product (i.e. supply) will rise.

At some point, a pharmaceutical manufacturer is constrained in the quantity of product that can be produced at its existing facilities and must choose whether to expand them if there is surplus demand that would absorb additional supplies. The ‘marginal cost’ of producing an additional unit may go up substantially when it can only be produced in a newly constructed manufacturing plant. This might explain price increases based on ordinary business requirements in some cases.

In light of the high prices charged for analogue insulin, in particular, it would be of interest to determine whether the three dominant suppliers are constrained to some degree in the potential output of their biologics manufacturing facilities, bearing in mind the possibilities for the outsourcing of production. Given the apparent wide difference between the estimated cost of producing insulin and the prices at which it is sold,¹⁰¹ it seems doubtful that high prices are necessary because of natural output constraints.

Output restriction could be applied in an indirect way, for example, by introducing new delivery devices such as pre-mixed vials and pens that are promoted as facilitating ease of use by insulin users. The prices for insulin in pre-filled pens and cartridges are higher than insulin presented in vials.¹⁰² A question is whether the companies at the same time are limiting the supply of product using less expensive and/or less sophisticated delivery devices so that high prices of the newer products are maintained.

99 Molly Lepeska and Margaret Ewen, ‘Global Access to Affordable Insulin: Understanding the Barriers’, ACCISS and HAI, presentation on file with authors, p. 6.

100 Cefalu et al., *supra* note 25, p. 1305.

101 See Dzintars Gotham, Melissa J. Barber and Andrew Hill, ‘Production costs and potential prices for biosimilars of human insulin and insulin analogues’, *BMJ Global Health* 3, no. 5 (2018). Available at doi: 10.1136/bmjgh-2018-000850, discussed *infra* text, note 129.

102 Ewen et al., *supra* note 8; Ball et al., *supra* note 73, p. 1.

v. Geographical allocation of territories

One customary type of behaviour is agreement among companies to allocate geographic territories among themselves. A number of companies may agree that a certain country market will be reserved for one supplier and that other excluded suppliers will not market within that country. The arrangement may involve agreement by excluded suppliers not to make any sales or deliveries in the reserved country, that is, prohibiting both active and passive sales, or it may prohibit excluded companies only from actively marketing within the reserved territory but allowing them to respond to externally generated inquiries, i.e. passive sales. As a general matter, a competition authority in one country pursues an enforcement action against such an arrangement based on the direct and substantial effect of the cartel within its own territory. This country's authority may use evidence regarding the establishment and maintenance of the cartel that it secures outside its territory, including through cooperative investigations with other countries' competition authorities. There is no 'global' competition authority per se with the power to prosecute all the potential interrelated activities of a multinational arrangement that affects multiple countries. It is up to individual country competition authorities to investigate and prosecute activities that affect their respective countries, although they may cooperate with each other.

Geographical allocation of territories may also occur within single national markets. Agreements among horizontal competitors to allocate markets within national territories are typically per se illegal. National rules on 'vertical' geographical allocation vary among countries. Whether a single company may allocate sales territories among its distributors may be assessed under a standard of rule of reason. The rationale for allowing geographical allocation among vertical distributors in appropriate circumstances is that this may encourage the provision of ancillary services such as advertising and promotion within that geographic area. Assuming the presence of horizontal competitors, there is likely to be downward pricing pressure on each of the distribution networks.

As with output restraints, an agreement among horizontal competitors to allocate geographic territories confers pricing power on the company with access to the territory/country. This is generally considered a per se violation of competition law.

There is evidence that a significant number of national markets worldwide are supplied with insulin products by only one or two of the three dominant suppliers.¹⁰³ This raises the question as to why potential competitors would elect to stay out of a national market. There may be reasonable business explanations for this, such as economies of scale, technological infeasibility and regulatory compliance costs. Furthermore, the market may be too small to accommodate several suppliers, there may be a physician/prescriber preference for a

¹⁰³ See Beren et al., 'Trade Flows', *supra* note 23, p. 730.

particular supplier, or there may be a single large national procurement contract. By contrast, the lack of presence of a potential competitor may raise questions about whether there is some form of geographical allocation of territories among the dominant suppliers.

vi. Bid rigging

Horizontal collusion often takes the form of bid rigging, or the gaming of procurement processes. A government authority or private purchaser typically requests offers or bids as a predicate to a purchase. In procurement tenders, the offering prices at which companies' bid are expected to be kept secret. Because prospective suppliers are bidding without knowledge of the prices being offered by competitors, each bidder in principle will offer its lowest business-sensible price. However, colluding suppliers may instead elect to share information with each other regarding the prices at which they intend to bid. They may choose to allocate the 'winning bid' to a particular supplier for one tender, with the understanding that a different colluding supplier will be allocated the winning bid on a subsequent tender. Alternatively, they might subdivide responsibility for fulfilling the contract once the tender has been accepted. In this way, the colluding suppliers benefit from higher prices.

Bid rigging is a form of price-fixing, but it may also involve elements of geographic allocation of territory, bribery and/or other anticompetitive practices.

There may be a legitimate business reason for single sourcing. But it is of interest to determine why the number of suppliers to a particular market is limited, particularly if prices in that market are higher than for other country markets.

vii. Agreements to refrain from competing

One characteristic practice in the pharmaceutical sector has been settlement agreements between a patent owner and a potential generic/biosimilar market entrant for the latter to drop its legal challenge of the patent in exchange for some valuable consideration. For instance, the US Federal Trade Commission (FTC) considers such agreements to be highly suspect under the competition laws, and for many years argued in court that patent challenge buyouts, or settlement agreements that involve substantial consideration, including cash payments, are illegal *per se*. The US Supreme Court in 2013 ruled that such agreements may violate competition laws but should be reviewed under a rule of reason standard. A payment not to compete by a dominant actor to a potential competitor, or some other form of indirect compensation (e.g. refraining from introducing an authorized generic/biosimilar)¹⁰⁴ may constitute an abuse of dominant position, i.e. unlawfully maintaining a monopoly.

104 Regarding the market effects of the introduction by originators of 'authorized generics' (i.e. off-patent versions of originator products introduced to compete with third-party generics), see N. Shcherbakova, M. Shepherd, K. Lawson and K. Richards, 'The role of authorized generics in the prescription drug marketplace', *Journal of Generic Medicines* 8, No. 1, Jan (2011), pp. 28–40; R. Gupta, N.D. Shah and J.S. Ross, 'Generic drugs in the United States: policies to address pricing and competition', *Clinical Pharmacology & Therapeutics* 105, No. 2, Feb (2019), pp. 329-37.

This type of conduct is also a form of horizontal anticompetitive conduct because it requires an agreement between the patent owner and the potential competitor, which is characteristic of a horizontal restraint. Abuse of dominant position and an anticompetitive agreement between undertakings may be found with respect to the same arrangement.¹⁰⁵

However, it is not only in the context of patent-owning dominant market actors that there may be anticompetitive agreements intended to preclude the entry of market competitors to preserve a market position. For example, in a case brought by the FTC against Mallinckrodt, the FTC charged that the pharmaceutical company had bought out the only potential competitor to an off-patent product in which it held a dominant position in the United States, recognizing that the product of the potential competitor would be sold at a much lower price than Mallinckrodt's product. This constituted anticompetitive abuse.¹⁰⁶

e. Potential vertical restraints

■ Product tying

Given that delivery devices are central to dosing, ease of use and convenience, product tying with devices can be particularly relevant in the insulin market. Such product tying can pose additional barriers for manufacturers of biosimilars or follow-on insulins if the insulin is incompatible with the administering devices or not as compatible as the products of the originator companies. Sophisticated administering devices are not easy to manufacture, and given that all biosimilars are not interchangeable products,¹⁰⁷ product tying of this nature may make it all the more difficult for generic/biosimilar companies to penetrate markets successfully.¹⁰⁸

¹⁰⁵ See *Generics (UK) v CMA*, Court of Justice of the European Union Judgement (Fourth Chamber), Case C-307/18, 30 January 2020.

