A cost sharing model to protect investments in pharmaceutical test data[1]

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Introduction

Before a new drug is launched into the market, evidence of its safeness, effectiveness and quality must be provided to the national drug regulatory authorities. This can be done by generating and submitting the pharmaceutical test data obtained from test and clinical trials or, as usually done by the generic industry, by relying on the test data submitted by others. There are economic, practical and ethical reasons why second / generic entrants into the pharmaceutical market should not replicate the test data. The tests may take several years to complete and delay the entry of cheaper generics into the market. Also, it is unethical to replicate some testing of drugs on human subjects.

The tests, particularly those involving human clinical trials, are expensive and require important investments. Therefore, there are several regimes that provide legal protection for the test data. These regulations are not needed to protect inventions -- which already benefit from patent protection -- but the investment made to generate the test data necessary to obtain registration and marketing approval.

From a public policy perspective, the test data protection should be balanced with public interest concerns because, if not, it can impose a burden on the registration of new products and it can become a barrier to generic competition.

The United States and the European Union grant a period of exclusive rights for the pharmaceutical test data that the originators generate and submit to national drug regulatory authorities. These regulations prevent national regulatory authorities from *relying upon* the originator's test data to approve generic applications during a pre-determined period of time[3].

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[2] Helpful comments were provided by Michael Palmedo.
[3] For a more detailed description of the U.S./E.U. legal models see: "US and EU Protection of Pharmaceutical Test Data" (CPTech Discussion Paper No. 1, 2006). Available online at: http://www.cptech.org/publications/CPTechDPNo1TestData.pdf

The United States and the European Union are trying to impose this approach on the rest of the world with several trade tools: unilateral pressure, such as the U.S. Special 301 List; and bilateral/regional trade agreements.

However, the granting of the exclusive right to rely upon test data is not required by the WTO TRIPS Agreement. The relevant provision in the TRIPS is Article 39.3.

> TRIPS/ Section 7: Protection of Undisclosed Information[4]
> Article 39.3: "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."

Article 39.3 by itself is not clear regarding the nature of protection the TRIPS Agreement requires. The TRIPS Agreement does not require Member States to recognize exclusive rights to the originator of the test data, and article 39.3 obligation is limited to the protection from "unfair" "commercial" "use" of "undisclosed" data, the origination of which involves a "considerable effort" and that is "used" to register "new chemical entities".

When negotiating trade agreements and/or considering modifications in national regulations, non-U.S. or E.U. models for pharmaceutical test data protection should be considered. Legal experts,[5] who have examined this issue and the legislative history of article 39.3, have concluded that a country can satisfy its TRIPS obligations by simply protecting regulatory data from disclosure, and that nothing in the TRIPS prevents a WTO member from allowing generic competitors to rely upon public information, evidence of foreign drug registrations, or non-disclosed data from another company (Non-disclosure/Non-appropriation model). Other non-U.S. or E.U. models for pharmaceutical test data protection have been presented.[6]

[4] Emphasis added

[5] For example, C. Correa: Protecting Test Data for Pharmaceutical and Agrochemical Products under Free Trade Agreements (Included in the book: Negotiating Health: Intellectual Property and Access to Medicines, Pedro Roffe, Geoff Tansey, David Vivas-Eugui, Earthscan Publications Ltd. 2006)

