Access to clinical trials data in the EU:
Balancing the implications for competition and public health

LLM Paper
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<tr>
<td>DG Competition</td>
<td>Directorate General for Competition</td>
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<td>DG SANCO</td>
<td>Directorate General for Health and Consumers</td>
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<td>CSR</td>
<td>clinical study report</td>
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<td>EFPIA</td>
<td>European Federation of Pharmaceutical Industries and Associations</td>
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<td>EMA</td>
<td>European Medicines Agency</td>
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<td>ECJ</td>
<td>European Court of Justice</td>
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<td>EU</td>
<td>European Union</td>
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<td>FTA</td>
<td>free trade agreement</td>
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<td>ICH</td>
<td>International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use</td>
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<td>TFEU</td>
<td>Treaty on the Functioning of the European Union</td>
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1. Introduction

Questions about the safety and effectiveness of medicines on the European market have reemerged following a series of serious adverse health events recently linked to the anti-diabetes medicine benfluorex (Mediator®) and the contraceptive, Diane 35®. It is postulated that adverse events and medicines of questionable efficacy can persist on the European market in part due to the widespread practices of “selective reporting” of positive test results rather than negative results, and the phenomenon of “publication bias”, in which the benefits of a medicine are reported or enhanced while its harms are downplayed. These practices are said to be in part responsible for hindering informed consumer decision-making about pharmaceutical therapy that can lead to the health and safety risks observed in these cases.

The production and sale of medicines in the EU is governed by Directive 2001/83/EC on medicinal products for human use (“Medicinal Products Directive”). The basis of its legal objective, to remove barriers to trade pharmaceutical products in the EU while maintaining a high standard of health protection, rests in Article 114 of the Treaty on the Functioning of the European Union (“TFEU”). The Medicinal Product Directive stipulates the requirements for a medicine to obtain a license to be marketed in the EU. License applications must include a variety of scientific and administrative information, including data gathered from clinical tests to establish a product’s safety and efficacy. A subsequent Regulation adopted in 2004 delegated much of the responsibility to evaluate a license application to the European Medicines Agency (“EMA” or “Agency”), and as a result, the Agency receives volumes of published and unpublished clinical trials data in market authorisation dossiers.

Public disclosure of clinical test data is one possible improvement to the poorly informed consumer decision-making described above. When public access is granted to this data, investigators such as the renowned researchers from the Cochrane Collaboration are able to

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2 P. C. Gøtzsche, ‘Why we need easy access to all data from all clinical trials and how to accomplish it’ (2011) 12 Trials 1 2 and 5
4 Ibid preamble 2-5
5 Consolidated version of the Treaty on the Functioning of the European Union [2010] OJ C 83/47 article 114(1) and (3)
6 Medicinal Products Directive 2001/83/EC chapter 3 and annex I
7 Ibid annex I
9 The Cochrane Collaboration is an international non-profit organisation that, through the participation of healthcare experts, produces systematic Cochrane Reviews, usually on healthcare interventions such as the use of a given medicine to treat a given condition. According to Cochrane’s website, systematic reviews ‘seek to collate all evidence that fits pre-specified eligibility criteria in order to address a specific research question’ and ‘aim to minimize bias by using explicit, systematic methods.’ Further reading about how a systematic review is conducted and how it contributes to evidence-based healthcare can be found at http://www.cochrane.org/about-us/evidence-based-health-care
produce an independent, systematic review of all available evidence of the effects of pharmaceuticals which can contribute to their safe use by consumers.  

Trials data is, however, valuable information that is not often readily disclosed. Clinical investigations are claimed to be the ‘most substantial investment from the drug developer in terms of time and cost’ in the drug development process, and these investments are not without risk. 11 Although there is ongoing debate about the true average cost spent on research and development of a single medicine, 12 global estimates range from 70.8 million Euro to 680.4 million Eur. 13 The EU’s pharmaceutical industry association, the European Federation of Pharmaceutical Industries and Associations (“EFPIA”), has stated that clinical trials investments in the EU amount to 20 billion Euro annually. 14 These investments are made amid the ever-present risk of a scientific setback that might delay or warrant the suspension of clinical investigations, and against the opportunity costs of prioritising one drug development line over another. 15 Trials data becomes all the more valuable as a crucial component of a product’s application for a market license in the EU, the granting of which is essential to recovering investments in drug development and generating future profit. Revenue can be maximised by companies who are the first to launch a new chemical entity (“first innovator”) on the market and those that enjoy market exclusivity free of competition from identical (“generics” or “second comers”) products. Investments into generating clinical trials data are of such great financial and strategic value that companies strive to maintain exclusive rights and/or other forms of confidentiality to exploit their data in the future development of their own product lines and to exclude competitors from deriving any similar direct or indirect advantages. 16

The Medicinal Products Directive applies the principles of document disclosure laid down in Regulation (EC) No 1049/2001 on public access to European Parliament, Council and

10 Other benefits in the public interest articulated by advocates of trials data disclosure include: the direct or indirect pressure to avoid the falsification of data or results in R. Verbeke and T. Tijdink, 'Scientific Fraud: The Hard Figures' Eos Magazine <http://eoswetenschap.eu/artikel/fraude-bij-een-op-de-twaalf-medische-wetenschappers> accessed 20 March 2013; the potential to minimise research costs by conducting a meta-analysis of existing data rather than conducting additional research in Gøtzsche p6; the potential to hasten emerging knowledge and thereby stimulate the development of innovative products and/or the launch of competing products (usually more affordable generic medicines) on the market in International Working Group, 'Transparency and accountability in drug regulation' 1996 2 <http://www.prescrire.org/docus/uppsalaEn.pdf> accessed 20 March 2013; the direct or indirect pressure to avoid the falsification of data or results in R. Verbeke and T. Tijdink, 'Scientific Fraud: The Hard Figures' Eos Magazine <http://eoswetenschap.eu/artikel/fraude-bij-een-op-de-twaalf-medische-wetenschappers> accessed 20 March 2013; the potential to minimise research costs by conducting a meta-analysis of existing data rather than conducting additional research in Gøtzsche p6; the potential to hasten emerging knowledge and thereby stimulate the development of innovative products and/or the launch of competing products (usually more affordable generic medicines) on the market in International Working Group, 'Transparency and accountability in drug regulation' 1996 2 <http://www.prescrire.org/docus/uppsalaEn.pdf> accessed 20 March 2013; the potential to minimise research costs by conducting a meta-analysis of existing data rather than conducting additional research in Gøtzsche p6; the potential to hasten emerging knowledge and thereby stimulate the development of innovative products and/or the launch of competing products (usually more affordable generic medicines) on the market


13 These figures, initially reported in USD as ranging between $92 million to $883.6 million, arise from a systematic review of academic literature seeking to calculate and report the average cost of drug innovation, excluding opportunity costs, from 1980 until 2009. In S. Morgan and others, 'The cost of drug development: A systematic review' (2011) 100 Health Policy 4


15 Morgan and others

16 In the context of the EU’s pharmaceutical sector, a competitor can be any company that would seek to employ the data for its own commercial use, such as the granting of a patent, a market license and/or data or market exclusivity for the same product as the first innovator. The concepts of competitors and non-competitors are described in A. X. Fellmeth, 'Secrecy, Monopoly, and Access to Pharmaceuticals in International Trade Law: Protection of Marketing Approval Data Under the TRIPs Agreement' (2004) 45 Harvard International Law Journal 443
Commission documents (“Transparency Regulation”), to the information held by the EMA. The Transparency Regulation foresees the widest possible access to EU documents with exceptions for certain protected commercial interests and an overriding public interest. A number of recent developments in relation to this EU law render this a timely discussion. In 2007, the European Ombudsman (“Ombudsman”) initiated his examination of the first-ever complaint against the EMA for refusing to disclose trials data requested by researchers from the Cochrane Collaboration. The Ombudsman’s recommendation three years later, that the trials data in question did not contain information that may damage a commercial interest and therefore may be disclosed, lead to a culture shift at the EMA. The Agency revised its access to documents policy and began releasing clinical studies reports and protocols to the public on request. However, the question of whether such documents risk a commercial interest rose again, this time before the European Court of Justice (“ECJ”). In 2013, at least one pharmaceutical company filed an action to annul the EMA’s decision to release clinical study reports (“CSRs”) and protocols relating to one of its medicinal products. Over the coming months, it is expected that the ECJ will examine closely the question of whether CSRs and protocols in question contain commercially confidential information. Meanwhile, these events have taken place against a backdrop of the European Commission’s (“Commission”) initiative to revise the legal framework governing the conduct of clinical trials taking place in the EU, announced in 2009. Following the necessary preparatory work, the Commission published a proposal for a regulation on clinical trials on medicinal products (“Clinical Trials Regulation”) in 2012, which the European Parliament (“Parliament”) is presently considering and will vote in plenary in October 2013. Transparency and provisions regulating access to trials data are widely-debated aspects of the present proposal and CSRs are at the center of the political discussion. Two groups of Members of the European Parliament (“MEPs”) have proposed amendments that would mandate the submission of 17 European Medicines Evaluation Agency, Rules for the implementation of Regulation (EC) No 1049/2001 on access to EMEA documents (EMEA/MB/203359/2006, 2006) 18 Medicinal Products Directive 2001/83/EC article 73 19 The Ombudsman investigates allegations of maladministration by EU institutions, bodies, offices, and agencies, excluding the ECJ, and provides non-binding recommendations in light of his examination. Maladministration is considered by the Office of the European Ombudsman to be ‘if an institution fails to respect fundamental rights, legal rules or principles, or the principles of good administration’ in Ombudsman, ‘Problems with the EU? Who can help you?’ 2013) <http://www.ombudsman.europa.eu/atyourservice/whocanhelpyou.faces#/page/4> accessed 8 May 2013 20 Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency 21 Ibid 22 European Medicines Agency, European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use) (POLICY/0043, 2010) 23 T-44/13 AbbVie v EMA [2013] OJ C79/31 24 ‘Medicinal Products for Human Use - Clinical trials’ (Commission, <http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm> accessed 19 May 2013 25 Ibid 26 Parliament, ‘Clinical trials on medicinal products for human use’ (Procedure File 2012/0192(COD) 2013) accessed 19 May 2013 27 Twenty-seven amendments governing data disclosure have been proposed to the report of the European Parliament’s rapporteur. In Parliament, Amendments 461 - 606 to the Commission’s proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (Amendments to the Draft Report 2012/0192(COD) March 2013, 2013) Also in Jim Murray, ‘Clinical trials directive: The Parliament’s political dilemma’ (EurActiv.com Opinion Article 19 April 2013, 2013) <http://www.euractiv.com/health/european-parliament-clinical-tri-analysis-518898> accessed 19 May 2013
CSRs to the so-called “EU Portal” to which the public would have access, in contrast to other amendments that seek to have only a summary of the data be publicly accessible.28

In contrast to the public and political debates, and in spite of these recent developments, few legal discussions have explored this tension. The vast majority of the legal scholarship concerning trials data access hinges around commercial interests in trials data and potential for greater competition to drive down prices in the pharmaceutical sector as a means to improve access to medicines in developing countries.29 Aside from the wave of prolific clinical specialists publishing calls for regulatory measures to ensure clinical data transparency in medical journals,30 few legal writers have joined this debate and only three authors have clearly juxtaposed the genuine interest of non-competitors in accessing trials data, not to speed market access but instead to complete the body of knowledge about medicinal products and enhance patient safety, with concerns about commercial confidentiality.31 Other articles draw the link between access to test data in the public interest of stimulating pharmaceutical innovation;32 however, no single research paper has conducted an in-depth analysis of the risk that data disclosure poses to commercial interests and the presence of an overriding public interest in the context of EU law.