¹⁰⁶ See FTC Case Summary, Mallinckrodt Ard Inc. (Questcor Pharmaceuticals), 14 July 2017. Available at www.ftc.gov/enforcement/cases-proceedings/1310172/mallinckrodt-ard-inc-questcor-pharmaceuticals:

"Mallinckrodt ARD Inc, formerly known as Questcor Pharmaceuticals, Inc, and its parent company, Mallinckrodt plc, agreed to pay \$100 million to settle charges that they violated the antitrust laws when Questcor acquired the rights to a drug that threatened its monopoly in the US market for adrenocorticotrophic hormone (ACTH) drugs. Acthar is a specialty drug used as a treatment for infantile spasms, a rare seizure disorder afflicting infants, as well a drug of last resort used to treat other serious medical conditions. The complaint alleges that, while benefitting from an existing monopoly over the only US ACTH drug, Acthar, Questcor illegally acquired the U.S. rights to develop a competing drug, Synacthen Depot. The acquisition stifled competition by preventing any other company from using the Synacthen assets to develop a synthetic ACTH drug, preserving Questcor's monopoly and allowing it to maintain extremely high prices for Acthar. In addition to the \$100 million monetary payment, the proposed stipulated court order, which must be approved by the federal court, requires that Questcor grant a license to develop Synacthen Depot to treat infantile spasms and nephrotic syndrome to a licensee approved by the Commission".

¹⁰⁷ Interchangeability for new insulin products will become a key consideration for people living with diabetes, doctors and insurance companies. A biosimilar or follow-on product does not automatically make it interchangeable, and currently none of the biosimilars are approved as interchangeable drugs.

¹⁰⁸ John White and Jennifer Goldman, 'Biosimilar and follow-on insulin: the ins, outs, and interchangeability', *Journal of Pharmacy Technology* 35, no. 1 (2019), pp. 25–35.

f. Potential abuse of dominant position

A company has a dominant position with respect to a particular product if it is able to raise and maintain a price higher than a competitive market price for an extended time without triggering third-party entry with competing products. If there are no substitutable products, various strategies or arrangements may allow a company to charge a price above a competitive market price such as a patent, trade secret or other market exclusivity.

i. Product market

It appears that human insulin and analogue insulin are substitutable products, although an analogue product or combination of analogues may present certain advantages to people living with diabetes. If insulin products are indeed substitutable, and regular human insulin is substantially cheaper than analogue insulin, the suppliers of analogue insulin should not, as a matter of principle, be able to charge substantially higher prices than suppliers of regular human insulin. Whether supplier companies that have pursued a policy of product improvement that qualifies as evergreening¹⁰⁹ is an important question.¹¹⁰ Studies have previously noted such extended patent protection to be the primary reason why insulin prices do not drop as expected.¹¹¹ Almost all country studies using the WHO/HAI methodology

109 See Roger Collier, 'Drug Patents: The Evergreening Problem', *Canadian Medical Association Journal* 185, (2013), pp. E385–E386: "Evergreening refers to possibilities through which the patent holder can artfully apply for new patents just before the end of its existing term, thus 'evergreening' its protection. Kumar and Nanda (2017) identify the following common strategies of evergreening: (a) combinations of two or more drugs; dosing range and dosing route; (c) biological targets for old molecule, (d) delivery profiles, mechanism of action; (e) derivatives and isomeric forms; (f) screening methods, dosing regimen; (g) packaging; and (h) different methods of treatment."

110 "Animal insulin disappeared in favour of human insulin created by recombinant DNA techniques, and human insulin is now being replaced by analogue insulin. Each change brought improvements in performance whose importance is contested, as well as prolonging patent protection and sustaining prices." Nigel Hawkes, 'The travesty of expensive insulin', *BMJ* 353 (2016). Available at doi:10.1136/bmj.i2933.

111 Enver Zerem, 'Dilemmas about instructions for administering drugs and indications for their use: is there negative effect of pharmaceutical industry?', *Clinical and Translational Medicine* 9, Issue 1 (2020), pp. 9–11, at p. 10: "It is well-known that new insulin formulations most often appear when the previous formulations of the same manufacturer are about to lose patent protection rights and when it is logical to expect a significant fall in the price of the drug. The most striking example, in this regard, is the inclusion of Glargine 300 IU as a new drug instead of Glargine 100 IU. Hence, it is logical to conclude, that the improvement of the treatment of patients was not in the foreground, but an attempt of the price protection of their drug (Glargine 100 IU) since its patent rights have expired and the emergence of new generic parallels would inevitably reduce its price. By establishing a very similar, virtually the same "new" drug (Glargine 300 IU) as a substitute for the "old" one (Glargine 100 IU), the patent rights are continued which prevents the impact of the new generic parallels on lowering the drug price. It goes a step further here, since, in most countries, the new drug is registered as a few percent cheaper than the old one, but the drug packaging is reduced by about 11% (1500 IU versus 1350 IU), practically meaning that the price has increased."

have expressed concerns about the dominance of analogue insulin,¹¹² even in countries where a number of local companies produce human insulin, and the persistent dominance of analogues could be associated with the abuse of dominant position conferred by many factors, including patents. A recent study of insulin availability in public- and private-sector outlets in Bengaluru, India concluded that despite the existence of cheaper human insulin, there was a preponderance of stocking of non-local, foreign analogue insulin in private pharmacies; the survey identified physician prescription practices, which can be influenced by marketing, as the reason for this.¹¹³ This is similar to accounts from the US market, which suggest that older insulins are continuously being replaced by newer analogues that remain covered by patents and other intellectual property protections,¹¹⁴ and people living with diabetes are prescribed the latest and most expensive insulin analogues.¹¹⁵

ii. Vertical allocation of territories

Information from interviews suggests that at least one of the three dominant insulin companies organizes its product distribution network on a regional basis, allocating exclusive supply rights to single distributors for different regions.¹¹⁶ Prices for insulin products are negotiated and established by the exclusive distributor, and potential alternative suppliers of the same product from the same manufacturer are not permitted to compete with those supplied by the exclusive distributor. The exclusive distributor may charge different prices for the same products for different countries in its region.

112 World Health Organization/HAI, 'Measuring medicine prices, availability, affordability and price components', WHO/PSM/ PAR/2008.3, Geneva, 2008.

113 "Responding to our observation that most surveyed pharmacies stocked insulin by Non-Indian companies, the wholesalers said that insulin uptake is largely driven by physician prescribing. Physicians continue to prefer insulin products marketed by Non-Indian companies over their Indian counterparts, even though the latter is often less expensive. Most patients adhere to the insulin brands prescribed by physicians, resulting in a persistent demand for insulin products marketed by Non-Indian companies." Gautam Satheesh, M.K. Unnikrishnan and Abhishek Sharma, 'Challenges constraining availability and affordability of insulin in Bengaluru region (Karnataka, India): evidence from a mixed-methods study', *Journal of Pharmaceutical Policy and Practice* 12, 31 (2019), pp. 2–19.

114 Jeremy A. Greene and Kevin R. Riggs, 'Why is there no generic insulin? historical origins of a modern problem', *The New England Journal of Medicine* 372, no. 12 (2015), pp. 1171–1175.