[6] Alternative models to the "EU/US exclusivity regime" have been presented (at least) by: J.R. Reichman: Undisclosed Clinical Trial Data Under the TRIPS Agreement and Its Progeny: A Broader Perspective, (UNCTAD-ICTSD Dialogue on Moving the Pro-Development IP Agenda Forward: Preserving Public Goods in Health, Education and Learning, 2004). Available online at: http://www.iprsonline.org/unctadictsd/bellagio/docs/Reichman_Bellagio4.pdf; R. Weissman: Data Protection: Options for Implementation (Included in the book: Negotiating Health: Intellectual Property and Access to Medicines, Pedro Roffe, Geoff Tansey, David Vivas-Eugui, Earthscan Publications Ltd. 2006); A.X. Fellmeth: Secrecy, Monopoly, And Access To Pharmaceuticals In International Trade Law: Protection Of Marketing Approval Data Under The Trips Agreement (45 Harvard International Law Journal 443, 2004); and R. Dinca: The "Bermuda Triangle" of Pharmaceutical Law: Is Data Protection a Lost Ship? (8(4) Journal of World IP 517, 2005). Earlier proposals for capping exclusivity when sales reach a certain level, and providing for compulsory licensing of the data were presented in an October 21, 1997 US Senate hearing, "Health Registration Data Exclusivity, Biomedical Research, and Restrictions on

Recognizing that several countries are facing U.S./ E.U. pressures to implement a TRIPS Plus model and reject the minimum non-disclosure/non-appropriation model on the protection of their pharmaceutical test data; the Consumer Project on Technology (CPTech) presents a particular approach to implementing TRIPS Article 39.3 obligation[7].

The approach addressed exceeds the minimum requirements of the TRIPS Agreement. It is a compromise between the very modest obligations of the TRIPS, and the very high levels of protection given to data in the United States or Europe.

The proposal presented in this paper involves cost sharing: During the period of protection, generic companies can rely upon the originator's test data if they make reasonable contributions toward the cost of the investments.

U.S. Regime for certain Agricultural Test Data

For countries that cannot avoid TRIPS-plus obligations on the protection of pharmaceutical test data, CPTech proposes the consideration of a model that is similar to that which the U.S. now uses to fulfill its article 39.3 TRIPS Agreement obligations to protect certain agricultural test data.

This involves a mandatory and automatic compulsory license on the originator's test data based on the principle of sharing the costs of originating the data, under the **Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)**[8], an environmental protection law.

> The relevant provision reads in part:
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> "The administrator (EPA) may, without the permission of the original data submitter, consider any such item of data (cited) in support of an application by another person ... if the applicant has made an offer to compensate the original data submitter. ... The terms and amount of compensation may be fixed by an agreement between the original data submitter and the applicant, or, failing such an agreement, binding arbitration….If, at the end of ninety days after the date of delivery to the original data submitter of the offer to compensate, the original data submitter and the applicant have neither agreed on the amount and terms of compensation nor on a procedure for reaching an agreement on the amount and

the Introduction of Generic Drugs," statement of James P. Love, Consumer Project on Technology, before the Subcommittee on Labor, Health and Human Services and Education and Related Agencies, Committee on Appropriations, U.S. Senate. Available online at: http://www.cptech.org/pharm/senhregd.html

[7] CPTech began working on problems relating the data exclusivity in 1991, in connection with the registration of Taxol, an unpatented cancer drug, and in a number of cases has advocated consideration of compensatory liability or mandatory compulsory licensing of rights in test data, including, for example, October 21, 1997 US Senate hearing (Ibid), and as an option for the CAFTA-US Free Trade Agreement in 2004 (http://www.cptech.org/ip/health/trade/cafta/joyspencercafta.html).

[8] The FIFRA Act is available online at:
http://www.access.gpo.gov/uscode/title7/chapter6_subchapterii_.html

