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Definition of Relevant Product Market in Reference to R&D Poles in Pharmaceutical Sector Mergers

JAEM03 Master Thesis

European Business Law
30 higher education credits

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Term: Spring 2015

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Summary

All competition analysis, including in the field of mergers, begins by defining the relevant market. Relevant market consists of the relevant product market and the relevant geographic market. Companies have large market shares under narrow market definitions, which indicate a high chance of successful anticompetitive effect. A broad market definition excludes that chance. Therefore, it is very important for effective competition in the market that the relevant market is defined as closely to the actual situation as possible.

In sectors where innovation plays a major role, the definition of the relevant market also takes into account the R&D efforts of the merging firms. One of the sectors where R&D poles can be identified early on is the pharmaceutical sector.

In order to be considered as a part of a market, the drugs must have reached the stage of clinical trials regardless of where these trials are being conducted. The test for defining the relevant product market definition regarding pipeline drugs differs depending on whether they compete with existing drugs or future products.

It seems as the Commission examines pipeline drugs as close as possible to finished dose pharmaceutical, including following the recent trend of narrowing the definition. The Commission has begun to define future markets in relation to different modes of action and administration.

The scope relevant market definition, when no products have been launched on the market yet, has an influence in assessing the merger's effect on competition in innovation, which depends on the amount of R&D poles left on the market post-merger. A product market consisting of only pipeline drugs is defined depending on the characteristics of the product and indications they will apply to in the future. The Commission, again, will look at the intended therapeutic by reference to the mechanism of action of the drug. This approach for future products could potentially be too stringent as future products could already be substitutable at a more general level and pipeline drugs have a low chance of ever being launched onto the market.

Preface

I would like to express my utmost gratitude to my supervisor Björn Lundqvist, for the support and enthusiastic encouragement throughout the project. I am especially grateful for your expertise on two of my favourite research topics, namely merger control and the pharmaceutical sector. I sincerely appreciate your guidance and advice in regards to my research. Your help and suggestions have been instrumental to the successful completion of this thesis

Abbreviations

API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Chemical
EphMRA	European Pharmaceutical Marketing Research Association
GSK	GlaxoSmithKline plc.
HHI	Herfindahl-Hirschman Index
IMS	Intercontinental Medical Statistics
LGSC	Low-grade serous carcinoma
M&A	Mergers and Acquisitions
OTC	Over-the-counter
R&D	Research and Development
Rx	Prescription only
SIEC	Significantly impeding effective competition
SSNIP	Small but Significant Non-transitory Increase in Price

Abbreviations of legislation

TFEU	Treaty on the Functioning of the European Union
Merger Regulation	Council Regulation (EC) No 139/2004 of 20 January 2004 on the control of concentrations between undertakings
Horizontal Merger Guidelines	Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings
Guidelines on Horizontal Cooperation Agreements	Guidelines on the applicability of Article 101 of the Treaty on the Functioning of the European Union to horizontal co-operation agreements
Market Definition Notice	Commission Notice on the definition of relevant market for the purpose of Community competition law

1 Introduction

1.1 Innovation and market definition

Innovation is a key concept in the pharmaceutical sector. While the R&D efforts require significant investments and are time-consuming, they can result in new treatments and care, which provide previously unimaginable benefits to patients. According to the Pharmaceutical Market Inquiry, innovation is an essential component of a competitive market economy and therefore promoting it is a task of competition law.¹ Innovation does not only create new markets or replace previous ones, but also happens on existing markets through the improvement of products.²

A merger between parties in control of major innovation poles for future markets may impede competition in innovation and hinder the launch of new innovative products onto the market.³ While the objective of mergers in pharmaceutical sector could be to avoid or limit competition, the Commission has full trust in the scrutiny under the EU and national merger control rules to avoid any loss in innovation.⁴

The purpose of merger control is the identification and prevention of transactions which create or enhance market power and in doing so significantly impede effective competition in a substantial part of the common market (Significantly impeding effective competition or SIEC).⁵ Market power is generally the ability of the

¹ European Commission, 'Pharmaceutical Sector Inquiry. Final Report' (Commission Staff Working Document, 2009)

<http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf> accessed 5 April 2015,

paras 8, 86

² Josef Drexl 'Anticompetitive Stumbling Stones on the Way to a Cleaner World: Protecting Competition in Innovation without a Market' 8(3) [2012] *Journal of Competition Law & Economics* 513

³ *Ibid* 524

⁴ European Commission, para 1568

⁵ Commission Notice on the definition of relevant market for the purpose of Community competition law [1997] OJ C 372/5 (Relevant Market Notice), para 10; Robert O'Donoghue and Jorge Padilla, *The Law and Economics of Article 102 TFEU* (Hart Publishing 2013) 209, Ioannis Kok-

merged firm or the firms remaining in the market post-merger to reduce the ability of competitors to function properly on the market. The possible existence of market power is usually determined through market shares, the calculation of which presupposes the definition of a market and the identification of firms that participate in it.⁶

‘Market definition is a tool to identify and define the boundaries of competition between firms. It serves to establish the framework within which the competition policy is applied by the commission.’⁷ The concept of market definition originates from the USA and is an analytical tool which is used in merger cases to ascertain the degree of dominance within said market. A broad definition of the market leaves market participants with comparatively small market shares leading to low likelihood of effective anticompetitive behaviour.⁸ A too narrow market definition, on the other hand, discourages innovation.⁹ As regarding the geographic market on pipeline pharmaceuticals, the Commission has been consistent in arguing that as R&D is global, the geographic scope of the market is global or at least EEA-wide.¹⁰

Therefore, the calculation of market shares directly depends on market definition. The Horizontal Merger Guidelines, based on case law, consider that market shares of 50% or more may in essence be evidence of an existent dominant position, but the ability to influence the market despite the level of market shares needs to be taken into account. Even firms created by a merger with less than 40% can lead to the creation or strengthening of a dominant position. Likewise, when the market share does not exceed 25%, there is an assumption of no anticompetitive effect on the market. Market shares are also used to measure concentration levels on the market through applying the HHI. The Commission is unlikely to find horizontal competition concerns in a market where the HHI is less than 1000. There is also a

koris and Howard Shelanski, *EU Merger Control: A Legal and Economic Analysis* (Oxford University Press 2014) 6.01

⁶ Kokkoris and Shelanski 6.01 - 6.03

⁷ Relevant Market Notice, para. 2.

⁸ Kokkoris and Shelanski 6.03 - 6.04

⁹ Jacob Westin ‘Defining Relevant Market in the Pharmaceutical Sector in the Light of the Losec-case – Just How Different is the Pharmaceutical Market?’ [2011] 32(2) ECLR 58

¹⁰ *Ciba-Geigy/Sandoz* (Case IV/M.737) Commission Decision [1996] OJ L201/1, para 51

low likelihood of competition concerns when no possible constraints listed in the Horizontal Merger Guidelines is present and:

- 1) The post-merger HHI is between 1000 and 2000 and the change in the HHI is below 250,
- 2) The post-merger HHI is above 2000, but the change in the HHI is below 150 .