115 Jing Luo, Aaron S. Kesselheim, Jeremy Greene and Kasia J. Lipska, 'Strategies to improve the affordability of insulin in the USA', *The Lancet Diabetes & Endocrinology* 5, no. 3 (2017), pp. 158–159.
Available at [www.thelancet.com/journals/landia/article/PIIS2213-8587\(17\)30041-4/fulltext](http://www.thelancet.com/journals/landia/article/PIIS2213-8587(17)30041-4/fulltext).

116 Certain individuals interviewed by the authors asked not to be identified because of their continuing role in insulin procurement.

From a competition law standpoint, the appointment of an exclusive distributor for a specific territory generally is not illegal per se, but rather is subject to assessment under the rule of reason. In the ordinary case of product distribution, there may be pro-competitive justifications for vertical geographic allocation of territories, such as to encourage the exclusive distributor to undertake advertising and promotion, or to provide ancillary services such as warranty repair that may be costly to provide. Price competition from alternative distributors that do not provide the same ancillary services may make their provision unsustainable and ultimately undercut the reputation of the brand owner.

There are, however, potential anticompetitive effects of vertical geographic allocation. When a manufacturer and its products are dominant in a particular market such that there are no alternative distributors of competitive products, geographical exclusivity may reinforce that dominance to an unacceptable extent from a competition law standpoint. Here, the anticompetitive effects of the vertical geographic allocation may outweigh the pro-competitive benefits.

One way in which the potential anticompetitive impact of vertical allocation of exclusive territories can be addressed is by the authorization of parallel importation of the manufacturer's same products that are first legitimately sold outside the country of importation. If products are placed on any national market at a lower price than in the importing country, they may be purchased and exported to the country where the exclusive distributor has control and without its consent. The parallel imports break up the pricing monopoly of the exclusive distributor.

Originator pharmaceutical companies attempt to prevent parallel importation, including by limiting the supply of products to any given national market. This restricts the possibilities for purchase of surplus product and its export.¹¹⁷

117 Margaret K. Kyle, "Parallel Trade in Pharmaceuticals: Firm Responses and Competition Policy," Chapter 13 in *International Antitrust Law & Policy: Fordham Competition Law 2009*, edited by Barry Hawk (Juris Publishing, New York, 2009). Available at www.margaretkyle.net/IntlAntitrust.pdf.

iii. Patents and other market exclusivities

The pharmaceutical sector, including the insulin market, is influenced by patents and other intellectual property rights, as well as the grant of regulatory market exclusivity.¹¹⁸ These types of exclusive rights effectively create a ‘legislatively granted monopoly’,¹¹⁹ although, as just noted, whether there is in fact a monopoly will depend on the availability of substitutable products. If a company legitimately secures a patent, maintains a trade secret or maintains regulatory market exclusivity, it may be challenged from a competition law standpoint only if it abuses that form of protection.

■ Obtaining a patent or regulatory exclusivity through fraud or other misadventure

A patent grants its owner the right to prevent third parties from making, using or selling the same product without the consent of the patent owner.¹²⁰ The exclusive right of the patent owner to market the product is often referred to as the ‘patent monopoly’. A patent monopoly is only legitimate from a competition law standpoint if it is obtained without abusing the application process (i.e. the process of securing the patent). If a company engages in a practice such as submitting false information to the patent authority, or knowingly withholding information that would adversely affect the application process, the resulting patent is not legitimate from a competition law standpoint. Invoking that patent may constitute a form of anticompetitive abuse.

One question that may be addressed in the context of inquiry into the insulin market is whether exclusive rights have been granted improperly using the patent application process. In addition to patents, the originator biologic drug may secure regulatory market exclusivity for 8 to 12 years in some jurisdictions by being the first to obtain approval from the drug regulatory authority for commercial marketing. As with the patent application process, it is possible that a biologic originator secured regulatory approval by knowingly providing false information. If so, invoking a regulatory marketing exclusivity obtained by defrauding the relevant regulatory authority may constitute an abuse of dominant position.

118 Regarding the insulin patent landscape, see Warren A. Kaplan and Reed F. Beall, ‘The global intellectual property ecosystem for insulin and its public health implications: an observational study’, *Journal of Pharmaceutical Policy and Practice* 10, no. 1 (2017), pp. 1–9. Available at doi: 10.1186/s40545-016-0072-8; Jing Luo and Aaron S. Kesselheim, ‘Evolution of insulin patents and market exclusivities in the USA’, *The Lancet Diabetes & Endocrinology* 3, no. 11 (2015), pp. 835– 837. Available at [http://dx.doi.org/10.1016/S2213-8587\(15\)00364-2](http://dx.doi.org/10.1016/S2213-8587(15)00364-2).

119 Patents are typically granted pursuant to national legislation that prescribes the basic features of domestic patent law. It is common for the day-to-day administration of the patent system to be conducted by an administrative body, often under the direction of the executive. This may include the adoption of detailed rules regarding how patent examiners should assess individual applications, which may in turn influence the types of technologies on which patents are granted. The ‘patent bureaucracy’ within a country may, therefore, play an important role in determining the scope of control that an originator industry has in the local market.

120 From a patent law standpoint, a third-party product may be the ‘same’ as the patented product even though there are minor or insignificant variations (‘equivalents’).

The European Commission successfully prosecuted a pharmaceutical manufacturer for abusively obtaining supplementary protection certificates extending patent terms in certain European Union Member States.¹²¹ Evidence of misconduct may arise in a related context when the exclusive rights owner seeks to enforce rights.

■ Abusive patent or regulatory exclusivity enforcement

A more prevalent type of anticompetitive abuse is the attempted enforcement of patents or other intellectual property rights in circumstances in which the owner of the intellectual property is aware that the complained-against party is not, in fact, violating the intellectual property owner's rights, but instead is merely seeking to delay or preclude market entry of a competing product.¹²² This may constitute an abuse of dominant position.¹²³

In the United States and several other countries, the process for obtaining approval of a biosimilar drug is extremely complicated, not only from the standpoint of demonstrating biosimilarity or interchangeability to the Food & Drug Administration (FDA), but also from the standpoint of overcoming potential patent challenges.¹²⁴ During the process of registration for regulatory approval at the US FDA, the originator may present a list of patents to the applicant that it contends should block market approval for the generic product, and the generic applicant may elect to challenge the applicability and/or validity of those patents. The parties may ultimately engage in litigation regarding whether the biosimilar infringes on an existing patent. This is a process that may take several years. It is possible that a biologic originator may assert patents that it knows are not valid or are not infringed merely for the sake of delaying market entry of the biosimilar competitor.

121 *AstraZeneca v European Commission*, Case C-457/10 P, Court of Justice of the European Union, 6 December 2012.

122 Purchasers of injectable insulin products brought a civil antitrust complaint against Sanofi in the US Federal Court, alleging, *inter alia*, that the originator improperly listed a patent in the US FDA Orange Book, and then invoked that patent to block entry of competitive injectable products (In *re: Lantus Direct Purchaser Antitrust Litigation*, Case No. 18-2086, US 1st Cir., February 2020). In particular, Sanofi listed a patent for a component of an injection device that did not claim any specific relationship to the insulin product as to which it asserted infringement, giving it the benefit of a 30-month automatic stay against market entry of generics. Overturning the District Court, the Court of Appeals for the First Circuit said that absence of clarity regarding the precise scope of the patents that can or should be listed in the Orange Book was not a defence to blocking actions by Sanofi based on a patent that was not connected to the product for which it sought to defend against generic entry. The First Circuit remanded the case to the District Court for further proceedings, including allowing Sanofi to offer proof that it had a good faith belief that it was listing the patent to comply with FDA rules, and thereafter invoking it in infringement litigation. This case remains pending in early 2020.

