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ARTICLE

Managing Intellectual Property Rights Over Clinical Trial Data to Promote Access and Benefit Sharing in Public Health

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Abstract The nature and scope of intellectual property protection, if any, which clinical trial data should receive in terms of Art. 39 of the TRIPS Agreement have been put back in the spotlight through recent events: First through suggestions by heads of the Dutch, French and UK regulatory authorities as well as the European Medicines Agency that such data should not be considered commercially confidential information. Secondly, courts in countries such as Argentina and Brazil have recently decided cases in which they had to balance rights over clinical trial data with competing public health priorities. Both courts decided that public health interests take priority over claims for exclusive rights over clinical trial data. These events raise pertinent ethical and legal concerns, which warrant considerations of strategies that can be used to manage intellectual property rights over clinical trial data with a view to fostering access and benefit sharing in public health. This paper draws lessons from these events and suggests possible options for strategic management of intellectual property rights over clinical trial data in order to cater to public health needs. The concept of access and benefit sharing, which has so far been debated in the fields of biodiversity and most recently in the human genome context is applied to public health with a view to initiating discussions on how it can inform decision making in the management of intellectual property rights over clinical trial data.

Keywords Benefit sharing · Clinical trials · Intellectual property · Public health · Test data · TRIPS Agreement

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1 Introduction

Intellectual property rights (IPRs) play an important role in many sectors of society. Public health is one such sector, which is, however, very sensitive to the manner in which IPRs are managed. This is the case because health is usually affected by struggles over who controls and benefits from the scientific and technological changes that are underway.[1]

Taubman's very humorous observation regarding the international scope of public health concerns is equally very relevant for appreciating the need to manage IPRs with a view to promoting access and benefit sharing (ABS) in public health:

> Pathogens show scant respect for national boundaries, human physiology is not shaped by national allegiance, and the flow of medical science is not neatly confined to discrete jurisdictions. The struggle to combat human disease and to promote health is inherently international in character and is recognized as an element of maintaining international peace and security.[2]

This observation seems to provide a good justification for encouraging data sharing among clinical researchers, yet a worrying trend has emerged whereby researchers often cite IPRs as a reason why results cannot be disseminated. This trend results in a potential conflict between the principle of sharing data and a system that supports wealth creation through protecting intellectual property.[3] Collaboration and access to information from clinical trials are essential to public health particularly because independent meta-analysis of the clinical trial reports may be necessary where there are concerns regarding the safety and efficacy of an approved drug. The importance of making clinical trial (CT) data available for independent scrutiny has been emphasised in the recent announcement by the *British Medical Journal* that with effect from January 2013 it will require a commitment by all clinical trial researchers, whether industry funded or not, "to make the relevant anonymised patient level data available on reasonable request," before results can be published in the journal.[4] Making data accessible in this manner is vital because the success of collaborative initiatives "between pharmaceutical companies, biotechnology firms and public research organisations … depends on developing strategies to manage access to proprietary knowledge and to share the benefits of discoveries from its use."[5]

The unwillingness to share data freely certainly means that some researchers consider their data proprietary "with a competitive advantage over other groups in terms of discovery and further acquisition of funds that would expand their research operations."[6] A possible reason for some researchers withholding data from their colleagues is the widespread practice of granting exclusive rights over CT data. This

[1] Tansey (2006, p. 2).

[2] Taubman (2008a, p. 526).

[3] The European Science Foundation (2009, p. 10).

[4] Godlee (2012, p. e.7304); *See also* Thomas (2012).

[5] Organisation for Economic Co-operation and Development (OECD) (2009, p. 152).

[6] Ad Carvalho et al. (2010, p. e9314).

is evident, for instance, from the pharmaceutical industry's concern that the "[d]isclosure of information about clinical trials (even without going as far as results disclosure) involves making public what industry refers to as 'the art of drug development.'"[7] The industry argues that the "[d]isclosure of such information, particularly early in the clinical trial process, may result in a loss of competitive advantage, which may deter companies from investing in drug development."[8] This argument provides a glimpse of the issues that are involved in managing IPRs over CT data. The magnitude of these issues can be appreciated by considering Gøtzsche's concern about the double standard, which the status quo creates, whereby trial participants are often willing to share data about themselves with investigators while the investigators are unwilling to share these data with trial participants and others.[9] He correctly concludes that this shows lack of respect for trial participants.

In current literature, little attention has been paid to the fact that data exclusivity may impede efforts by clinical researchers, regulatory authorities and other stakeholders to ensure benefit sharing (BS) with clinical research participants. This is essentially a public health concern, which seems to be overshadowed by preoccupation with warding off unfair competition from the generic industry. A balance thus needs to be struck between the need for data confidentiality and the need to foster academic freedom/ability to publish and disseminate research results and to promote public welfare.[10]

Pugatch has correctly observed, that the ongoing debate over data exclusivity

> seems to mark a shift from the conventional debates over patent protection and drug prices … [as it] involves both developed and developing countries, is characterized by political and economic interests, as well as by safety issues that guarantee to make it one of the more interesting as well as heated subjects in the IPR field.[11]

At a practical level, these debates have set different interests on a collision path in the field of data exclusivity. The first two main parties whose interests are at stake in CT are the pharmaceutical companies that invest in CTs in order to deliver products to end users and the communities that expect to benefit from the research. Both parties have their own legitimate expectations. The pharmaceutical companies

> demand rules and enforcement that will protect their income streams, justifying a high return on the investment as necessary to drug development … [while the] community demands rules and measures to reduce the social cost of patents, to reduce expenses for governments, businesses and individual consumers, as well as to exercise greater control over the direction of research.[12]

[7] Health Canada (2005, p. 16).

[8] Health Canada (2005, p. 16).

[9] Gøtzsche (2011, p. 249).

[10] Leibowitz and Sheckler (2006, p. 289).

[11] Pugatch (2006, p. 129).

[12] Abbott (2006, p. 36).

"Communities" in this context includes stakeholders such as researchers who expect to share information with their peers since "scientific communities thrive on collaboration, which requires sharing information."[13]

Conflicting interests also exist between the pharmaceutical companies, as data originators, and generic drug companies who would like to obtain marketing approval through regulatory authorities' reliance on data without necessarily disclosing the data to the generic companies. Conflict arises from the fact that regulatory authorities grant marketing authorization based on the provided CT data, and this makes the availability of such data a condition for obtaining marketing approval of new products, modifications or new uses of existing products.[14] The emerging practice of providing sui generis protection of CT data is therefore a real concern since, as Correa correctly observes, it implies that "the research-based pharmaceutical … industry, actively seeks to ensure a period of exclusive use of the data after marketing approval. During this period, national authorities would be prevented from *using* or *relying* upon the data for marketing approval of generic versions of the already registered products."[15] Apart from the worrying data exclusivity period, it has to be noted that the product, which is granted marketing authorization, may in most cases already be protected by a basic patent right and a supplementary protection certificate (SPC) whose validity continues to run even after the basic patent right has expired.[16] The practical consequence is that competitors cannot place their products on the market when the first entrant's product is still protected under the SPC. It would therefore make sense, for purposes of encouraging research for the benefit of public health, for the data to be made easily available since there is no risk of unfair commercial use by competitors.

The general public equally has an interest at stake because CT data confidentiality hinders the possible use of raw clinical data by other researchers for developing predictive models for orienting patients to appropriate treatments. Evidence is, for instance, available to show that the randomized controlled trials data sets have been used to develop such predictive models.[17] This would not have been possible without disclosure of raw data.

Without a proper interpretation and understanding of the scope of CT data protection under Art. 39.3 of TRIPS, public health implications are far more serious because in situations where the data generator's competitors are compelled to duplicate preclinical and/or clinical trials to develop new test data, such trials cannot meet the ethical requirements under paragraph 32 of the Declaration of Helsinki (DoH). The paragraph, which will be discussed in more detail in the second part of

[13] Lipkus et al. (2010, p. 8).

[14] Correa (2006, p. 82).

[15] Correa (2006, p. 83).

[16] *See*, for example, Art. 13 of the EU Council Regulation (EEC) No 1768/92 of 18 June 1992, which provides that the SPC "shall take effect at the end of the lawful term of the basic patent for a period equal to the period which elapsed between the date on which the application for a basic patent was lodged and the date of the first authorization to place the product on the market in the Community reduced by a period of 5 years." available at http://eur-lex.europa.eu/LexUriServ/site/en/consleg/1992/R/01992R1768-20070126-en.pdf; *see also* Moore (1998, p. 137–140); de Pastors (1995, p. 189–192).

[17] *See* Selker et al. (2011, p. 10–16); (Kent et al. (2002, p. 104–111).

this paper, requires new interventions to be tested against the best current proven interventions, except in justifiable circumstances.

Conflicts originate from the different constructions of Art. 39.3 of TRIPS. The Article provides that

> Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.

The Article does not require data exclusivity, yet there is a tendency to grant CT data exclusive protection on the basis of this Article. It should be noted that although the TRIPS Agreement is considered "the first multinational agreement ever to require … [test data] protection"[18] it is however "not a model IP law, and … its text is ill suited to be converted directly into domestic legislation …"[19] This is the case because it "is an international agreement between trading partners on what they can legitimately expect of one another as far as IP protection is concerned, and on the actions they can and cannot take when those expectations, inevitably, are significantly frustrated."[20]

Much has been written on the underlying problems with protecting CT data.[21] It may thus be akin to opening a can of worms to delve into these debates in the context of public health in this paper. Consequently, the paper does not delve into such underlying problems but aims at suggesting ways in which IPRs over CT data can be managed by collaborating researchers, technology transfer offices (TTOs) and regulatory authorities in a manner that fosters ABS in public health. The underlying concerns that arise from these debates are, however, useful for informing the management options that are proposed in this paper. For instance, most of the alternatives to data protection that have been suggested[22] ideally require the direct involvement of the stakeholders on which this paper focuses, and yet very little has been written on the role of these relevant stakeholders.

The first part of the paper discusses issues that arise when regulatory authorities rely on data submitted by originator pharmaceutical companies to approve generics and possible conflicts that may arise from such reliance. The second part deals with situations where CT data may be disclosed on public interest grounds. ABS and public health concerns that arise from protecting CT data are discussed in the third part, which lays the foundation for the discussion of how to manage these complex

[18] Pugatch (2006, p. 110).