One of the abovementioned constraints includes a situation where one or more merging parties are important innovators in ways not reflected in market shares.¹¹

In the pharmaceutical industry, in the field of human health, the Commission groups markets according to thresholds of market shares as follows:

Table 1: Groups in pharmaceutical market

	Parties' joint market share	The increment
Group 1	>35%	>1%
Group 2	>35%	<1%
Group 3	15-35%	

The Commission generally focuses its market investigation on markets belonging to Group 1 as the other two groups do not usually pose competition concerns.¹²

Unlike the assessment of dominance under Art.102 TFEU, the EU merger control assesses the existence of dominance ex ante, which means that it looks whether a notifiable transaction would lead to a SIEC-situation. Consequently, in addition to looking at whether there is existing evidence of a dominant position, the competi-

¹¹ Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings [2004] OJ C 31/5 (Horizontal Merger Guidelines), paras 16-20

¹² *Teva/Cephalon* (Case COMP/M.6258) Commission Decision [2011] OJ C 46/1, para 15; *Teva/Ratiopharm* (Case COMP M.5865) Commission decision [2010] OJ C7/5, paras 12-14; *Abbott/Solvay Pharmaceuticals* (Case COMP/M.5661) Commission Decision [2010] OJ C89/1, paras 50-52

tion authority also needs to assess whether the situation will continue to exist or arise as a result of the merger.¹³

The evaluation of dominance-inducing effects is especially difficult in technology and research-based areas, such as the pharmaceutical industry, where the potential effects on future technologies and products require detailed assessment.¹⁴ The CJEU has found that the analysis in merger control requires great care as it does not entail the examination of past events, but rather attempts to predict whether future events are more or less likely to occur as a result of a merger.¹⁵ The evidence used to define a relevant product market includes information of substitution in the recent past, quantitative tests, reasoned answers of customers and competitors, customer preferences, barriers and switching costs, categorisation of customers and price discrimination.¹⁶

1.2 Research question

The thesis aims to answer the question of how to define relevant product market concerning R&D poles in pharmaceutical sector mergers.

1.3 Method and material

The most prominent legal research is the legal doctrinal research under which belongs this thesis as well. The legal doctrinal or legal dogmatic research method aims to investigate what the law is in a particular area. This method entails the collection and analysis of a body of case law and relevant legislation. The supporting material includes secondary sources, such as journal articles and commentaries on cases and legislation.

The research is limited to EU merger control procedures, which belong under the competence of the European Commission. In order to achieve the aims set for the

¹³ Sally Shorthose (ed), *Guide to EU Pharmaceutical Regulatory Law* (3rd edn, Kluwer Law International 2012) 8.68; Robert O'Donoghue and Jorge Padilla, *The Law and Economics of Article 102 TFEU* (Hart Publishing 2013) 209

¹⁴ Ibid

¹⁵ Case C-12/03P *Commission v Tetra Laval* [2005] ECR I-987, para 42

¹⁶ Relevant Market Notice, para 38-43

research, the main body of case law consists of European Commission decisions in the field of pharmaceutical mergers. To set the relevant legal background, the research also refers to EU secondary legislation, relevant Commission guidelines and other documents.

1.4 Research limitations

The pharmaceutical industry offers a large variety of different medicinal products from APIs to medical equipment, and products for the treatment of human or animal care. All these products lead by R&D belong to different markets,¹⁷ the discussion of which would become too broad a task. Hence, the research scope is limited to the European Commission merger control investigations into pharmaceuticals in the human health industry.

1.5 Structure

The thesis is structured to begin from a more general perspective on market definition, gradually moving to a more specific one. The study is divided into four parts. Firstly, the introduction describes the connection between innovation and mergers and explains the role of market definition in protecting competition in innovation. Next is an overview of the principles for defining relevant product markets for finished dose pharmaceuticals. This will give an understanding on what considerations are important in assessing pharmaceutical products as competition in innovation is also present on existing markets. The third chapter focuses entirely on how to define products on innovation markets. This chapter also includes an overview of Commission assessment in the Novartis/GlaxoSmithKline Oncology Business merger decision in which the Commission analysed the role of

¹⁷ *Sanofi-Aventis/Genzyme* (Case COMP/M.5999) Commission Decision [2011] OJ C226/2, para 11. See also *Johnson & Johnson/Johnson & Johnson MSD Europe* (Case COMP/M.3394) Commission Decision [2004] OJ C 111/9; *Novartis/Hexal* (Case COMP/M.3751) Commission Decision [2005]; *Sanofi Aventis/Zentiva* (Case COMP/M.5253) Commission Decision [2009] OJ C66/24; *Eli Lilly/Novartis Animal Health* (Case COMP/M.7277) Commission Decision [2014] OJ C8/2, para 8.

R&D efforts on both existing markets as well as keeping the future in mind. The final chapter provides a conclusive analysis on the topic.

2 Market definition

2.1 Principles of market definition

2.1.1 General principles

The EU Courts have confirmed that ‘(...) a proper definition of the relevant market is a necessary precondition for any assessment of the effect of a concentration on competition.’¹⁸ In fact, relevant market definition is the first necessary step in any competition law analysis as it determines the scope of the analysis and, as explained before, has a major influence over the result.¹⁹

The methodology of defining the relevant market and the concept of relevant market definition can be found in the Notice on the definition of the relevant market. The relevant product market is defined as comprising of all products and/or services, which can be seen as interchangeable or substitutable by the consumer depending on the characteristics, price and intended usage of the products.²⁰ The Notice distinguishes three key sources of competitive constraints – demand substitutability, supply substitutability and potential competition.²¹

Demand substitutability is measured by cross-price elasticity or the responsiveness of the quantity demand for a certain product to changes in the price of another product.²² The assessment of demand substitution entails the determination of the product, which the consumer considers as substitutes, and the readiness to switch between them. This can be estimated through the hypothetical monopolist or SSNIP test, which assesses whether a 5-10%, permanent price increase results

¹⁸ Case C–68/94 and C–30/95 *France and Société commerciale des potasses and de l'azote and Entreprise minière and chimique v Commission* [1998] ECR I-1375, para 143

¹⁹ Sally Shorthose (ed), *Guide to EU Pharmaceutical Regulatory Law* (3rd edn, Kluwer Law International 2012) 557

²⁰ Commission Notice on the definition of relevant market for the purpose of Community competition law [1997] OJ C 372/5 (Relevant Market Notice), para 7

²¹ *Ibid* 13

²² Ioannis Kokkoris and Howard Shelanski, *EU Merger Control: A Legal and Economic Analysis* (Oxford University Press 2014) 6.14

in an unprofitable situation due to the increase of sales of substitutes. In that case, the goods belong to the same market.²³ The SSNIP test is more efficient in merger cases compared with abuse of dominance cases, as the prevailing price is taken as a starting point, lessening the risk of a cellophane fallacy.²⁴

Supply-side substitutability can be taken into account when its effects are equivalent to those of demand substitution in terms of effectiveness and immediacy.²⁵

The third possible constraint, potential competition, is only carried out after defining the market and when the positions of companies on the relevant market have been ascertained and give rise to completion concerns.²⁶

Nevertheless, when no competition concerns arise even if the market was hypothetically defined in the strictest manner, the merger procedure is not based on market definition.²⁷

2.1.2 Pharmaceutical market specification

The general principles of definition of a relevant product market listed in the Notice are not sufficient for all sectors. The pharmaceutical market is divergent mainly due to three major differences:

First, the price of prescription drugs is often regulated as many national markets are in the form of a monopsony of the Government as the single buyer. In such cases, pharmaceutical companies cannot freely set prices, and especially cannot increase them over time despite the profitability of such actions.²⁸ These firms may, however, decrease prices in response to strong competition.²⁹

²³ Relevant Market Notice, paras 15-17

²⁴ Kokkoris and Shelanski, 6.17

²⁵ Relevant Market Notice, para 20

²⁶ Ibid, para 24

²⁷ Leigh Hancher and Wolf Sauter, *EU Competition and Internal Market Law in the Health Care Sector* (Oxford University Press 2012) 8.71

