Regulatory Data Protection in Pharmaceuticals and Other Sectors

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ABSTRACT

Generating data to secure regulatory approval in sectors, such as pharmaceuticals and agricultural chemicals in which product safety and efficacy is paramount, has become ever more extensive and expensive. There is thus a need to provide an incentive to undertake such data-generation efforts by protecting the investment in them against free riding. Article 39.3 of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) recognizes as an intellectual property right the need for such protection in those sectors. This chapter discusses how certain jurisdictions, and in particular the European Community, have implemented the TRIPS requirement involving regulatory data protection regimes. Such protection is not provided by the patent system, which instead protects invention.

1. INTRODUCTION

When a company or institution spends the time and money to demonstrate that a product is safe and efficacious, the investment pays off, in part, by protecting the data generated through this effort. This protection has become crucial in highly regulated sectors, such as pharmaceuticals and agricultural chemicals, where product safety and efficacy are paramount. The importance of protecting such data is reflected in their recognition by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), Article 39.3, as intellectual property (IP) rights. The need for such protection has arisen because the testing required to secure regulatory approvals has become more extensive and expensive. Thus, greater incentives for undertaking such work are needed, especially since no other forms of protection may be available for a product that regulatory agencies have authorized for the market.

The protection of data generated for regulatory purposes prevents direct or indirect use of the data filed in support of a marketing authorization by subsequent applicants seeking marketing authorization for the same product. The protection applies unless the subsequent applicant has obtained the consent of the party that first filed the data and obtained the original marketing authorization. It is often uneconomic for subsequent applicants to generate their own data independently, so this exclusivity effectively confers a de facto right in favor of the first applicant. However, the protection is for a limited time, so that subsequent applicants can use it after an appropriate period. This avoids the need for repetitive testing, which whether on animals or people, is undesirable both from economic and ethical points of view.

2. REGULATORY DATA PROTECTION VERSUS OTHER FORMS

2.1 *How regulatory data protection differs from confidential information protection*

Although the protection of regulatory data has its origins in laws regulating confidential information

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(including trade secrets), and indeed is addressed in the same article of TRIPS that mandates the protection of confidential information, it is a separate right that requires separate analysis.[1] The two types of IP right are different, and a balance between private and public interests struck in one should not affect how that balance is struck in the other. For example, while there would seem to be no compelling reason why the protection afforded to confidential information should ever be limited in duration, the term of regulatory data protection *ought* to be limited.

Some experts might argue that there is no need for a separate legal regime to protect regulatory data because the data can be protected under the law governing confidential information. Indeed, viewed from an English common law perspective, regulatory data is typically confidential in nature and is communicated to regulatory authorities with an obligation of confidence. However, trade secrets law has proved inadequate for protecting data filed with regulatory authorities. First, the issue has not been about the disclosure of data but about its use (although freedom of information considerations today make a limited measure of disclosures inevitable, which can undermine its confidential nature.) Second, it is unclear whether regulatory authorities in fact do "use" the data in a way that is subject to the law of confidential information, especially when officials merely rely on the existence of such data and do not actively refer to it. Third, even assuming that such reliance does constitute use, is there some "public policy" or "implied permission" defense that permits this use?

On this third point the various *Cimetidine* cases,[2] each of which was decided effectively on public policy or implied-permission grounds, demonstrated the difficulties faced by those who file confidential regulatory data in the common law countries of England, Australia, and New Zealand. When regulators assessed in these cases an application for approval of an equivalent medicinal product by a generic competitor, the original data filings could not be protected via traditional concepts of confidential information. The law of confidential information could not prevent the regulatory authority from referring to the originator's file or from relying on the mere fact of the earlier authorization.[3] Thus the decision of the House of Lords in the English *Cimetidine* case confirmed that the information was confidential and that a breach of confidentiality would have occurred if the information had been disclosed to third parties or the information used for purposes unrelated to the function of the regulatory authorities. But that was not the case. Instead, the regulatory authorities had been using the data to carry out the regulatory function. The legal decision went on to confirm that regulatory authorities have a right and duty to make use of such information. The court observed that "*the licensing authority should not be deterred from exercising its rights and powers so as to ensure public safety....*"

2.2 *Regulatory data protection versus patents*

Some experts argue that the protection of innovation in regulated areas, such as pharmaceuticals and agrochemicals, ought to be left to the patent system, and that no other system of protection is needed. This objection, however, fails to recognize that proving safety and efficacy for regulatory authorities is a very different matter from demonstrating that an invention is patentable. From a regulatory perspective, much of the required expenditure of time and money is directed to R&D that rarely yields patentable inventions.

Indeed in some cases, patent protection for a product approved by regulatory authorities may be very weak or impossible to obtain, especially when the patent protection is not for a new chemical entity or other new active substance but is instead for a new physical form, new formulation, new synthetic process, or new use of an old substance. Such "second generation" patents are at greater risk of successful attacks on their validity, because patent validity depends less on the work done to bring inventions to market, or to prove that inventions are safe and efficacious, than on the discovery of the invention in the first place. Such patent validity considerations are wholly unrelated to regulatory data protection, which may therefore provide the sole protection for a medicinal product. The ability of patents to give only limited protection—and thus to

provide a limited incentive for completing the important work required to secure a marketing authorization—was recognized in the English patent case *Merck & Co. Inc.'s Patents.*[4] Having found invalid certain patents for the medical uses of alendronate, a compound used to treat medical disorders of excess bone destruction, the trial judge observed:

Accordingly I hold both patents invalid. I do so with some regret. Merck [has] only had a few years' exclusive exploitation of alendronate. [The company] must surely have had to make a very considerable investment and incurred considerable risk in bringing [the product] to market. And mankind is better off as a result. But the patent system does not confer monopolies on those who develop obvious or old products, even if they have never been exploited. A workable system for that might be a good idea, particularly in the field of medicine and analogous fields.