1.1 Structure of this paper

This paper aims to critically examine the claim that commercial interests could be undermined by the disclosure of clinical trials data after a market license has been granted. An analysis of this claim will consider the unique EU legal context in order to identify potential risks to commercial interests and bring them into balance with the overriding public interest in informed consumer decision-making. Chapter 2 serves to narrow the focus of this paper on a specific set of trials data, the CSR. CSRs offer an interesting case study as a subject of disclosure on account of their contents and structure, in addition to the growing attention paid to them in EU legal documents and political debates. The pharmaceutical life cycle is an important factor that will be considered in formulating the scope of CSRs that will be dealt with in this paper. Chapter 3 explores the various forms of intellectual property and other protection that may be afforded to CSRs. A brief exploration of the TRIPS agreement will be

made to understand how the protection of trials data by regulatory authorities has been codified from global norms. An assessment is made of whether CSR data falls into the scope of the applicable EU legislative tools, to conclude with an understanding of the legal status of this type of trials data in the EU jurisdiction. Chapter 4 will briefly sketch transparency regulation in the EU, its application at the EMA and the impact of recent changes on CSR disclosure by the Agency. Chapter 5 examines the insight offered to the present debate by recent case law from the ECJ. Persistent uncertainties about the scope of an overriding public interest will be identified, followed by an analysis of future guidance that may be expected from the ECJ in relation to commercial and public interests. Chapter 6 describes a novel two-part balancing test that can be applied to find an equilibrium between a protected commercial interest in trials data secrecy and an overriding public interest in information disclosure. A further distinction between the nature of CSR data is made. Chapter 7 identifies precisely how free-riders could benefit directly or indirectly from disclosed data in the EU legal framework. Beginning with a clearly defined concept of competitive advantages, this chapter analyses several scenarios in which these advantages could be accrued by competitors from disclosed CSRs. Other factors that may influence likelihood of competitors accruing advantages from disclosed data are examined. Chapter 8 determines whether the qualities of safety data and/or efficacy data is caught by the scope of an overriding public interest. The result is further analysed to determine if the same public interest objective can be determined through an alternative data source or format, or the act of another agency. Chapter 9 will draw key conclusions from the two-part balancing test. Two foregoing chapters to identify a reasonable balance between data protection and disclosure. Knowledge gaps and future research directions will be identified.
2. Refining the concept of clinical trials data

A number of different proposals have been put forward as to which data would contribute best to the public understanding of the effects of pharmaceuticals if it were to be disclosed. The variety of these proposals illustrate the diversity of what is considered to be “trials data”. Scientists have demonstrated that ‘chemical, biological, and phenotypic properties of drugs’ found in early stage pre-clinical tests could be used to reliably predict adverse events in certain medicines. Although health researchers have, until recently, predominantly focused on obtaining “raw data” resulting from clinical trials. Raw data is generally understood as individual uncoded patient level information, the rich detail of which allows for the investigation of a variety of questions about the use of the product in humans, in addition to the primary outcomes studied in that specific trial. Recently, however, researchers from the Cochrane Collaboration have pressed on for public access to CSRs in medical literature following the Ombudsman’s recommendation to the EMA. Given this diversity, it is not surprising that the Commission and the EMA clearly define specific aspects of trials data rather than attempt to extend an all-encompassing definition to the concept under EU law.

2.1 Clinical study reports

The choice to examine CSRs in this paper is based on the nature of these documents, their standard format and the increasing attention paid to CSRs as an object of disclosure in EU law. First, considerable interest has been shown by the medical research community in access to CSRs due to their contents, which have been described by researchers from the Cochrane Collaboration as…

…a distillation and summary of the raw data from a given individual trial, but importantly, [clinical study reports] are unabridged reports that (depending on study size) can be thousands of pages in length. They should report a trial’s background and rationale, methods, results and discussion…

Besides including the data and results from a single study, note that this description includes the study protocol, which is a lengthy and insightful document that describes the study methodology and data analysis plan. Nordic Cochrane Center Director, prof. dr. Gøtzsche

34 Jefferson and others 148
35 Doshi and Jefferson And Doshi, Jefferson and Del Mar And Jefferson and others And T. Jefferson and others, ‘Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children’ Cochrane database of systematic reviews (Online) <http://www.ncbi.nlm.nih.gov/pubmed/22258996> accessed 13 April 2013
36 See, for example, the definitions in Annex I ‘Analytical, pharmacological and clinical standards and protocols in respect of the testing of medicinal products’ in Medicinal Products Directive 2001/83/EC
37 Jefferson and others 148
38 Clinical trial protocols, a sub-set of study reports, have been described by the EMA as documents that ‘describe the objectives, design, methodology, statistical considerations, and organisation of a clinical trial. Protocols usually also give the background and reasons for conducting the trial… [and they] …contain a study plan on which the clinical trial is based.’ In ,
explains that an independent analysis requires a thorough description of the study methods and data analysis which are described in the protocol, in order to understand how to interpret the data and to evaluate the scientific rigor of the study. Although access to CSRs will not alleviate what Gotzsche calls “the incentive to cheat” in study and results reporting, the CSR is a suitable data source for secondary analysis by clinical researchers, and for these same reasons, could also be of interest to potential competitors. Therefore, the nature of CSRs yields a natural playground to experiment with varying degrees of disclosure and to examine the potential effects on commercial and public interests.

Second, CSRs are presented in a common format and structure – a global standard – according to ‘guidelines developed by the industry regulatory collaborative effort ‘the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use’ (hereafter “ICH”). ICH has developed guidelines intended to yield ‘a report that is complete, free from ambiguity, well organised, and easy to review’ in order to be used globally by trials sponsors and regulators. Therefore, the results of this examination of CSRs could be applicable to other regulatory contexts.

Third, increasing attention is being paid to CSRs as an object of disclosure in EU law. In the past eleven years, an evolution has been observed. The early laws of 2001 scarcely mention a CSR. These documents are only mentioned in an annex of the Medicinal Products Directive, while the phrase is absent entirely from Directive 2001/20/EC on the implementation of good clinical practice in the conduct of clinical trials on medicinal products (“Clinical Trials Directive”). Over a decade later, several MEPs have proposed to include express references to CSRs as an object of disclosure in the text of the proposed Clinical Trials Regulation, which the Parliament will vote on in October 2013. Moreover, the Ombudsman and the ECJ have, at different points in time, been tasked with adjudicating the commercial interest in CSR disclosure, which will be explored further in chapter 3. This change could be interpreted as an evolution in the relative importance of CSRs in the eyes of EU legislators, and potentially in EU law itself.

However, achieving the systematic release of CSR submitted to the EMA will not ensure that all existing trials data is disclosed, and the documents themselves are not without flaws. CSRs are developed and maintained by trial sponsors who have an inherent interest in the success of the product being tested. For this and other reasons, researchers have identified that the data reported in CSRs ‘may not be reliable’. This reality could be aggravated by, what Business

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Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 47

Gotzsche 8

Ibid 6

Doshi and Jefferson 1-2


This concern was also implicitly raised by researchers who made provisions for the verification of the reliability of the CSRs, their data source, in their study design. In Jefferson and others 150 And in J. S. Ross and others, 'Pooled analysis of rofecoxib placebo-controlled clinical trial data: lessons for postmarket pharmaceutical safety surveillance' (2009) 169 Archives of internal medicine 1976 1977 1977
Law Professor D. Cahoy labels, the “transparency paradox” or the danger that greater statutory transparency may lead to less de facto data disclosure.\(^{46}\) Applied in this situation, this theory could mean that companies may limit what is disclosed in CSRs if it is known that the documents may or will be released publicly by the EMA at a later stage. The only safeguard against this risk is that CSRs adhere to the global standards established by the ICH. Required reporting of an agreed level of detail in each field in a CSR can mitigate the risk that the richness of data will diminish as a result of mandatory disclosure.\(^{47}\)

For these reasons, CSRs will be considered as a primary object of disclosure in this paper. In a complaint to the Ombudsman concerning access to CSRs, the EMA advanced the following concise definition of a CSR, which will be applied in this paper:\(^{48}\)

> Clinical and statistical descriptions and analyses are integrated in a single report and, among other things, comprise the following information: the protocol; sample case report forms; investigator-related information; information relating to the drugs to be tested, including active control comparators; technical statistical documentation; related publications; patient data listings; and certain technical statistical details.\(^{49}\)

### 2.2 Disclosure and the pharmaceutical life cycle

A discussion of trials data disclosure can not be had in a vacuum without considering at what point in the product’s ‘lifecycle’ data might be publicly released. The timing of disclosure impacts upon a sponsor’s commercial interest in maintaining the confidentiality of the information and to the public interest in knowing the effects of medicines. Market approval is a prominent distinction in the lifecycle of a medicine. At this point a medicine’s status changes from being the subject of years of research and development activities to a product that may be sold on the market and used by consumers.

Stakeholders involved in the ongoing political debate about data disclosure hold varied opinions about the potential and different effects of publication prior to and following market authorisation. Research-based pharmaceutical companies are represented in EU policy debates by their industry trade association, the European Federation of Pharmaceutical Industries and Associations (hereafter “EFPIA”). Much of EFPIA’s key communications on the topic suggest that this trade association and its partners are closed to discussing data disclosure prior to market approval for a number of reasons, including to prevent the ‘competitive disadvantage’ of companies.\(^{50}\) Less than a year ago, the EMA hosted a first-ever


\(^{47}\) Ibid

\(^{48}\) A definition of CSRs has been put forward as an amendment to the text of the proposed Clinical Trials Regulation. In Glenis Willmott, Draft Report on the proposal for a regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (2012/0192(COD)) January 2013, 2013) p18. However, this definition will not be considered in this paper as the Regulation has not been adopted.