²⁸ Case C-468/06 *Sot. Lélos kai Sia* [2008] ECR I-7139, para 59

²⁹ Jacob Westin 'Defining Relevant Market in the Pharmaceutical Sector in the Light of the Losec-case – Just How Different is the Pharmaceutical Market?' [2011] 32(2) ECLR 57; Andrea Coscelli, Alan Overd 'Market Definition in the Pharmaceutical Sector' 28 (5) [2007] ECLR 294

Secondly, the most important decision maker in the choice of medicines that any given patient needs is their doctor.³⁰ The ultimate consumer also very often differs from the payer, which is to say the national insurance service or a private health insurance provider.³¹ Therefore, price usually plays a limited role in consumer decision-making.³²

Thirdly, originator pharmaceutical companies compete in innovation and investment in R&D to bring new, patented products on the market. Generics may enter the market only after patent expiry inducing price competition.³³

As competition in the pharmaceutical sector is based essentially on non-price grounds and there are restrictions on the freedom to price, many authors argue that the demand elasticity cannot be estimated. Thus, the investigation in pharmaceutical sector should be based on more sector specific criteria and less focused on the SSNIP test and other price-related grounds for analysis.³⁴

2.2 Approved drugs

2.2.1 ATC classification

The Commission usually subdivides pharmaceuticals according to the ATC classification devised by EphMRA and maintained by EphMRA and IMS.³⁵ The ATC classification has 16 categories,³⁶ each with four levels from the most generic to

³⁰ Howard Morse 'Product Market Definition in the Pharmaceutical Industry' 71 [2003] *Antitrust Law Journal* 661-662

³¹ Case C-501/06 P *GlaxoSmithKline Services and Others v Commission and Others* [2009] I-9291, para 45; Pieter-Augustijn Van Malleghem, Wouter Devroe 'Astrazeneca: Court of Justice Upholds First Decision Finding Abuse of Dominant Position in Pharmaceutical Sector' 4(3) [2013] *Journal of European Competition Law & Practice* 230,

³² Westin 57; Coscelli and Overd 294

³³ Josef Drexl 'Anticompetitive Stumbling Stones on the Way to a Cleaner World: Protecting Competition in Innovation without a Market' 8(3) [2012] *Journal of Competition Law & Economics* 511

³⁴ Coscelli and Overd 294-295; Westin 57-58, Sangin Park 'Market Power in Competition for the Market' [2009] 5(3) *Journal of Competition Law & Economics* 571, 578

³⁵ *Watson/Actavis* (Case COMP/M.6613) Commission Decision [2012] OJ C180/11, para 6; *Pfizer/Wyeth* (Case COMP/M.5476) Commission Decision [2009] OJ 262/1, p 15

³⁶ *Pfizer/Wyeth*, para 15

the most specific.³⁷ The third level of the ATC classification (ATC3) groups pharmaceuticals in terms of their therapeutic indication and is generally used as the starting point for the definition of relevant product markets³⁸ in competition cases, in particular for competition between innovator companies.³⁹

In some cases, pharmaceuticals need to be assessed at a higher, lower or mixed level or further subdivided.⁴⁰ Moreover, in recent cases involving generic companies a narrower market definition has been systematically used – the ATC4 level, the exact same molecule or API level or based on a group of molecules⁴¹. The need for a narrower definition in competition with generic medicines stems from the fact that these drugs can normally be viewed as the closest substitute to originator drugs.⁴² The definition based on molecule level is particularly important when:

- 1) Doctors may, or are required to, prescribe medicines using the international non-proprietary name of the molecule
- 2) the reimbursement is based on the price of a generic version of the originator medicine or
- 3) pharmacies may, or are required to, offer the patient the opportunity to substitute an originator medicine with a generic equivalent.⁴³

2.2.2 Different galenic forms

Since the *Sanofi-Aventis/Zentiva* decision in 2009, the Commission in its decisions⁴⁴ has differentiated medicines not only by their active ingredient(s), but also

³⁷ *Takeda/Nycomed* (Case COMP/M.6278) Commission Decision [2011] OJ C240/1, para 9; EphMRA /PBIRG Classification Committee, ‘Who we are What we do 2015’ (2015) <http://www.ephmra.org/user_uploads/ephmra%20who%20we%20are%202015%20final.pdf> accessed 5 April 2015, para 6

³⁸ *Pfizer/Wyeth*, para 15, *Reckitt Benckiser/Boots Healthcare International* (Case COMP/M.4007) Commission Decision [2006] OJ C92/12, para 9

³⁹ *Pfizer/Wyeth*, para.15.

⁴⁰ *Reckitt Benckiser/Boots Healthcare International*, para 9

⁴¹ *Teva/Ratiopharm* (Case COMP M.5865) Commission decision [2010] OJ C7/5, para 12; *Watson/Actavis* (Case COMP/M.6613) Commission Decision [2012] OJ C180/11, para 7

⁴² *Teva/Ratiopharm*, paras 12, 17

⁴³ *Sanofi Aventis/Zentiva* (Case COMP/M.5253) Commission Decision [2009] OJ C66/24, para 18

⁴⁴ *Valeant Pharmaceuticals International/Bausch & Lomb Holdings* (Case COMP/M.6969) Commission Decision [2013] OJ C247/1, paras 16-17; *Novartis/Alcon* (Case COMP/M.5778) Commission Decision [2010] OJ C20/8, para 16; *Galenica/Fresenius Medical Care/Vifor Fresenius Medi-*

by their galenic form as recognized by the European regulatory framework for medicines for human use, by their posology, pharmaceutical form and method and route of administration, which may limit their substitutability.⁴⁵

The route of administration and pharmaceutical form is sometimes, but not always, reflected in the ATC product categorisation.⁴⁶ For a single galenic form or a small group of closely related galenic forms, the Commission begins to define the relevant product market by first identifying the active ingredient and only then the galenic form. The Commission is of the view that the correct market definition is most likely to consider possible distinctions between different galenic forms.⁴⁷

The dosage and form of a pharmaceutical are not always interchangeable, especially in paediatrics. Some forms of medicine, especially OTC medicines, can be substituted when they pursue convenience rather than medical benefits.⁴⁸ Different galenic forms are not considered to exist on the same relevant product market merely due to supply-side substitutability. The effects of such substitutability are not equivalent to those of demand substitution regarding effectiveness and immediacy as the development of new galenic forms of an existing generic medicine generally takes two to three years or longer. The Commission has found that certain common galenic forms are generally not found to be substitutable on either the demand or the supply side. These include as oral syrups, tablets, rectal forms, injectable forms and parental forms. Different forms serve the needs of different types of patients, such as children, patients with the risk of vomiting etc, although this distinction must be confirmed on a case-by-case basis.⁴⁹

cal Care Renal Pharma Jv (Case COMP/M.6091) Commission Decision [2011] OJ C 33/3, para 19

⁴⁵ Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use [2001] OJ L 311, arts 9, 11.