The framework for such a workable system has existed for some time in the law of regulatory data protection, which in the United Kingdom provided longer effective protection than did the patents at issue in this case.[5] However, the regulatory data protection system for medicinal products, at least in Europe and as mandated by Article 39.3 of TRIPS, provides for only limited compensation for the shortcomings of the patent system. This is because regulatory data protection is available only for data filed in support of a new active chemical and not (with one exception only recently introduced) for data filed in support of a new indication, new formulation, or new dosing schedule of an already-authorized active chemical. The exception, discussed further below, extends the total period of data protection for all uses of a medicinal product by one year, if one or more new therapeutic indications are authorized that are held to bring significant clinical benefits in comparison with existing therapies. To fail to protect data filed in support of a new indication, new formulation, or new dosing schedule of an already authorized active chemical has two baleful consequences. It not only discourages development work on existing medicinal products, but also encourages work on new medicinal products that may be no better in practice than those they replace. This robs from investments in public health since the "innovations" add no benefit to the public but still require resources to be spent for new research and market authorization. Clearly, the pursuit of better IP protection in this case is a perverse incentive. A revised approach is needed, one that recognizes the differences between regulatory data protection and patents. In short, the former differs from patents in three ways: (1) its apparently shorter duration; (2) the lack of any need to comply with conventional concepts associated with patentability, such as novelty and obviousness; and (3) it protects only the regulated product. Table 1 lays out these differences in more detail.

Notwithstanding the fundamental conceptual differences between the two systems of protection, some links between the systems have been created. The regime in the United States for granting authorizations for medicinal products (and as required to a degree, by many bilateral trade agreements between the United States and third countries) provides that, when a patent protects a product, in most cases the term of regulatory data protection is extended for 30 months or longer. In Europe, however, if there is no sample submission to the regulatory authorities (which itself would constitute an infringing act under applicable patents in Europe), the mere application for a marketing authorization does not constitute an act of patent infringement. In fact, a marketing authorization may be granted to any party that complies with the applicable technical requirements without, thereby, infringing any patent[6].

2.3 *Regulatory data protection versus other forms of marketing exclusivity*

Rights protecting regulatory data need to be distinguished from and contrasted with other types of marketing exclusivity conferred for other reasons. Because both provide a form of market exclusivity, the distinctions are not always very clear.

Internationally, one example of market exclusivity that contrasts with regulatory data protection is the exclusive marketing rights conferred

under Article 70.9 of TRIPS for pharmaceuticals and agricultural chemical products in those countries that did not provide full product patent protection for such chemicals when TRIPS came into force.

Another type of marketing exclusivity is available in both Europe and the United States for *orphan* medicinal products. Because of their small potential market, these products require incentives for development over and above the norm. In a sense, the exclusivity for orphan medicinal products could be said to protect indirectly the data submitted by the entity that secures the first such orphan-drug authorization, but it goes much further. During the term of orphan-drug marketing exclusivity, a second applicant will not be able to obtain market authorization even if it submits its own data. Thus orphan-product status does not simply protect regulatory data but confers true marketing exclusivity.

As is to be expected for a right that has only recently been developed and is only now starting to be analyzed in detail, there was considerable international variation in the protection afforded to regulatory data. This was the case when the text of TRIPS was finalized in 1994 and it remains the case today in 2007. In consequence, Article 39.3 leaves much latitude in relation to its national implementation (see Box 1).

Table 1: Patents and Regulatory Data Protection Contrasted

	Patent	Data Protection
Protects	claimed compound and analogues, and/or uses, and/or formulations, and/or synthetic processes	compound (and sometimes formulation) which has an authorization to market
Prevents	• manufacture, sale, use, or import of a claimed product or the direct product of a claimed process • use of a claimed process • indirect infringement	grant to a subsequent applicant of an authorization to market based on originator's data
Relevant excepted use	- private and noncommercial use - use for purposes of securing regulatory authorization - experimental use relating to the subject matter of the invention (outside the United States)	any use which does not require an authorization to market
Period of protection	20 years from application	variable, but typically 5–10 years from the first authorization to market
Requires	patentability: novelty, inventive step, sufficiency, etc.	demonstration of safety and efficacy

Box 1: Article 39.3 of TRIPS

Propositions as to the scope of Article 39.3 TRIPS

The importance of regulatory data protection and its international recognition as a sui generis type of intellectual property right are embodied in Article 39.3 of TRIPS. This embodiment, together with Article 39.1 and Article 39.2, (which are expressed in somewhat different terms and mandate the protection of confidential information) provides:

1. In the course of ensuring effective protection against unfair competition as provided in Article 10 *bis* of the Paris Convention (1967), Members shall protect undisclosed information in accordance with paragraph 2 and data submitted to governments or government agencies in accordance with paragraph 3.

2. Natural and legal persons shall have the possibility of preventing information lawfully within their control from being disclosed to, acquired by, or used by others without their consent in a manner contrary to honest commercial practices so 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 dealt 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.

Note: For the purpose of this provision, "*a manner contrary to honest commercial practices*" shall mean at a minimum practices such as breach of contract, breach of confidence, and inducement to breach, and includes the acquisition of undisclosed information by third parties who know, or were grossly negligent in failing to know, that such practices were involved in the acquisition.

3. Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilise 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 steps are taken to ensure that the data are protected against unfair commercial use.

To date, there have been no cases brought under the WTO (World Trade Organization) dispute-resolution mechanism in relation to Article 39.3 to provide guidance. Nonetheless, the following propositions about the minimum thresholds of protection that it mandates can be advanced:

- Article 39.3 addresses two issues: *use* of the data in its first sentence and *disclosure* in the second. However the data to be protected are in each case the same.