[19] Taubman (2011, p. 12).

[20] Taubman (2011, p. 12).

[21] *See* Reichman (2009, p. 1–68); Taubman (2008b, p. 591–606).

[22] Weissman (2006, p. 151–178).

concerns in the fourth part of the paper. Some thoughts on how to move forward, particularly by including public health concerns in the debate, are provided in the concluding section of the paper.

2 Reliance on CT Data in the Abridged Approval Process

CT data can generally be defined as data resulting from clinical trials of drugs.[23] Some regulators, in a bid to provide a more comprehensive description of what CT data consists of, have suggested that it should include the full raw data set as well as data at the patient level.[24] This essentially means that CT data should consist of full clinical study reports.

Taubman provides a very useful analysis of the type of information that CT data may contain. He explains that:

> The information content of test data can be viewed (and regulated) at several levels: (i) as empirical information about the physical properties of chemical substances; (ii) as information that test data establish a substance as safe, acceptably non-toxic, sufficiently efficacious, etc.; (iii) as information that the substance is approved for use by a certain regulator on the basis of test data submitted.[25]

Taubman observes that it is easier to exclude access to information at level (i) than at levels (ii) or (iii), and that a rival product may be approved without direct reference to level (i) at all.[26] These observations are useful for the discussions on the disclosure of CT data on public interest grounds but it should be noted that the ease with which access to information at level (i) can be controlled depends on the jurisdiction in question. This is the case in so far as in some national legislation, for instance in Switzerland, there is a set of chemical data that cannot be considered as "undisclosed information."[27]

There are different views on the scope of protection that should be given to CT data.[28] These divergent views can be attributed to the fact, as Taubman observes, that TRIPS created "strong expectations of effective protection of regulatory data, but did not reconcile the differing views on the appropriate scope of protection that emerged during the TRIPS negotiations."[29] As a result of divergent practices, different countries protect regulatory data for different periods.[30] This is evident

[23] *See* Taubman (2008b, p. 591).

[24] Eichler et al. (2012, p. e1001202).

[25] Taubman (2008b, p. 591).

[26] Taubman (2008b, p. 591).

[27] I owe this useful observation to Dr Dannie Jost, Senior Research Fellow and Science Advisor, World Trade Institute, University of Bern.

[28] *See* Reichman (2006, p. 133–150).

[29] Taubman (2008b, p. 594).

[30] *See* Pugatch (2006, p. 101–110) for a detailed discussion of these approaches at the domestic and international levels. *See also* Meitinger (2005, p. 128–130).

from the following two main approaches to the regulatory approval of generics that are used in different regimes[31]:

(a) Abridged approval procedures are currently used in Argentina, Brazil, Europe, Japan, Israel and the USA. In terms of this procedure, generic companies cannot rely on the data submitted by the first applicant, but regulatory authorities rely on the data submitted by the first applicant for a similar product, provided that its physicochemical attributes are equivalent to the first applicant's;
(b) Regulatory authorities may also opt to rely on an approval, which has been granted in a foreign country.[32] Reichman argues in this regard that in terms of Art. 39.3 of TRIPS, "WTO Members have no duty to 'require … the submission of undisclosed test or other data.' If a state foregoes such a requirement – for example, by relying upon the health and safety decisions of other jurisdictions or on the published medical literature, or a combination of both – it arguably incurs no liability whatsoever under Art. 39.3."[33]

It is worth explaining the rules of reliance on the confidential information relating to CT data in some of the jurisdictions that are mentioned above, particularly in view of the fact that the WHO has stated that generic companies should not be required to repeat clinical trials since it is sufficient for regulatory authorities to rely on the safety and efficacy that has been established through the original CT data for previous marketing approvals that have been granted.[34] This position is compatible with the requirements of Art. 39.3 and the public health exceptions, which are explained in the third part of this paper.

In the USA, the Food and Drug Administration (FDA) treated CT data as confidential and did not allow generic companies to rely on such data. The FDA could not even accept applications for marketing approval without the initial registrant's permission. The rationale for this approach, which was adopted in Europe and other developed countries, was to solve the problem of duplicative clinical testing.[35] Commentators raised valid concerns that such unqualified data exclusivity was eschewed because "many drugs are not discretionary purchases, but correlate highly with the quality and even preservation of human life."[36] The situation prevailed until the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act) of 1984 led to the creation an Abbreviated New Drug Application (ANDA) process for bioequivalent products without duplicating clinical trials.[37]

The prevalent practice of granting sui generis protection of CT data warrants a consideration of how data exclusivity differs from patents in order to appreciate the magnitude of the problem. A patent is a right, which enables the holder to exclude a

[31] Correa (2006, p. 83).

[32] Correa (2006, p. 84).

[33] Reichman (2006, p. 141).

[34] Arkinstall et al. (2011, p. 16); *see also* World Health Organization (2006a).

[35] Fellmeth (2004, p. 447).

[36] Fellmeth (2004, p. 472).

[37] Baker (2008, p. 305). *See also* Federal Food, Drug, and Cosmetic Act, 21 U.S.C. Sec. 3550 (2000 & Supp. 2005).

third party from utilizing an innovation pertaining to a new medication for commercial purposes. CT data, on the other hand, contains no additional information about the medication. Technically this data is not being used by the third party; rather, it is the regulatory authority that relies on the data that it already has available from the first party to grant marketing authorization to a generic manufacturer of the same medication. As such, technically, the data is never seen by the third party, thus it is not disclosed.[38] This position of course raises the question of whether reliance on the data by a regulatory authority would constitute an unfair commercial use. Since the word "use" is not defined in Art. 39 TRIPS, member states are free to interpret reliance as use or not use. The more prevalent interpretation is that it is not use.[39] The two cases that are discussed below show that courts in Brazil and Argentina have taken this approach.

The Brazilian Law 9.279 of 1996 (Intellectual Property Law) and Act No. 10.603/2002 do not provide for data exclusivity. The latter Act only provides for data exclusivity in respect of veterinary pharmaceutical products though the original version of the Act (Provisional Decree No. 69/2002) also provided for data exclusivity in respect of human pharmaceutical products, but this category was expressly rejected by the Brazilian National Congress and consequently omitted from the final version of the Act.[40] This means that there is no legal provision for data exclusivity in human pharmaceuticals in Brazil, hence the lack of clarity that has persisted on the interpretation of Art. 39.3 TRIPS. The current requirement is that applicants for the regulatory approval of generics do not have to repeat clinical trials that were previously conducted for the innovator drug so long as the generic applicants can demonstrate pharmaceutical equivalence and/or bioavailability.[41]

Some legal commentators are, however, of the view that test data that is submitted to the Brazilian National Health Surveillance Agency (Agência Nacional De Vigilância Sanitária, hereinafter ANVISA), for marketing approval "is protected by Brazilian law and cannot be used by ANVISA or any third party for any subsequent marketing approvals whatsoever, except when previously authorized."[42] Di Blasi offers the following arguments in support of this interpretation: first, ANVISA's reliance on the test data would constitute "unfair commercial use" in so far as the registering competitor would have a low production cost. Secondly, the use of previously generated test data may pose a threat to safety and efficacy since "the formulation of generic and similar copies can actually differ … in terms of quality control of the active principle ingredients and vehicles, which can impact bioavailability" and thirdly, the protection of such data "is fundamental to the financial compensation of all investments made by the sponsor company."[43]

[38] Discussions with Dr Dannie Jost, Senior Research Fellow and Science Advisor, World Trade Institute, University of Bern.

[39] Ho (2011, p. 77).

[40] See Fischmann (2012, p. 221).

[41] Barra and Albuquerque (2011, p. 72).

[42] Di Blasi (2009, p. 35). The TRIPS Agreement has been incorporated into the Brazilian law by virtue of Decree number 1355.

[43] Di Blasi (2009, p. 34).

The above views cannot be accurate because of the very clear position as stated by Barra and Albuquerque in the preceding paragraph and the judicial opinion that was recently expressed in the famous antidepressants case, *The National Health Surveillance Agency (ANVISA) and Lundbeck,*[44] which was heard by the Federal District Court and the Superior Court of Justice.[45] The case before the courts involved the registration of generic and similar medicines based on the active ingredient escitalopram, an antidepressant. The Federal Court judge found that *ANVISA* had violated Art. 39.3 TRIPS and ordered *ANVISA* to refrain from granting registration to an unauthorized third party if they used the test results and data of the dossier sent by Lundbeck Brazil Ltda., the producer of Lexapro, a reference drug, to receive the registration for the drug. The court also ruled that "any drug registration already granted based on this dossier, in particular those obtained by companies Aché Pharmaceutical Laboratories S/A and Biosintética Pharmaceuticals Ltd., Manufacturers of similar drugs were invalid."[46]

In August 2011, the Superior Court of Justice suspended the Federal court's decision on the basis that its suspension was "subject to the existence of a manifest public interest in order to avoid harm to public order, security, health or economy."[47] As a result of the Superior Court of Justice's decision, the biotechnology industry in the USA has recommended to the United States Trade Representative that Brazil be elevated to the Priority Watch List.[48] The reason is that the industry is concerned that Brazil's lack of data protection for pharmaceuticals is inconsistent with TRIPS Art. 39.[49] The industry equally considers the decision to have been made purely on "political grounds". The Superior Court of Justice's decision certainly entailed a balancing act in respect of which socio-economic, ethical and human rights considerations were brought to bear. Such factors cannot accurately be considered as purely political in nature. The legal consideration of ethical principles in this case is commendable since the decision focused on public health implications of data exclusivity. As the court succinctly put it;

> … it is recommendable that the suspension of the decision of the first instance be granted in order to avoid the risk of weakening the national public policy concerning generic drugs, which is unquestionably valuable to the population, especially its segment with lower purchasing power.[50]

The National public policy, which is mentioned in the court's decision, is enshrined in Law 9.787 of 1999. Pursuant to the enactment of this law, which provides the legal

[44] The National Health Surveillance Agency (ANVISA) and Lundbeck case (2011).