\(^{49}\) Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 46

\(^{50}\) EFPIA and others, 'The Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases' (Joint Position, 2008) 3

stakeholder workshop 2012 to discuss how greater data disclosure could be realised in the EU. In EMA’s workshop report, a representative of EFPIA is said to have explained that

…the industry would like to see data access reviewed on a case-by-case basis and with decisions makers taking a range of factors into account, including the nature of the product, the data being presented, its place in its lifecycle and the method of release.\(^{51}\)

The workshop documents do not capture any explanation of how the EU legal framework could allow for commercial interests to be harmed through data disclosure.

Similarly, communications from the EU institutions about trials data disclosure consistently refer to publication after an application for market approval is made, and not prior. In an article recently published in the medical press, the Executive Director of the EMA and co-authors from other European regulatory authorities restricted their discussion of disclosure ‘to data on drugs for which the regulatory benefit-risk assessment has been completed.’\(^{52}\)

Moreover, the Commission’s representative, Mr. Stefano Soro, head of Medicinal Products unit at DG SANCO and responsible figure in the Commission for the Clinical Trials Regulation proposal, made a concerted effort to steer a debate on transparency in medical research away from disclosure before market approval. Beginning his speech at a Lunch Seminar in the Parliament hosted by several MEPs in 2012, Mr. Soro clearly ring-fenced the debate he wished to have around disclosure after market approval. His statement suggests that the Commission only views the need for disclosure as the result of market approval.\(^{53}\)

The subject of the proposal for the Clinical Trials Regulation… is not what data are necessary for a market authorisation and hence what data must be disclosed. It is about the authorization process for all clinical trials, commercial and non-commercial, linked to the development of a medicine.\(^{54}\)

The purpose of describing these divergent views of which data ought to be disclosed and when, is to illustrate the complexity of the issue at hand, and to emphasise the role that timing plays in balancing the public and commercial interests in data secrecy or release. In line with the recent political and somewhat understated legal debate, this article will focus on achieving a balance of interests in the disclosure of data in CSRs after a license has been granted to a prescription medicine by the EMA.

\(^{51}\) European Medicines Agency, Access to clinical-trial data and transparency (Workshop report, 2012) 2
\(^{52}\) H. G. Eichler and others, ‘Open clinical trial data for all? A view from regulators’ (2012) 9 PLoS medicine e1001202 1
\(^{53}\) Stichting Health Action International (HAI) Europe, Opening up EU clinical trial data: Mr. Stefano Soro (DG SANCO) (2012) 0:00 - 1:42
\(^{54}\) Ibid 1:17 onwards
3. Legal protection of commercial interests

This chapter will consider the range of intellectual property and other protection applied in EU law and whether CSRs fall into the scope of these measures. In this way, the toolbox of protection measures that may apply to CSRs under EU law will be elucidated and built on in subsequent chapters.

Elucidating the legal status of clinical trials data begins with the question of data ownership. “Study sponsors”\(^\text{55}\) are the financiers and the entities with legal responsibility for clinical trials in which a product is administered to groups of human test subjects as part of clinical research.\(^\text{56}\) In many cases, study sponsors are recognised as the owners of the results.\(^\text{57}\)

3.1 Patent exclusivity

A global framework of intellectual property protection was introduced following the World Trade Organisation’s Agreement on the Trade-Related Aspects of Intellectual Property Rights (hereafter “TRIPS”) in 1994.\(^\text{58}\) TRIPS Article 28 describes a patent as a form of legal protection of an invention that prevents third parties from ‘making, using, offering for sale, selling, or importing’ an innovative product or process without the owner’s consent.\(^\text{59}\) Intended to provide time-limited rewards for innovation, patents in the EU provide 20 years of protection from the time of filing, which in turn is intended to simulate innovation by developers seeking to secure a patent for subsequent novel products.\(^\text{60}\)

Patents are routinely relied on to protect new pharmaceutical inventions in the EU.\(^\text{61}\) Although a single ‘European’ patent does not exist, the European Patent Convention harmonises patentability criteria in Europe to a large extent.\(^\text{62}\)

Clinical trials data are excluded from the scope of patent protection. C. Correa, Professor of Law at the University of Buenos Aires and recognised expert in the field of intellectual property protection of biotechnology,\(^\text{63}\) has aptly described test data as the result of ‘routine

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\(^\text{55}\) The ‘study sponsor’ is classified under EU law as falling into one of two categories: an industry sponsor or a non-commercial sponsor such as an academic institution or foundation. Data from the European Commission show that industry sponsors execute 60% of the clinical studies in the EU. In Commission, Impact assessment report on the revision of the “Clinical Trials Directive” 2001/20/EC Annex I (Staff Working Document SWD(2012) 200 final, 2012) 14 p11 and p14.

\(^\text{56}\) Ibid p14

\(^\text{57}\) Determined through a study of clinical study protocols by P. C. Gotzsche and others, ‘Constraints on publication rights in industry-initiated clinical trials’ (2006) 295 Journal of the American Medical Association 1645


\(^\text{60}\) Commission, Pharmaceutical Sector Inquiry (Final Report 8 July 2009, 2009) paragraphs 251-252

\(^\text{61}\) Ibid paragraph 253

\(^\text{62}\) Ibid paragraph 258

scientific practices’ that are applied to an innovative product, and not an innovation of themselves. Similarly, Professor J. Reichman at Duke University Law School juxtaposes patent exclusivity and data exclusivity (discussed below) by stating ‘clinical trial results improve upon existing technological know-how, without adding an inventive step to the prior art.’ Therefore, patent exclusivity offers no direct protection to trials data.

3.2 Data and market exclusivity

Global standard setting in protection of market authorisation data, was achieved in by the TRIPS Agreement, which arguably brought clinical test data into the scope of intellectual property. Article 39.3 sets out the framework of protection that national regulatory authorities should afford to test data submitted to their agencies. This framework has been concisely summarised by Correa as pertaining to only those previously unpublished disclosures which are obliged by regulators as part of the license application to market a new chemical entity. Data meeting these requirements should be protected from unfair commercial use ‘except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.’

Much has been written about the concept of ‘unfair use’ in TRIPS, which refers to the idea that a competitor may benefit from the investments made and risks taken by a first innovator without being required to make its own investments in testing or to financially compensate the owner. Several scholars have argued that the TRIPS responsibilities placed on Member States to protect regulatory data against unfair commercial use are to be applied narrowly. Commenting on Member States’ discretion to interpret TRIPS obligations, Professor E. Kitch of the University of Virginia School of Law has stated that ‘agencies have inherent power to control their records and, in the absence of statutory provisions prohibiting disclosure…, an agency is free to choose to disclose.’ Moving one step further, Reichman argues that in spite of TRIPS obligations, agencies ‘remain free to make non-commercial uses of the data and to make other uses of them that are “fair”, even if such uses product a commercial impact.’

Turning now to the EU legal framework, the data exclusivity provisions introduced in EU law can arguably be traced to the protection norms enumerated in TRIPS. It is useful to first explain that under the Medicinal Products Directive, generic copies of off-patent first innovators may be licensed in the EU without the need for duplicative clinical testing. Instead, generic competitors may obtain a license by demonstrating their bioequivalence to the reference product.

Reliance on the safety and efficacy data of a reference product is not permissible in all cases.

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64 Correa 14
65 Reichman 43
66 Correa 13
67 Ibid 14-16
68 ‘Trade-Related Aspects of Intellectual Property Rights’ article 39(3)
69 Fellmeth 464
71 Reichman 19
72 Medicinal Products Directive 2001/83/EC article 10(2)(a)
73 Ibid article 10(2)(a)
The EU’s data exclusivity regime, introduced in 2004 through amendments to the Medicinal Products Directive, applies the so-called “8 + 2 + 1 formula” of protection to new chemical entities licensed in the EU. This system provides new chemical entities with an initial period of eight years during which time second comers may not rely on a reference product’s data to obtain market approval (called data exclusivity). Thereafter, a second comer may reference originator data in a license application to the EMA; however, an additional two-year period of market exclusivity impedes a second comer from marketing its product during that time. In addition, a subsequent year of market exclusivity (called the eleventh year) may be granted to a first innovator that licenses the same product for one or more new indications that offer ‘significant clinical benefit in comparison to existing therapies’ within the first eight years of data exclusivity. In this way, the exclusivity regime protects against the direct use of an originator’s data to obtain a market license for an identical product. Long-standing economics professor at Duke University and commentator on pharmaceutical economics, Professor H. Grabowski asserts that exclusivity regimes can stimulate research and development into new indications.  

3.3 Commercial confidentiality

According to the EMA, commercial confidentiality is a broad concept that includes two distinct categories:

- confidential intellectual property, “know-how” and trade secrets (including e.g. formulas, programs, process or information contained or embodied in a product, unpublished aspects of trade marks, patents etc.);

- commercial confidences (e.g. structures and development plans of a company).

3.3.1 Trade secrets

As patents have been addressed above, attention will be turned to trade secrets, which are loosely considered by the Commission to be:

...know-how that has not or not yet been registered as industrial property rights but that is actually or potentially valuable to its owner and not generally known or readily ascertainable by the public, and which the owner has made a reasonable effort to keep

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74 Ibid article 10
75 Ibid article 10(1)
76 Ibid article 10(1)
A list of the potential advances that satisfy the criterion of a significant clinical benefit can be found in Commission, Guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in order to benefit from an extended (11-year) market protection period, 2007) 4
79 European Medicines Agency, Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents, 2007) 3
Trade secrets currently lack harmonised protection at the EU level. Companies are left to rely on provisions in national law that requires the data owner to maintain the secrecy of trade secrets by preventing their release into the public domain. Perhaps the lack of legislation to protect trade secrets accounts for the imprecise scope employed by the Commission. The Ombudsman has previously considered ‘formulae, manufacturing or control processes’ of medicinal products to fall in the category of trade secrets. Considering the above definition together with these examples, it appears that the clinical safety and efficacy data contained in CSRs is outside the scope of a trade secret.

### 3.3.2 Commercial confidences

Turning to a vaguer category, commercial confidences are offered no formal protection under EU law. The EMA elucidated the scope of this category in relation to medicinal products as being ‘[i]nformation that could be of benefit for a competitor, the disclosure of which could cause a disproportionate prejudice to and seriously harm the commercial interest of the party.’