⁴⁶ *Merck/Schering-Plough* (Case COMP/ M.5502) Commission Decision [2009] OJ C13/10, para 46

⁴⁷ *Teva/Ratiopharm*, paras 20-21

⁴⁸ *Sanofi Aventis/Zentiva*, para 129, *Teva/Ratiopharm*, para 17

⁴⁹ *Teva/Ratiopharm*, paras 18-19

2.2.3 Prescription v. OTC drugs

The Commission also separates between prescription only ("Rx") and over-the-counter ("OTC") drugs.⁵⁰ The division between those categories stems from the differences in medical indications, side effects, legal framework, distribution and marketing. Usually consumers choose and purchase OTC drugs themselves and therefore these drugs are advertised to the general public. As mentioned before, the choice of prescription drugs is made by a doctor and the price is often reimbursed to the patient, therefore the marketing of the pharmaceutical is targeted at the prescriber.⁵¹

Products available OTC that are reimbursable when bought on prescription exist on the same market. This could be the case depending on the defined conditions of the patient, for example drugs exclusively for patients such as children or pregnant/breastfeeding women, or when some of the same brand name drugs are sold OTC while others Rx depending on the packaging size, dosage or galenic form.⁵² In the latter case, the patients might prefer to buy the medicine on their own expense depending on the price of the OTC to avoid the inconvenience of obtaining a prescription for a reimbursable alternative.⁵³

2.2.4 Originator v. generic drugs

Even though the Commission has admitted that there could be differences in the demand for originator and generic pharmaceuticals, even when they are bioequivalent,⁵⁴ they are still found to exist on the same product market as the aim of generics is to compete with originators.⁵⁵ Generics are usually less expensive versions of originator drugs and the producers need to demonstrate that the generic version has identical quality and purity and that it is bioequivalent to the origina-

⁵⁰ *Watson/Actavis* (Case COMP/M.6613) Commission Decision [2012] OJ C180/11, p.10, *Teva/Ratiopharm*, para 22; *Novartis/Alcon*, paras 12-14; *Abbott/Solvay Pharmaceuticals* (Case COMP/M.5661) Commission Decision [2010] OJ C89/1, para 11

⁵¹ *Pfizer/Wyeth*, para 17, *Merck/Schering-Plough*, para 13

⁵² *Sanofi Aventis/Zentiva*, paras 22-23

⁵³ *Teva/Ratiopharm*, para 23

⁵⁴ *Sanofi Aventis/Zentiva*, para 26, *Teva/Ratiopharm*, para 26

⁵⁵ *Watson/Actavis*, para 12

tor drug to receive approval.⁵⁶ After patent expiry, originators tend to lose market share to generics unless the price is reduced. Substitution is especially efficient if the regulatory system encourages switching⁵⁷ and therefore a merger can cause a significant loss of competition where the producer of an originator acquires a significant or sole producer of its generic equivalent on the market.⁵⁸ For this reason, the distinction between originator drugs and generics is taken into account when assessing the closeness of competition in the markets investigated.⁵⁹

2.2.5 Biopharmaceutical products v. synthetic drugs

The Commission has made a distinction in product market definition between biological medicinal products and small molecule chemical drugs.⁶⁰ ‘Biological medicinal products are medicines whose active substance is made by or derived from living organisms (e.g. immunological products and medicines derived from human blood and plasma).’⁶¹ Biopharmaceutical products also include biosimilars. The market for biosimilars has not been around for long as the first biosimilars – growth hormones – were launched in Europe in 2006 following the adoption of regulatory guidance on the approval of biosimilar products at the EU level.⁶² Biosimilar drugs are new versions of originator biopharmaceutical drugs with an identical therapeutic mechanism and clinical attributes. Unlike the small molecule generics, also known as synthetic generics as they are produced by chemical synthesis, biosimilars are not exact copies of the originator pharmaceuticals. The

⁵⁶ *Teva/Ratiopharm*, para 25, *Sanofi Aventis/Zentiva*, para 25

⁵⁷ *Valeant Pharmaceuticals International/Bausch & Lomb Holdings* (Case COMP/M.6969) Commission Decision [2013] OJ C247/1, para 14; *Novartis/Alcon* (Case COMP/M.5778) Commission Decision [2010] OJ C20/8, para 15; *Teva/Barr* (Case COMP/M.5295) Commission Decision [2008] OJ C10/1, para 14; *Pfizer/Wyeth*, para 19

⁵⁸ *Sanofi Aventis/Zentiva*, paras 18-19

⁵⁹ *Valeant Pharmaceuticals International/Bausch & Lomb Holdings*, para 14; *Watson/Actavis*, para 12

⁶⁰ *AbbVie/Shire* (Case COMP/M.7339) Commission Decision [2014] OJ C397/1, paras 16, 27

⁶¹ *Sanofi-Aventis/Genzyme* (Case COMP/M.5999) Commission Decision [2011] OJ C226/2, para 15

⁶² *Lonsa/Teva/JV* (Case COMP/ M.5479) Commission Decision [2009] OJ C9/4, para 13; European Medicines Agency, ‘Guideline on Similar Biological Medicinal Products ‘ (Guideline CHMP/437/04, 2005)

<http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=W C500003517> accessed 4 March 2015

active ingredient of a biosimilar, due to its manufacturing process, is never exactly the same as the biological originator product and is subject to significantly more complex and costly R&D and regulatory approval processes.⁶³ The R&D process of a biosimilar is more similar to the R&D of originator drugs rather than synthetic generics as it requires clinical trials and takes considerably longer time from development to marketing with a higher risk of failure of R&D.⁶⁴

⁶³ *Lonsa/Teva/JV*, para 12; *Teva/Ratiopharm*, paras 28-29

⁶⁴ *Teva/Ratiopharm*, para 29

3 Relevant market for future products

3.1 Future products

Pharmaceutical firms are under heavy pressure to undertake significant R&D. New innovative products and having promising research and pipeline allow pharmaceutical firms to face competition with less vulnerability.⁶⁵ Large pharmaceutical companies depend on the profitability of a small number of products and the portfolio of patents on their new products.

R&D can be carried out in-house by the pharmaceutical firms themselves or by academic or commercial laboratories.⁶⁶ While ideas for new products are often bought in, the R&D projects are executed by very large pharmaceuticals, which have the resources to bring the innovative products to market.⁶⁷ The investments needed for R&D can only be financed if a company can obtain the necessary funds during the relevant period of patent protection of the product development, thus it is necessary to launch new products on the markets of large industrialised countries as quickly as possible.⁶⁸ Unlike other new-market economies that are led by innovation and significant investments in R&D, such as telecommunications or internet-based businesses, the pharmaceutical industry largely lacks network effects based on technical compatibility. Therefore, the industry cannot be characterised by "quick and frequent entry and exit."⁶⁹ One of the ways companies secure a stream of new products is to increase in size and combine drug portfolios

⁶⁵ Dror Ben-Asher 'In Need of Treatment? Merger Control, Pharmaceutical Innovation, and Consumer Welfare' [2000] 21 The Journal of Legal Medicine 277-278

⁶⁶ *Monsanto/Pharmacia & Upjohn* (Case COMP/M.1835) Commission Decision [2000] OJ C143/4, para 92

⁶⁷ Daniel J. Gifford, Robert T. Kudrle 'Antitrust Approaches to Dynamically Competitive Industries in the United States and the European Union' [2011] 7(3) Journal of Competition Law & Economics 700

⁶⁸ *Monsanto/Pharmacia & Upjohn*, para 92

⁶⁹ Gifford and Kudrle 699-700

through M&A.⁷⁰ According to the Horizontal Merger Guidelines such mergers also bring about pressure on competitive companies to innovate.⁷¹