- In each case the data protected are *required* "*as a condition of approving the marketing of pharmaceutical or of agricultural chemical products,*" suggesting that this does not require that data submitted for these products for other purposes, or submitted as a condition of approving the marketing of other types of product, be protected. (The European Community, for example, also provides for regulatory data protection in other fields, such as animal feedingstuffs and biocidal products but TRIPS does not recognize it).
- In each case, the data protected are *required* "*as a condition of approving the marketing of … products which utilise new chemical entities.*" The expression *new chemical entity* is not defined. Thus this provision does not necessarily impose a patent standard of novelty, and indeed it should not be expected that it do so, given the different nature of the right. In any event, if one were to apply a patent standard of novelty, would this be absolute (worldwide) or relative (local)? TRIPS is silent on this issue with regard to patents, and although over time there has been a trend to absolute novelty, it has by no means been universally adopted. It should be noted that the term *new chemical entity* is widely used in a regulatory context. Accordingly, a new chemical entity could be regarded as an active substance approved for the first time within a particular regulatory framework, since the same chemical may have activity within the context of different regulatory frameworks. Moreover, because in some regulatory systems the term *new chemical entity* is in practice limited to "small molecules" (as opposed to the "large molecules" that designate biotechnology products, such as therapeutic proteins, and are usually termed *new active substances* in such systems), the term ought to be regarded as comprising new active substances. However, this does not mandate the protection of new data, no matter how much effort their origination has involved, for an old, or already authorized, chemical entity or active substance, although such protection ought to be regarded as desirable on public policy grounds.
- In each case, the origination of the data protected must "*involve a considerable effort.*" This no doubt would cover safety and efficacy data, such as that generated in the course of clinical trials for pharmaceuticals or field trials for agricultural chemicals, but it leaves open the question of what other data should also be protected on these grounds.
- In relation to prohibited use, the use must be "*unfair commercial use.*" This expression is not defined, but clearly excludes non-commercial use, such as for public health and safety. As to commercial use, such as that made when a subsequent applicant relies on the existence of such data (whether or not actually referred to), or to be more accurate, when the regulatory authority assesses the second applicant's application in light of the data provided by the original applicant, the issue is whether or not such use is unfair. It is in this context that such matters arise as the appropriate term of protection and whether or not the protection should be an exclusive right or merely a remuneration right (and thus available for compulsory licensing).
- In relation to disclosure, such data must be protected except in two cases: where it is either "*necessary to protect the public*" or where "*steps are taken to ensure that the data are protected against unfair commercial use.*" Thus, in these two alternative cases there is

no absolute prohibition on the disclosure of such data. The first permitted exception, namely that of "*[necessity] to protect the public*" appears narrow in scope and should not properly be equated with transparency, which is the principle behind disclosures under freedom of information considerations. Thus in relation to disclosures for purposes of transparency, TRIPS would appear to require that "*steps [be] taken to ensure that the data are protected against unfair commercial use.*" This would appear to require the regulatory authority not to treat information disclosed for such purposes as detracting from the undisclosed nature of the underlying data. Indeed, in the European medicinal products regime, the Notice to Applicants expressly provides that the information set out in a European Public Assessment Report (EPAR) cannot be used to apply for a marketing authorization for a medicinal product on a bibliographic or published data basis (see also Box 2 at the end of this chapter).

The Background to and Negotiating History of Article 39.3 TRIPS

Before TRIPS came into force on 1 January 1995, regulatory data was already protected throughout the European Community and in the United States by statutory provisions for both pharmaceuticals and agricultural chemicals. Since 1987, the member states of the European Community have provided protection for data filed in support of marketing authorizations for medicinal products, and since 1991 for data filed in support of marketing authorizations for plant protection products. Similarly since 1982, the United States has had its own regulatory data protection provisions for pesticides, and since 1984, such provisions for medicines. Moreover, as discussed earlier, in both jurisdictions the case law had made plain the limitations of the law of confidential information as a means for protecting regulatory data.

Moreover, TRIPS was not the first multinational agreement to mandate that its Member States provide regulatory data protection. This honor fell to the North American Free Trade Agreement (NAFTA)[7], paragraphs 5 through 7 of Article 1711 of which provide:

5. If a Party requires, as a condition for approving the marketing of pharmaceutical or agricultural chemical products that utilize new chemical entities, the submission of undisclosed test or other data necessary to determine whether the use of such products is safe and effective, the Party shall protect against disclosure of the data of persons making such submissions, where the origination of such data involves considerable effort, except where the disclosure is necessary to protect the public or unless steps are taken to ensure that the data is protected against unfair commercial use.
6. Each Party shall provide that for data subject to paragraph 5 that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter's permission, rely on such data in support of an application for product approval during a reasonable period of time after their submission. For this purpose, a reasonable period shall normally mean not less than five years from the date on which the Party granted approval to the person that produced the data for approval to market its product, taking account of the nature of the data and the person's efforts and expenditures in producing them. Subject to this provision, there shall be no limitation on any Party to implement abbreviated approval procedures for such products on the basis of bioequivalence and bioavailability studies.
7. Where a Party relies on a marketing approval granted by another Party, the reasonable period of exclusive use of the data submitted in connection with obtaining the approval relied on shall begin with the date of the first marketing approval relied on.

The "*not less than five years*" term of protection that the North American Free Trade

Agreement (NAFTA) accepts in Article 1711(6) as "*reasonable*" reflected, no doubt, the U.S. position regarding pharmaceuticals,[8] but such a term is now widely regarded on the research-based side of the pharmaceuticals industry as inadequate. However, the NAFTA formulation has a significant place in the history of regulatory data protection because it is the first to reflect the principles of regulatory data protection in treaty language and because its language parallels that found in TRIPS.

3. THE E.U. AND U.S. IMPLEMENTATIONS OF ARTICLE 39.3 TRIPS

3.1 *Background*

Although the obligations mandated under Article 39.3 are generally expressed, it is instructive to consider how they have been implemented by the world's two major trading blocks—the European Union and the United States—especially since it has become increasingly common for each to try to impose its own IP norms on trading partners through regional or bilateral trade agreements.