A pivotal Complaint 2560/2007/BEH (“Complaint to the Ombudsman”) submitted to the Ombudsman in 2007 by Danish Cochrane researchers, including Gøtzsche, (hereafter “the Applicants”) provoked an examination of the scope of commercial confidences in relation to trials data. The EMA argued that ‘in the event of disclosure, competitors would be able to gather valuable information on the long-term clinical development strategy of the sponsoring company’, although the Ombudsman’s investigation found that the CSRs and protocols in question did not contain such information. As a result, the Ombudsman concluded that the EMA failed to indicate precisely ‘why and how disclosure of documents could enable the development of the same or similar drug’ and thereby ‘specifically and actually undermine commercial interests.’ However, claims that the release of CSRs would damage commercial interests have recently been raised by at least one pharmaceutical company applying to annul the EMA’s decision to release these documents. It therefore appears that the question of the presence of confidential commercial interests in CSRs and the risk of jeopardising such interest has not been sufficiently investigated.

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80 Commission, Protection of trade secrets/confidential business information from misappropriation and misuse by third parties, 2012 2
81 Ibid interestingly, in 2012 DG Market published a roadmap outlining the EU policy options that may be explored to offer greater protection of trade secrets from use by third parties.
82 Fellmeth 462-263
83 Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 78
84 European Medicines Agency, Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents 2
85 Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 75
86 Ibid
87 Ibid 82
88 Ibid 81
89 Ibid 83
90 T-44/13 AbbVie v EMA
3.4 Conclusion

Under the Medicinal Product Directive, trials data including CSRs are directly protected from use by competitors to obtain a license in the EU, for a maximum of eleven years. Other forms of exclusivity, such as patents, do not directly catch trials data in their scope, while a common protection framework for trade secrets and commercial confidences is lacking at the EU level. There is an ongoing debate, now taken before the ECJ, concerning whether CSRs contain confidential commercial information. Against this understanding of the EU’s framework of test data protection, the following chapters aim to assess if and to what extent commercial interests could be harmed through the release of CSRs.
4. Access to trials data under EU law

This chapter aims to contextualise the application of EU transparency laws, under which the release of CSRs has been granted, at the EMA. A critical assessment will be made of several recent developments and their influence on the EMA’s own policy on access to documents.

4.1 The right of access to EU documents

European citizens’ right of access to documents of the EU institutions is enshrined in Article 15 of the TFEU, which serves as a legal basis for the Transparency Regulation. Aimed at securing citizens’ rights to the widest possible access to documents, the scope is any matter ‘falling within the institution’s sphere of responsibility’, irrespective of its medium. This definition lends itself to the nature of clinical data that may be held not only in the format of a CSR written on paper but also in an electronic database. Under this law, all Union documents are to be publicly accessible unless several exceptions enumerated in Article 4 apply. The applicable article in the context of this paper states:

2. The institutions shall refuse access to a document where disclosure would undermine the protection of:

— commercial interests of a natural or legal person, including intellectual property,
— court proceedings and legal advice,
— the purpose of inspections, investigations and audits,

unless there is an overriding public interest in disclosure.

In summary, the Transparency Regulation has established a hierarchy of norms in which non-disclosure is warranted in order to protect commercial interests unless there is an overriding public interest in the disclosure of the material. Although other exceptions to disclosure, such as the protection of personal data, must be brought in balance with the right to access documents, they will not be addressed in this paper.

4.2 Application of the Transparency Regulation by the EMA

In 2006, the EMA adopted Rules for applying the Transparency Regulation to the Agency’s documents (hereafter “Transparency Rules”). In an annex, the Transparency Rules further described the classification nomenclature applied to EMA documents as being public,

91 Natural or legal persons registered in a member state
93 Ibid article 3(a)
94 Ibid article 4(2)
restricted or confidential in nature. Of note is that “restricted” documents were defined as those whose ‘premature disclosure might be prejudicial to the interests of… applicants for and holders of marketing authorisations’.

These rules were tested in 2007 in the Complaint to the Ombudsman which appealed the EMA’s decision to deny the Applicants access to the CSRs and protocols submitted as part of the license applications for two anti-obesity medicines. Three years later, the Ombudsman’s decision that the CSRs and protocols in question do not risk commercial interests, has indisputably altered the EMA’s handling of access requests for these documents. In particular, the EMA adopted a revised access policy in 2010, titled the ‘EMA policy on access to documents related to medicinal products for human and veterinary use’ (“Transparency Policy”).

A brief analysis of the revised Transparency Policy illustrates the evolution of data disclosure at the EMA. The legal basis of the Transparency Policy remains the right of access to documents in the TFEU and the Transparency Regulation in particular. Unlike the preceding Transparency Rules, there is no longer any reference to TRIPS as a foundation for this internal policy. This approach brings the revised policy wholly in line with the Agency’s purpose, to evaluate the safety, efficacy and quality of medicines as well as to coordinate pharmacovigilance activities, and not to protect intellectual property, as a reference to TRIPS might suggest.

Although the general principle of ensuring the widest possible access unless a protected interest can be identified, the EMA now states that the presence of a commercial interest will provoke a balancing exercise between the right of protection of the commercial interest and the right of public access. This nuance stands in sharp contrast to the EMA’s preceding Transparency Rules which merely reproduced the text of the Transparency Regulation and showed few signs of weighing the risks of disclosure. Moreover, unlike the preceding Transparency Rules, the EMA has explicitly defined the notion of commercially confidential information as being ‘any information which is not in the public domain or publicly available and where disclosure may undermine the economic interest or competitive position of the owner of the information’ in its revised Transparency Policy. Additional evidence of the impact of the Ombudsman’s recommendations can be found in the Heads of Medicines Agencies and EMA’s joint guidance document produced to accompany the implementation of

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95 European Medicines Evaluation Agency
96 Ibid 6
97 Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 6
98 The EMA’s Transparency Policy does not supersede its Transparency Rules; instead it appears to be read alongside the Rules in order ‘to build-up a more robust system, capable of handling in a more efficient and consistent way increasing demands for access to a wide variety of EMA documents, hence facilitating the day-to-day operation of public access to EMA documents.’ In European Medicines Agency 1-2
99 Ibid 1
100 Ibid 1
101 The juxtaposition of the core tasks of the EMA to the unrelated task of granting patent protection was first made by the European Ombudsman in Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 77
102 European Medicines Agency 4
103 Ibid 4
its Transparency Policy. Here specific documents submitted to the EMA in the market application are coded according to level of allowable disclosure. Notably, all sub-sections in the module on CSRs are labeled as ‘can be released’ indicating disclosure by default unless limited exceptions apply.

This shift in policy has been publicised by the Senior Medical Officer at EMA in the medical press and in public debates in the Parliament. In a commentary on access to clinical trials data published in 2012, Dr. Hans-Goerg Eichler, together with the Agency’s Executive Director and representatives of three national regulatory bodies in Europe, went on record to express their agreement ‘that clinical trial data should not be considered commercial confidential information.’

4.3 Impact of the EMA’s revised Transparency Policy

The revised policy has been credited by Cochrane researchers as facilitating their access to unpublished data in CSRs in the process of evaluating the safety and efficacy of Tamiflu. Dr. Tom Jefferson explains the impact of the EMA’s revised Policy during his presentation at the 2012 HAI Europe Open Seminar:

We had identified that we couldn’t trust the statements made in publications, so we decided we were only going to use regulatory information for our [systematic] reviews. … Now, of course, all this was facilitated by the EMA’s change of policy and by the lightning-fast reaction of the EMA to our questions, and to our requests. The EMA sent us all they had, which was parts of 16 trials of Tamiflu.

Cochrane researchers were not the only applicants for access to EMA documents under the revised policy. Following the revision in 2010, requests to access documents dramatically increased in 2011, reaching an all-time high of 574,420 pages released on request by the Agency, which is over 75 times higher than the number of pages released the year before. The table below illustrates the absolute increase in number of pages released on request by the EMA in the years leading up to and following the adoption of its Transparency Policy. The Agency states the majority of requests received in 2011 pertained to clinical studies reports and that 90% of the applications were product-specific requests. It has been suggested that

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105 Ibid 39-40

106 Dr. Eichler explained the EMA’s new approach and its opposition to the industry’s view that clinical trials data is commercially confidential at the lunch debate ‘Opening up medical research data for an ethical and efficient EU policy’ hosted by Members of the European Parliament in Brussels on 6 June 2013. His comments were published by Peter O’Donnell for APM Health in Peter O’Donnell, ‘Calls echo round European Parliament for wider access to clinical trial data’ *APM Health* (Brussels 6 June 2013) <http://tacd-ip.org/archives/6682> accessed 9 May 2013

107 Eichler and others 1

108 Stichting Health Action International (HAI) Europe, *Dr. Tom Jefferson on lack of access to Tamiflu clinical trials* (2012)

109 Ibid from 21:51 to 22:28

greater requests have been received from companies seeking information on competing products, although little information can be found to verify if this is actually the case.\textsuperscript{111}

<table>
<thead>
<tr>
<th>Year</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
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<td>7,603</td>
<td>7,090</td>
<td>574,420</td>
<td>381,000</td>
</tr>
</tbody>
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Table 1. Absolute number of pages released on request in the second quarter of each year. Information sourced from EMA mid-year reports.\textsuperscript{112}

**4.4 Conclusion**

The EMA’s policy on granting access to documents is not only influenced by its legal basis in the TFEU and the Transparency Regulation, but also by recommendations from the Ombudsman to take CSRs outside of the scope of commercial interests. Recent revisions to the EMA’s Transparency Policy have seen an unprecedented number of pages released, most of which hail from CSRs. Public health researchers have taken advantage of this policy change to access unpublished clinical data to inform their analyses of the effects of oseltamivir. At the same time, it has been suggested that pharmaceutical companies are requesting CSRs to gain insight into the products of their competitors. These distinct interests in CSRs highlight the crux of the present debate. The following chapter will analyse recent guidance from the ECJ that may aid in striking a balance between protecting commercial interests from undue risks and serving the public interest in access to information.

\textsuperscript{111} MEP Peter Liese mentioned this phenomenon in his introduction at the lunch debate ‘Opening up medical research data for an ethical and efficient EU policy’ hosted by himself, MEP Christel Schaldemose and MEP Magrete Auken in the European Parliament in Brussels on 6 June 2013.

5. Guidance from the European Court of Justice

A number of ECJ decisions have progressively defined the scope and formed non-exhaustive principles that guide the application of the Transparency Regulation. Much has been examined about the scope of a protected commercial interest; however, the criteria to assess an overriding public interest as it relates to trials data is still unclear. Through an analysis of the foregoing precedents established by the EMA and the Ombudsman, this chapter will raise crucial unanswered questions about the assessment of these interests and examine the potential for future ECJ decisions to offer guidance in the present debate.