[45] *Agência Nacional De Vigilância Sanitária – ANVISA v. Lundbeck Brasil Ltda*: Suspensão De Liminar E De Sentença No 1.425–DF (2011/0184444-8) (Superior Tribunal de Justiça). *See* Fischmann (2012, p. 220) for a commentary on this decision.

[46] Brazilian Court rejects data exclusivity, available at http://donttradeourlivesaway.wordpress.com/2011/08/24/brazilian-court-rejects-data-exclusivity/.

[47] Fischmann (2012, p. 218).

[48] These are countries that are considered to have "serious IPR deficiencies that warrant increased bilateral attention concerning the problem areas or practices." *See* Masterson (2004, p. 20). Argentina, Brazil, Canada, Chile, China, India, Indonesia, Israel, Thailand and Venezuela are currently on this list.

[49] Biotechnology Industry Organisation (2012, p. 11).

[50] Quoted in Fischmann (2012, p. 219).

framework for generic medicines, ANVISA has issued guidelines that regulate the manufacture and approval of generic medicines.[51] The clear position in terms of this legal framework is that ANVISA can rely on previously submitted CT data to approve a generic medicine that establishes pharmaceutical equivalence and/or bioavailability.

The consequences of Brazil remaining on the Priority Watch List should not, however, be underestimated because under Sec. 301 of the US Trade Act of 1974, the USTR can use its annual review process to initiate WTO dispute settlement proceedings against countries whose IPR practices are inconsistent with TRIPS or it can eliminate unilaterally granted tariff preferences or impose unilateral trade sanctions if the country in question is not a member of the WTO.[52] For example, on 30 May 2000, the US requested consultations with Argentina concerning Argentina's legal regimes governing *inter alia*, data protection in Law 24,766 and Regulation 440/98. The US in this consultation considered that Argentina fails to protect against unfair commercial use of undisclosed test or other data submitted as a requirement for market approval of pharmaceutical or agricultural chemical products.[53] The WTO's dispute settlement body (DSB) did not, however, deal with the case because on 31 May 2002 the US and Argentina notified the DSB that they had reached an agreement on all the matters.

The final decision on the merits of the case is still pending, and as such Brazil's Superior Court of Justice's decision entailed an assessment based on a balance of convenience in lifting the preliminary injunction that had been granted by the Federal court. This notwithstanding, the decision is commendable for putting socio-economic, ethical and human rights considerations before trade interests. It should also provide a clear example of the correct application of Art. 39.3 TRIPS, which does not provide for data exclusivity. The decision clarifies the practical position regarding generic companies' access to CT data. The correct position is that these companies "do not use originator's data – in fact they do not even have access to them. The regulatory body relies on the originator's data, but normally does not actually use or revisit them."[54] Timmermans correctly argues that such reliance on the data by regulatory authorities is not commercial use and that "it does not seem justified to suddenly label longstanding regulatory practices as 'unfair'."[55] This argument is also supported by the position of the World Health Organization's (WHO) Commission on Intellectual Property Rights, Innovation and Public Health. The Commission has stated that Art. 39.3 "… does not create property rights, nor a right to prevent others from relying on the data for the marketing approval of the same product by a third party, or from using the data except where unfair (dishonest) commercial practices are involved."[56] The commission's statement implies that rights over CT data, in terms of the Article, are not similar to ordinary real property rights.

The above clarifications are useful in view of the fact that the scope of the TRIPS Agreement is often misconstrued to such an extent that TRIPS-plus obligations end

[51] *See* Barra and Albuquerque (2011, p. 72) for a detailed discussion of these policies.

[52] Masterson (2004, p. 21).

[53] Argentina – Certain Measures on the Protection of Patents and Test Data (WTO Dispute DS196).

[54] Timmermans (2007, p. 0206).

[55] Timmermans (2007, p. 0207).

[56] World Health Organization (2006b, p. 124).

up being imposed on countries.[57] The aim of Art. 39.3 is to protect the undisclosed information, which is submitted for regulatory approval purposes, against "unfair commercial use."[58] For information to meet the requirements of the Article, it "must be undisclosed (as defined in para[graph] 2) and the origination of data must result from a 'considerable effort'."[59]

Paragraph 2 of the Article provides that the information shall be protected as long as such information:

> (a) is secret in the sense that it is not, as a body or in the precise configuration and assembly of its components, generally known among or readily accessible to persons within the circles that normally deal with the kind of information in question;
> (b) has commercial value because it is secret; and
> (c) has been subject to reasonable steps under the circumstances, by the person lawfully in control of the information, to keep it secret.

The protection provided by Art. 39 is an intellectual property right since Art. 1(2) TRIPS defines the term "intellectual property" to include all categories of IP that are the subject of Subsections 1–7 of Part II, and Art. 39 falls within this range. The scope and the interpretation of Art. 39.3 are, however, rather contested. Correa, for instance, argues that the protection of test data does not confer exclusive rights in terms of Art. 39.1, read together with Art. 10^{bis} of the Paris Convention for the Protection of Industrial Property but only confers "the right to take legal action against whoever has obtained commercial advantage by means of dishonest practice."[60]

Article 39.1 requires member states to protect undisclosed information against unfair competition as provided in Art. 10^{bis} of the Paris Convention[61] if the information satisfies the requirements of paragraph 2 of the Article. This interpretation is in accordance with Arts. 31 and 32 of the Vienna Convention on the Law of Treaties.[62] Consequently, the requirement for a period of exclusivity, as required and implemented by the US and the EU in free trade agreements (FTAs) signed with developing countries[63] is a TRIPS-plus measure and does not flow from Art. 39. It thus follows that the liability, which is envisaged by this Article is limited

[57] *See* the discussions of Brazilian and Argentinean cases in this paper.

[58] Abbott (2006, p. 32).

[59] Gervais (2008, p. 2.337).

[60] Correa (2006, p. 84).

[61] The Article prohibits any acts of competition that "are contrary to honest practices in industrial or commercial matters …".

[62] Article 31 of the treaty is a customary rule of interpretation of public international law, available at http://untreaty.un.org/ilc/texts/instruments/english/conventions/1_1_1969.pdf.

[63] The European Parliament, in its Resolution on the TRIPS Agreement and access to medicines (12 July 2007) called on the European Council "to restrict the Commission's mandate so as to prevent it from negotiating pharmaceutical-related TRIPS-plus provisions affecting public health and access to medicines, such as data exclusivity, patent extensions and limitation of grounds of compulsory licences, within the framework of the EPA negotiations with the ACP countries and other future bilateral and regional agreements with developing countries." Available at http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+TA+P6-TA-2007-0353+0+DOC+XML+V0//EN.

to the competitors who make commercial use of the undisclosed information or individuals who disclose the information without the data originator's authorization.[64] It is equally clear that honest governmental regulatory authorities' practices, such as relying on CT data to grant approval for a competitor's product without necessarily disclosing the data to the competitor, are excluded from the reach of this Article.[65]

A clear illustration of the exemption of governmental authorities' reliance on CT data is the case of *Novartis Pharma AG v. Monte Verde SA & Varios Propiedad industrial e intellectual*,[66] which shed light on the prevailing obscure interpretation of Art. 39.3 TRIPS. The court had to consider whether Argentine Law No. 24,766 (the Confidentiality Act) that regulates the protection of test data does not offer effective data protection thus making it inconsistent with Art. 39.3 TRIPS. Article 5 of the Confidentiality Act and Arts. 3 and 4 of Executive Order No. 150/92 provide for an abridged approval of similar medicines that are already registered in selected countries or in Argentina. The effect of this approval process is that an applicant does not need to conduct its own trials and to submit test data for medicine that was previously approved and already registered.

Novartis filed this case in which it requested the court to order its competitor, Monte Verde, to stop using confidential information related to any product containing the active principle imatinib mesilate. Monte Verde had requested and obtained marketing approval in Argentina for its Leucimat pharmaceutical product, which also contained imatinib mesilate. Novartis requested the court to rule that test data submitted abroad for the approval of an original pharmaceutical product be protected in Argentina in accordance with Art. 39.3 TRIPS. It further asked the court to stop the use of submitted information in the approval of competitors' products and to declare that the clauses of the law and of the ruling decree that support the abridged approval process are unconstitutional because they are contrary to the National Constitution and the TRIPS Agreement.

Novartis relied on the following arguments to support its case:

(i) It had undertaken research (pre-clinical and clinical studies) and invested funds in order to obtain marketing approval for its Glivec product in the US and Europe;
(ii) The confidential information that it had obtained is protected under Art. 39.3 TRIPs; and
(iii) Although Glivec is not patented in Argentina, Arts. 14 and 17 of the Argentine Constitution protect Novartis' property rights, and Art. 39.3 TRIPS also protects such data against unfair competition carried out through disclosure or unfair commercial use.

In dealing with Novartis' case, the court noted that Novartis had previously obtained marketing approval for several original pharmaceutical products in Argentina based on the same rules that establish the abridged registration procedure

[64] *See* Cottier and Meitinger (2000, p. 57); Meitinger (2005, p. 126–127).

[65] Cottier and Meitinger (2000, p. 57).

[66] Sala III, Camara Nacional de Apelaciones en lo Civil y Comercial Federal (Division III of the Federal Civil and Commercial Court of Appeals in Argentina), Case No. 5.619/05 (decided on 1 February 2011).

to which it objected on this occasion. Secondly, the court held that a strict requirement that every company must perform its own trials of active principles already researched and authorized would obstruct public access to pharmaceutical products, which is an essential aspect of the right to health, and would make such products more expensive, mainly in those countries that have adopted the generic-drug policy. Thirdly, the court stated that Art. 39.3 TRIPS can be implemented by member states either through the rules on unfair competition, in which case marketing approval in favor of a third party based on the similarity registration process does not entail non-compliance with Argentina's obligation to protect data from unfair commercial use; or through a system of exclusive rights on the undisclosed data during a specific term, which does not exist in Argentina.

The court considered Novartis' arguments and confirmed the court of first instance's decision, which had rejected Novartis' complaint. Some of the court's findings are worth highlighting here because they strengthen the arguments that are advanced in this paper to support easy access to CT data. The court noted that Novartis did not prove that the data, which was relied on for the approval of Monte Verde's product had been submitted or filed by Monte Verde. As such a case of unfair commercial use was not established by Novartis. The court also concluded that the approval of "similar products" does not imply, by itself, non-compliance with the guaranty assumed by Argentina to protect the unfair commercial use of the data in question.[67] This decision shows the laudable manner in which the court balanced all the competing interests that were at stake in the application before it.