123 *Federal Trade Commission v. AbbVie Inc., et al.*, Case No. 2:14-cv-05151-HB, FTC File No. 121-0028 (complaint filed seeking a permanent injunction and other equitable relief on 8 September 2014; global settlement entered with Teva on 19 February 2019). Recently affirmed regarding a sham litigation claim against AbbVie involving Perrigo in *FTC v. AbbVie*, US Ct. of Appeals for Third Circuit, Case No. 18-2748, decided 30 September 2020. Available at www2.ca3.uscourts.gov/opinarch/182621p.pdf.

124 See description of the 'patent dance' process in *Sandoz v. Amgen*, 582 U.S. 137 S. Ct. 1664 (2017).

In addition, there are administrative processes involving the FDA that allow the filing of ‘citizen petitions’, which allow an interested person to challenge the basis on which a drug may be approved for marketing.¹²⁵ In recent years, the originator pharmaceutical industry has routinely used petitions to try to delay regulatory approvals of generic drugs by the FDA, including in circumstances where the factual grounds for asserting a claim were suspect.¹²⁶ Such action might constitute abuse of the administrative process and an anticompetitive action by a dominant actor.

There has already been substantial litigation initiated in the United States by the three dominant insulin market actors, seeking to block entry of biosimilar or interchangeable competitors into the market.¹²⁷ The competition law question is whether such litigation has been undertaken in good faith, or whether there may be evidence of abuse of the approval pathway process.

Because each national system for the approval of biologic drugs such as insulin is different, it will be necessary for each national competition authority to examine the points in the system at which it can be abused by patent and regulatory market exclusivity holders.

Another set of issues regarding potential patent abuse involves delivery devices, such as injection pens and pump devices. There has been insufficient study of the possibilities for third parties to introduce generic versions of devices that perform the same function as those of the patent owners, and whether the dominant market actors may have improperly tried to block the entry of competitors.¹²⁸ Possibly, patents on some delivery devices should not have been granted and may be subject to validity challenge, even if improper conduct was not used to secure them.

125 A citizen petition is a vehicle that stakeholders outside of FDA can use to ask FDA “to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action” (21 CFR 10.25(a) and 10.30, at p. 3). Under the governing regulations, petitioners can request, for example, that the Agency:

- disapprove a drug product application;
- add warnings to the labelling of a drug; and/or
- change products from prescription to over-the-counter (OTC) status.

FDA regulations also provide for the submission of petitions for ‘stay of action’ to delay the effective date of an administrative action, such as the approval of certain drug applications (21 CFR 10.35). US Department of Health and Human Services, ‘Seventh Annual Report on Delays in Approvals of Applications Related to Citizen Petitions and Petitions for Stay of Agency Action for Fiscal Year 2014’, Washington, DC, 2014.

126 See, for example, *Federal Trade Commission v. Reckitt Benckiser Group plc*, Case No. 1:19-cv-00028, FTC File No. 1310036 (complaint filed 11 July 2019; stipulated order for permanent injunction and equitable monetary relief entered on 12 July 2019). Available at www.ftc.gov/news-events/press-releases/2019/07/reckitt-benckiser-group-plc-pay-50-million-consumers-settling-ftc.

127 See, for example, *Sanofi-Aventis Deutschland GmbH v. Mylan Pharmaceuticals Inc*, U.S. Court of Appeals for the Federal Circuit, Available at <https://fingfx.thomsonreuters.com/gfx/legaldocs/byprjmonxpe/IP%20SANOFI%20PATENTS%20brief.pdf>.

128 See *In re: Lantus*, *supra* note 122.

■ Abusive delay of entry of biosimilars through interference with development (e.g. withholding samples)

Initiating production of a biosimilar product entails a process of development that may require the availability of samples of the originator biologic product. This may be only for the purpose of undertaking comparative analysis, although it may also be for the purpose of creating the biosimilar product. In any case, biologic originator companies have been known to refuse to provide samples in the commercial quantities that are necessary for drug development by biosimilar companies.¹²⁹ This inhibits market entry of competing products. Depending on the circumstances, such withholding of samples may constitute abuse of dominant position.

■ Trade secret and biologics production processes

It has been suggested that patent protection may not constitute a principal barrier to the introduction of biosimilar insulin products because, among other reasons, many of the initially secured key patents are expiring or have expired. There are non-patented technologies that may remain significant in terms of the pace at which biosimilar or interchangeable insulin products may be placed on the market. These may include manufacturing processes that are held in secret by originator companies.

Ordinarily, a company is not under an obligation to furnish trade secret production process information to a potential competitor. However, there may be some circumstances in which a company with a dominant market position seeks or maintains that dominant position by abusing trade secret protection. For example, in *FTC v. Mallinckrodt*, the company had purchased a potentially competing product and trade secrets regarding the manner in which the product was produced to protect its dominant market position. As part of a settlement with the FTC, the company was obliged to license trade secret technology to a third party.¹³⁰

129 See Kelly Davio, 'FDA Names Companies that Restrict Access to Drug Samples for Generic Testing', *AJMC*, 17 May 2018 (referring, *inter alia*, to US FDA, 'Statement from FDA Commissioner Scott Gottlieb, M.D., on new agency efforts to shine light on situations where drug makers may be pursuing gaming tactics to delay generic competition', Washington, DC, 17 May 2018). See also Complaint for Injunctive and other Equitable Relief, *FTC and State of New York v. Vyera Pharmaceuticals, et al.*, 20 CV 00706, S.D.N.Y. filed 27 January 2020 (involving chemical drug).

130 See *supra* note 106, FTC Case Summary, *Mallinckrodt Ard Inc. (Questcor Pharmaceuticals)*.

g. Potential excessive pricing

Monopoly or dominant position, whether obtained through intellectual property or another mechanism, may enable a pharmaceutical supplier to charge a price that is excessive. Competition law in many jurisdictions recognizes abuse of dominant position by the charging of an excessive price as a form of anticompetitive conduct.

The claim that an insulin supplier is abusing dominant position to charge an excessive price does not require that the supplier colludes in some way with a third party. It is the decision to charge an excessive price as such that is the basis of the claim.

The major source of competition law jurisprudence with respect to excessive pricing comes from the Court of Justice of the European Union (CJEU), although it has not rendered a decision on these grounds involving the pharmaceutical sector.¹³¹ The CJEU has prescribed a two-step test tracing back to its seminal decision in *United Brands v. Commission*.¹³² As the first step, the analysis addresses whether the price charged by the manufacturer/supplier is excessive by establishing a baseline price set preferably by determining the cost of producing the product plus a reasonable profit, then comparing that baseline price with the price charged by the manufacturer/supplier. The question at the first stage is whether the margin is excessive. In the second step, the analysis addresses whether the price is either unfair in itself or unfair in comparison with comparable products. In this sense, in the view of the CJEU, a price may be excessive yet not unfair.

It would seem that insulin would be subject to reasonably objective analysis from a cost-plus standpoint. Regular human insulin was developed a century ago, and a cost assessment would not need to accommodate research and development (R&D) and other product introduction risk factors. Similarly, most of the analogue insulins have been on the market for a considerable period. Costs and risks of R&D have likely been recovered by the suppliers. Although establishing a baseline reasonable price may factor in an increment for funding future R&D, these products might be looked at now largely from the standpoint of the cost of production plus a reasonable profit in terms of a baseline price.