Pipeline products are products, which are at an advanced stage of development, but are not yet on the market.⁷² After a pipeline drug has been successful at pre-clinical trials, an application is filed with relevant national authorities in Europe to begin clinical trials. R&D projects undergo three different phases of clinical testing on humans. The Commission refers to the statements by the parties in the *GibaGeigy/Sandoz*⁷³ decision when talking about success rates of clinical trials. Phase I starts eight to ten years before a product is marketed and generally have no more than a 10% rate of success. Phase II starts four to five years before the product is marketed and has a success-rate of ~30%. Phase III involves testing the medicines on patients in clinics and hospitals, usually in multiple different countries and aims to confirm the efficacy and safety of the test compound versus placebo and/or standard of care for a given disease. Phase III, which starts three years before the marketing of the product, has a failure-rate of over 50%.⁷⁴ Therefore, potential competition by pipeline products is already regarded as actual competition to an extent as pipeline products that are in phase III or beyond are already in use.⁷⁵

While pharmaceutical mergers incentivise competitors to make R&D efforts, a merger between innovators may impede effective competition. The Horizontal Merger Guidelines brings examples of major innovators with pipeline products related to a specific product market seeking to merge and a firm with relatively small market share but promising pipeline products.⁷⁶ Regarding pipeline products, the Commission looks at the R&D efforts in terms of both existing and future

⁷⁰ Ben-Asher 277-278

⁷¹ Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings [2004] OJ C 31/5 (Horizontal Merger Guidelines), para 38

⁷² *Glaxo Wellcome/SmithKline Beecham* (Case COMP/M.1846) [2000], para 70.

⁷³ *Ciba-Geigy/Sandoz* (Case IV/M.737) Commission Decision [1996] OJ L201/1, para 57-58

⁷⁴ *Pfizer/Wyeth* (Case COMP/M.5476) Commission Decision [2009] OJ 262/1, para 27; *Bristol Myers Squibb/Du Pont* (Case COMP/M.2517) Commission Decision [2001] OJ C367/30, para 23; *Glaxo Wellcome/SmithKline Beecham* (Case COMP/M.1846) Commission Decision [2000], para 70

⁷⁵ *Pfizer/Wyeth*, para 35

⁷⁶ Horizontal Merger Guidelines, para 54. For an example of pipeline products of one merging party likely to compete with the other party's pipeline or existing products, see *Glaxo Wellcome/SmithKline Beecham*, para 188

market situations. Unless the future products intend to replace existing products, the relevant market for these products cannot be defined in the same way as existing products.⁷⁷ In addition to assessing the effects of the merger on the existing and potential product market, the Commission does indeed take into account competition in innovation as well.⁷⁸

The Commission has considered that products in R&D could be relevant for the assessment of the competitive situation on both the existing product market and on possible future markets.⁷⁹ Therefore, the Commission assesses situations where there are a) actual overlaps between existing products, b) potential overlaps between existing products and R&D projects in Phase III (market-to-pipeline) and c) potential overlaps between the merging companies R&D projects in Phase II (pipeline-to-pipeline).⁸⁰

The potential overlaps involving pipeline drugs about to enter into competition with other products which are either on the market or at the development stage are assessed based on identifying the ATC3 category, by reference to their characteristics and intended therapeutic use, in which the relevant pipeline product would most likely fall upon release.⁸¹ In relation to the importance of R&D for future markets, the relevant product market definition can be less clear-cut than for existing products and left open and is based either on existing ATC classes or primarily by the characteristics and indications to which the future products are to be applied.⁸²

⁷⁷ *Bristol Myers Squibb/Du Pont*, para 24

⁷⁸ *Novartis/GlaxoSmithKline Oncology Business* (Case COMP/M.7275) Commission Decision [2015] OJ C95/14, para 89

⁷⁹ *Takeda/Nycomed* (Case COMP/M.6278) Commission Decision [2011] OJ C240/1, para 10; *Novartis/Alcon* (Case COMP/M.5778) Commission Decision [2010] OJ C20/8, paras 111-113; *Teva/Ratiopharm* (Case COMP M.5865) Commission decision [2010] OJ C7/5, para 37.

⁸⁰ *Takeda/Nycomed*, para 13; *Novartis/GlaxoSmithKline Oncology Business*, para 47

⁸¹ *Takeda/Nycomed*, para 13; *Pfizer/Wyeth*, paras 15-16; *Glaxo Wellcome/Smithkline Beecham*, paras 70-72; *Novartis/GlaxoSmithKline Oncology Business*, paras 25-27, 67

⁸² *Giba-Geigy/Sandoz*, paras 42-49, *Glaxo Wellcome/Smithkline Beecham*, para 72, *Novartis/GlaxoSmithKline Oncology Business*, para 68

3.2 Competition in innovation

Competing R&D poles are defined as ‘R&D efforts directed towards a certain new product or technology, and the substitutes for that R&D, that is to say, R&D aimed at developing substitutable products or technology for those developed by the co-operation and having similar timing’⁸³

The Guidelines on Horizontal Cooperation Agreements, which also applies in the field of mergers,⁸⁴ includes the concept of competition in innovation or R&D efforts. Competition concerns may arise when the merger takes place between innovators currently developing new products or technologies ‘which either may – if emerging – one day replace existing ones or which are being developed for a new intended use and will therefore not replace existing products but create a completely new demand.’ These Guidelines distinguish two scenarios depending in the nature of innovation in the industries.⁸⁵

The latter scenario includes innovative efforts in an industry where R&D poles cannot be identified and thus the Commission will try to avoid assessing the impact of the R&D on innovation and focus on existing markets related to the R&D.⁸⁶

In the former scenario, the process of innovation is structured so that competing R&D poles are identifiable at an early stage. The aim of the assessment is to analyse whether there will be a sufficient number of remaining R&D poles left on the market after the agreement. The Commission starts with analysing the R&D of the parties, followed by identifying credible competing R&D poles. The aspects considered for the assessment of the credibility of competing poles include the nature, scope and size of any other R&D efforts, their access to financial and human resources, know-how/patents, or other specialised assets as well as their timing and their capability to exploit possible results. R&D poles that cannot be seen as close

⁸³ Guidelines on the applicability of Article 101 of the Treaty on the Functioning of the European Union to horizontal co-operation agreements [2011] OJ C 11/1 (Guidelines on Horizontal Cooperation Agreements), para 120

⁸⁴ Ibid, para 6

⁸⁵ Ibid, para 119

⁸⁶ Ibid, para 122

substitutes, due to access to resources or timing for example, cannot be regarded as credible competitors. In addition to changes in innovation market, a new product market could also be affected. Even though this market does not yet exist as such, the analysis of it can often implicitly be incorporated in the competition in innovation analysis. This scenario is typical to the pharmaceutical industry⁸⁷

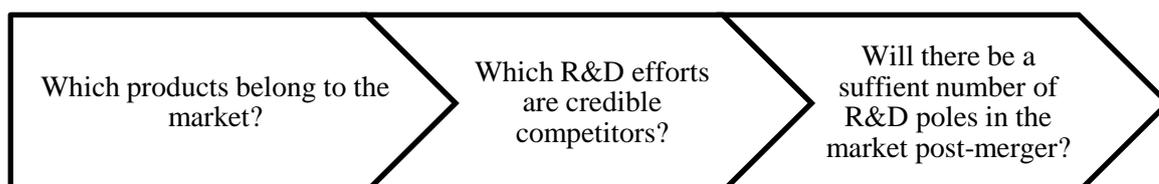


Figure 1: Assessment process of competition in innovation according to Guidelines on Horizontal Cooperation Agreements

The wording of the Horizontal Merger Guidelines⁸⁸ covers competition from potential rivals about to enter a market but also allows a preview of the future market situation as a result of current R&D potential and leaves the Commission wide discretion in assessing mergers in innovation markets.⁸⁹ The Commission has primarily focused on the “future market” approach i.e. focused exclusively on the protection of competition on future product market.⁹⁰