3 Disclosure of CT Data on Grounds of Public Interest

The disclosure of CT data by regulatory authorities may be viewed as problematic, but such disclosure can be justified on public interest and ethical grounds. The need to disclose CT data is evident from the manner in which the release of previously unpublished details of test data has radically changed public knowledge of the safety and efficacy of drugs.[68] This shows the extent to which confidentiality hinders health research. The experience in Tamiflu also confirms that the limited information that is usually reported in biomedical journals is inadequate, and access to study reports is necessary.[69] This is the case because such reports represent a complete synthesis of planning and execution results of a clinical trial. Independent researchers from the Cochrane group only gained access to additional clinical study reports for Tamiflu through a freedom of information request to the European Medicines Agency (EMA).

An independent critical analysis of the clinical study reports revealed *inter alia* that serious adverse events that occurred in the trials were not reported in the published papers, and the manufacturer's (Roche's) claim of Tamiflu's mode of action was inconsistent with evidence from the trials.[70] These revelations confirm

[67] *See* Otamendi (2011).

[68] Doshi et al. (2012, p. e1001201), *see* Table 1.

[69] Doshi et al. (2012, p. e1001201).

[70] Doshi et al. (2012, p. e1001201), box 1.

the fact that confidentiality in CT data perpetrates bias in reporting the outcome from clinical trials such that other independent researchers are deprived of the opportunity of verifying the claims made by CT data owners. Selective reporting also makes it difficult for doctors to choose the best treatments for their patients.[71]

In view of the fact that Art. 39.3 TRIPS does not confer exclusive rights on CT data, Reichman argues that a state "remains free to make noncommercial uses of the data and to make other uses of them that are 'fair', even if such uses produce a commercial impact. For example, governmental use to avoid health or safety risks revealed by the data in the local environment [is] fair by definition."[72] He equally argues that "the promotion of research and science in the public interest would presumably allow some uses of the data that would be both non-commercial and fair, consistent with any research exemption embodied in the domestic patent laws."[73] It is also worth noting that disclosure to the data originator's non-competitors such as a public interest organisation, a university or a hospital to enable them to "review and verify the accuracy, reliability, and completeness of the data" is acceptable within these exceptions.[74]

WTO member states, however, need to beware of incurring liability as a result of TRIPS-plus obligations that they have contracted through FTAs. In practice, some clinical researchers also tend to relinquish their entitlements, to rely on their domestic laws, by signing clinical trial agreements in terms of which they agree to be governed by the laws of their foreign sponsors rather than their domestic laws. In such cases, if the sponsor's laws confer exclusive rights over CT data, then Reichman's arguments may not be of much help to such member states or clinical researchers who are bound by the contracted TRIPS-plus obligations. Such obligations can give rise to serious ethical issues. For instance, is it ethical to duplicate clinical trials using a placebo or lower standards while "the best current proven intervention" as required by paragraph 32 of the Declaration of Helsinki (DOH) exists, but such best intervention is the subject of exclusive rights that cannot be availed to the competitors?

For purposes of putting the discussion of the ethical implications in context, a brief explanation of the status of the DOH suffices here. The DOH provides widely accepted ethical guidance, and some of its sections have been incorporated in other international and national instruments, guidelines, laws and regulations relating to research on human participants.[75] The general understanding is that ethics guidelines are not legally binding, but it should be noted that such guidelines are regarded in current legal literature as customary international law.[76] An ethics guideline must be supported by the consistency and generality of a practice to

[71] Gøtzsche (2011, p. 249).

[72] Reichman (2009, p. 19).

[73] Reichman (2006, p. 141).

[74] Arkinstall et al. (2011, p. 464).

[75] Human and Fluss "The World Medical Association's Declaration of Helsinki: Historical and Contemporary Perspectives", available at http://www.wma.net/en/20activities/10ethics/10helsinki/draft_historical_contemporary_perspectives.pdf.

[76] Andanda et al. (2013).

qualify as customary international law.[77] Some general and consistent state practices can be gleaned in the government funding of national and international clinical trials[78] that are required to comply with ethics guidelines, particularly the DOH.

Paragraph 32 of the DOH provides as follows:

> The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:
> – The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
> – Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.[79]

Correa therefore correctly concludes that "when test data for an approved drug already exists, repeating tests with placebo or otherwise creating risks for patients is clearly unethical and would be unacceptable under many health regulations."[80] For instance, an ethics review committee is unlikely to approve a protocol that is submitted by a generic company seeking to use a placebo while an effective medication is withheld purely for commercial reasons. In this regard Timmermans correctly concludes that withholding CT data "renders it de facto impossible for generic companies to repeat clinical trials."[81]

Concerns about the ethical implications of CT data protection have led to calls on patients, in their capacity as those who contribute most to the success of clinical research and also stand to benefit from successful drug development, to sign consent documents only if such documents commit pharmaceutical companies to making CT data widely available.[82] The ethical basis for this call is that failure to share data creates an incomplete knowledge base, which leads to redundant research that is unethical and renders participants' informed consent illusionary as patients and their doctors can only access biased information.[83] In this regard, Chalmers and Glasziou have suggested that new research should only be initiated if the question proposed to be addressed cannot be answered satisfactorily with existing evidence.[84] This suggestion is in line with paragraph 32 of the DOH, which requires new interventions to be tested against the best current proven intervention.

[77] Brownlie (2003, p. 7).

[78] Fidler (2001, p. 326).

[79] World Medical Association (2008).

[80] Correa (2006, p. 93).

[81] Timmermans (2007, p. 207).

[82] Editorial Nature Biotechnology (2012).

[83] Gøtzsche (2011, p. 249).

[84] Chalmers and Glasziou (2009, p. 86–89).

The consequences of linking research participants' consent to the pharmaceutical companies' commitment to share CT data cannot be underestimated since such resembles the move that the Indonesian government made when it withheld samples of avian influenza virus A (H5N1) from the WHO in 2007. This led to a crisis in global health because the WHO collects virus samples for distribution to pharmaceutical research units for the development of vaccines that target specific strains of H5N1. Indonesia's action was prompted by a breakdown in mutual trust as a result of the WHO's acknowledgment that patents had been obtained on modified versions of H5N1 samples shared through the Global Influenza Surveillance Network without the consent of the countries that supplied the samples.[85] Indonesia was among the contributing countries and the Indonesian Health Minister's concern was that even though Indonesian samples were crucial to the development of vaccines, the results would be unaffordable to its citizens.[86] After negotiations, the Indonesian government resumed contributing samples. It is worth noting that following this incident; the World Health Assembly's Resolution 60.28 stressed "the need for effective and transparent international mechanisms aimed at ensuring fair and equitable sharing of benefits, including access to, and distribution of, affordable diagnostics and treatments, including vaccines."[87] This incident raised a BS issue and it is commendable that it was resolved by recognizing the need for fairness by sharing benefits from research with countries that contribute vital resources for vaccine research. This strengthens the argument for including the ethical principle of BS in the debates over the protection of CT data as well.

Countries are free to make suitable rules to govern disclosure of data. The rules governing the disclosure of CT data in Japan provide an example in this regard. The rules can be glimpsed through the case of *Yakugai Ombudsperson Kaigi v. Ministry of Health, Labour and Welfare of Japan*.[88] The case specifically dealt with a request by third parties (groups representing patients suffering from side effects of drugs) for the disclosure of clinical study reports, which had been submitted to the Ministry by AstraZeneca KK (AZ) for marketing approval. In January 2002, AZ submitted a new application to the Ministry of Health, Labour and Welfare (MHLW) for the approval of the importation and marketing of a new drug for lung cancer called Iressa. The application was submitted together with non-clinical and clinical study reports, which had been prepared by AZ's parent company, AstraZeneca PLC. The application was approved under priority review process in July 2002 and AZ specified interstitial pneumonia as a serious side effect in the package insert of Iressa. Since the launch of the drug in July 2002, interstitial lung disease (ILD) and interstitial pneumonia occurred as side effects in many patients who were taking it. AZ also reported 26 cases of ILD to the Ministry of Health, Labour and Welfare of Japan (MHLW) whereupon, on MHLW's instructions, AZ sent a letter to doctors containing a warning about ILD and also included the additional warning on Iressa's

[85] For more details on this case, *see* Sedyaningsih et al. (2008, p. 482–488); Fidler (2008, p. 88–94).

[86] Caplan and Curry (2007, p. 1–2); *see also* Walsh (2007).

[87] World Health Assembly (2007, p. 1–3).

[88] Decision of the Tokyo High Court on 16 November 2007; *see* the translation and report by Fujimoto (2010, p. 616–619).

package insert. By December 2002, 358 ILD cases including 104 deaths were reported to MHLW by AZ.

The above adverse events prompted the third parties (plaintiffs) on 4 April 2003 to request MHLW "to disclose documents that contain information on cases of death in Iressa's Phase I and Phase II clinical trials."[89] MHLW disclosed the side-effect reports on 3 June 2003 after deleting patients' personal information but refused to disclose the clinical study reports on the basis that such disclosure "was likely to cause harm to the competitive position of AZ."[90] The clinical study reports in question contained methods of the clinical trials, results, evaluations, conclusions, references and appendices. The plaintiffs were aggrieved by MHLW's refusal to disclose the information and applied to the Tokyo District Court, requesting disclosure of the reports under the Act on Access to Information held by Administrative Organs (AAI). Under Sec. 5 of the AAI, an administrative organ can disclose information that it holds subject to the following exemptions, which are relevant for the purposes of this paper:

> … information concerning legal entities is exempted from the general rule of disclosure when the disclosure is likely to cause harm to the rights, competitive position, or other legitimate interests of the legal entities ... "information which is found necessary to be disclosed in order to protect a person's life, health, livelihood, or property" shall be disclosed even though disclosure of the information is likely to cause harm to the rights, competitive position, or other legitimate interests of the legal entities.[91]

On the basis of this Section, the district court decided against the disclosure of the clinical study reports and the plaintiffs appealed to the Tokyo High Court.