Gotham, Barber and Hill published a study in 2018 of estimated prices for biosimilars of human and insulin analogues including production costs, operating margins (20 percent), transport (20 percent), and estimated cost of bringing the biosimilar to market that may provide some foundations for an inquiry regarding excessive pricing, as shown in Table 2.

¹³¹ See, generally, Frederick M. Abbott, 'Excessive pharmaceutical prices and competition law: doctrinal development to protect public health', *UC Irvine L. Rev.* 6 (2016), p. 281. Available at SSRN: <https://ssrn.com/abstract=2719095>.

¹³² Case 27/76, 1978 E.C.R. I-207. See also *Aspen Italia et al. v. Italian Competition and Market Authority*, Council of State (Italy), Section Six, N. 01832 / 2020 REG.PROV.COLL., N. 08447/2017 REG.RIC., 13/03/2020.

TABLE 2. Estimated prices for insulins

Compound	Price of API per kilogram (US\$)	Typical dose per day (mg)	API cost per day (US\$)	Estimated cost price of production for 10mL (1,000 units) vial (US\$)	Estimated price for 10mL (1,000 units) vial (US\$)	Estimated price per year (US\$)
Regular human insulin	24,750	1.40	0.03	2.28–3.37	3.29–4.86	48–71
Insulin NPH	23,282	1.56	0.04	2.32–3.42	3.35–4.93	49–72
Glargine	68,757	1.46	0.10	3.69–5.13	5.32–7.38	78–108
Lispro	100,000	1.40	0.14	4.52–6.16	6.51–8.87	95–130
Aspart	100,000	1.40	0.14	4.51–6.16	6.50–8.86	95–129
Glulisine	100,000	1.40	0.14	4.47–6.11	6.44–8.80	94–128
Detemir	100,000	5.68	0.57	13.47–17.35	19.40–24.99	283–365
Degludec	100,000	1.46	0.15	4.66–6.34	6.71–9.13	98–133

Source: Data reproduced from Dzintars Gotham, Melissa J. Barber and Andrew Hill, 'Production costs and potential prices for biosimilars of human insulin and insulin analogues', *BMJ Global Health* 3, no. 5 (2018).

Notes: API: active pharmaceutical ingredients; NPH: Neutral Protamine Hagedorn. *Calculations are based on 40 units for use per person per day.

In the second stage, an analysis would first look at the difference between baseline prices and selling prices in the market, and whether there is any reasonable justification for the spread or difference. If the difference is unjustifiable, the prices charged by the suppliers may be considered intrinsically unfair. The alternative analysis of comparison to other products would raise some interesting questions. It may be that the price of analogue insulin should be compared with the price of regular human insulin, and it seems probable that on the basis of such a comparison, the high price of analogue insulin may be unfair. In addition, analogue insulin prices vary widely across national markets, and higher prices in some markets may be unfair when there are lower prices in others. It may be that the three dominant analogue insulin manufacturers charge similar prices and that a comparison between their prices would not show a significant difference. However, given that these are market-dominant companies, this comparison can probably be discounted.

It is possible that a claim of excessive pricing as such with respect to the insulin market would be joined with other types of anticompetitive behaviours, such as price-fixing, geographical allocation of markets and output restraints.

Expert research suggests that analogue insulin can be produced at prices far lower than the prices at which these products are marketed.¹³³ And, in a number of cases, analogue insulin products have lost their primary patent protection, although there may be secondary patents and/or process patents protecting elements associated with these products.¹³⁴ Ordinarily, drug products that have gone off-patent will face generic or biosimilar competition that brings down the prices. This does not appear to be happening to a significant extent in the analogue insulin supply market, recognizing that the scale of price decreases in biosimilars markets may not be as great as those in markets for small molecule chemicals. In addition, the three dominant insulin manufacturers are introducing delivery devices (e.g. pre-mixed injector packages) that are protected by patents.¹³⁵

The situation is further complicated in some countries, such as the United States, by a distribution system in which pharmaceutical benefit managers (PBMs) purchase insulin from manufacturers at a published list price and receive a rebate from the manufacturer for a percentage of that price, which is in effect, a discount. The revenues received by the manufacturer may be less than the listed price. The pricing/rebate arrangements between the manufacturers and the PBMs are not publicly disclosed, and the net after-rebate prices received by the manufacturer may be difficult to determine.¹³⁶ A recent study on the topic of profit flows and payments across the insulin supply chain for the United States concludes that the three companies have seen higher net revenues between 2010 and 2018, amounting to an average increase of 44 percent when compared to 2009.¹³⁷ This study, which draws

133 Gotham et al., *infra* text at note 101, p. 1:

“Results – The manufacturing processes for RHI and insulin analogues are similar. API prices were US\$24,750/kg for RHI, US\$68,757/kg for insulin glargine and an estimated US\$100,000/kg for other analogues. Estimated biosimilar prices were US\$48–71 per patient per year for RHI, US\$49–72 for neutral protamine Hagedorn (NPH) insulin and US\$78–133 for analogues (except detemir: US\$283–365). *Conclusion* – Treatment with biosimilar RHI and insulin NPH could cost ≤US\$72 per year and with insulin analogues ≤US\$133 per year. Estimated biosimilar prices were markedly lower than the current prices for insulin analogues. Widespread availability at estimated prices may allow substantial savings globally.”

134 See Beran et al., ‘Current Challenges’, *supra* note 23, pp. 11–12; and Luo and Kesselheim, *supra* note 118.

135 Beran et al., ‘Current Challenges’, *supra* note 23, p. 24: “Unlike for many other medicines, intellectual property is not an issue for insulin itself. As was shown in this report, human insulin is off patent and many analogue insulin formulations are either already off patent or will no longer be protected in the next few years. Of concern is the increase in patent protection on the delivery devices.”

136 The Senate Staff Insulin Report, *supra* note 88, highlights the role of PBMs in the pricing strategies of the three major insulin pharmaceutical companies. It also highlights the extent to which insulin pricing in the United States is affected by factors different from those in other countries, including the particular characteristics of the US healthcare system. See, for example, Natalie Shure, ‘The Insulin Racket’, *The American Prospect*, 24 June 2019. Available at <https://prospect.org/health/insulin-racket>.

137 These results are part of an ongoing study by Lazonick and Collington. See Rosie Collington, ‘Who Benefits When the Price of Insulin Soars?’, *Institute for New Economic Thinking*, 16 April 2020. Available from: www.ineteconomics.org/perspectives/blog/who-benefits-when-the-price-of-insulin-soars.

data available from financial reports of companies, is supported by recent figures published on net price increases of branded insulin prices in the US market.¹³⁸

There is a class-action lawsuit currently ongoing in the United States that is in part directed toward the activities of the PBMs in the insulin supply market, including potential collusion with the manufacturers.¹³⁹ Because the US insulin supply market is distinct from other countries and markets, it may be that the elements of this particular legal action will not be relevant for other markets. But it highlights that the ex-manufacturer prices are not the only area for study with respect to potential anticompetitive practices relating to insulin supply. Equally importantly, a detailed consideration of drug retail chains with attention to pricing practices at the wholesale or retail levels due to lack of retail or wholesale competition is required, along with a review of factors such as tariffs and taxes that may impact final prices.

Within national markets, as highlighted, there are structural health-sector features that might account for price variations. But at the same time, as explained above, available price data do not fully support the suggestion that insulin suppliers differentiate their prices based on national gross domestic product (GDP) levels or similar indicators, and that prices are tiered reflecting these levels.¹⁴⁰ Although other explanations are possible, insulin price differences across national markets raise the prospect of markets prone to price discrimination by monopolistic companies with the intent of catering to the high-paying segments across all markets. Such a pricing strategy generally implies large social welfare losses due to a combination of high prices and low access to all countries as a result of anticompetitive practices. It also raises the possibility that dominant market power may be used to influence markets.