5.1 The overriding public interest criterion: Unanswered questions

The scope and criteria of an overriding public interest have been seldom addressed, in spite of extensive communication from the ECJ, the EMA and the Ombudsman concerning exceptions to the disclosure of EU documents. First, questions arise concerning what constitutes an overriding public interest. The ECJ has offered guidance on this question in relation to an allowable derogation of any of the four freedoms. Overriding public interests upheld in ECJ judgments include, but are not limited to, the protection of the environment in relation to the movement of goods, the maintenance of ‘a permanent population and an economic activity independent of the tourist sector’ for regional planning purposes in relation to the movement of capital, and the protection of workers in relation to the movement of services. A portion of these overriding public interests have subsequently been enshrined in the TFEU. Specifically, permissible derogations to the free movement of goods include ‘public morality, public policy or public security; the protection of health and life of humans, animals or plants; the protection of national treasures possessing artistic, historic or archaeological value’ [emphasis added]. Notably, the protection of public policy, public security and public health have been mentioned in relation to grounds for allowable derogations to the free movement of workers and the right of establishment. These presumably non-exhaustive examples of what may constitute a public interest in the context of the ‘four freedoms’ may be applicable to the assessment of an ‘exception to an exception’ in the Transparency Regulation.

Questions also arise about the criteria required to demonstrate the existence of an overriding public interest. The need for this guidance in relation to CSRs is demonstrated by the

113 The ECJ, an institution that functions independent of the EU institutions and national governments, provides a binding interpretation of the content and procedures enshrined in EU law. In Treaty on the Functioning of the European Union Article 228(1) and (3) and Section 5
114 C-142/05 Åklagaren v Percy Mickelsson and Joakim Roos [2009] ECR I-04273 paragraphs 30-44
116 C-341/05 Laval un Partneri Ltd v Svenska Byggnadsarbetareförbundet, Svenska Byggnadsarbetareförbundets avdelning 1, Byggetan och Svenska Elektrikerförbundet [2007] ECR I-11767 paragraph 102-103
117 Treaty on the Functioning of the European Union article 36
118 Ibid article 45(3) and 52(1)
proceedings in the Complaint to the Ombudsman. The Applicants and the EMA fundamentally disagreed about the presence of an overriding public interest in the disclosure of CSRs. Unfortunately, the course of the Ombudsman’s examination did not necessitate his evaluation of an overriding public interest. Nonetheless, considerations such as what criteria must be fulfilled and how much evidence is necessary to prove the presence of an overriding public interest would offer useful guidance to the assessment of similar cases in the future.  

Finally, applicants seeking access to a document may be, by nature of their position, in a disadvantaged situation to prove the existence of an overriding public interest in disclosure. The Applicants in the Complaint to the Ombudsman expressed difficulty in adequately arguing an overriding public interest in their submission to the Ombudsman. They contended that due to the limited availability of objective information to assess the health effects of the medicines in question, it would be difficult for any entity besides the trials sponsor and the EMA properly determine whether a public interest in disclosure exists. Interestingly, an alternative approach has since been taken in the EMA’s revised Transparency Policy, which is now more closely aligned to the ECJ case law. The Agency explains that an overriding public interest ‘can be identified by the Agency, either further to a request for access to documents, or on its own initiative.’

5.2 Undecided cases before the ECJ

Few recent ECJ decisions provide relevant insight into the nature of documents that fall within the scope of protected commercial interests in Article 4.2, as it relates to trials data. However, three cases have recently been lodged before the ECJ that may shed additional light on the uncertainties raised above. The first case concerns an undecided appeal of the ECJ’s prior finding that granting access to preparatory documents from the European Council’s Working Party on Information would not undermine the decision-making process protected by Article 4.3 of the Transparency Regulation. The present appeal case is expected to address the degree of evidence required to demonstrate adverse effects on protected

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119 It is noteworthy that voluminous guidelines have been developed jointly by the EMA and the HMA following the Agency’s Transparency Policy to set out the criteria of disclosure to be applied to a commercially confidential document in Heads of Medicines Agencies and European Medicines Agency, Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation, 2010). However, in contrast, similar guidance has been provided neither by the Ombudsman nor by the EMA concerning the assessment of an overriding public interest.

120 In their submission, the Applicants contended that they could use their medical knowledge to extrapolate that ‘as a likely consequence of EMA’s position, patients would die unnecessarily and would be treated with inferior and potentially harmful drugs’, however the Applicants recognised that evidence needed to prove these statements was the subject of the contended access request. In , Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 16

121 The ECJ has stated ‘it is for the institution concerned to strike a balance between the public interest in disclosure and the interest which is served by a refusal to disclose, in the light, where appropriate, of the arguments put forward by the applicant in that connection.’ In T-36/04 Association de la presse internationale ASBL (API) v Commission [2007] ECR II-3201 paragraph 94

122 European Medicines Agency 3

123 This is the only relevant result following a search of the Curia database was made for all cases including the terms ‘access to documents’ and ‘commercial interests’ in the last three years.

interests. If the ECJ determines that disclosure would damage a protected interest, then an interpretation of an overriding public interest may be expected.

The second and third cases are similar in that depending on the outcome of the evaluation of the presence of a commercial interest, the ECJ may also give guidance on the overriding public interest in disclosure. One case awaiting judgment is *ClientEarth and International Chemical Secretariat v European Chemicals Agency*, in which public access to manufacturing information about chemicals alleged to be harmful to public health has been denied in order to protect commercial interests. The third case will undoubtedly yield the greatest insight into the fine balance between disclosure and protection of CSRs. Abbvie, a pharmaceutical company, applied in January 2013 to annul the EMA’s decision to release the CSRs of one of Abbvie’s products, in line with the EMA’s Transparency Policy and the Transparency Regulation. The applicants claim that disclosure would violate their ‘fundamental rights to the protection of confidential commercial information; [and] … the obligation to state reasons as regards the application of Article 4(2) of the Transparency Regulation.’ In light of this action to annul, it seems imminent that the ECJ will further define the scope of commercial interests as it applies to test data. If CSRs are found to risk a commercial interest, then further guidance on the determination of an overriding public interest may be provided.

### 5.3 Conclusion

Several undecided cases have the potential to further carve out the scope of a protected commercial interest under the Transparency Regulation. Considering the persistent gaps in understanding an overriding public interest, the greatest insights may be offered by the ECJ’s own assessments of this exception, should it prove necessary. The following chapter will build on this knowledge of the most recent issues addressed by the ECJ in relation to the transparency of EU documents to propose a novel test to balance the competing interests in trials data disclosure.

125 *C-280/11 P Council of the European Union v Access Info Europe* [2011] *OJ C238/6*  
126 *T-245/11 ClientEarth and International Chemical Secretariat v European Chemicals Agency* [2011] *OJ C194/20*  
127 It has been reported that a second case has been brought by a second pharmaceutical company against the EMA, although no information was available on the ECJ website at the time of writing this article.  
128 *T-44/13 AbbVie v EMA*
6. Balancing Test

The competition between commercial and public interests in trials data disclosure has been captured in respective intellectual property law and medical literature for the last three decades. The relative scarcity of academic legal writing to explore and balance these interests in the context of EU law warrants a thorough study of this issue in relation to CSRs. The proposed test to carry out this study is the product of adaptations and developments of established legal tests from case law and concepts raised in academic literature. The two-part test applied in the MyTravel case is a useful departure point provided by the General Court, which has stated that ‘exceptions to the general right of access’ should assess:

…first, whether access to the document would specifically and actually undermine the protected interest and, secondly, in the circumstances referred to in Article 4(2) and (3) of Regulation No 1049/2001, whether there was no overriding public interest in disclosure.\(^{129}\)

The first assessment, whether access to the document would actually and specifically undermine the protected interest, must be focused and tailored to the specific commercial interests in the case of trials data. Professors of Law, T. McGarity and S. Shapiro, have rightly identified that damage to commercial interests in the context of trials data actually references the potential to hurt returns on investment in medical product innovation.\(^{130}\) That potential arises from whether, in the words of McGarity and Shapiro, disclosure will grant competitors ‘significant licensing and intelligence advantages’ that would detract from investor’s reward for bringing an innovative product to the market.\(^{131}\) Following the approach by the ECJ, ‘the risk of an interest being undermined must be reasonably foreseeable and not purely hypothetical’,\(^{132}\) and it must be demonstrated that disclosure would ‘specifically and actually undermine commercial interests’.\(^{133}\) These principles will be applied to the evaluation of whether granting access to CSRs would confer significant licensing and intelligence advantages on competitors.

The second assessment of an overriding public interest in disclosure should be made in two parts, first by assessing whether an overriding public interest is present and then whether the same public interest objectives could be achieved through other means not requiring data disclosure. This approach, including an analysis of the proportionality and objective necessity of disclosure, has been applied by the ECJ in examining a public interest exception to one of the four freedoms.\(^{134}\) The present discussion warrants a specific examination of whether information from another source or whether the act of another agency, neither of which require the disclosure of CSRs, could achieve the same objective.

\(^{129}\) T-403/05 MyTravel Group plc v Commission [2008] ECR II-02027 paragraphs 32-33

\(^{130}\) McGarity and Shapiro 852

\(^{131}\) Ibid

\(^{132}\) C-39/05 P and C-52/05 P Sweden and Turco v Council [2008] ECR I-4723 paragraph 43

\(^{133}\) T-403/05 MyTravel Group plc v Commission paragraphs 32-33

\(^{134}\) C-142/05 Åklagaren v Percy Mickelsson and Joakim Roos paragraphs 32-40
The question arises of whether a workable balance of interests could best be achieved by applying the above test to CSRs in their entirety or to sub-sections of CSRs. To this end, A. Kesselheim and M. Mello, lawyers at the Harvard School of Public Health, have proposed that the effects of medicines can be roughly divided into categories (a medicine’s safety profile and its efficacy to treat a given indication) and the disclosure of data in each category may have varying degrees of potential competitive disadvantages and/or public interest benefits. Relying on this theory, Kesselheim and Mello specifically suggest that safety data disclosure optimises the public interest benefits while minimising the potential competitive disadvantages. An alternative view comes from P. Lurie, the former Deputy Director of Public Citizen’s Health Research Group, who has argued that the disclosure of efficacy data from clinical investigations would achieve the appropriate compromise between public interests and commercial protection. In conclusion, a sharper distinction between safety data and efficacy data in CSRs will be made in order to examine the feasibility of various interest balances in the context of EU law.

135 A. S. Kesselheim and M. M. Mello, ‘Confidentiality laws and secrecy in medical research: improving public access to data on drug safety’ (2007) 26 Health Affairs 483 489
136 Ibid
7. Risk of undermining commercial interests

This chapter first clearly defines the concept of a commercial interest in CSRs. Considering the EU’s exclusivity regime and the scope of its protection offered to trials data described in Chapter 3, this chapter analyses several scenarios in which disclosed CSRs could be used by a competitor to achieve commercial benefits. In doing so, a differentiation is made between the relative risks to commercial interests evoked by safety as by efficacy data. Finally, other factors that could affect the likelihood of competitors accruing advantages from disclosed data are examined.