The Commission also looks on the effects of mergers on R&D and innovation as innovation is seen as a beneficial by-product of effective competition to consumers, similar to a low price or high quality of products.⁹¹ Considering efficiencies, the Commission takes into account consumer welfare as long as it does not form an obstacle to competition.⁹² The priority is short-term welfare, even though the

⁸⁷ Ibid, paras 120 -121

⁸⁸ However, in some circumstances, the Commission may take into account future changes to the market that can reasonably be predicted. Ibid, para 9

⁸⁹ Carsten Reimann ‘Essential Function vs Essential Facility: Defining the amount of R&D protection in high-tech industries after IMS and Microsoft’ [2004] 1(2) The Competition Law Review 59

⁹⁰ Benjamin R Kern ‘Innovation Markets, Future Markets, or Potential Competition: How Should Competition Authorities Account for Innovation Competition in Merger Reviews?’ [2014] 37(2) World Competition Law and Economic Review 189

⁹¹ Horizontal Merger Guidelines, para 8

⁹² Council Regulation (EC) No 139/2004 of 20 January 2004 on the control of concentrations between undertakings [2004] OJ L 24/1 (Merger Regulation), art 2(1)(b), Horizontal Merger Guidelines, para 76

Commission may accept a long-term consumer welfare standard in exceptional cases.⁹³

The reduction of competition in innovation, on the other hand, will reduce the number of new products within the same market, leading to negative consequences for both patients and healthcare providers. The future products would be, to a significant extent, demand substitutes and the results of lessening competition are higher prices for patients and healthcare systems. Moreover, a reduced number of differentiated products in future markets in terms of tolerability and safety profile leads to less variety of choices available to match the needs of patients.⁹⁴

3.3 Novartis/GlaxoSmithKline Oncology Business merger

In 2014 Novartis and GSK signed an agreement according to which Novartis would acquire sole control over GSK's portfolio of oncology pharmaceutical products composed of ten marketed products and two pipeline products for the treatment of advanced cancers.⁹⁵

The Commission used the definition for the R&D efforts set out in the Guidelines on Horizontal Cooperation Agreements⁹⁶ – clinical research programmes are competing when they are aimed at developing substitutable products and have similar timing. Whether these future products could potentially substitute each other was assessed by reference to

- 1) the products' characteristics together with the intended therapeutic use, in particular, by reference to their mechanism of action
- 2) the cancer types the products aimed to treat.

⁹³ Ariel Ezrachi and Maria Ioannidou, 'Buyer Power in European Union Merger Control' 10 European Competition Journal 69 75

⁹⁴ *Novartis/GlaxoSmithKline Oncology Business* (Case COMP/M.7275) Commission Decision [2015] OJ C95/14, para 110

⁹⁵ *Novartis/GlaxoSmithKline Oncology Business*, para 4

⁹⁶ "Competing R&D poles are R&D efforts directed towards a certain new product or technology, and the substitutes for that R&D, that is to say, R&D aimed at developing substitutable products or technology for those developed by the co-operation and having similar timing." Guidelines on Horizontal Cooperation Agreements, para 120

In assessing the timing, the Commission used the Phases of the clinical trials as reference points.⁹⁷

The overview of the Competition's line of investigation and considerations in defining the market is only given regarding the treatment for advanced melanoma and ovarian cancer and in the field regarding competition between pipeline drugs in future markets. While there were more markets involved, the Commission found no competition concerns in those markets and left the definition thus open.

3.3.1 Advanced melanoma

Novartis had a B-Raf inhibitor and a MEK inhibitor in Phase III clinical trials for the treatment of advanced melanoma, which were also in Phase III trials for combined treatment.⁹⁸ GSK had a B-Raf inhibitor and a MEK inhibitor approved as monotherapies for the treatment of advanced melanoma and was undergoing Phase III clinical trials for their use in combination.⁹⁹

This was the first time the Commission assessed the relevant product market definition for pharmaceuticals treating melanoma.¹⁰⁰ In accordance with the Commission's previous decisions on the product market definition for pipeline pharmaceuticals, it assessed whether the B-Raf and MEK inhibitors and immunotherapies belonged to the same product market.¹⁰¹ Both targeted therapies and immunotherapies were new forms of cancer therapies. Immunotherapies support the immune system to increase its natural ability to fight cancer. B-Raf and MEK inhibitors are both used as targeted therapies which inhibit proteins which carry the signal for cells to reproduce. They are primarily used at advanced stages of the tumour with the aim of slowing down cancer progression and elongate the life of the patient.¹⁰²

The Commission used the pipeline products as the starting point for defining the relevant product market in accordance with previous case law, looking at the

⁹⁷ *Novartis/GlaxoSmithKline Oncology Business*, para 90

⁹⁸ *Ibid*, paras 35-37

⁹⁹ *Ibid*, paras 38-40

¹⁰⁰ *Ibid*, para 23

¹⁰¹ *Ibid*, paras 27,28

¹⁰² *Ibid*, paras 10-11

characteristics of the future products and the indications to which they will be applied.¹⁰³ The market investigations showed that targeted and immunotherapies would be used in different settings depending on the mutation and aggression of the tumour. Likewise, the targeted therapies could not be substituted with chemotherapy.¹⁰⁴ Therefore, the relevant product market was the market for targeted therapies for the treatment of advanced melanoma but the further, more detailed definition, was left open as the Commission had doubts of the compatibility of the transaction already at this stage.¹⁰⁵ This market definition created three horizontal overlaps within the market:¹⁰⁶

Table 2: Horizontal overlaps in Novartis/GSK Oncology merger in advanced melanoma market

	B-Raf inhibitors	MEK inhibitors	B-Raf/MEK combination
Novartis	Phase III	Phase III	Phase III
GSK	Approved	Approved	Phase III

In the competitive assessment for the advanced melanoma market, the Commission took into account that, according to the market investigation, the B-Raf and MEK inhibitors, particularly in combination, would become the standard care in treatment. The only competitor for the parties in the market was Roche holding a B-Raf inhibitor already on the market and B-Raf and MEK combination that has successfully completed III clinical trials – likely to be approved in EEA in 2015.¹⁰⁷ Furthermore, the market investigation showed that the merger would reduce potential credible competition for the use of B-RAF and MEK inhibitors as monotherapies as well as in combination as Roche would not exert competitive pressure on the post-merger entity. The Commission concluded that it is likely that Novartis will not launch their inhibitors as the Roche products are at a more advanced stage of trials, benefiting the GSK’s B-Raf and MEK combination and

¹⁰³ Ibid, paras 24-28

¹⁰⁴ Ibid, paras 29-30

¹⁰⁵ Ibid, para 31

¹⁰⁶ Ibid, para 41

¹⁰⁷ Ibid, paras 49, 52

thereby reducing the number of inhibitors that would be available on the market without the transaction.¹⁰⁸

3.3.2 Ovarian cancer

Both Novartis and GSK had MEK-inhibitor in Phase III clinical studies for the treatment of low-grade serous carcinoma, a rare type of ovarian cancer, while GSK also had an AKT inhibitor in Phase I/II clinical studies in combination with chemotherapy for the treatment of recurrent platinum-resistant ovarian cancer.¹⁰⁹ The Commission used a similar assessment for the definition of the market as for the advanced melanoma treatment and considered the product market for pipeline pharmaceutical as guided by the characteristics of the product and indications to which they apply.¹¹⁰ The Commission found potential pipeline-to-pipeline overlaps in the treatment of ovarian low-grade serous carcinoma between the MEK-inhibitors of the parties.¹¹¹