Because insulin is generally considered a biologic drug, in some countries it may be treated differently from small-molecule chemical drugs from both drug regulatory and marketing

138 The data compiled by Hernandez et al. on seven insulin products in the US market show that list prices of insulin increased by 262 percent, whereas net prices went up by 51 percent between 2007 and 2018: Inmaculada Hernandez, Alvaro San-Juan-Rodriguez, Chester B. Good and Walid F. Gellad, 'Changes in list prices, net prices, and discounts for branded drugs in the US, 2007-2018', *JAMA* 323, no. 9 (2020), pp. 854–862.

139 In re Insulin Pricing Litigation, Civil Action No. 3:17-Cv-00699 (BRM) (LHG), Amended Class Action Complaint, United States District Court, District of New Jersey, filed 17 March, 2017. See also Katie Thomas, 'Drug Makers Accused of Fixing Prices on Insulin', *New York Times*, 30 January 2017.

140 All three companies argue that they have some form of differential pricing for LMICs, but existing reviews find these to be insufficient to cater to the needs of the poorest, and prices are often not related to GDP. For example, the Base of the Pyramid (BoP) project is a public-private partnership led by Novo Nordisk to facilitate access to diabetes care for the poorest (the base of the economic pyramid), i.e. LMICs. In Kenya, despite the prevalence of the programme, penetration was found to be low, and a large number of those who need access to the project had not been included: Geordan D. Shannon, Hassan Haghparast-Bidgoli, Winnie Chelagat, Joseph Kibachio and Jolene Skordis-Worrall, 'Innovating to increase access to diabetes care in Kenya: an evaluation of Novo Nordisk's base of the pyramid project', *Global Health Action* 12, no. 1 (2019). Available at doi: 10.1080/16549716.2019.1605704.

exclusivity regulatory standpoints.¹⁴¹ The multinational biotechnology industry has lobbied intensively for extended periods of regulatory market exclusivity for biologic drugs, leading to the creation of 8 to 12 years of regulatory market exclusivity in a number of jurisdictions.¹⁴²

In the United States, there is a stringent and complex system for the approval of biosimilar¹⁴³ versions (i.e. biosimilar or interchangeable) of originator biologic drugs, which raises substantial barriers to entry for large and small biosimilar manufacturers.¹⁴⁴ About 10 years ago, the country introduced a regulatory pathway for insulin products to be treated as biosimilar or interchangeable products similar to the European Medicines Agency pathway, rather than using the regulatory pathway for small molecule chemical products.¹⁴⁵ Because of the complexity and expense involved, the regulatory pathway, which is designed to protect the health and safety of the population, is a substantial obstacle to market entry for biosimilar insulin even without abuse of the system. Adding anticompetitive abuse of the pathway can further increase the obstacles.

A competition law inquiry into the insulin supply market could attempt to determine whether the high prices and wide variations in prices found in national markets are the result of conduct among the suppliers and/or other actors in the supply chain directed towards suppressing competition or of ordinary business judgments and natural market forces. In addition to conduct directed towards suppressing competition, a competition law inquiry into the insulin supply market might also consider whether manufacturers and/or other actors in the supply chain are engaged in an abuse of a dominant position through excessive pricing as such. This would inherently require establishing a comparator based on what is a reasonable price for insulin in its various forms. Available evidence on the market structure suggests the presence of a number of factors that, from a purely economic perspective, promote collusion and the undue use of market power, including: the continued presence of some companies that have approximately equal market shares signalling a not-so-dynamic market structure; the presence of significant entry barriers due to patents, regulatory requirements, etc.; the frequent interaction among the few companies that maintain significant market shares in

141 See, for example, Michael A. Carrier and Carl J. Minniti III, 'Biologics: the new antitrust frontier', *U. Ill. L. Rev.* (2018), p. 1.

142 Wong, Jenny, "Data Protection for Biologics – Should the Data Exclusivity Period Be Increased to 12 Years?" [2016] UNSWLawJISuS 7; (2016) UNSWLJ Student Series No 16-07. Available at <http://classic.austlii.edu.au/au/journals/UNSWLawJISuS/2016/7.html>.

143 See Box 2 regarding terminology.

144 See, for example, a description of the biosimilars' regulatory pathway in Leah Christl, 'FDA's Overview of the Regulatory Guidance for the Development and Approval of Biosimilar Products in the US', PowerPoint (2015), and the US Supreme Court's description of the 'patent dance' in *Sandoz v. Amgen*, 582 U.S. (2017).

145 See FDA Center for Drug Evaluation and Research, Transcript of Meeting, 'The Future of Insulin Biosimilars: Increasing Access and Facilitating the Efficient Development of Biosimilar and Interchangeable Insulin Products', Washington, DC, 13 May 2019.

national bidding processes, among others; and the forecast of growing markets for the future, which promotes incentives for collusion and price-fixing.¹⁴⁶

a. Evidence-gathering and developing a theory of the case

The preceding parts of this paper have addressed the types of practices that might constitute some form of anticompetitive abuse. It was noted that pricing and access features of the insulin market raise some significant questions from a competition law standpoint. For example:

- Why is there such a wide variation in insulin prices within and between countries?
- Why do the prices of both human insulin and analogue insulin products appear to be substantially in excess of estimated manufacturing costs including normal profit margins, even taking into account the costs of R&D?
- Why are there a substantial number of markets where one of the major insulin manufacturers is the sole supplier of insulin products?
- What accounts for the dominance of three multinational suppliers even in the market for regular human insulin where the technology is not protected by patents or regulatory market exclusivity and where alternative suppliers are capable of supplying products?
- Why are insulin products often closely tied to the mode of delivery?

Other related questions also emerge, such as:

- Why do some governments not procure insulin at all in many markets despite rising public health needs?
- Why do some governments not purchase human insulin, which is much cheaper?
- What impediments, other than the obvious technological barriers, explain the relatively low presence of what should otherwise be a thriving biosimilars market, given the growing global demand for the products?
- What is the role of intermediaries, doctors and standard-setting organizations in these outcomes?

Some of these questions might be answered based on ordinary market factors, including factors specific to the pharmaceutical sector and/or to insulin as a product. The three dominant companies have so far provided some responses on their pricing and access-related practices, particularly given the amount of public interest that these practices have generated. However, a competition inquiry would require a more substantive and in-depth response.

¹⁴⁶ Marc Ivaldi, Bruno Jullien, Patrick Rey, Paul Seabright and Jean Tirole, 'The Economics of Tacit Collusion', Final Report for DG Competition (European Commission, 2003), p. 19. The authors note: "There is more scope for collusion when the same firms compete repeatedly. Relatedly, firms will find it easier to sustain collusion when they interact more frequently."

There are two general approaches – sector inquiry and targeted evidence-gathering – that can be pursued by competition authorities in attempting to develop an objective evidence based explanation for manufacturer/supplier behaviour and a potential theory for a case.

i. Sector inquiry

Pursuing a sector inquiry is intended to create a blueprint or map of an industrial sector at the national level, including information about the entity and management structure of the industry; the way the industry is financed, including private and public funding; the process by which new products are developed, approved, introduced into the market and distributed; the role of intermediaries; the regulatory environment in which the industry operates, including any forms of legal benefits (e.g. patent and market exclusivity protection) that are conferred on the industry; the characteristics of supply and demand for the industry products that may shape volume and pricing decisions, including the extent to which particular products may act as substitutes for each other; the impact of the industry on consumers and public interests; and dynamic changes that may be affecting the sector.