The risks of data use by a competitor are best illustrated by leading scholars in this field. Many suggest that data disclosure could convey product insights and related advantages on competitors who have not borne the related research costs, or so-called ‘free-riders’. The EMA has made these same claims in relation to the information in a CSR which could ‘be used by competitors to start developing the same or a similar medicinal product on their own, using the information and data for their own economic advantage.’

Commentators such as Grabowski and Fellmeth warn that the practice of disclosing trials data could ultimately have a cooling effect on the incentive to innovate. Fellmeth suggests that the practice of ‘free-riding’ or inadequately compensated exploitation would be an ‘insufficient incentive’ for data owners to innovate and develop new products if they were not assured that their advances would be protected from unfair commercial use by competitors. Moreover, Grabowski explains that ‘uncertainty about recoupment periods and the ability to earn a risk adjusted return on particular new product candidates will result in fewer of these candidates being taken forward into development.’ Therefore, the question guiding the assessment in this chapter is whether competitors could gain advantages from release CSRs that could give them significant licensing or intelligence advantages.

7.1 Exclusivity laws in the EU protect against marketing copies

Concerns have been raised about the potential for disclosed data to be used by another inventor to secure a patent for the same product. These arguments have recently been cited by industry associations in response to initiatives to voluntarily register clinical trials. EFPIA and partner associations state that ‘exceptionally, public disclosure of certain data elements could jeopardise the granting of a patent’. Given that CSRs provide more detail than trial registries, it is conceivable that similar patent concerns would be extended to CSRs although few have emerged in recent literature. However, T. Lemmens, Associate Professor at the University of Toronto Faculty of Law with appointments in the Faculty of Medicine, suggests that ‘[t]he patent fear seems unfounded’ given that ‘[p]atent applications are filed as soon as industry sees promise in a new compound or medical device or in a new use of an existing

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138 In the Complaint to the Ombudsman, however, no evidence of how insight into drug development could be possible through the release of CSRs was found, considering that these documents do not contain compositional data. Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency 81
139 Fellmeth 468–9
140 Grabowski and DiMasi 9
141 EFPIA and others 3
Important decisions must be made about how to allocate resources to minimise risk of R&D failure and maximise potential profit. Products to develop further are identified and, in most cases, patented well before they reach the clinical trial phase, during which time the act of research can lead to various forms of publicity that would pose risks to an unpatented product, as described in more detail below. Therefore, the potential for competitors to seek a patent in the EU for an identical product using the information obtained in a CSR appears to be quite limited.

Patent exclusivity also extends limited protection against use of disclosed data by competitors. This is achieved in a similar way as the protection of the product itself. Filed patent applications are published and circulated in the interests of raising awareness of the latest scientific and technological advances, ultimately to stimulate further innovation. Fears about this information stimulating imitation products are placiated by patents that exclude competitors from marketing an identical product. Similarly, any incentive to produce an imitation product, stimulated by the publication of a CSR, would be futile when the first innovator benefits from patent protection.

EU law provides new chemical entities entering the market with a period of data exclusivity during which second comers may not reference the first innovator’s safety and efficacy data to obtain market approval. Moreover, any attempt to secure a product license on the basis of trials data sourced directly or indirectly through access or so-called “freedom of information” requests is strongly discouraged by the Commission. This protection effectively obliges potential competitors seeking to market the same product, to either wait to launch the generic product until data and market exclusivity expires or to invest in the ‘independent development’ and clinical investigations required to obtain a license. For a number of reasons explored further below, the result is often ‘sequential licensing’ in which generic competitors are kept from entering the market until exclusivity has expired.

7.2 Indirect commercial advantages in the EU

A second comer may invest the time and financial resources to build on or employ the insight it has gained through disclosed test data in the ‘independent development’ of the same product. Assuming in the scenarios below that the first innovator is off-patent, then both the first innovator and the second comer may be simultaneously licensed. Even if the innovator benefits from data exclusivity, it will offer no protection against a competitor that has made its own investments in research and development to bring the same chemical entity to the market. The precise advantages that may be enjoyed by the second comer in this case will depend upon what point in the product’s life cycle a market license is sought.

142 Lemmens and Telfer 24
143 Ibid 24
144 The Pharmaceutical Commission, an advisory group to the European Commission has emphasised at its 65th annual meeting in 2009 that such an action ‘would lead to a circumvention of the data protection rules of Directive 2001/83/EC’. Commission, 65th meeting of the Pharmaceutical Committee - Human (Summary Record, 2009) 5
145 The terms ‘sequential’ and ‘simultaneous’ licensing have been used by Owais in his presentations to WIPO in 2012 on data exclusivity and generic market entry.
146 McGarity and Shapiro 850
In one scenario, a new chemical entity may be launched on the market and within the first eight years of its data exclusivity, a second competitor may independently license the same chemical entity for a new indication. Aside from greater competition, this scenario could have a negative impact on the first innovator if it were attempting to license its product for the same new indication. Recall that under EU law, the first innovator may enjoy an additional year of market exclusivity (called the *eleventh year*) if it licenses its product for a new indication during the first eight years of data exclusivity. If a second comer’s own independent development outpaces that of the first innovator and yields a license for a new indication, then the former may encroach on the first innovator’s benefit of the eleventh year of the exclusivity rights it may have otherwise enjoyed.

In a second scenario, a new chemical entity may be launched on the market and following its eight years of data exclusivity, an identical product may be independently licensed by a competitor for a new indication. Contrary to the first scenario, here the first innovator would experience relatively limited impact on its exclusivity rights and remain entitled to enjoy the maximum non-cumulative ten or eleven years of market exclusivity, which is determined by the results of its own development and licensing activity during the first eight years of exclusivity.

Safety data and efficacy data independently provide the necessary yet insufficient evidence base to alone support a license application. It is the combination of both types of data that allow regulators to judge a product’s benefit-risk balance for each condition it treats. In the context of licensing known products for new indications, efficacy data has the potential to offer useful insights to a competitor that are not conferred by safety data. For that reason, safety data disclosure may pose greater risks to first innovators’ commercial interests than safety data.

Aside from exclusivity rights, one of the greatest risks that first innovators would face in the above scenarios is damage to their market share and profits as a result of identical competing products reaching the market. DG Competition labels the market effects of generic entry “profound”. Evidence provided by the Commission in the context of the Pharmaceutical Sector Inquiry shows that the ‘average prices dropped by almost 20% after the first year following LoE [loss of exclusivity] and about 25% after two years.’ In EU Member States, price decreases of 50% are achieved on average within two years of generic entry after loss of exclusivity. Moreover, ‘generic companies built up a more than 50% share by value and volumes’ in the first year of their entry to the German and Czech markets. This reduction in market shares and product prices usually results in lower profits for earlier marketers. This is a strong reminder of Grabowski’s point that ‘data exclusivity does not provide an innovator with either a monopoly or marketing exclusivity from competitors with therapeutic alternatives’, and therefore, first innovators are subject to competition if their products lose patent exclusivity.

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147 See Chapter 3, sub-heading ‘Data and market exclusivity in the EU’
148 Commission, *Pharmaceutical Sector Inquiry* paragraph 209
149 Ibid paragraph 212
150 Ibid paragraph 225
151 Ibid paragraph 234
152 Grabowski and DiMasi 4
7.3 Licensing advantages in foreign markets

The risk of competitors relying on the trials data of products marketed in the EU to directly obtain a license for the same product in a foreign jurisdiction has been identified by many scholars. A full evaluation of this risk would require an examination of the market approval laws in third countries and the resulting impact, if any, of foreign trade agreements on the licensing process. Most bilateral and regional trade agreements between the US or the EU and third countries secure a period of data exclusivity, and many bilateral trade agreements with the US go as far as to prohibit regulators in the target country from relying on market approval from foreign jurisdictions. The pertinent question is: if and to what degree free trade agreements ("FTAs") govern a competitor’s use of test data obtained through an access request, to secure a license for the same product in a third country.

Although full consideration of the prevailing legal frameworks necessary to answer this question lie beyond the scope of this paper, there may be protective features of selectively withholding certain data in the disclosure of a CSR. One way forward under this theory would be to publish only the clinical safety and efficacy data in a CSR and withhold the pharmacokinetic and pharmacodynamics data. A second comer would then have knowledge of the product’s safety and efficacy profile; however, it would lack the evidence of bioavailability, which is essential to obtaining a license for a generic product in many, although not all, jurisdictions.

7.4 Other factors that influence competitors’ use of trials data

The potential for a number of additional factors outside of the EU’s legislative framework that may offer protection to previously unpublished trials data will be examined below.

7.4.1 ‘Cost-benefit’ ratio of independent development

The potential for second comers to reap these advantages from insight into clinical trials data must be weighed against the disincentives to invest in independent development. Reichman argues that the ‘cost-benefit ratio’ of independent development is a significant deterrent to generic competitors choosing to repeat clinical trials. Significant costs include the time and resources required to conduct trials as well as the reduced ability to recoup these costs from the marketed product because it ‘by definition lacks a patent’.

153 McGarity and Shapiro 848
154 Insight into this question may be offered by doctoral candidate Owais Hassan Shaikh, affiliated with the International Max Planck Research School for Competition and Innovation, whose unpublished research has explored the impact of data exclusivity provisions in various bilateral free trade agreements on generic market entry. ‘International Max Planck Research School for Competition and Innovation’ <http://www.imprs-ci.ip.mpg.de/en/pub/staffandresearchers/doctoralcandidates/2013/owais_hassan_shaikh.cfm> accessed 11 May 2013
156 Ibid
157 Reichman 5
158 Ibid 5
implausibility of second comers conducting their own safety and efficacy studies, Karin Timmermans of the World Health Organization offers an additional deterrent:

‘[t]he repetition of clinical trials raises serious ethical questions, since it would imply withholding medicines that are already known to be effective from some patients (the control group), solely for commercial purposes. It is unlikely that withholding medicines in this way would pass the scrutiny of ethical review committees, which renders it de facto impossible for generic companies to repeat the clinical trials.’

These barriers to independent development become even greater when considering the natural incentives for first innovators to employ their existing knowledge to bring a product to market and minimise what Grabowski titles ‘development delay’. Using the example of biological medicinal products, Grabowski explains that, as a result of a delay in development, first innovators could experience

…lower revenues on a present discounted value basis from the firm’s perspective at the beginning of development, a lower likelihood of gaining first mover advantages, and greater competition from different drugs and biologics that treat the same conditions during the biologic’s period of market exclusivity.