3.2 *Pharmaceuticals*

A variety of national regulatory data protection regimes for pharmaceuticals have emerged. The regimes differ both in terms of the length of protection and the categories of data protected. For example, European Community Member States previously provided (depending on the country or the regulatory route followed) six or ten years protection for data filed in support of an authorization for a new pharmaceutical chemical entity, but none for data relating to a new indication for an already-authorized pharmaceutical. For new chemical entities authorized as pharmaceuticals in the European Community after October 2005, second applicants may apply for a marketing authorization eight years after the first authorization is granted, but such authorization cannot be granted less than ten years after the date of such first authorization.[9] In each case the protection runs from the first authorization in the Community. Under the new system, the ten-year period is extended by a further year if authorization for a significant new indication for the pharmaceutical is secured before the eight-year period expires.

In the United States, a second applicant cannot (assuming no patents cover the product) apply for such an authorization until five years after the first marketing authorization.[10] Assuming a typical review period of 18 months, the result is a total effective protection period of six and a half years. However, the more usual situation is that the relevant regulatory authority (the U.S. Food and Drug Administration (FDA)) has been advised that one or more patents apply to the pharmaceutical in question, in which case the link between the regulatory regime and the patents regime comes into play (see section 2.2).[11] This link exists in the United States but not in the European Union.

In the United States, a company wishing to market a generic version of a pharmaceutical by relying on the first applicant's regulatory data must certify one of the following to the FDA: (1) no patent applies, (2) the relevant patent has expired, (3) approval is sought only after the patent expires; or (4) there is a patent but it is asserted to be invalid or not to be infringed. Once a generic manufacturer provides a certification that it considers the patent to be invalid or not infringed (a "Paragraph IV Certification"), the manufacturer must notify the patentee, which then has an immediate right to sue for patent infringement. A patent infringement action filed within 45 days of notice delays approval of the first generic authorization for 30 months.[12] The practical result of the linkage is thus to extend the effective regulatory-data protection period by at least 30 months to seven and a half years, even when the Paragraph IV certification proves to be correct and the listed patent turns out to be either invalid or not infringed. Thus at first sight the duration of protection in the United States for data filed in support of an authorization for a pharmaceutical as a new chemical entity may seem less than that afforded by the European Community. In practice however, the difference is much less, especially because of this patent linkage.

Moreover, in the United States, data based on new clinical investigations (other than

bioavailability studies), relating to an already-authorized product, that are essential to a further authorization (such as that required for a new indication) are protected for three years. Although the protection for new data in support of a new indication for an old product is apparently more generous in the United States than in the European Community, which provides for an extension of only one year, it is important to appreciate that in the European Community the protection is extended for all indications and not just, as in the United States, for the new indication.

3.3 *Agricultural Chemical Products*

In general, the agricultural-data protection systems for authorizations in the European Community and the United States provides for a longer period of protection than for pharmaceuticals. They also give a considerably higher level of protection for new data used in relation to old active compounds than that mandated in the pharmaceutical systems.

The system in the European Community, subject to special provisions for products already on the market when the system came into force, provides for ten years of Community-level protection for a new active compound.[13] The system also provides ten years of protection at a national level (running from the first such authorization in the Community) for data filed in support of a formulated plant protection product containing an already authorized active compound. However, these periods of protection are subject to provisions intended to promote data regarding vertebrates to be shared, so that duplicate testing on animals can be avoided. Failing agreement on this issue, Member States are empowered to compel sharing of such data, which typically involves arbitration over compensation. As a result of these compulsory licensing provisions, test data derived from vertebrate animals does not benefit from exclusivity. The conferred data protection can to this extent thus be seen as a remuneration right rather than an exclusive right.

For pesticides, in the U.S. regulatory data for old and new products is protected for a ten-year period.[14] For a further five-year period, others can use the data only when the would-be users have offered to compensate the first filer of the data (in the absence of agreement as to the level of compensation, there are provisions for arbitration), but after this 15-year period there is no restriction on use. Thus the protection for the last five years of the 15-year period of protection is not exclusivity but remuneration.

3.4 *Regulatory data protection in bilateral and regional trade agreements*

NAFTA is an example of a regional free trade agreement, but since the negotiation of TRIPS, both the United States and the European Community have entered into a number of bilateral trade agreements with third countries. There have also been some regional trade agreements. Such agreements typically contain chapters addressing IP, including regulatory data protection. The approach of the European Community Trade Agreements, such as that with the Ukraine, is simply to require the trading partner to harmonize its laws with European Community standards. In contrast, the U.S. free trade agreements (FTAs) contain specific provisions to tighten up matters left vague by the TRIPS Agreement. Several FTAs are in force, including one with Australia. The texts of several others have been finalized, and negotiations are under way on a number of others.[15] The texts spell out the approach to be adopted in implementing the TRIPS standards. The obligations, expressed as mutual obligations, usually require the other party to adopt at least some elements of the U.S. implementation. This is the approach in the provisions concerning regulatory data protection.

In most cases, the FTAs that the United States has negotiated specify minimum five-year periods of regulatory data protection for pharmaceuticals and ten-year periods for agricultural chemicals. Some countries permit the granting of marketing approval based upon the existence of an approval for the same pharmaceuticals in another country. In some of these cases, the FTAs require the second country to protect the regulatory data filed in the first country for the same length of time as the first country does, or for an independent period.[16] Protection is sometimes required for test data submitted in support not

only of authorizations for pharmaceutical products incorporating new chemical entities, but for any pharmaceutical product.[17] In comparison, Europe offers such protection for new data filed in relation to an old active compound in a pharmaceutical product only when such data is filed in support of one or more new indications that bring a significant clinical benefit. However, regulatory data protection in the European Community for data filed in support of an authorization of a new pharmaceutical chemical entity is longer than the minimum five years required under the FTAs.

Several of the FTAs also require the parties to adopt the U.S. system for pharmaceutical products: the patent holder is notified of any attempt by a second applicant generic company to apply for a marketing authorization before patent expiry.[18] Indeed, in many cases, the regulatory authority is prohibited from granting a marketing authorization before patent expiry.[19] The impact of the FTA provisions requiring a link between marketing approval and patent protection, which is not mandated by TRIPS, depends very much upon the precise mechanism involved. Some mandate mere notification. Others mandate that no authorization be granted while patents continue in force, the effect of which is to increase considerably the effective period of protection. Moreover, unless they have an incentive to challenge patents in the form of their own brief period of generic exclusivity as provided by the U.S system, they may be unlikely even to try, because all they will achieve is to clear the path for other generic competitors.