The parties requested that the GSK MEK-inhibitor be left out of assessment as the Phase III clinical trials for the treatment of the ovarian low-grade serous carcinoma were conducted in an Investigator Sponsored Study (ISS) sponsored by the National Cancer Institute, which is part of a US government agency and accountable for all aspects of the study.¹¹² The Commission refused the request and used a hypothetical situation where the results of the ISS trials were positive and trial conditions answered to the European Medicines Agency requirements to file for registration, in which case, GSK could enter the market.¹¹³

Similarly to the market for advanced melanoma treatment, the parties had only one competitor with a pipeline product in Phase II clinical studies. Consequently, the Commission again considered that there was a likely elimination of Novartis' pipeline resulting in a loss of competitive pressure.¹¹⁴

¹⁰⁸ Ibid, paras 56-58

¹⁰⁹ Ibid, para 62

¹¹⁰ Ibid, paras 67-68

¹¹¹ Ibid, para 76

¹¹² Ibid, para 73

¹¹³ Ibid, para 77

¹¹⁴ Ibid, paras 78, 82

3.3.3 Innovation in the MEK and B-Raf inhibitor.

Both parties had ongoing Phase I and II clinical trials for MEK and B-Raf inhibitors potential use either as monotherapies or in combination for a number of types of cancer. Novartis also had an ongoing Phase II clinical trial for the use of its MEK inhibitor in uveal melanoma.¹¹⁵ The Commission concluded that the approach set out in the Guidelines on horizontal Co-operation Agreements could be applied in order to define the market for this pipeline-to-pipeline situation.¹¹⁶

According to the market investigation, the parties' MEK and B-Raf inhibitors were based on the same mechanism of action, were expected to address similar presently unmet medical needs, were likely to identify the same cancer types and were at similar stages of clinical development. Thus, they were likely to be substitutes to each other. Correspondingly to the findings for market definition for the treatment of advanced melanoma, research programmes based on immunotherapies were found rather complementary than competing. Consequently, the market was defined as development of MEK and B-Raf inhibitors for the treatment of colorectal cancer, non-small-cell lung carcinoma and advanced melanoma brain metastases.¹¹⁷

Therefore, the Commission assessed whether there would be sufficient number of clinical research programmes left after the merger. As mentioned before, Roche had MEK and B-Raf inhibitors potentially competing with the parties' MEK and B-Raf inhibitors as combined therapies – where there is more interest for competition than for monotherapies.¹¹⁸ The merger would combine under the same ownership two among three competing clinical trials based on MEK and B-Raf inhibitors that aimed to serve the same unmet medical needs.¹¹⁹

¹¹⁵ Ibid, para 84

¹¹⁶ Ibid, para 89

¹¹⁷ Ibid, paras 91-94

¹¹⁸ Ibid, paras 101, 102

¹¹⁹ Ibid, paras 97, 102-104

Table 3: Competing R&D efforts based on the MEK and B-Raf inhibitors for the treatment of certain cancers

	B-Raf inhibitor	MEK inhibitor	B-Raf/MEK combination
Colorectal cancer			
Novartis	Phase I/II	Phase I/II	-
GSK	-	-	Phase II
Roche	Phase II	-	-
Non-small-cell lung carcinoma			
Novartis	Phase II	Phase II	Phase II
GSK	Phase II	-	Phase II
Melanoma brain metastases			
Novartis	-	-	Phase II
GSK	Phase II	-	Phase II
Uveal melanoma			
Novartis	-	Phase III	-

The Commission considered that the parties' incentive to invest in their R&D programmes, driven by future sales, would be curtailed. Post-merger investment in one of the clinical research programmes would cannibalise future sales of its other clinical research programme. The pharmaceutical products based on different active principal ingredients differentiate to some extent, for example in terms of tolerability and safety for certain groups of patients. The trials to identify these differences is a common practice in oncology clinical research as part of sales strategy and could still provide some incentive to develop two parallel research programmes if the differentiation would compensate and reward the incremental cost of running the clinical research programme. The sales of the competing, parallel developed, product would still decrease as a result. Therefore, there was a likelihood of reduced innovation post-merger due to the lack of competition and

incentive to invest in both MEK and B-Raf clinical research programmes in parallel.¹²⁰

Due to the degree of uncertainty in pharmaceutical R&D, it is likely that products at a more advanced stage of research would be preferred. As GSK's products are on the market for the treatment of advanced melanoma, it is likely that the pair will also be prioritised in development for other types of cancer, potentially leading to the abandonment of Novartis' products. The market investigation showed that the B-Raf and MEK inhibitors, especially combined, would have significant importance in cancer treatment in the future. The abandonment of Novartis' clinical trials also meant the end of clinical trials for the treatment of various, sometimes even rare cancers, such as uveal melanoma. Even if clinical research for these cancers were to be launched for GSK products, there would be a substantial delay due to the time necessary for designing and completing completely new clinical trials. Thus, the variety of MEK and B-Raf therapies and therefore competition would possibly be restricted.¹²¹

¹²⁰ Ibid, paras 104-105

¹²¹ Ibid, paras 106 -114

4 Conclusion

A correct market definition might reveal a situation where the pipeline drugs overlap with either products that are already on the market or other future products. Just like a merger between firms with competing existing products might cause competition concerns, it can have an impeding effect on competition between R&D research programmes. The purpose of mergers involving innovators could be either to acquire new research programmes or to reinforce market power. The concern for future innovation becomes even greater when the fact, that so far studies have not shown mergers to have any actual positive influence on innovation, nor to produce incentives for other companies to innovate, is taken into account.¹²² This means that despite the theory that mergers between innovators serve the incentivising role for competitors to initiate new R&D efforts, there is a higher likelihood of loss of innovation in the pharmaceutical sector. Therefore, from competition perspective, a relevant product market definition, which reflects the actual market situation, plays a key role in assessing the potential outcomes regarding both competition and innovation.

The main concept the Commission uses for relevant product market definition is demand substitutability. The R&D poles are examined for the purpose of defining the market in two occasions. In the first situation, the R&D efforts aim to significantly change existing products or to replace them. In this case, the market should be easier to define, mainly, because there is a product on the market, which the pipeline product substitutability can be compared to. The nature of this circumstance calls for a narrow product market definition. Based on the developments on the definition of a relevant product market for finished dose pharmaceuticals, it is likely that also the pipeline drugs will be more strictly assessed in order to be able to compare them. The evidence of this progress is most clear regarding pipeline generic drugs where the Commission already divides the relevant ATC3 classes to molecular level when possible and takes the mode of administration into ac-

¹²² Carmine Ornaghi, 'Mergers and Innovation in Big Pharma' 27 *International Journal of Industrial Organization* 70 78

count.¹²³ This could be seen as equivalent to differentiating between finished dose pharmaceuticals depending on their galenic form.

As can be illustrated by the *Novartis/GlaxoSmithKline Oncology Business* decision, the market definition begins with defining the disease that the drug is meant to treat. While the B-Raf and MEK inhibitors were both used, either separately or in combination for cancer treatment, the Commission assessed different cancer types as the basis of different markets. From there on, the Commission examined which treatments for those cancers are substitutable regarding indications to which they will be applied. The Commission also took into account pipeline drugs which are not in clinical trials in Europe, but are elsewhere. While the Commission explained the decision to consider these trials in their assessment by the fact that in principle, if the trials conditions correspond to European Medicines Agency requirements, it is possible file for drug registration also in Europe, the inclusion is also in conformity with the presumption that R&D is global.