Therefore, it seems inconceivable that any insight offered by trials data would be the sole driver of ‘independent development’ that is not already underway. The incentive is further diminished considering that, in the absence of patent protection, additional competitors engaging in own product development may enter the same product market at any time. Thus the more likely scenario is one in which an innovator’s trials data provides insight to a competitor’s development process that is already underway.

McGuinty and Shapiro argue that the first innovator’s own ‘headstart’ is a powerful advantage afforded to the first innovator and could mitigate any risk of product imitation posed by insight into trials data. However, the actual headstart advantage enjoyed by first innovators is likely be highly subjective second comers’ stage of independent development. The precise advantage that this insight may offer is difficult to estimate; however, it may be sufficient to recognise that the greatest risk of free-rider insight driving own development and a second comer exists when the innovator has the least headstart advantage.

Besides considerations of time and resources, Gøtzsche contends that the phenomenon of publication bias observed in unpublished trials data offers little incentive to engage in independent development of the same product. It must be said that, although the phenomenon of publication bias is widely recognised in academic literature, it is an insufficient argument to stave off drug development by a second comer and thereby indirectly offer protection to commercial interests. The question of whether or not test data will yield a

159 Timmermans 0207
160 Grabowski and DiMasi 24
161 Ibid 24
162 McGarity and Shapiro 884
163 Gøtzsche also cited reasons specific to the CSRs and unique to the clinical studies conducted on the two medicines that were the subject of the Complaint to the Ombudsman, which due to their specificity to his particular case, are not explored here. Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 55
positive or negative overall view of the potential for the medicine being tested is highly subjective to the clinical study at hand. Moreover, it can be assumed that the EMA receives sufficient CSRs and clinical evidence from which an overall positive benefit-risk is determined given that EU market licenses have been granted to a number of products. Additionally, competitors would still benefit from another’s investment into the generation of negative or less favorable results, albeit not to the same degree if the results were more positive. Negative test results may provide useful insight that could provoke a competitor to make beneficial changes to its development strategy. Examples of investigational adaptations include investing in solving a particular problem observed in clinical studies or re-directing a line of development to a more promising innovation (i.e. dosage form, indication, chemical entity). This is one concept behind the widely-discussed theory that access to test data can stimulate pharmaceutical innovation,\textsuperscript{164} which lies outside the scope of this paper. Although the disclosure of unpublished data may not yield “positive” test results, that information has the potential to nonetheless confer valuable knowledge leading to potential benefits for competitors.

### 7.4.2 ‘Market imperfections’

The protection of intellectual property rights and the EU’s competition laws sometimes appear to be at odds with one another. In the context of the present debate, it should be considered whether commercial interests that fall outside the well-defined scope of patent and data exclusivity in the EU are worthy of additional confidentiality measures in order to protect against its disclosure. In response to concerns about the potential abuse of intellectual property protection and other measures to hamper competition in the EU pharmaceutical sector, DG Competition initiated the Pharmaceutical Sector Inquiry in 2007.\textsuperscript{165} The Sector Inquiry found a number of strategies used by companies directly or indirectly block competition from generics, including:

…filing for a large number of patents in relation to a single medicine (so-called "patent clusters"…, engaging in disputes with generic companies leading to… reported patent litigation, concluding more than 200 settlement agreements with generic companies which partly restrict generic entry and lead in certain instances to value transfers…\textsuperscript{166}

The Inquiry’s findings illustrate that certain ‘market imperfections’ exist, which McGarity and Shapiro argue ‘can protect the ability of an innovator to reap monopoly benefits’.\textsuperscript{167} The ‘market imperfections’ documented in DG Competition’s study between 2000 and 2007 demonstrate company behavior that could delay the entry of generic medicines onto the market in Europe and therefore, artificially extend the first innovator’s exclusivity. Although the Commission has engaged in monitoring activities of so-called ‘pay-for-delay’ settlements between originators and generics,\textsuperscript{168} and is closely examining individual cases of alleged anti-
competitive company behavior, it is conceivable that all potentially anti-competitive behavior can not be eliminated and some aspects of the ‘toolbox’ used by companies will persist. These ‘market imperfections’ could afford commercial interests unintended protection in the face of data disclosure, as McGarity and Shapiro have suggested.

7.4.3 The act of research reveals commercial interests

Gøtzsche has argued that the clinical study protocols are made available to all scientific collaborators and therefore, it is highly unlikely that the protocols would contain commercially sensitive information. It can be argued that this reasoning could be extended to the CSR, which includes the protocol and patient data. Lemmens stresses that study participants are required by law to give their informed consent and such a decision would necessitate a reasonably detailed explanation of ‘the product, its risk and its intended use.’ Such informed consent safeguards can, however, fail to provide patients with crucial information, which raise questions about how detailed or thorough the consent procedure may be. Therefore, it must be recognised that Lemmens’ assertion that much information could conceivably be gathered from such a process may not hold in every case.

7.5 Conclusion

The foregoing analysis demonstrates that the disclosure of CSRs may encroach upon a first innovator’s commercial interests in maximising its sales revenue. Specifically, second comers may seek to gain commercial benefits from a combination of its own product development and indirect insights offered by trials data, which may lead to licensing an identical product in the EU. Although a competitor’s interest in relying on disclosed CSRs to seek a license in a foreign jurisdiction, this risk was not explored in detail. A number of other factors, such as the development stage of the second comer and the legal framework in foreign jurisdictions, render it difficult to conclude with certainty to what degree such commercial interests would be harmed in these specific circumstances. Commercial interests in maintaining market exclusivity raise the question of where an acceptable balance between intellectual property protection and fair competition should be found.

spark scrutiny from the competition authorities, have been said to have ‘stablized at a low level’ over the monitoring periods. Commission, 3rd Report on the Monitoring of Patent Settlements, 2012) 15


170, Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency paragraph 56

171 Lemmens and Telfer 26

172 US consumer organisation Public Citizen launched a campaign for greater safeguards in health research in April 2013 after it came to light that over 1000 premature babies were enrolled in clinical studies at US medical centers without their parents’ knowledge of the increased risks of blindness and death. In Public Citizen, ‘HHS-Funded Experiment Exposed Babies to Risk of Death and Blindness Without Informing Parents’ (Press Release 11 April 2013, 2013) <http://www.citizen.org/pressroom/pressroomredirect.cfm?ID=3859> accessed 13 April 2013
8. Overriding public interest in disclosure

Once it has been established that there may be commercial interests in disclosing the data, an analysis must be made of the overriding public interest in the information. This test begs three novel questions adapted from EU law principles. First, it is assessed whether informed consumer decision-making is caught by the scope of a justifiable overriding public interest. This is followed by an evaluation of whether the overriding public interest can be achieved through less damaging means, particularly by not necessitating disclosure. To this end, alternative data sources and formats, as well as acts of other agencies, are considered.

8.1 The presence of an overriding public interest

In the absence of an exhaustive list, any public interest exception to internal market provisions initially established by the ECJ and later enshrined in the TFEU may be invoked as an overriding public interest in the present debate. The previous exploration has shown that ‘the protection of health and life of humans’ may be considered an overriding public interest that is applicable in this case.173

8.1.1 The purpose of informed consumer decision-making

It must now be assessed whether disclosed CSRs can achieve informed consumer decision-making which contributes to the protection of human health and safety. Two distinct aims of informed consumer decision-making will be evaluated. First, having a complete and accurate understanding of the safety profile of a medicine is arguably of great importance to facilitate the ‘accurate evaluation of drug safety’ by consumers.174 Second, access to information about the effectiveness of a medicine to treat a given condition is necessary for prescribers and patients to choose the most appropriate therapy.

Concerning the evaluation of drug safety, several prominent safety concerns resulting from delayed public knowledge of the safety risks associated with taking certain medicines have been reported in the media. One example is of the medicine rofecoxib (Vioxx®), marketed to treat arthritis and eventually voluntarily removed from the global market in 2004 due to its link with adverse events including heart attack and stroke.175 A subsequent meta-analysis of the adverse events recorded in all published and unpublished trials data revealed that a significant risk of a suffering a heart attack or death as a result of taking the medicine could have been identified as early as June 2001 if trials data had been published as it was generated.176 This and other cases described by Gøtzsche illustrate the potential for safety data disclosure to protect human health and safety through the early detection of serious adverse

173 See Chapter 5, sub-heading ‘The overriding public interest criterion: Unanswered questions’
174 Kesselheim and Mello 483
176 One source of data was unpublished trials made available through the rofecoxib litigation in the USA. In Ross and others
events and preventing the continued use of potentially harmful medicines by European patients.  

Concerning the selection of the most appropriate therapy, the availability of trials data to make comparative analyses of therapies would aid prescribers and patients to choose the most effective product to meet their health needs. One example of the importance of efficacy data can be drawn from the recent concerns raised about the effectiveness of oseltamivir (Tamiflu®) at treating symptoms of influenza. In 2012, Cochrane researchers stated their continued inability to draw clear and reliable conclusions about oseltamivir’s effectiveness due to the methodological flaws of available studies and the inaccessibility of all unpublished CSRs held by the drug manufacturer, Roche. This conclusion has emerged nearly three years after governments around the world, including many EU Member States, have spent substantial sums of money to stockpile oseltamivir and other influenza vaccines for use in the event of a pandemic. These stockpiles are considered by commentators to be a waste of public funds, as only a fraction of the stockpiles have been used to date, and the limitations to their use considering their questionable effectiveness and their finite shelf-lives. Gøtzsche concisely summarises patients’ interest in efficacy information with his statement ‘[i]f Tamiflu does not reduce complications, there is little rationale for using this expensive drug.’

### 8.1.2 Which data can protect human health and safety

Against the above understanding of what safety and efficacy data can independently contribute to public health, it must now be determined to what degree either or both types of data achieve the protection of human health and safety. On one hand, safety data is chiefly aimed at documenting and quantifying any adverse event or other health risk experienced as a result of taking the medicine. Therefore, it can be said that the disclosure of safety data can make a significant contribution to protecting human health. On the other hand, doubts can be raised about whether the need for comparative information and cost-effective treatments directly contributes to the protection of human health and safety. Although promoting rational healthcare decisions and the financial viability of public healthcare systems in the EU are noble objectives, their achievement is arguably more distantly related to the protection of human health.

A comparison of the effects of using unsafe medicines and of non-effective medicines can yield interesting insight in this exercise. While both scenarios pose potential dangers to public health, immediate negative effects will surely be felt by a healthy user of an unsafe medicine.