A sector inquiry may be used by the competition authority to address the preliminary question whether the behaviours in the sector are explainable as may be expected under ordinary market conditions. If the market appears to be functioning normally on preliminary inspection, the competition authority may decide that its further attention can be directed elsewhere. By contrast, the sector inquiry might generate data suggesting that the market is not behaving normally, and that there may be some form of collusion among the market participants and/or abuse of a dominant position by a market participant that merits more in-depth probing into the behaviour of specific industry actors. At that point, the competition authority might open a targeted investigation.

There is no single answer to the question whether participation by industry actors in a sector inquiry is voluntary or compulsory. Whether recipients of voluntary requests for information will provide adequate responses to allow a reasonably robust market evaluation may depend on how the recipients of the request view the alternatives. If a sector inquiry is presented as an alternative to the initiation of targeted investigations, this might induce reasonable cooperation. It appears preferable that a sector inquiry be undertaken with some form of formal government authorization that includes compelling (i.e. requiring, including with potential enforcement measures) recipients of requests to provide accurate and complete responses. So, for example, European Commission competition staff carried out the pharmaceutical sector inquiry leading to the publication of the 2009 ‘Pharmaceutical Sector Inquiry Final Report’ under the authority of a Council Regulation, making clear that the Commission had the authority to compel the production of evidence, and following a formal

decision by the Commission to initiate and undertake the inquiry.¹⁴⁷ The Chilean Competition Authority (FNE) has carried out a recent, detailed study of its pharmaceutical sector under legislative authority empowering it to request information from private undertakings for the execution of market studies and the possibility of imposing administrative sanctions for infringement of the duty of collaboration with FNE.¹⁴⁸

ii. Targeted evidence-gathering and developing the complaint

The competition authority may have information from any number of sources that gives it reason to suspect that some form of anticompetitive behaviour may be affecting a particular market. This can include information from media reports, complaints from consumers or competitors, whistle-blowers providing information from inside a company, public documents filed by companies, and so on. It may come from government departments that either procure products, carry out health technology assessments, or otherwise interact with the industry. A government or non-governmental organization might compile a research report and make it available to the competition authorities.

In reviewing information about behaviour deemed to be reasonably reliable, the competition authority might develop a suspicion regarding anticompetitive conduct. There are various approaches that can be followed. The choice of approach may depend on the type(s) of information that has been secured and whether the competition authority has reason to believe that such evidence is vulnerable to destruction if there is advance warning to a potential target of its investigative interests.

It is not uncommon for a competition investigation to begin with a voluntary request for information to a company regarding which the competition authority has some suspicion of anticompetitive conduct. Informal interviews and exchange of documents may be pursued. After a voluntary exchange, the concerns of the competition authority may be alleviated and the matter set aside. Alternatively, the target of the informal investigation might acknowledge that a certain practice or behaviour has at least the appearance of anticompetitive abuse

147 See Commission Decision of 15 January 2008 initiating an inquiry into the pharmaceutical sector pursuant to Article 17 of Council Regulation (EC) No 1/2003 (Case No COMP/D2/39.514). Regarding the investigatory basis, the 2009 Final Report states (note 16):

Art. 17 (1) 1st paragraph of Council Regulation 1/2003 reads:

“Where the trend of trade between Member States, the rigidity of prices or other circumstances suggest that competition may be restricted or distorted within the common market, the Commission may conduct its inquiry into a particular sector of the economy or into a particular type of agreements across various sectors. In the course of that inquiry, the Commission may request the undertakings or associations of undertakings concerned to supply the information necessary for giving effect to Articles 81 and 82 of the Treaty and may carry out any inspections necessary for that purpose.”

148 Information provided by FNE to UNDP and incorporated in ‘Supplement to the UNDP Guidebook for Low and Middle-Income Countries: Using competition law to promote access to health technologies’, (2022). See the Final Report of the Pharmaceutical Market Study, available at: www.fne.gob.cl/wp-content/uploads/2020/01/Informe-Final.pdf (Spanish).

and agree to modify its practices. This can be achieved with or without acknowledgement of potential culpability, depending on the circumstances. Finally, either because the targeted entity is uncooperative or because information developed during the informal investigation stage raises deeper concerns that may include criminal misconduct, the competition authority may proceed to initiate a more formal investigation using its power to compel the production of evidence.

The procedures and scope for competition authorities to compel the production of evidence depends on the national legislative framework, including constitutional mandates and protections, regulations and internal procedures. National competition authorities typically have some form of internal process pursuant to which staff members present a case to a senior authority with the power to authorize a formal investigation. Once authorized, the staff including prosecutors will prepare compulsory demands for production of information/evidence by the target of the investigation. Such demands typically inform the target of the reason or basis for the request (e.g. a theory of the violation), and specify the types of evidence that the competition authority wishes to secure. In addition to identifying the types of evidence in terms of substance, the compulsory request may specify the format of the potential evidence, such as documents and records including digital files, audio and video recordings, records including transcripts of telephone communications, emails, digital and/or social media postings and other formats in which information today is conveyed and stored, including in digital and physical archives.

Following transmission of the request to the target, the competition authority and target may organize a meeting at which the parties may seek to clarify the scope of the request, timing or other matters. The target may refuse to comply with the request, either by failing to respond or by objecting to its scope, or other matters. This may require the competition authority to seek judicial enforcement of the compulsory demand for information/evidence.¹⁴⁹

As noted earlier, there are situations in which the competition authority does not want to alert the target of its investigation about a demand for information/evidence because of concerns that evidence may be moved or destroyed by or on behalf of the target. The competition authority may seek the assistance of legal enforcement officers and conduct an unannounced visit to the premises of the target to secure information and evidence. These investigatory actions may include search and seizure of materials from the target premises and might even involve the detention and questioning of individuals. Unannounced site visits are a standard tool in the arsenal of competition authorities. A search of the premises of a target, whether unannounced or announced, may require specific authorization (e.g. a

¹⁴⁹ See, for example, US Federal Trade Commission, Enforcement, Cases and Proceedings, Petitions to Quash, at p. 6. Available at www.ftc.gov/enforcement/cases-proceedings/petitions-quash.

search warrant) that is issued by a judge, particularly if the investigation involves criminal or potentially criminal misconduct. The competition authority making the request will identify the reason for the search and seizure, the location and the types of records or property that it intends to examine and/or seize.

Once the competition authority reviews the gathered information and evidence, it may decide to interview or depose individuals identified as potential participants in and/or witnesses to anticompetitive conduct. These individuals are often accompanied by legal counsel and are under legal obligation to provide truthful responses. Conveying falsehoods, i.e. lying, to government authorities may be punishable by civil and/or criminal penalty. It is not uncommon for competition authorities to offer leniency or immunity to some witnesses as an incentive to furnish information.

The process of information and evidence gathering allows the competition authority to make a threshold determination whether anticompetitive conduct has taken or is taking place, and to decide whether it wants to formally prosecute the target(s). If it decides to proceed, the competition authority prepares a complaint laying out its theory of the case and outlining its evidentiary support. It describes the remedies sought. Prior to filing a complaint in the relevant court or administrative body, the competition authority may open discussions with the target(s) regarding a potential settlement that avoids litigation. If there is no settlement, or to encourage settlement, the competition authority may then file the complaint with the relevant judicial or administrative body.