> terms of compensation, either person may initiate binding arbitration proceedings by requesting the Federal Mediation and Conciliation Service to appoint an arbitrator from the roster of arbitrators maintained by such Service. The procedure and rules of the Service shall be applicable to the selection of such arbitrator and to such arbitration proceedings, and the findings and determination of the arbitrator shall be final and conclusive, and no official or court of the United States shall have power or jurisdiction to review any such findings and determination, except for fraud, misrepresentation, or other misconduct by one of the parties to the arbitration or the arbitrator where there is a verified complaint with supporting affidavits attesting to specific instances of such fraud, misrepresentation, or other misconduct. The parties to the arbitration shall share equally in the payment of the fee and expenses of the arbitrator.
> If the Administrator determines that an original data submitter has failed to participate in a procedure for reaching an agreement or in an arbitration proceeding as required by this subparagraph, or failed to comply with the terms of an agreement or arbitration decision concerning compensation under this subparagraph, the original data submitter shall forfeit the right to compensation for the use of the data in support of the application…..
> If the Administrator determines that an applicant (second) has failed to participate in a procedure for reaching an agreement or in an arbitration proceeding …., or failed to comply with the terms of an agreement or arbitration decision concerning compensation …., the Administrator shall deny the application or cancel the registration of the pesticide in support of which the data were used ….”
>
> 7 U.S.C. Chapter 6, Subchapter II, § 136a. Registration of pesticides
> FIFRA § 3(c)(1)(F)(iii)

How do the data-sharing provisions of the FIFRA work[9]?

1. In order to obtain marketing approval for some agricultural test data, originators provide the U.S. Federal Government with the data and the cost to generate the data (similar to the U.S. Orange Book obligations to submit patent information[10]). If the originators do not provide information on the cost of the data, they can face a negative presumption during the arbitration determination of the actual cost.

2. The originator gets ten years of market exclusivity, but for the ten years afterwards, the originator is granted a limited remuneration right subject to procedures for non-voluntary licenses by third parties.

[9] For an analysis of the FIFRA cost sharing model read M. Cresence Stanfford and James C. Wright: “Data Citation, Compensation and Cost Sharing: Pitfalls and Traps for the Unwary”. Available online at: http://www.pesticide.net/x/article/stafford20021210.pdf

[10] As described in the CPTech Discussion paper on linkage. See: “Patent-Registration Linkage” (CPTech Discussion Paper No. 2, 2006). Available online at: http://www.cptech.org/publications/CPTechDPNo2Linkage.pdf

3. Generic/ second applications have an automatic right to use the data and can register products relying on the data, if they pay an adequate remuneration to the test data originator within a limited period of time.

The issue, of course, is what an "adequate remuneration" is. The FIFRA system begins with a requirement to resolve this issue voluntarily. Once the EPA (US Environmental Protection Agency) has issued a second entrant registration, the second applicant has to submit the test's originator an "offer to compensate" and the parties have to try to reach an agreement.

However, if the parties do not reach an agreement, 90 days after the delivery of the offer[11], either party can start a **binding arbitration**[12] with the Federal Mediation and Conciliation Service that will decide what compensation is adequate.

There is no explicit compensation standard set forth in FIFRA. However, since 1975, arbitration decisions have often been resolved based on a **cost-sharing approach,** meaning that the second applicant should share the cost of generating the test data with the originator.

The concrete allocation of costs between the parties is a controversial issue. The cost for the second applicants has sometimes been based upon their **relative/actual market share**[13], meaning that compensation is linked to the value of the data to each company, which depends on resulting sales. The argument is simple: if one party (A) has a market share larger than the other (B), (A) will benefit more than (B) from its registration; and since (A) can be expected to benefit more than (B), it should pay more of the costs of the data development program.

[11] Or **60 days** after a party offers to share the cost or jointly develop the data for FIFRA § 3(c)(2)(B)(iii) situations: "*If, at the end of sixty days after advising the Administrator of their agreement to develop jointly, or share in the cost of developing, data, the registrants have not further agreed on the terms of the data development arrangement or on a procedure for reaching such agreement, any of such registrants may initiate binding arbitration proceedings by requesting the Federal Mediation and Conciliation Service to appoint an arbitrator from the roster of arbitrators maintained by such Service. The procedure and rules of the Service shall be applicable to the selection of such arbitrator and to such arbitration proceedings, and the findings and determination of the arbitrator shall be final and conclusive, and no official or court of the United States shall have power or jurisdiction to review any such findings and determination, except for fraud, misrepresentation, or other misconduct by one of the parties to the arbitration or the arbitrator where there is a verified complaint with supporting affidavits attesting to specific instances of such fraud, misrepresentation, or other misconduct. All parties to the arbitration shall share equally in the payment of the fee and expenses of the arbitrator. The Administrator shall issue a notice of intent to suspend the registration of a pesticide ….if a registrant fails to comply with this clause*."