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177 Gøtzsche
179 According to Public Service website, the UK government spent around £500 million to purchase Tamiflu in 2009. , ‘£500m Tamiflu spend to be investigated’ Public Service (14 December 2012) <http://www.publicservice.co.uk/news_story.asp?id=21714> accessed 9 May 2013
181 Gøtzsche 4
On the other hand, healthy users would experience few or no adverse effects from taking a non-effective medicine. Admittedly, a medicine of limited efficacy may not improve an ill patient’s condition and for that reason, pose a risk to public health. However, the fact remains that an unsafe medicine will be dangerous to all users while a non-effective medicine will only pose risks to those who require it to treat a condition.

8.2 Proportionality

Similar to the ECJ’s approach to seek out the least restrictive means to achieve internal market objectives, the remainder of this chapter evaluates whether there are less damaging means than the disclosure of CSRs to achieve the same degree of human health protection. As the disclosure of safety data has been demonstrated to be most closely related to public health protection, only safety data will be considered in the remainder of this chapter. An evaluation of two criteria will be made, namely whether another data source or format or whether the act of an alternative agency could provide the necessary information to achieve informed consumer decision-making.

8.2.1 Alternative data sources or formats

When considerations of a different source or format are made to achieve the same goal, the substitution of CSRs in two specific scenarios can be evaluated: substitution with another data source documenting the same trial or substitution with a CSR from a different study on the same product.

Several data sources documenting the same trial warrant consideration as potential substitutes for CSRs. First, although statements about the safety of a medicine, its indication and any safety warnings are printed on the so-called patient information leaflet that consumers receive with a medicine at the point of sale,182 studies show that this information about important health risks associated with taking the medicine can be incomplete or inconsistent.183 Moreover, patient information leaflets are not the appropriate publication or format to provide a description of clinical tests and their results suitable for a systematic review in a way that CSRs do. Second, it has been suggested that trial registries could serve as an information source for researchers examining the effects of pharmaceuticals. Although publicly accessible registries provide an important record of the trial taking place, academics have found that trial entries contain little usable information for research purposes; the study methods section is particularly weak in comparison to the detail available in CSRs.184 Finally, in comparison to trials described in journal articles, researchers have demonstrated that CSRs include ‘substantially more information and detail on the intervention being tested than published versions of the same trial’.185 Therefore, CSRs provide the greatest degree of detail of safety

182 Medicinal Products Directive 2001/83/EC  Title V
185 Doshi and Jefferson
and efficacy data conducive to public health research, and for that reason, can not be substituted with another data source of the same trial.

At first sight, a publicly available CSR from a different study on the same product could conceivably substitute for an unpublished CSR. The phenomena of ‘publication bias’ and ‘selective reporting’ of the benefits and downplaying the harms of a medicine in published data is precisely what renders published data unsuitable for the purpose of informed consumer decision-making. Moreover, the objective behind conducting a systematic review or a meta-analysis is to capture and investigate all the existing information on the effects of a pharmaceutical product, as each trial contributes to the global understanding of the medicine’s benefit-risk profile. Therefore, it is of little use to these scientific inquiries into safety and efficacy to substitute an unpublished CSR with more readily accessible published data.

**8.2.2 Acts of another agency**

It could be thought that independent analysis of data submitted to the EMA merely replicates the examination carried out by these regulatory authorities or other public agencies. It will be demonstrated that the scope of the EMA’s examination of products, by its legal basis in EU law and its execution in practice, addresses fundamentally different objectives than those of third party public health analysts.

First, there are several reasons why the benefit-risk evaluation of the EMA could not substitute for the analyses of unpublished CSRs by public groups such as the Cochrane Collaboration. First, the EMA regulators are responsible to evaluate the safety, efficacy and quality of medicines to be marketed to the general population in the EU. Drug regulatory authorities base a marketing decision on the safety profile of a product and its efficacy at treating a given indication. The threshold of scientific judgment required by regulators is arguably low; the product in question must be more effective at treating an indication than a placebo. Regulatory evaluations can rarely consider the safety and effectiveness of medicines in certain sub-population groups, such as children, pregnant women and the elderly, by virtue of the fact that these patient groups are often excluded from clinical tests. In addition, the submission of clinical data from comparative studies using similar products is not obligatory in order to receive a standard market license for a prescription medicine from the EMA.

Second, unpublished data submitted to the EMA in license applications is exempt from the peer review process, which is applied in scientific research to debate findings and to progress the understanding of pharmaceutical effects. Although the peer review process is not

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186 Gøtzsche 2 and 4
188 Gøtzsche 2
190 Medicinal Products Directive 2001/83/EC Annex I Part I 5.2.5.1. However, as stated in Article 10(1), comparative data must be submitted in order to obtain an eleventh year of exclusivity for licensing a medicine to treat a new indication and offers ‘a significant clinical benefit in comparison with existing therapies’.
191 McGarity and Shapiro
infallible, it is the best alternative currently available to advance scientific thought. Without the peer review process, new observations may not be readily identified and discrepancies and conclusions may not be questioned, leading to a stagnation in the collective completeness of society’s knowledge base of the effects of a medicine.

8.3 Conclusion

Informed consumer decision-making about medicines was demonstrated to be closely linked with the protection of human health and safety, an overriding public interest established in the TFEU. While both safety and efficacy data disclosure can be related to public health protection, the former is notably more intrinsically and immediately linked to the protection of human health and safety than the latter. This chapter demonstrated that it is the nature of unpublished CSRs that make these documents valuable to independent researchers seeking to analyse the complete body of evidence of the effects of medicines. Furthermore, a safety analysis could not be undertaken by another public agency.

192 There have been a number of instances of fraud in medical research among even peer-reviewed publications. In Verbeke and Tijdink
9. Looking forward

Recent reports of adverse health effects and the threat of contagious influenza have led European medical researchers, regulators and politicians to re-examine what is known about the effects of pharmaceuticals on the EU market. Evidence has shown that unpublished clinical test data held by the EMA could make a unique contribution to the body of scientific knowledge and ultimately promote informed consumer decision-making about medicines use. However, concerns have been raised about the potential for greater transparency of test data to undermine the commercial interests of pharmaceutical companies, which is no better illustrated than by a pharmaceutical company’s recent action to annul the EMA’s data disclosure policy. Nearly absent from this EU debate, however, are legal scholars. Few attempts have been made to balance interests in secrecy and disclosure through the lens of EU law.

It has long been suggested that the disclosure of clinical trials data could jeopardise the commercial interests of its owners. This paper sought to evaluate the validity of this claim in the context of EU law and to bring it into balance with the overriding public interest in informed consumer decision-making. In this analysis, the subject of disclosure was narrowed to a standardised CSR which is uniquely developed in relation to a single clinical test of a medicinal product, and which submitted to the EMA in a license application.

This paper critically examined the legal protection afforded to test data in the EU and the EU’s transparency framework that has been strongly influenced by the Ombudsman and the EMA’s policies on disclosure. It was shown that the EU’s data exclusivity regime is the only form of direct protection against CSR use by competitors, in certain circumstances. Other forms of protection, such as patent exclusivity, are not applicable to data or, in the case of trade secrets and commercial confidences, are not harmonised at the EU level.

A brief exploration of recent guidance from the ECJ was shown to contribute little to the understanding of whether CSRs fall into the scope of a protected commercial interest. Several undecided cases before the ECJ have the potential to shed light on this outstanding query, and specifically the case of Abbvie v. EMA is of great interest to this debate.

In the absence of guidance from the ECJ, a novel two-part test has been proposed to first evaluate the presence of a protected commercial interest, followed by an overriding public interest.

The evaluation of potential risks to commercial interests in the first part of the balancing test suggests that patent and data exclusivity laws in the EU protect, to a large extent, against freeriding within Europe; however, similar concerns exist for foreign jurisdictions lacking the EU’s legal framework. Two scenarios based on the EU’s exclusivity laws, were proposed to evaluate the potential for competitors to gain significant intelligence and licensing advantages from disclosed CSRs. These scenarios elucidated the ever-present risk that insight from CSRs may contribute to a competitor licensing an identical product through its own independent development. In such a case, it was shown that the first innovator would stand to lose market share and revenue, in addition to the potential of risking an eleventh year of market
exclusivity in certain circumstances. The foregoing analysis demonstrates that some insight offered by CSRs may not be unique to that source, but may actually be derived in an unsystematic way from a number of pre-existing and publicly accessible sources, or CSRs may offer little incentive or little novel insight to stimulate competitive innovation.

The second part of the balancing test examines an overriding public interest in disclosure. This analysis has demonstrated that certain types of data that may be disclosed in a CSR have been demonstrated to serve an overriding public interest. Safety data has been shown to be more intrinsically linked to the public interest in human health protection and safety than efficacy data. Further analysis of the public health conclusions that may be drawn from the safety data in CSRs has proven that the same degree of human health and safety protection could not be achieved through the use of another data source, nor format, nor by the act of another agency that may not require disclosure.

Taken together, the results from the analysis of a risk to a commercial interest and the presence of an overriding public interest lead to convergent conclusions. While the disclosure of CSR data may encroach upon a commercial interest in maintaining the secrecy of that data, the risk of its use by competitors can be attenuated. Releasing only the safety data in CSRs would be a prudent approach to mitigate the risks of any direct or indirect licensing or intelligence advantage from being accrued by competitors. At the same time, this paper has demonstrated that safety data disclosure can make a significant contribution to the protection of human health and safety. Efficacy data disclosure, on the other hand, raises concerns about the potential for its use, however indirectly, to the commercial benefit of competitors, while its disclosure would deliver less immediate benefits to the achievement of human health protection and safety. The proposed way forward therefore minimises the risks to commercial interests while maximising the public interest benefits.

Future investigations may seek to refine this balance in consideration of the potential impacts of CSR disclosure on product competition and commercial interest protection in foreign jurisdictions. Moreover, as medicines regulation becomes increasingly more transparent, alternative clinical data sources may become available that offer greater insight for consumer decision-making, that pose a lower risk of competitors deriving commercial benefits, or that yield clinical data from jurisdictions beyond the EU. Moreover, important questions have risen from this paper about the interplay between intellectual property protection and competition law. Further research may address to what degree the risk of independent drug development by a competitor ought to be avoided or stimulated in certain scenarios.

193 Recall that applications made to the EMA will not include CSRs from all trials undertaken on a given product, nor are the CSRs required to be submitted in their entirety. CSRs may lack appendices, including the individual and anonymised patient data that provide the most detailed, useful information as compared to the summaries found within the CSR itself. In Doshi and Jefferson and Jefferson and others, The EMA only receives CSRs in market license applications for the EU jurisdiction; European regulators do not have access to evidence in license applications made outside the EU. This dilemma has played in a central role in the Cochrane Collaboration’s inability to draw clear conclusions about the efficacy of oseltamivir. See Chapter 8, sub-heading ‘The presence of an overriding public interest’
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