The decision of the high court focused on the issue whether the clinical study reports, which the plaintiffs requested contained information about the reasons for the medical doctors' evaluation regarding the causal relationship between Iressa and the adverse effects on the lungs. The court was of the view that for information to be disclosed by an administrative organ in terms of the exemption under Sec. 5(ii) of the AAI, "there must exist a clear and direct relationship between the disclosure of the information and the protection of a person's life or health."[92] Though the court considered the information contained in the clinical study reports to concern a person's life or health, it concluded that the plaintiffs in this case had failed to prove that the reports contained information about the doctors' evaluation of the causal relationship between Iressa and the adverse effects on the lungs. The court, therefore, decided that the disclosure of the reports would not change the total assessment of Iressa since AZ had already sent a letter to the doctors with the warning of ILD and included a warning in the package insert, which could enable patients to determine whether or not to take Iressa. On the basis of this reasoning, the court refused to grant the request for the disclosure of the reports.

[89] Fujimoto (2010, p. 617).

[90] Fujimoto (2010, p. 616–619).

[91] *See* Sect. 5 exemption (ii)(a).

[92] Fujimoto (2010, p. 618).

The court's decision in Iressa seems to have been made on technical grounds taking into consideration the nature of the plaintiffs' request. The plaintiffs were clearly non-competitors of AZ; they can be described as a public interest group and the only attribute that they were lacking in order to enjoy the public health exceptions under Art. 39.3 was to demonstrate that they needed to review and verify the data as contained in the reports. Although the court's decision cannot be faulted in view of this technicality, concerns ought to be raised concerning the manner in which the court seemed to be preoccupied with warding off generic companies instead of protecting public health. This preoccupation was based on the fact that the Japanese Pharmaceutical Affairs Act does not require generic companies to submit any self performed clinical study reports.[93] The decision illustrates the existence of broad views regarding the status of CT data in the current debates. Two views are worth highlighting here:

- Protecting CT data represents "an attempt to create pragmatic mechanisms for financing specific public goods to respond to the market failure represented by reluctance to develop such data, to share it with regulators and other public interest users, and ultimately to bring new products to the market."[94]
- "The drive to protect clinical trial data internationally is but the latest and most far-reaching consequence of the deep structural problems that flow from the failure to treat clinical trials as a national and international public good."[95]

What seems common in the two approaches is the recognition of the public-good nature of clinical trials, which is an appropriate starting point, particularly for arguing in favor of data sharing on the basis of the ethical principle of BS, which is discussed in the next section of this paper.

Reichman observes that "the demand for global protection of clinical test results arises from the underlying concerns about free riding on private-sector research & development (R&D) investments."[96] Such underlying concerns are, for instance, evident in Taubman's argument that "the absence of protection would create a manifest free rider problem with deleterious impact on the public interest."[97] The notion that there is an economic logic for protecting CT data lies at the centre of these observations. However, the economic logic of protecting CT data is not easily justifiable. For instance, Reichman notes that the estimated cost of US $800 million to US $1 billion per approved drug[98] "may be disputed at the margins, [as] it necessarily includes the cumulative high costs of clinical trials incurred for many drugs that fail to win approval."[99] Most importantly, it has been established that pharmaceutical companies in the USA have not been transparent enough to open

[93] Fujimoto (2010, p. 618).

[94] Taubman (2008b, p. 596).

[95] Reichman (2006, p. 134).

[96] Reichman (2006, p. 134).

[97] Taubman (2008b, p. 596).

[98] *See* DiMasi et al. (2003, p. 151–185). It has been argued that the report is based on proprietary and unverifiable data [*see* Ho (2011, p. 267)].

[99] Reichman (2006, p. 133).

their books to independent public inspection to prove these R&D costs.[100] An equally relevant observation is the fact that the same estimated costs are usually relied on by the pharmaceutical industry to argue in favor of patent protection. It can therefore be concluded that the recovery of these costs is catered for through patent protection.[101]

The concept of free riding seems more relevant to commercial competitors. The limited scope of this concept warrants two points of clarification: First, as has already been established in the preceding part of this paper, reliance on the submitted data by regulatory authorities to grant marketing authorization to competitors does not amount to free riding by such authorities. Secondly, independent researchers who are interested in conducting a meta-analysis of the data for safety and efficacy studies cannot be classified as free riders. It follows that the justification for data exclusivity is focused on warding off free riding without much attention to these two points and such exclusivity can have negative public health implications.

Clinical research warrants careful attention due to the important role that it plays in public health. The use of human volunteers as participants and researchers' dependence on the results to inform medical decisions imply that clinical research is very important for public health.[102] Clinical research is also important for measuring and obtaining information about the safety and data necessary for seeking marketing approval of drugs and devices.[103] The following two reasons have been given in literature to support broader disclosure and dissemination of data:

> Trial participation by humans is predicated on the concept that the trial will add to "medical knowledge," which requires dissemination of the results. In addition, it is not possible for a volunteer or an IRB [institutional review board] to assess the risks and benefits of participation in a clinical trial if an unknown proportion of data on the proposed interventions is not publicly available.[104]

The two reasons justify the need to make CT data easily accessible to the public. In fact, heads of the Dutch, French and UK regulatory authorities as well as the European Medicines Agency (EMA) have recently made a statement suggesting that CT data should not be considered commercially confidential information.[105] Their suggestion is based on the fact that non-disclosure of complete trial results undermines the clinical trial participants' philanthropy insofar as most of them agree to participate with a view to contributing to medical knowledge.

[100] Light and Lexchin (2005, p. 959).

[101] Ho (2011, p. 264).

[102] Zarin and Tse (2008, p. 1340–1342).

[103] Leibowitz and Sheckler (2006, p. 289).

[104] Zarin and Tse (2008, p. 1342).

[105] Editorial Nature Biotechnology (2012).

4 ABS and Public Health Concerns

Data exclusivity has two consequences on public health. First, unless an abridged approval process is used, generic drug companies cannot obtain marketing approval for generic drugs on the basis of the protected CT data during the period of exclusivity.[106] Secondly, compulsory licensees may also be precluded from getting their products approved during the data exclusivity period.[107] Meitinger, however, argues that a compulsory licence for a patent under paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health should be treated differently and not be required to provide test data for a product that has already been approved before.[108] The two consequences essentially mean that generic drug companies and compulsory licensees are compelled to duplicate clinical trials in order to produce their own test data. The duplication of preclinical and/or clinical trials to develop anew the test data necessary for regulatory approval of a drug also raises ethical concerns.[109]

The intricate nature of the debates over data exclusivity warrants a consideration of ethical principles in attempting to establish strategies for managing IPRs over CT data. It is in this regard that this paper calls for the inclusion of the novel ethical principle of benefit sharing (BS) in the ongoing debates as a way of giving public health concerns the importance that they deserve. ABS has so far been debated in the fields of biodiversity and most recently in the human genome contexts. BS is a mechanism that can be used to counter the possibility of exploiting research participants since it means the "… provision of benefits to those who may lack reasonable access to resulting products and services."[110] ABS should be relevant to both industry-sponsored trials and public funded trials. This broad application of ABS is justified on the basis that the public is always a partner in both types of trials in the sense that it contributes trial participants and infrastructure that is needed for research.[111]

There are two other relevant arguments for supporting BS in the context of clinical research, which are worth noting for the purposes of the discussion in this part of the paper. First, BS should be viewed as a "compensatory activity, geared towards those who have taken risks and accepted the possible inconveniences that are necessary for research to take place and possibly succeed."[112] This argument is plausible and can be used as a basis for supporting BS with research participants. It equally supports the view that participants and the society at large that they represent should be the owners of the CT data.[113] The second argument, which is based on the principle of solidarity, views BS "as a social- and/or global-justice

[106] Correa (2006, p. 89).

[107] Correa (2006, p. 91).

[108] Meitinger (2005, p. 137).

[109] Correa (2006, p. 93).

[110] Schroeder (2007, p. 207).

[111] Gøtzsche (2011, p. 249).

[112] Simm (2007, p. 496).

[113] Gøtzsche (2011, p. 249).

concern … [that] defines the way in which access to research results is provided or denied to everyone else."[114] This argument can be used for urging BS in a broader context by including other parties such as collaborating researchers and the public at large as beneficiaries.

The rationale of extending the concept of ABS to clinical research may be questioned in view of the widespread belief that "people participate in the research process out of 'altruism' …"[115] However, there is evidence that

> a growing number of bioethicists, policy-makers, legal scholars, patient groups, and other critically involved parties have recently, and vociferously, started calling for [the use of BS as] … a new ethical principle to supplant the long-reigning notion of altruism, and to supplement the key tool in the bioethical toolbox, informed consent.[116]

Most importantly, the concept of ABS has recently found its way into the clinical research context through the World Medical Association's (WMA) Declaration of Helsinki (the Declaration), which requires the provision of post-study access as a form of benefit sharing.

Paragraph 30 of the earlier version of the Declaration (2000) provided that "at the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study."[117] The paragraph was limited to patients and implied that clinical trial participants were the only ones who were entitled to benefit from post-trial access to the developed products. In 2004 the following note of clarification was added to the Declaration:

> The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care.[118]

This note of clarification added the phrase "access to other appropriate care" and changed the term "patients" to "study participants", which means that the scope of benefits is extensive, and healthy volunteers can also benefit from post-trial access.

The 2008 version of the Declaration changed the concept from "post-trial obligation" to "post-study obligation" and introduced two additional paragraphs, 14 and 33, which relate to BS and are relevant for the discussion in this paper. Paragraph 14 states that "the protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits." This paragraph essentially expanded the scope of beneficiaries to other volunteers who may not directly be involved in

[114] Simm (2007, p. 496).

[115] Hayden (2007, p. 730).

[116] Hayden (2007, p. 731).

[117] World Medical Association (2000).

[118] World Medical Association (2004).

the clinical trials, which can include pre-clinical or epidemiological research participants as well.

Paragraph 33 stipulates that:

> At the conclusion of the study, patients entered into the study are entitled to be informed of the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.