4. CONCLUSIONS

Regulatory data protection provides an important incentive for developing safe and efficacious pharmaceuticals and agricultural chemicals. It is an incentive that patents alone cannot provide. The obligations in TRIPS Article 39.3 concerning the protection of regulatory data are broadly expressed and permit numerous flexibilities of implementation. However, the United States and the European Union, as the two major trading entities, have each developed specific implementations of these obligations, each with its own carefully crafted checks and balances. Each adopts a different approach to protecting regulatory data for pharmaceuticals and for agricultural chemicals. Each is also in the process of extending its specific approach to implementing these obligations to some of its trading partners. They are doing this through trade agreements that specify the minimum standard of IP protection that the parties must afford. It is important, therefore, to be aware of the differences between the U.S. and European Community systems for protecting regulatory data for pharmaceuticals and agricultural chemicals, the different checks and balances within such systems, and the reasons for and consequences of such differences. Such differences make it dangerous to cherry-pick only certain aspects of such systems, or indeed to try to merge and harmonize their respective features into one system, for doing so is likely to result in an upward harmonization that will produce a system of regulatory data protection that is more stringent than that provided by either system on its own. ■

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1 Article 39.2 TRIPS mandates the protection for confidential information. There are, however, considerable disparities in the manner in which countries comply or enforce this protection (even within the European Community), in the remedies conferred (for example, are they are enforced in the criminal or civil courts?), and in the legal bases for such laws (are they contractual or, as tends to be the case in common law jurisdictions, equitable? Or are they seen as a species of unfair competition, as tends to be the case in civil law countries?)

2 *Smith Kline & French Laboratories Ltd. v Attorney General* FSR 418 (1989), *In re Smith Kline & French Laboratories Ltd.* 1 AC 64 (1990) (England), *Smith Kline & French Laboratories (Australia) Ltd. v Secretary to the Department of Community Services and Health*, and *Alphapharm Ltd. v Secretary to the Department of Community Services and Health* FSR 617 (1990), relating respectively to New Zealand, England, and Australia.

3 Likewise in the United States, *Ruckelshaus v Monsanto Co.* (467 U.S. 986, 1019–20 (1984)) shows the reluctance of the courts to impose an unqualified restriction on regulatory authorities' use of the data filed with them. *Ruckelhaus* was analyzed extensively in the Australian *Cimetidine* case *Alphapharm Ltd. v Secretary to the*

Department of Community Services and Health [1990] FSR 617.

4 *Merck & Co. Inc's* FSR, p. 498 (2003).

5 However, one of the patents in issue in this case was for a new dosing schedule (seven days as opposed to one, with a concomitant difference in dose), and neither the old regulatory data protection law in Europe, nor the current one that replaces it, protects new data in support of a new dosing schedule for an old active compound, as was confirmed under the old law in the unsuccessful challenge to the grant of a marketing authorization to a second applicant in *The Queen on the application of Merck Sharp and Dohme Limited v The Licensing Authority (acting by the Medicines and Healthcare products Regulatory Agency, and Approved Prescription Services (U.K.) Ltd., Generics (U.K.) Ltd. and Arrow Generics Ltd*. EWHC 710 (Admin, 2005) (Moses J, 28 June 2005).

6 The earlier regulatory data protection regime in Europe as introduced by the amendments made in 1987 by Directive 87/21/EEC to Directive 65/65/EEC allowed Member States the option not to confer regulatory data protection for medicinal product "after patent expiry" and thus undermine the effect of regulatory data protection in such countries. However, although some countries, such as Denmark, initially availed themselves of this option, they rapidly abandoned it. The current regulatory data protection regime in Europe, which applies to active compounds the application for the first marketing authorization of which was made since November 2005, provides no such option.

7 NAFTA was signed on 12 August 1992 and entered into force (subject to transitional provisions) on 1 January 1994.

8 Although, as observed in Section 3.2 where the pharmaceutical is the subject of a patent, this can in practice prove to be rather longer.

9 For specifics of the current European Community system for the regulatory data protection of medicinal products see Box 2 of this chapter.

10 See the Federal Food Drug and Cosmetic Act (21 U.S.C. 355), "New Drugs," and in particular the amendments here introduced by the Drug Price Competition and Patent Term Restoration Act 1984 (Hatch-Waxman Act).

11 Such declarations are listed in the so-called Orange Book, the electronic version of which is available at www.fda.gov/cder/ob/.

12 There is an exception to this in the unlikely event that a final judgment disposes of the patent in less than 30 months. The U.S. system also provides an incentive to be the first applicant to file a Paragraph IV Certification: no other such applicant can go to market until 180 days after the first applicant to file such a certification goes itself to market or disposes of the patent in a final judgment.

13 See Articles 13 and 14 of Directive 91/414/EC of 15 July 1991 concerning the placing of plant protection products on the market.

14 See the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 136a), "Registration of pesticides."

15 Details of those U.S. FTAs signed to date and the progress of the others can be found at www.ustr.gov/Trade_Agreements/Bilateral/Section_Index.html.

16 For example United States-Australia FTA Article 17.10, CAFTA Article 15.10, United States-Jordan FTA Article 4(22), United States-Bahrain FTA Article 14.9.

17 For example United States-Jordan FTA, Article 22 Footnote 10, United States-Singapore FTA, Article 16.8.

18 For example United States-Chile FTA Article 17.10, United States-Singapore FTA Article 16.8(4), CAFTA Article 15.10(3).

19 For example United States-Singapore FTA, United States-Chile FTA, CAFTA, United States-Australia FTA, United States-Morocco FTA.

20 Namely, "*any substance or combination of substances presented as having properties for treating or preventing disease in human beings*" or "*any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunologic or metabolic action, or to making a medical diagnosis*."