In the second case, the competition in the market will happen in the future. The Commission assesses these situations by with the aim of protecting competition on future markets and protecting future innovation. That is, the Commission considers whether the merger will result in loss of competition on the future relevant product market and whether enough R&D poles will remain. Identification of R&D poles and the assessment of the impact of a merger on innovation is the key to relevant market definition according to the Guidelines to Horizontal Cooperation Agreements.

Defining the relevant product market for products that do not exist yet is a lot more difficult, yet important task. Not only is the assessment based on predictions on the future importance of the product on the market, there might not exist a suitable ATC class which would provide a reference point for the definition. Thus, the relevant product market for competing future products cannot be as precise as it is in case of market-to-pipeline overlaps.

¹²³ *Actavis/Allergan* (Case COMP/M.7480) Commission Decision [2015] OJ C 123/6, paras 23, 34-36

The step-by-step logic of the Commission for the relevant product market definition for future products derived from the *Novartis/GlaxoSmithKline Oncology Business* decision consists of three steps:

- 1) Determining the mode of action
- 2) Identifying the scope of application
- 3) Determining the stage of clinical development.

The accuracy of relevant product market definitions determines the range of products and the position of companies operating on the market in the future. The variety of products offers a choice to consumers depending on their specific needs and preferences while the competition in the market exerts pressure on pricing. These benefits accompany effective competition regardless of whether the pipeline drugs will compete with existing or other future products. Even though defining the relevant market precedes competitive analysis, possible competition concerns should already be taken into account at this stage of the assessment.

The Commission begins defining the market on a rather general level, the therapeutic use, and in recent years, the relevant product market has been defined more and more stringently. The process of defining the market ends, as also demonstrated in the *Novartis/GlaxoSmithKline Oncology Business* decision, as soon as competition concerns arise. The practicality of a narrow market definition has already raised doubts among legal scholars and practitioners as it suggests that any pharmaceutical with novel biochemical action protected by patent is likely to be considered possessing market power, which discourages innovation.¹²⁴ These concerns were first raised after European Court of Justice confirmed the Commission's finding that H2 blockers and PPIs do not belong to the same market despite having the same therapeutic use, but different biochemical mode of action.¹²⁵

Pharmaceuticals with the same or similar therapeutic use aim to treat the same medical problems. Taking the market definition to a mode of action, or to an even further level, means that every future product with an innovative mode of action

¹²⁴ Matthew Cole 'Pharmaceuticals and Competition: First Strike to the Commission?' 34(5) [2013] ECLR 230; Jacob Westin 'Defining Relevant Market in the Pharmaceutical Sector in the Light of the Losec-case – Just How Different is the Pharmaceutical Market?' [2011] 32(2) ECLR 57

¹²⁵ Case C-457/10 P *AstraZeneca v Commission* [2012] ECR, para 50

or molecule is creating its own new market. This indicates market power even if there are already existing treatments for the same medical needs, which could even be preferable from the viewpoint of medical practitioners or patients. In the *Novartis/GlaxoSmithKline Oncology Business* decision, the Commission also regarded mode of action as basis for the assessment of which future products compete in innovation. The B-Raf and MEK inhibitors were found to exist on the same future market even though the trials, with the exception of uveal melanoma, were only in either Phase I or Phase II trials.¹²⁶ It is important to bear in mind that the prognosis for the success of R&D efforts even at Phase III trials is gloomy as less than half of these products will eventually be launched onto the market. In addition to the likelihood of the failure of clinical trials, the possible substitutability is only revealed during the end-phase of the trials or when the product is actually in use in the market.

The amount of R&D poles on the market play a significant role on the assessment of competition in such markets. It is important to protect R&D efforts from being eliminated as a competition strategy and therefore the assessment of competition in innovation cannot be excluded. Nevertheless, the realistic predictions on which products would be competing on the market in the future should be taken into account. With a success rate of approximately 30%, pipeline drugs in Phase II will probably never be launched and compete with each other on actual market. In the end, recognising the uncertainty surrounding R&D poles concerning their future use and chances of success, turning back to future product market definition based on therapeutic use and considering only those pipeline drugs that have reached Phase III trials might reflect the actual competitive situation better.

Excluding programmes in Phase I and Phase II trials may also raise competition concerns. Both Horizontal and Non-Horizontal Merger Guidelines acknowledge that the effects of innovation on the market may not be reflected in the market shares in relation to calculating HHI.¹²⁷ Nevertheless, the market shares of inno-

¹²⁶ Table 3

¹²⁷ Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings [2004] OJ C 31/5 (Horizontal Merger Guidelines), para 20(b), Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings [2008] OJ C 265/6, paras 25-26(a)

vating biotech companies or other commercial labs may not be sufficient to result in a post-merger HHI above 1000, which is likely to exclude the finding of competition concerns by the Commission. It is therefore understandable why the Commission decided to take research programmes in an early stage into account in market definition.

It is difficult to assess which relevant product market definition protects the market most efficiently. On one hand, the Commission has chosen to narrow down the variety of products on future markets according to their chemical composition or mode of action while on the other, broadened it by taking into consideration research programmes in an earlier stage of research. The purpose of such considerations is probably to find balance and avoid defining the relevant product market either too broad or narrow. It is easier to assess the impact of narrowing down the definition regarding characteristics of the chemical compound according to their use in treatment. It is probably almost impossible to predict whether broadening the amount of clinical trial phase would have a remarkable desired effect of broadening the variety of products on the future market due to the uncertainty of the success of R&D efforts.

The Commission has recently been in scrutinizing reverse payment settlements that block or delay the launch of generic drugs onto the market.¹²⁸ A similar result can be achieved through mergers which, moreover, can be preferable from an economic perspective to entry deterrence.¹²⁹ The discontinuation of a R&D programme is a likely outcome when the merging parties' existing or future products could be seen as substitutes to each other, thus, lessening competition in innovation and on future markets. In connection with reverse payment settlements, additionally to finding subsequent breaches of Article 101 TFEU, the Commission has also pursued scrutiny under article 102 TFEU.¹³⁰ Theoretically, the Commission could also apply article 102 TFEU in merger cases. Both merger control and anti-

¹²⁸ European Commission, 'Pharmaceutical Sector Inquiry. Final Report' (Commission Staff Working Document, 2009) <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf> accessed 5 April 2015 para 1608. See also *Perindopril (Servier)* (Case COMP/AT.39612) [2014]

¹²⁹ Laurent Granier and Sébastien Trinquard, 'Entry Deterrence and Mergers under Price Competition in Pharmaceutical Markets' 42 *Applied Economics* 297 302-304

¹³⁰ *Perindopril (Servier)* (Case COMP/AT.39612) [2014]

Article 102 TFEU cover the concept of dominance, the first ex ante and the latter ex post. It is already the task of merger control to avoid the creation or enhancement of dominant position, which would impede effective competition. The application of article 102 TFEU to subsequent mergers would mean that ex ante assessment of these mergers has failed. Such situation could be a result of a too broad market definition, which had not reflected actual competitive situation. While the application of article 102 TFEU is possible, it is more likely that the Commission prefers to narrow down market definitions to avoid the necessity of remedying the situation.

Overall, relevant market definition should not be viewed in isolation. Because the relevant market definition is of decisive importance to the result of the assessment and as to whether a merger will or will not be approved on certain conditions, it is not possible to start defining the market without thinking ahead. The possible effects of the merger on competition on future markets and in innovation should be taken into account from the very beginning.

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