The most interesting aspect of this paragraph, which is relevant for the discussion in this paper, is the requirement to inform the participants regarding the study outcome. Such information conventionally takes the form of either positive or negative outcome of the study. Paragraph 33 can be used to argue in favour of the "public-goods" nature of CT data insofar as the participants are entitled to be informed of some of the contents that might be undisclosed if data exclusivity is recognized by regulatory authorities. Such contents can for instance relate to safety, efficacy and approval status of the substance that is being tested. Consequently, failure to disclose less-favorable results and adverse effects amount to exploiting participants for commercial or career gains.[119] Failure to publish relevant research results promptly and lack of public access to full results have in fact been identified as causes of avoidable waste in the production and reporting of research evidence.[120]

The Declaration also recognizes the publication of research results as an ethical obligation. Paragraph 30 provides that:

> Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty *to make publicly available the results of their research on human subjects* and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication … [emphasis added]

Authors, in this context, include clinical researchers who are obliged to ensure the publication of the research results, which may be included in the protected CT data. In this regard, clinical researchers have a very important role in fostering ABS by making the results publicly available as required by paragraph 30 of the Declaration.

Part of managing IPRs over CT data would thus require such researchers to ensure that for the benefit of clinical research participants, they reserve the right to publish the findings from the research expeditiously and share data with their peers. The prevailing practice of pharmaceutical industry sponsors demanding the right to review proposed publications in order to ensure that prospects of obtaining IPRs are not prejudiced by the publications has been established, in current literature, to be

[119] Gøtzsche (2011, p. 249).

[120] Chalmers and Glasziou (2009, p. 87).

impractical because there is rarely information that can compromise commercial interests.[121] This approach is bound to raise some tension when dealing with pharmaceutical companies in view of some authors' recommendation to these companies to "refrain from undertaking any actions that could result in the disclosure of data, for example, through publication of the data in an academic journal."[122] The emerging tensions may need to be managed by balancing ethical obligations to research participants and collaborating researchers who are entitled to access the information with the commercial interests of pharmaceutical companies. In this regard, ethical obligations ought to take first priority in the interest of public health. Article 39.3 TRIPS in fact contains two exceptions that can be used in this balancing act. In terms of these exceptions, the information can be disclosed "where necessary to protect the public, or [where] steps are taken to ensure that the data are protected against unfair commercial use." This Article can be relied on to extend the regulatory authorities' obligation to disclose information in order to ensure, as was suggested by the British House of Commons Health Committee, that society's obligations towards participants in trials and all other patients take precedence over commercial interests.[123]

Admittedly, there is no agreement on what constitutes unfair commercial use of test data but Correa provides very useful examples that can be used in the above balancing act. He states that unfair commercial use "may include competitor's misrepresentation, fraud threats, defamation, disparagement, enticement of employees, betrayal of confidential information [or] commercial bribery ..."[124] These examples can help authors in making decisions on the publication of clinical trial results and guide regulatory authorities on sharing information that may have public health relevance.

As the expectations, which have been discussed in the first part of this paper, play out in the field of clinical research, they shift the spotlight to the need to manage IPRs over CT data with a view to meeting the parties' legitimate expectations. A starting point for discussing the management of IPRs would be to consider Gibson's argument that "in order to deliver the right to health, not only must the possible limitations on access to products be addressed, but also the influences and factors relevant to the innovation process itself."[125]

Notably, IPRs play an important role in the innovation process. For instance, Gibson argues that "access is not necessarily restricted by the intellectual property framework itself … [since] arguably the patent system provides for access in industries where the same knowledge would otherwise be protected by trade

[121] Chan et al. (2004, p. 2457–2465).

[122] Lemmens and Telfer (2012, p. 82). The authors do however acknowledge the importance of a system of transparency of data "for the promotion of evidence-informed medicine and the protection of public health." *See* p. 89.

[123] House of Commons Health Committee. The influence of the pharmaceutical industry. Fourth Report of Session 2004 available at http://www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/42.pdf.

[124] Correa (2002, p. 41).

[125] Gibson (2009, p. 142).

secrets."[126] This argument is reinforced by Taubman's observation that the "IP system itself is intended to be one means of producing public goods."[127] He defines a public good as "a technical economic concept, referring to goods that are not used up when anyone benefits from them ('non-rivalrous') and that no-one can be prevented from enjoying ('non-excludable')."[128] In view of this consideration, the move to collocate "clinical test data within the provisions regulating unfair competition"[129] under Art. 39.3 TRIPS may be questioned. The collocation essentially provides separate and additional protection to CT data, as undisclosed information, while there may already be underlying patent protection for the product being tested. This position is confirmed in the prevalent practice in some FTAs in terms of which exclusive rights over test data "operates, in some cases, like a substitute for the patent protection, thereby removing from public domain products that should be freely available."[130] Reichman mentions a very valid concern regarding the above collocation insofar as it implies that "the pharmaceutical industry has quietly but successfully pursued this alternative intellectual property right in the results of clinical trials, independent of and cumulative with the patent rights that everyone takes for granted."[131]

5 Managing Intellectual Property Rights Over Clinical Trial Data

Intellectual property management has been identified as an important tool that can be used by research consortia for maximizing the chances of translating research findings into vital products such as diagnostics, pharmaceuticals and vaccines for public health benefit.[132] Managing IP issues calls for maintaining a delicate balance between protecting commercial interests and promoting public health, which requires the delivery of safe and effective products to the public. The balance is important in view of the debates over the nature of IP protection, which should be accorded to CT data under international and national legal frameworks.

The fact that TRIPS as an international standard setting instrument does not confer exclusive rights over CT data but leaves member states free to manage these issues essentially means that there is space for considering other management strategies for IPRs over such data. The second basis for making free decisions over the management of CT data should be Art. 7 TRIPS, which provides that

> the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation into the transfer and dissemination of technology, to the mutual advantage of producers and users

[126] Gibson (2009, p. 142).

[127] Taubman (2011, p. 165).

[128] Taubman (2011, p. 165).

[129] Reichman (2009, p. 19).

[130] Correa (2006, p. 95).

[131] Reichman (2009, p. 6).

[132] Chokshi et al. (2006, p. 383).

of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations.

The decision of the Brazilian Superior Court of Justice in *National Health Surveillance Agency (ANVISA) and Lundbeck* and the Argentinean Commercial Court of Appeals decision in *Novartis Pharma AG v. Monte Verde SA & Varios Propiedad industrial e intellectual*, which have been discussed in this paper, illustrate how the rights and obligations of parties ought to be balanced in practice.

The management of IPRs over CT data is viewed in this paper in a more practical manner by including the ethical principle of BS. This approach is in line with the nature of such data as "public goods" and such public goods, as Taubman correctly argues, "are not achieved through theoretical legal debate or even the formulation of binding international law. They are ultimately practical concerns, a consequence of the accumulated impact of numerous discrete choices and practical steps."[133] Taubman further observes that "much controversy and analysis of these issues and the formal legal options available to governments occur downstream and in international or bilateral contexts, often at a [distance removed] from the core context of the practice of regulation."[134]

The above observation and argument are helpful for locating the correct level at which the management strategies that are proposed in this paper should be implemented. Taubman and Reichman in fact provide a solid basis on which it is argued in this paper that research consortia, regulatory authorities and technology transfer offices (TTOs) can adopt strategies that can foster the expeditious publication of results from clinical research thus sharing scientific information with peers and other stakeholders. Regulatory authorities can in turn rely on such scientific information for the approval of registration of products by competitors, based on the published information. This approach can also address safety and ABS concerns since the information would be available to other researchers who can replicate it and expedite the approval process for new products without having to contend with the intricate data exclusivity debates.

The concern, which has been raised by Lemmens and Telfer, that "regulators of smaller countries with limited resources for drug approval may find it difficult to conduct a serious investigation in the source of the data when a generic drug company submits these to support an application"[135] can equally be addressed through this approach since the authorities would be relying on published scientific information as opposed to relying exclusively on test data submitted by an originator whose authenticity may be difficult to verify.

Attempts to create clinical trial databases, which could deal with concerns relating to data exclusivity have yet to yield tangible results as these attempts still face resistance on the basis that "posting results on unapproved compounds or new applications of marketed products could erode intellectual property protections."[136]

[133] Taubman (2011, p. 169).

[134] Taubman (2008b, p. 595).

[135] Lemmens and Telfer (2012, p. 35).

[136] Fisher (2006, p. 181).

This is the position notwithstanding the recognition of the fact that "timely and transparent reporting of clinical trials results is essential to effective healthcare decision-making and public confidence."[137]

In situations where significant progress has been made towards disclosure of clinical trial information, some sectors of the pharmaceutical industry, particularly in Canada, have committed to disclosing "results of exploratory trials where results are deemed to have significant medical importance or impact on labeling."[138] Such limited disclosure is based on "[t]he argument … that if a product does not go to market, it does not affect health care decisions."[139] The argument is not plausible because the disclosure of such information is not only required for health care decisions but influences the conducting of clinical trials such that non-disclosure leads to the duplication of clinical trials with a view to establishing anew the undisclosed information. As already pointed out, the duplication of clinical trials raises ethical concerns. The publication of such information is equally an ethical obligation under paragraph 30 of the Declaration of Helsinki.

A number of suggestions have been given in literature on how IPRs over CT data can be managed for public health benefits. These are explained in this paper in terms of current trends/approaches and forward-looking strategies.

5.1 Current Trends and Approaches

5.1.1 It is Important to Draw a Distinction Between the Data Itself and the Health and Safety Outcome to which the Data Lead

Reichman for instance argues that

> governments that merely cross-reference the conclusions reached on the basis of data submitted elsewhere, or that allow competitive production of bioequivalent products for local consumption once marketing approval has been granted, will arguably not have committed any actionable "unfair commercial use" of regulatory data submitted by any firm, domestic or foreign within the purview of Art. 39.3. In such cases, it is not the confidential data themselves that are being unfairly used, even if a first comer is compelled to submit them in order to meet health and safety requirements. It is the health and safety outcome to which the data lead that is being used (a matter of public record ...).[140]

The argument is in line with the WHO's statement that generic companies should not be required to repeat clinical trials.

[137] Fisher (2006, p. 181).

[138] Health Canada (2005, p. 21).