21 *Separate* is here meant in the sense that an authorization secured under one system cannot form the basis for securing another authorization in the other system. One exception to this is provided by Article 3(3) of the Regulation, which allows Member States to apply the Article 10 abridged authorization procedure to grant a national authorization for a generic medicinal product of a reference medicinal product first authorized by the Community.

22 The centralized system has long been obligatory for medicinal products produced by most biotechnological processes, and has with effect from 20 November 2005 been obligatory also for medicinal products for human use containing a new active substance for the treatment of AIDS, cancer, neurodegenerative disorder, and diabetes, and for medicinal products that are designated as orphan medicinal products. It is optional for other new active substances and for medicinal products shown by the applicant to constitute "*a significant therapeutic scientific or technical innovation or that the granting of authorisation in accordance with [the] Regulation is in the interests of patients or animal health at Community level*." This latter provision provides a theoretical possibility of securing an entirely new period of data protection via the centralized route in relation to an active compound that has already been authorized via the national route.

23 See Article 14(11) and 89 of the Regulation, paralleling part of Article 10 of the Directive, as amended, and Article 2 of the amending Directive.

24 See Article 6 of the Regulation, incorporating by

reference, inter alia, Articles 10, 10a and 10b of the Directive, as amended.

25 Moreover by New Article 10(5) "*... where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication*." The precise application and scope of this provision (which was added at the final stage of the legislative process and for which there are no *travaux preparatoires*) is yet to be established. The EMEA takes the view that the expression *well-established substance* means that the product no longer benefits from data exclusivity, and that the new period of data protection can be granted independently at any time after the initial protection period has expired, but can only be granted once.

26 Case C-368/96, *R v Licensing Authority, ex parte Generics (UK) Ltd*. 2 CMLR 181 (1999).

27 The proviso under the old regulatory regime stated, "*However, where the medicinal product is intended for a different therapeutic use from that of the other medicinal products marketed or is to be administered by different routes or in different doses, the results of appropriate toxicological and pharmacological tests and/or of appropriate clinical trials must be provided*."

28 In Case C-106/01, *v R v Licensing Authority, ex parte Novartis* the abridged authorization that the ECJ held to be lawful concerned a formulation of an active that was suprabioavailable to the formulation that had been authorized for longer than the data protection period but was bioequivalent to a formulation for the same active that had been authorized for less than that period. In Case C-36/03, *v R v Licensing Authority, ex parte Approved Prescription Services* the abridged authorization that the ECJ held to be lawful concerned a pharmaceutical form of an active compound that was different to the pharmaceutical form that had been authorized for longer than the data protection period but was the same as that for the same active that had been authorized for less than that period. In Case C-74/03, *SmithKline Beecham plc v Laegemiddelstyrelsen*, the abridged authorization that the ECJ held to be lawful concerned a different salt of the active moiety to that in the originally authorized product.

29 Whether or not such a mechanism was in effect implicit in the old regulatory regime was the subject of a challenge to a Commission Decision under the old regulatory regime concerning a human growth hormone product in Cases T-15/04 & T-105/04 *Sandoz GmbH v Commission of the European Communities*. However as the product in question (Omnitrop (somatropin)) has now received an authorization under the new regime, this litigation may well not continue.

30 See www.emea.eu.int/pdfs/human/ewp/309702en.pdf and www.emea.eu.int/pdfs/human/bwp/320700en.pdf for already-adopted general guidelines and the listing at www.emea.eu.int/htms/human/biosimilar/biosimilardraft.htm for various draft guidelines including specific draft guidelines as to recombinant EPO, G-CSF, human insulin, and somatropin.

31 C-440/93, *R v Licensing Authority of the Department of Health (Norgine intervening) ex parte Scotia Pharmaceuticals Ltd*. 3 CMLR 657 (1995).

32 "*The Parties acknowledge that, at the time of entry into force of this Agreement, neither Party permits third persons, not having the consent of the person that previously submitted information concerning the safety and efficacy of a product in order to obtain marketing approval in another territory, to market a same or similar product in the territory of the Party on the basis of such information or evidence of prior marketing approval in another territory.*" [Footnotes 17 and 18 in original Annex].

33 "*As an alternative to this paragraph, where a Party, on the date of entry into force of this Agreement, has in place a system for protecting information submitted in connection with the approval of a pharmaceutical product that utilizes a previously approved chemical component from unfair commercial use, the Party may retain that system, notwithstanding the obligations of this paragraph*." [Footnotes 17–19 in original Annex].

Box 2: Regulatory Data Protection for Medicinal Products in the European Community (extracts)

Introduction

This section sets out in detail the provisions relating to regulatory data protection for medicinal products for human use in the European Community.[20] Parallel provisions, which differ with regard to certain specifics involving regulatory data protection, apply to veterinary medical products. The legal basis for such provisions changed as from:

- 30 October 2005, the date by which Member States were mandated to bring the provisions of Directive 2004/27/EC amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (for medicinal products in the national systems) into effect
- 20 November 2005, the date on which the relevant provisions of Regulation 726/2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use (for medicinal products in the centralized Community system), and replacing those under Regulation 2309/93, comes into effect.

The relevant extracts from the Directive as amended are set out at the end of this Box. However, it should be noted that certain aspects of the former provisions (notably the period of protection and the nonavailability of extended protection for new uses) continue to apply to medicinal products for which an application for authorization was submitted before such dates, and since much of the litigation concerning the scope and effect of the old provisions informs the interpretation of the new ones, it is appropriate also to bear in mind the old provisions when discussing the new ones. Moreover, it is convenient to analyze these issues by reference to the Directive, dealing with medicinal products in the national, decentralized, and mutual recognition systems, rather than by reference to the Regulation, which deals with the generally separate, from a regulatory perspective,[21] centralized system,[22] because the substantive law in each case is the same as a result of the Regulation either repeating,[23] or in some cases incorporating by reference the relevant provisions of the Directive.[24]

This Box does not address the separate system of protection that may also be available in some cases under Regulation (EC) No 141/2000 (the Orphan Medicinal Products Regulation).