The process or procedure by which competition authority investigations are conducted, as well as the process or procedure by which private-party civil investigations are conducted, varies sometimes substantially across national jurisdictions. For instance, the US Department of Justice published a detailed manual of its investigative procedures,¹⁵⁰ as does the European Commission Competition Directorate.¹⁵¹ The situation in the EU is complicated by the concurrent presence of a central competition authority, and individual Member State competition authorities, each of which has its own processes and procedures. The EU recently adopted a directive, the ECN+, intended to assure common practices among the EU competition authorities.¹⁵²

¹⁵⁰ See US Department of Justice, 'Chapter III. Investigation and Case Development', in *Antitrust Division Manual*, 5th edition, Washington, DC, 2015. Available at www.justice.gov/atr/division-manual.

¹⁵¹ See Commission notice on best practices for the conduct of proceedings concerning Articles 101 and 102 TFEU. Available at <https://op.europa.eu/en/publication-detail/-/publication/7b804daf-ce95-4fdd-8abd-88b6c21d0d9e/language-en>.

¹⁵² Directive (EU) 2019/1 of the European Parliament and of the Council of 11 December 2018 to empower the competition authorities of the Member States to be more effective enforcers and to ensure the proper functioning of the internal market. Available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019L0001&from=EN>.

b. Types of demands for information and evidence

In framing a request for information or evidence, the competition authority should present a substantive basis for its inquiry and make its more specific demands.

Consider a factual predicate that in certain national markets the price of analogue insulin may be substantially higher than in other national markets, and that the higher prices are comparable among the three major suppliers. The competition authority might assume that if the same companies are able to sell at substantially lower prices in other countries, then one or more of them should be attempting to gain market share in its country by lowering its prices. The companies may have agreed with each other not to compete on the basis of price, without disregarding the possibility that other factors may explain the high prices.¹⁵³ The competition authority might demand:

Any and all documents, information and records, in [the company's] possession or under its actual or constructive custody or control including, but not limited to, documents and information in the possession, custody, or control of [the company's] directors, officers, employees, and other agents and consultants, in whatever form or format, including physical and digital, on any and all medium, that contain, involve or refer to correspondence, conversations, meetings, agreements, tacit understandings and/or other forms of arrangement that relate to the price or pricing of insulin products, and/or the quantities of insulin products that are or will be produced and/or supplied to the market, and/or that allocate or suggest the allocation of market segments (whether geographic or by type/category of purchaser) between or among two or more manufacturers or other distributors of insulin products.¹⁵⁴

Another form of horizontal anticompetitive undertaking, which can also involve abuse of dominant position, is an agreement by an originator manufacturer with a potential biosimilar competitor to refrain from entering the market before or after the expiration of a patent covering the originator product or to settle patent or market exclusivity challenges to preserve originator market exclusivity. The competition authority might demand:

Any and all documents, information and records, in [the company's] possession or under its actual or constructive custody or control including, but not limited to, documents and information in the possession, custody, or control of [the company's] directors, officers, employees, and other agents and consultants, in whatever

¹⁵³ The substantive explanation of competition law refers to 'horizontal' restraints involving agreements between undertakings, such as price-fixing, output restraints and geographic allocation of territories, which are typically per se violations of competition law.

¹⁵⁴ A demand by a competition authority is likely to be more detailed than the illustrative example above, also because the competition authority will have more specific information regarding the matter it is pursuing.

form or format, including physical and digital, on any and all medium, that contain, involve or refer to correspondence, conversations, meetings, agreements, tacit understandings and/or other forms of arrangement relating to the time at which a third-party product that is therapeutically competitive with [originator insulin product] will be permitted to enter the market, including but not limited to those arrangements which involve a transfer of payment or other form of consideration between [originator producer] and the producer or distributor of a therapeutically competitive product.¹⁵⁵

A competition authority may decide to proceed against one or more dominant or monopoly manufacturers based on a suspicion of excessive or unfair pricing. The scope of inquiry that is conducted depends significantly on whether the alleged excessive pricing is directed towards generic (i.e. off-patent and post-regulatory market exclusivity) or new originator products. To date, almost all competition enforcement actions directed towards excessive pricing in the pharmaceutical sector have involved generic manufacturers that pursued large and unexplained price increases. In these circumstances, a competition authority might demand:

Any and all documents, information and records, in [the company's] possession or under [its] actual or constructive custody or control including, but not limited to, documents and information in the possession, custody, or control of [the company's] directors, officers, employees, and other agents and consultants, in whatever form or format, including physical and digital, on any and all medium, that contain, involve or refer to correspondence, conversations, meetings, agreements, tacit understandings and/or other forms of arrangement relating to the pricing of the [generic product] and the basis for any and all pricing decisions in [the relevant period]. The documents and records shall include all information regarding the cost of producing the [generic product], the cost of distribution, revenues from sales of the product (including information regarding financial arrangements with distributors and purchasers), and the cost of any product improvements introduced during [the relevant period].¹⁵⁶

If the investigation concerns a new originator product whose price would factor in expenses related to R&D and other elements specific to new drug development, compared to the development of the generic product, a competition authority might frame its demand to encompass other potential pricing variables:

Any and all documents, information and records, in [the company's] possession or under its actual or constructive custody or control including, but not limited to, documents and information in the possession, custody, or control of [the

¹⁵⁵ Ibid.

¹⁵⁶ Ibid.

company's] directors, officers, employees, and other agents and consultants, in whatever form or format, including physical and digital, on any and all medium, that contain, involve or refer to correspondence, conversations, meetings, agreements, tacit understandings and/or other forms of arrangement relating to the pricing of [new product], including costs and expenses associated with the research and development (R&D) of the new product, including but not limited to clinical trial and other costs associated with regulatory approval of the new product, acquisition costs of technology from third parties, facilities and employee costs. Documents and records shall encompass reports, conversations and data with any and all external consultants with respect to determinations on pricing. Documents and records shall identify contributions to R&D from external sources, including financial and/or scientific contributions from external sources, including national research funding sources, university collaborators, teaching hospitals and others. Documents and records shall identify any and all tax, subsidy or other incentives received in respect of R&D on [new product].¹⁵⁷

The four examples of civil investigatory demands provided above are drafted at a broad level of generality. When it prepares and issues an investigatory demand, a competition authority is likely to have in its possession previously developed information that will allow it to more specifically identify areas where information/evidence is sought, likely in addition to making a more general inquiry. The foregoing illustrations are also not intended to exhaust possible avenues of inquiry; no doubt others are or will be suggested by research on the insulin market by various interested stakeholders.

c. Enforcement litigation, settlement and remedies

The competition authority or a civil complainant ultimately must persuade a judge or jury that anticompetitive abuse has taken or is taking place, and that remedies are warranted. Potential remedies include civil monetary penalties, injunctions, compulsory licensing and sharing of technologies and know-how, oversight of pricing practices and/or criminal penalties including fines and imprisonment. From the standpoint of the insulin purchaser and user, the principal positive effect of a competition enforcement action will be to enhance access to insulin products.

¹⁵⁷ Ibid.

Competition law is an important tool available to increase innovation and access to health technologies, but its application can sometimes be difficult or inefficient, including for LMICs that do not have appropriate competition law frameworks and national competition authorities. Governments and interested stakeholders have various tools available to promote access to insulin, including regulatory and procurement interventions (e.g. ensuring genuinely competitive bidding), increased transparency to improve price negotiation outcomes, and exercise of government power to regulate drug prices. Direct price regulation is one of the more efficient ways to address problematic pricing. Global regulatory improvements, such as the recent extension of the WHO prequalification programme to include insulin, are also important: they play a significant role in assuring quality while increasing the number of suppliers in the market. Using competition law, including by pursuing exemplary inquiries and cases, may increase transparency and access to key information, and may dissuade manufacturers and distributors from engaging in abusive conduct, thereby enhancing the effectiveness of this and complementary approaches to enhance access.



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