[139] Health Canada (2005, p. 21).

[140] Reichman (2006, p. 142).

5.1.2 Cost-Sharing Approach

This approach has been proposed as a solution to free riding. Reichman suggests that this should be "built around the 'take and pay' liability rules for value-adding uses of innovation …"[141] He argues that

> if this approach were applied to clinical trials, it would at the very least allow governments and third parties to rely upon both test data and positive regulatory outcomes for authorizing the marketing of equivalent or competing products otherwise permitted under international intellectual property law, provided that the second comers paid a reasonable royalty to the data originators to help defray their costs of R&D.[142]

This approach is equally supported by Weissman who argues that the payable amount by the competitors "is based on the actual cost of generating the data and the proportionate global market share obtained by the generic competitor."[143] The approach seems to be based on speculation, which raises a fundamental question: what happens in the event that no subsequent generic enters the market? The consequence would be that the first entrant bears all costs of generating the CT data. The argument in the cost sharing approach does not equally make sense in view of the fact that the first entrant's product will most likely be sold at premium prices, unlike the generic and consequently, the first entrant is already compensated for its expenditures through higher margins. It is equally relevant to consider whether the pharmaceutical industry would be transparent enough to disclose actual R&D costs to be utilized for calculating the payable cost by competitors. The answer to this issue is no in view of the observation that this approach is supported mostly by public health advocates but is not popular with the pharmaceutical industry.[144]

Notably, Reichman and Weissman's suggestions essentially address concerns about free riders, which were mentioned earlier. The suggestions can however be contested on the basis that clinical research data have a public good character, coupled with the fact that the exact costs of R&D that are incurred in generating such data has not been established with precision. Pugatch has attempted to offer an explanation that could be used to counter these contentious arguments by observing that "even if there is no academic consensus about the accurate costs of pharmaceutical R&D, clearly the process of developing and testing a new pharmaceutical product, including clinical trials, requires major financial resources and time."[145] The observation is, however, skewed towards favoring the pharmaceutical industry's commercial interests without adequate public health considerations. For instance, the argument that risks encountered by others in generating data be taken into consideration[146] seems not to feature in this observation. A

[141] *See* Reichman (2006, p. 145).

[142] *See* Reichman (2006, p. 145).

[143] Weissman (2006, p. 155).

[144] Ho (2011, p. 270).

[145] Pugatch (2006, p. 116).

[146] *See* Cottier and Meitinger (2000, p. 63).

consideration of such risks would entail the inclusion of research participants' efforts thereby limiting the data generators' exclusivity claims. The precise argument by proponents of cost sharing, that if a WTO member provides for a compensation system, then it must be adequate and fair[147] seems misplaced when risks are considered in a broader sense, which includes risks encountered by research participants. This is the case because it is practically difficult for WTO members to ensure adequacy and fairness vis-à-vis the risks encountered by clinical trial participants in consenting to participation and the public in contributing its infrastructure.

So far, the approach of cost sharing has been tested in agricultural chemical registration in the USA[148] and the European Community[149] but such chemicals differ significantly from the CT data context. The contribution of research participants to the generation of CT data cannot certainly be adequately factored into the actual costs that the approach relies on in advocating this TRIPS-plus strategy.

A second suggestion by Reichman is to treat clinical trials as a public good. He argues that

> if clinical trials were properly viewed and treated as a global public good, it would still be necessary for governments around the world who participated in such a scheme to contribute a fair share to the aggregate costs of clinical trials, adjusted for the relative capacities to pay and to per capita gross domestic product (GDP).[150]

The concern mentioned already, relating to the inability to practically assess the value of research participants' and the public's contributions in generating CT data, is relevant to this suggestion too. Reichman's suggestion would have been more helpful if he specifically referred to CT data since treating clinical trials as a public good does not necessarily guarantee the treatment of CT data by regulatory authorities as such.

5.1.3 Public Health Variants of the Data-Exclusivity Approach

Broad consensus exists on the fact that test data, which includes CT data, are public goods.[151] On the basis of such consensus and due to the fact that TRIPS is "not a kind of model domestic law"[152] there is space for countries to provide for public health variants to the data-exclusivity approach. The seven variants that have been proposed in literature are explained below.

[147] *See* Meitinger (2005, p. 135).

[148] Weissman (2006, p. 156).

[149] Meitinger (2005, p. 135).

[150] Reichman (2006, p. 147).

[151] *See* Reichman (2009, p. 1–68); Taubman (2008b, p. 591–606).

[152] Taubman (2008b, p. 601).

5.1.3.1 Restricting Data Exclusivity to Products Consisting of New Chemical Entities (NCEs) and not to All New Pharmaceutical Products The rationale for this approach is that "… the investment for reformulated products, products sold for new indications or derivative products will be less than for NCEs."[153] The approach is in line with Art. 39.3 TRIPS to the extent that the Article only requires the protection of test data in relation to products that utilize NCEs. However, the idea of data exclusivity is a TRIPS-plus proposal with no adequate support since "protection" is not equivalent to granting data exclusivity status.

5.1.3.2 Restricting Data Exclusivity to Unpublished Information This approach would allow generic firms to gain market authorization "if they are able to establish bioequivalence to products to which safety and efficacy has been shown in published literature."[154] It would require the contribution of researchers/collaborating consortia to facilitate the publication of information. Weissman argues that "tying data exclusivity to lack of disclosure gives pharmaceutical companies an incentive not to publish their clinical testing data."[155] In this case, researchers and TTOs need to be strategic in the licensing and clinical trial agreements by ensuring that terms that would facilitate data sharing with the scientific community are included. A good example of this approach can be learnt from Unitectra, a Swiss technology transfer organization, which supports scientists of the Universities of Basel, Bern and Zurich and of their associated university hospitals in their collaborations with industry and the commercialization of research results.[156]

Unitectra ensures that the researchers' right to publish research results is clearly provided for in the clinical trial and research agreements. In the case of sponsor/investigator initiated trials, the investigator's university reserves full publication rights. Publication may, however, be delayed for a period of three months to enable a collaborating party to apply for the patenting of any related invention. In cases where the trial is initiated by a commercial company, it reserves the right to review the data, but if the company does not publish the data within a period of one year, then the collaborating university reserves the right to do so with a view to facilitating data sharing.[157] Unitectra's role has been hailed in Europe,[158] which is a clear confirmation that researchers and TTOs can play an important role in the management of IPRs.

[153] Weissman (2006, p. 163).

[154] Weissman (2006, p. 167). This is already practised in Chile, Colombia as well as a number of countries in Eastern Europe and Asia.

[155] Weissman (2006, p. 168).

[156] Information about Unitectra is available at http://www.unitectra.ch/index.php?lang=en.

[157] Personal discussion with Ms Aleksandra Goes and Dr Daniel Gisi, contract manager and technology transfer manager respectively at Unitectra's Bern office on 24 November 2011.

[158] Swiss Technology Transfer Organisation Unitectra wins the 2011 European BIOTECHNICA Award, *Biotechnica* 2011 (11–13 October), pp. 1–3. The BIOTECHNICA award recognized Unitectra's exceptional contribution to the initiation and promotion of cooperation between the publicly funded research community and business.

5.1.3.3 Waiving Data-Exclusivity Protection in Cases of Compulsory Licensing Related to Patents Generic companies are usually required to obtain marketing approval even under compulsory licences. Data exclusivity would be an obstacle in such cases.[159]

5.1.3.4 Waiving Data-Exclusive Protection for Patented Products The basis of such waiver is that data originators already have patents to help them recoup their investment costs.[160] Interestingly, Ho suggests banning the use of data exclusivity for drugs that are not patented as a way of catering for the interests of countries where there is currently no requirement to provide patents on drugs.[161]

5.1.3.5 Compulsory Licensing System for Registration Data The proposal in this case is that countries should be free to determine conditions under which compulsory licenses should be granted over registration data.[162] Regulatory authorities can work together with TTOs to ensure that terms that facilitate compulsory licensing are included in the licensing agreements.

5.1.3.6 Shortening the Term of Data Exclusivity This approach is already being used by Unitectra, which ensures that collaborating researchers at universities reserve the right to publish data if the commercialising company does not do so within a period of one year. Weissman also points out that a country can decide to shorten the term since the periods that are usually granted in practice are not based on any criteria.[163]

5.1.3.7 Adjusting Start Date of Data Exclusivity Under this approach, the start date could be that of the first worldwide registration of the product in respect of which data exclusivity is granted.

The seven variants seem to promote equitable and fair access to data while respecting the underlying IPRs. However, given the public goods nature of CT data, might it not be more suitable to argue for the promotion of free access to such data? In posing this question, I am not oblivious to the current arguments in literature regarding the undesirable consequences of free riding by competitors. The concept of free riding is however rather limited and does not include stakeholders who would benefit from such free access.

In view of the argument in this paper that clinical researchers can play an important role in data sharing in a manner that does not need to contend with data exclusivity complications, it is worth mentioning a practical suggestion that has been provided in literature, which can help researchers to share information from CT data freely. Lipkus and colleagues have suggested that early filing for patent rights can facilitate free sharing of information since subsequent disclosure does not

[159] Weissman (2006, p. 169).

[160] Weissman (2006, p. 170).

[161] Ho (2011, p. 271).

[162] Weissman (2006, p. 172).

[163] Weissman (2006, p. 175).

compromise patentability.[164] The difficulty with applying this suggestion to CT data sharing, particularly where the main reason for withholding data is the claim of exclusive rights over the data, is that the suggestion relates to patent rights while exclusive rights over data, as was pointed out earlier, are different from the underlying patent rights.

5.1.4 The Misappropriation Approach

This approach is intended to reflect TRIPS' flexibilities by providing for the non-disclosure of registration data while at the same time enabling generic companies to rely upon approval by regulatory authorities of originator products.[165] In countries where this approach has been implemented, it prohibits disclosure of the data by government officials to third parties but "they empower government agencies to grant marketing authorization by relying upon the fact of prior approval of essentially similar products for which registration data was submitted."[166] The approach is advantageous for two main reasons: it "enables generics to reach the market as fast as possible, and with no extra registration data-related costs [; and it] is simple to administer as it imposes no regulatory burdens on governments."[167]

The approach, however, has its disadvantages too. For instance, Weissman argues that "it will undermine brand name company investment in research and development … and … it denies fair return to brand name companies."[168] This takes us back to the issues that have been noted in this paper regarding the contested R&D costs in clinical trials and the "public-good" nature of CT data, particularly given that human participants equally contribute to the generation of the data.