General Principles

The regulatory data protection provisions for medicinal products operate by providing an exception, after a specific period, to the requirement for someone seeking a marketing authorization for a medicinal product to provide the results of toxicological and pharmacological tests or the results of clinical trials for such medicinal product if such a medicinal product has already been the subject of an authorization. Thus these provisions enable the authorization of a generic version of an already authorized product after such period and without such data. Such an authorization may conveniently be termed an *abridged authorization*.

Term of Protection

Where a medicinal product has been the subject of an authorization submitted before November 2005, then the periods of protection under the old regime (old Article 10(1)(a)(iii)) apply, by which a product must have been authorized within the Community, in accordance with Community provisions in force, for not less than a six or ten-year period, and be marketed in the Member State for which the application is made. The ten-year period applies to medicinal products authorized under the centralized procedure of the Regulation and its predecessor, throughout the Community, and also in respect of authorizations secured nationally in those Member States that elected to apply it, namely Belgium, France, Germany, Italy, Netherlands, Sweden and the United Kingdom The six-year period applies to authorizations secured nationally in other Member States. This is the regime that will continue in effect for abridged authorizations for some time to come.

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Box 2 (continued)

Where a medicinal product is the subject of an authorization submitted after October 2005, then the periods of protection under the new regime apply. By new Article 10(1), an application for an abridged authorization cannot be filed until a period of eight years after the first marketing authorization in the Community has been granted, but a product so authorized cannot be placed on the market less than ten years from the first marketing authorization in the Community. This ten-year period is extended to 11 years when, during the first eight years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications that, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. The first requests for abridged authorizations under the new regime cannot be filed before November 2013.

Variations and Line Extensions of an Already Authorized Medicinal Product: New Indications, New Strengths, Pharmaceutical Forms, Administration Routes, Presentations, and so on

As noted earlier, the new ten-year period of protection available to medicinal products the subject of an authorization submitted after October 2005 will be extended to 11 years where, during the first eight years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.[25] No such provision existed under the old regulatory regime, it having been established in the *Generics* case[26] that new indications for an already authorized active did not secure a new period of protection running from the date of authorization of such new indication, and that accordingly an abridged authorization for a particular medicinal product could be granted with respect to all indications already authorized for that particular medicinal product as at the date of such abridged authorization. This case also established that new dosage forms, doses, and dosage schedules likewise did not secure a new period of protection running from the date of authorization of such new dosage forms, doses and dosage schedules, and that accordingly an abridged authorization for a particular medicinal product could be granted in respect of all dosage forms, doses and dosage schedules already authorized for that particular medicinal product as at the date of such abridged authorization.

The decision in the *Generics* case was based on the determination under the old regulatory regime that the product the subject of the abridged authorization was properly to be regarded as "*essentially similar,*" as the term was used in Article 10(1)(a)(iii), to the originally authorized product, if it satisfied "*the criteria of having the same qualitative and quantitative composition in terms of active principles, of having the same pharmaceutical form and of being bioequivalent, unless it is apparent in the light of scientific knowledge that it differs significantly from the original product as regards safety and efficacy*." Subsequent cases under the old regulatory regime established that even where there might not be such essential similarity, the proviso to Article 10(1)(a)[27] allowed for bridging data to be filed, or for bridging data filed by the originator to be relied on, provided that the originally authorized product and the product that is the subject of the abridged authorization had the same active principle.[28]

These principles have been retained under the new regulatory regime by virtue of new Article 6 and Article 10(1). Article 6 clarifies the issues of interpretation addressed in the *Novartis* and *Approved Prescription Services* cases by introducing the concept of the global marketing authorization which covers "*any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions*." Article 10(1) requires the applicant for an abridged authorization to demonstrate that the medicinal product that is the subject of the application "*is a generic of a reference medicinal product which is or has been authorized under Article 6 for not less than eight years in a Member State or in the Community*." The definition of *generic medicinal product* under Article 10(2)(b) preserves the concept of essential similarity as refined by ECJ case law in *Generics* and subsequent cases.

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Box 2 (continued)

New Combinations

New Article 10b replaces old Article 10(1)(b) and concerns medicinal products containing active substances used in the composition of authorized medicinal products but not hitherto used in combination for therapeutic purposes. In such a case, the results of new preclinical tests or new clinical trials relating to that combination shall be provided, but it is not necessary to provide scientific references relating to each individual active substance. The matter has not been the subject of litigation, but it has generally been accepted that, by virtue of this provision, a new combination has its own period of data protection calculated from the date of the first marketing authorization for that particular combination in the Community, as if that new combination were a new active substance.

Biological Medicinal Products

New Article 10(4) provides a framework that did not exist under the old regulatory regime.[29] It would enable guidelines to be established by which biological medicinal products could be authorized without full results of toxicological and pharmacological tests, or the results of clinical trials, on the basis of an earlier authorization for a "biosimilar" product. The EMEA is at present developing such guidelines, but so far the only specific guidelines that have so far been published concern certain specified recombinant proteins.[30]

Bibliographic Applications

New Article 10a replaces old Article 10(1)(a)(ii) and, as before, allows for an authorization to be sought without full results of toxicological and pharmacological tests or the results of clinical trials but which does not refer to an authorized reference product where "*the active substances of the medicinal product have been in well-established medicinal use within the Community for a period of at least ten years, with recognised efficacy and an acceptable level of safety*". It is under this provision that authorization can, for example, be sought for medicinal products containing active substances such as aspirin for the relief of pain. The narrow scope of the provision was emphasized under an earlier version of the provision under the old regulatory regime in the *Scotia* case.[31]

Relevant Provisions of Directive 2001/83/EC on the Community Code in Regard to Medicinal Products for Human Use as Amended by Directive 2004/27/EC

Article 6

1. No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive or an authorisation has been granted in accordance with Regulation (EEC) No. 2309/93.

   When a medicinal product has been granted an initial marketing authorisation in accordance with the first subparagraph, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 10(1).

Article 10

1. By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he [or she] can demonstrate that the

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Box 2 (continued)

medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 6 for not less than eight years in a Member State or in the Community.

A generic medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed from the initial authorisation of the reference product.

The first subparagraph shall also apply if the reference medicinal product was not authorised in the Member State in which the application for the generic medicinal product is submitted. In this case, the applicant shall indicate in the application form the name of the Member State in which the reference medicinal product is or has been authorised. At the request of the competent authority of the Member State in which the application is submitted, the competent authority of the other Member State shall transmit within a period of one month, a confirmation that the reference medicinal product is or has been authorised together with the full composition of the reference product and if necessary other relevant documentation.

The ten-year period referred to in the second subparagraph shall be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorisation holder obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their authorisation, are held to bring a significant clinical benefit in comparison with existing therapies.

2. For the purposes of this Article:

   (a) "reference medicinal product" shall mean a medicinal product authorised under Article 6, in accordance with the provisions of Article 8;

   (b) "generic medicinal product" shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters, or derivatives of an authorised active substance must be supplied by the applicant. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required of the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.

3. In cases where the medicinal product does not fall within the definition of a generic medicinal product as provided in paragraph 2(b) or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration, vis-à-vis the reference medicinal product, the results of the appropriate pre-clinical tests or clinical trials shall be provided.

4. Where a biological medicinal product which is similar to a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided.

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Box 2 (continued)

The type and quantity of supplementary data to be provided must comply with the relevant criteria stated in the Annex and the related detailed guidelines. The results of other tests and trials from the reference medicinal product's dossier shall not be provided.

5. In addition to the provisions laid down in paragraph 1, where an application is made for a new indication for a well-established substance, a non-cumulative period of one year of data exclusivity shall be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication.

6. Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.

Article 10a

By way of derogation from Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests or clinical trials if he can demonstrate that the active substances of the medicinal product have been in well-established medicinal use within the Community for at least ten years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in the Annex. In that event, the test and trial results shall be replaced by appropriate scientific literature.

Article 10b

In the case of medicinal products containing active substances used in the composition of authorised medicinal products but not hitherto used in combination for therapeutic purposes, the results of new pre-clinical tests or new clinical trials relating to that combination shall be provided in accordance with Article 8(3)(i), but it shall not be necessary to provide scientific references relating to each individual active substance.

Article 10c

Following the granting of a marketing authorisation, the authorisation holder may allow use to be made of the pharmaceutical, preclinical and clinical documentation contained in the file on the medicinal product, with a view to examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form.

Box 3: Regulatory Data Protection Provisions of the United States-Australia FTA Articles 17.10: Measures Related to Certain Regulated Products

1. (a) If a Party requires, as a condition of approving the marketing of a new pharmaceutical product, the submission of undisclosed test or other data concerning safety or efficacy of the product, the Party shall not permit third persons, without the consent of the person who provided the information, to market the same or a similar product on the basis of that information, or the marketing approval granted to the person who submitted such information, for at least five years from the date of marketing approval by the Party.

(b) If a Party requires, as a condition of approving the marketing of a new agricultural chemical product, including certain new uses of the same product, the submission of undisclosed test or other data concerning safety or efficacy of that product, the Party shall not permit third persons, without the consent of the person who provided the information, to market the same or a similar product on the basis of that information, or the marketing approval granted to the person who submitted such information, for ten years from the date of the marketing approval of the new agricultural chemical product by the Party.

(c) If a Party permits, as a condition of approving the marketing of a new pharmaceutical or agricultural chemical product, third persons to submit evidence concerning the safety or efficacy of a product that was previously approved in another territory, such as evidence of prior marketing approval, the Party shall not permit third persons, without the consent of the person who previously submitted information concerning safety or efficacy, to market the same or a similar product on the basis of evidence of prior marketing approval in another territory, or information concerning safety or efficacy that was previously submitted to obtain marketing approval in another territory, for at least five years, and ten years for agricultural chemical products, from the date of marketing approval by the Party, or the other territory, whichever is later.[32]

(d) For the purposes of this Article, a *new product* is one that does not contain a chemical entity that has been previously approved for marketing in the Party.

(e) If any undisclosed information concerning the safety or efficacy of a product submitted to a government entity, or entity acting on behalf of a government, for purposes of obtaining marketing approval is disclosed by a government entity, or entity acting on behalf of a government, each Party is required to protect such information from unfair commercial use in the manner set forth in this Article.

2. With respect to pharmaceutical products, if a Party requires the submission of: (a) new clinical information (other than information related to bioequivalency) or (b) evidence of prior approval of the product in another territory that requires such new information, which is essential to the approval of a pharmaceutical product, the Party shall not permit third persons not having the consent of the person providing the information to market the same or a similar pharmaceutical product on the basis of the marketing approval granted to a person submitting the information for a period of at least three years from the date of the marketing approval by the Party or the other territory, whichever is later.[33]

3. When a product is subject to a system of marketing approval in accordance with paragraph 1 or 2, as applicable, and is also subject to a patent in the territory of that Party, the Party shall not alter the term of protection that it provides pursuant to paragraph 1 or 2 in the event that the patent protection terminates on a date earlier than the end of the term of protection specified in paragraph 1 or 2, as applicable.

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Box 3 (continued)

4. Where a Party permits, as a condition of approving the marketing of a pharmaceutical product, persons, other than the person originally submitting the safety or efficacy information, to rely on evidence or information concerning the safety or efficacy of a product that was previously approved, such as evidence of prior marketing approval by the Party or in another territory:

   (a) that Party shall provide measures in its marketing approval process to prevent those other persons from:

      (i) marketing a product, where that product is claimed in a patent; or

      (ii) marketing a product for an approved use, where that approved use is claimed in a patent, during the term of that patent, unless by consent or acquiescence of the patent owner; and

   (b) if the Party permits a third person to request marketing approval to enter the market with:

      (i) a product during the term of a patent identified as claiming the product; or

      (ii) a product for an approved use, during the term of a patent identified as claiming that approved use, the Party shall provide for the patent owner to be notified of such request and the identity of any such other person.