At a practical level, experience shows that "in bilateral and regional free trade agreement negotiations with industrialized countries, developing countries that have suggested little more than the misappropriation approach have found their positions unsustainable."[169]

5.2 Forward-Looking Strategies

The suggestion that future legislation and, I would add, management strategies on the protection of CT data should be based upon proper balance of all interests involved[170] is vital for the discussion in this part of the paper. Two forward-looking strategies are discussed here: shifting the default position from confidentiality to one of disclosure, and an abridged approval process, which is currently used in some countries.

[164] Lipkus et al. (2010, p. 8).

[165] Weissman (2006, p. 153).

[166] Weissman (2006, p. 153).

[167] Weissman (2006, p. 153).

[168] Weissman (2006, p. 153).

[169] Weissman (2006, p. 155).

[170] Cottier and Meitinger (2000, p. 71).

5.2.1 *Shifting the Default Position from Confidentiality to One of Disclosure*

International calls for CT data sharing are on the increase.[171] Since November 2010, EMA took steps to improve transparency in CT data sharing by granting wider access to documents such as clinical trial reports submitted as part of marketing authorization applications.[172] The fact that EMA granted Cochrane's independent analysts access to Tamiflu clinical reports through a freedom of information request serves as evidence that there is already a shift in the current default position of confidentiality. It also shows the key role that regulatory authorities can play in ensuring access to CT data that may be required for medical research. Such developments in EMA are commendable in view of the fact that it was previously very difficult to get information. For instance, before the new system came into force, it took Gøtzsche and his colleagues from the Nordic Cochrane centre three years and a complaint to the European Ombudsman to get access to clinical study reports for two anti-obesity drugs at EMA.[173] The arguments that EMA relied on to avoid disclosing the documents were: the protection of commercial interests; disclosure would involve an administrative burden as there were no overriding public interests; and that after the data had been redacted by EMA, it would be worthless to the requesting researchers.[174] These reasons are indicative of the extent to which the reach of Art. 39 TRIPS seems to be overextended while at the same time public interests are undermined.

Proponents of this strategy are not oblivious to the possible problems that may arise from making CT data easily accessible. Three problems that may arise are: possible disclosure of personal data or breach of patient confidentiality, data may become vulnerable to distortion due to financial interests, and potential for data misuse may increase.[175] The benefits of data sharing also need to be considered together with these possible problems: more information about the true benefits and harms of interventions would be available for decision-making in healthcare; the incentives for cheating would be reduced; important research questions would be answered using existing data; and access to raw data would make meta-analysis of trials much more reliable.[176] When all these benefits are considered, it is safe to conclude that mechanisms already exist, which can be used to address possible problems of making CT data more accessible, and the benefits far outweigh the problems since there would be competition at a more ethical level. Besides, the ethical concerns that have been explained in this paper clearly warrant a shift in the current default position.

One major limitation that has been noted in using this strategy is that regulatory authorities may not be in possession of the full clinical test reports. This essentially

[171] *See* Gøtzsche (2011, p. 249), Appendix 1 for a detailed report on the most recent international calls for data sharing.

[172] Pott (2011, p. d3838).

[173] Gøtzsche (2011, p. 249).

[174] Gøtzsche (2011, p. 249).

[175] Eichler et al. (2012, p. e1001202).

[176] Gøtzsche (2011, p. 249).

means that if the default position has to be changed, means should be established of gaining access to the full reports in line with the exceptions under Art. 39.3 TRIPS, which allows disclosure where necessary to protect public health and where data is protected against unfair commercial use. We have established in this paper that in some cases, public health needs require an analysis of the full clinical test reports by independent researchers and possibility of unfair use in this context would be minimal or non-existent.

Experience from Tamiflu shows that access to regulatory information is essential. This is because the mandate of regulatory authorities enables them to conduct thorough evaluations of the clinical trial programme. Independent clinical test report analysis would therefore benefit from such authorities' reports. This strategy cannot, however, work in practice without first addressing the underlying issues of data exclusivity and data protection. A clear illustration of this problem can be glimpsed in the protracted exchange, which ensued between Roche and the Cochrane group in the Tamiflu case. Roche withheld some information from Cochrane's independent analysis by citing patient confidentiality, data exclusivity and the protection of IPRs. Moving forward with this strategy therefore requires, as has been argued in this paper, that all relevant stakeholders' attention be drawn to the fact that data exclusivity is a TRIPS-plus approach, which needs to be toned down by focusing on the exclusions in Art. 39.3 TRIPS, and patient confidentiality can always be properly managed through applicable de-identification/anonymization techniques in accordance with data protection directives that are in force.

The difficulties that have been pointed out notwithstanding, this strategy can be helpful since the current approaches that have been discussed leave all the clinical research documents within the domain of regulatory authorities who have no capacity to scrutinize them and therefore rely on the data owners' trust.[177] As mentioned earlier, public health needs require that independent researchers conduct a meta-analysis, and this can only be possible if an approach that EMA is currently using is adopted.

Regulated means of granting access to CT data can possibly be made along the lines of clear exceptions under the Japanese AAI, which have been discussed under the *Iressa* case. Most jurisdictions already have legal frameworks that can be used in this regard. The Brazilian constitution, Art. 5, XXXIII, provides that everyone has the right to receive information of his own interest or public interest from public entities. Article 22 of Federal Law No. 8.159/1991 also provides for full right of access to public documents. In Argentina, the constitution does not provide for a general right of access to public documents or information, but the Access to Public Information Regulation of 2003 provides for the right of access. The Regulation applies to any agency, entity, organism or entity established by the executive. It has established a presumption of publicity of all documents held by the subjects that it regulates.[178] The only documents exempted from access are those that affect "national defence, foreign policy, trade secrets, legal advice of government counsel, privacy and intimacy and sensitive data under the Data Protection Act, and

[177] Gøtzsche (2011, p. 249).

[178] Banisar (2006, p. 38).

information that may risk someone else's life".[179] CT data or clinical research reports do not clearly fall within the exempted category of information.

In the EU, Member States are not obliged to enact freedom of information laws, but it has adopted directives that require Member States to adopt laws to provide access to information in specific areas, notably consumer protection and re-use of public information.[180] In the USA, the Freedom of Information Act[181] allows any interested party to request access to records held by federal government agencies. Discretionary exemptions apply in respect of "national security, internal agency rules, information protected by other statutes, business information, inter and intra-agency memos, personal privacy, law enforcement records, financial institutions and oil wells data."[182] There seems to be space, within these jurisdictions' legal frameworks, for interested third parties to request access to CT data on public health grounds in terms of the exceptions under Art. 39.3 TRIPS.

5.2.2 Abridged Approval Process

As mentioned earlier, this process is currently used in Argentina, Brazil, Europe, Japan, Israel and the USA where regulatory authorities rely on the data submitted by the first applicant for a similar product, provided that its physico-chemical attributes are equivalent to the first applicant's. The process has the public health merit of sparing more research participants from being involved in research, which duplicates questions that have already been answered through the existing data.

Details concerning this approach have already been discussed with the aid of Argentina's Commercial Court of Appeals decision in *Novartis Pharma AG v. Monte Verde SA & Varios Propiedad industrial e intellectual*, and it would belabour the point to repeat them in this part of the paper.

6 Conclusions

The two fundamental principles, which are the basis of data sharing mentioned earlier, namely minimizing impediments to research processes and making the products of scientific research widely available to the people who need them, should be used in assessing the suitability or otherwise of the management options that are discussed in the preceding part of this paper. The other factor to bear in mind is the fact that the strategies cannot work in practice if, as Lemmens and Telfer have correctly suggested, changes do not target international trade regimes as well in view of the fact that "existing international trade agreements oblige countries to respect the secrecy of clinical trials data and are invoked to resist trial registration and results reporting obligations."[183] This definitely calls for the correct

[179] Banisar (2006, p. 38).

[180] Banisar (2006, p. 12).

[181] 5 USC 552, 1966.

[182] Banisar (2006, p. 159).

[183] Lemmens and Telfer (2012, p. 90).

understanding and interpretation of Art. 39.3 TRIPS, which would enable countries to exercise more freedom in negotiating FTAs and in enforcing data-exclusivity-related claims at the domestic level. The approach that courts have used in Brazil and Argentina provide good examples in this regard.

Apart from changes that are aimed at the international trade regimes, strategic approaches can be used by researchers, TTOs and regulatory authorities since they are better placed to apply the paramount ethical principle of BS in their daily operations and would also appreciate the fact that research participants' and public health interests should be considered in decision-making.

The main strategic approaches that have been identified in this paper are summarized below.

i. Researchers should ensure that they reserve the right to publish clinical research findings expeditiously when they sign clinical trial agreements and TTOs that negotiate licensing agreements with the pharmaceutical industry, on behalf of researchers, should equally be sensitized to the need to protect this right since it is an ethical obligation under paragraph 30 of the Declaration of Helsinki.
ii. Regulatory authorities should exercise discretion by drawing a clear distinction between the data itself and the health and safety outcome to which the data lead. This approach should enable regulatory authorities to exercise the freedom to register competing products based on proven health and safety outcomes if bioequivalence can be established by the applicant. This is acceptable under Art. 39.3 TRIPS.
iii. Regulatory authorities should be allowed through domestic legislation to rely on published scientific information to approve competitors' products. As was noted earlier, TRIPS is not a model law to be copied at the domestic level, and due to the contested interpretations of Art. 39.3, it would be useful for countries to provide clarity in their legislations, which would enable regulatory authorities more freedom in decision making.
iv. Regulatory authorities should adopt the strategy, which EMA has so far used to facilitate access to full clinical research reports for independent meta-analysis for public health benefits. This calls for a shift in the current default position from confidentiality to one of disclosure. The strategy equally requires the enactment of access to information legislation to regulate the disclosure of information and clear exceptions such as those contained in the Japanese AAI.

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