[12] For the official arbitration rules of FIFRA test data compensation/ cost sharing disputes (29 C.F.R. Part 1440) see: http://www.pesticide.net/x/cfr/arb_rule.htm

[13] For example, Dupont v. Griffin and Drexel/Docket No. 16-171-0080-86M (1988) Decision available at http://www.pesticide.net/x/comp/dupont1.htm. American Cyanamid v. Aceto / Docket No. 13-171-0800-85 (1989) Decision available at http://www.pesticide.net/x/comp/aceto.htm. Ciba-geigy v. Drexel Chemical / Docket No. 16 171 00321 92G (1994). Decision available at http://www.pesticide.net/x/comp/ciba.htm

The usual practice is that:

- The arbitration decides the amount of compensation and the second applicants' entrance into the market is not delayed because the generic companies have an automatic right to use the data and these disputes are resolved while the generic product is on the market.

- Arbitration costs are shared equally between parties.

- The regime does not allow the possibility to appeal the decision, except for fraud, misrepresentation, or other misconduct by one of the parties or the arbitrator, where there is a verified complaint with supporting affidavits attesting specific instances.

- The basis is the actual cost incurred by the originator, not how much it would cost to replace the data. The arbitrators require originators to provide evidence to support cost claims and the burden of proof is on the originator, since they are in a better position to know the actual cost of generating the data.

In at least one decision, a U.S. District Court has judicially confirmed a FIFRA final arbitration order[14]. In 1984, the U.S. Supreme Court reviewed the FIFRA data-sharing provisions on the Ruckelshaus case and declared that the provisions were constitutional and that there was no improper "taking" of property without just compensation.[15]

Cost Sharing Model for Pharmaceutical Test Data

CPTech proposes the FIFRA model be used by countries being pressured in trade negotiations to provide TRIPS Plus protection for pharmaceutical test data.

Originators should be required to disclose their real investment costs on originating the test data and provide documental evidences.

An international organization, such as WIPO or WHO, could create a public database that would centralize the collection of data on the costs of the clinical trials worldwide. This might even be considered in connection with a larger database that include medical information.

The generic/second applicants should be allowed to use/rely upon the originators test data from "day one" and no data exclusivity periods should be applicable.

[14] U.S. District Court for the District of Columbia in Cheminova A/S v. Griffin L.L.C., 182 F. Supp. 2d 68 (D.D.C. 2002) available online at: http://www.pestlaw.com/x/comp/cheminova02.html

[15] Ruckelshaus v. Monsanto Co., 467 U.S. 986 (U.S. 1984). Some relevant language: "But Monsanto has not challenged the ability of the Federal Government to regulate the marketing and use of pesticides. Nor could Monsanto successfully make such a challenge, for such restrictions are the burdens we all must bear in exchange for the advantage of living and doing business in a civilised community."

Under the proposed model, the originator of the test data would get a remuneration right during a limited period of time of 3 to 5 years. The generic/second applicants would contribute to the cost of generating this data by paying the originator an adequate and reasonable remuneration.

Again, determining the adequate remuneration is the key point. Two different approaches should be considered:

a) A "reasonable royalty" model, where generics could pay a percentage representing a modest share of the generic's revenues.

b) A "pro-rata share of costs" model, where generics could pay a contribution based upon their share of the global market sales for the product.

This second option is similar to the one that some FIFRA arbitrators have designed for agricultural test data. A possible adjustment could be introduced for risk of investments and cost of capital[16]. The adoption of an arbitration system, similar to the U.S. agricultural data one, could also be considered for pharmaceutical data.

For the second option, it is essential that the implementing legislation makes it clear that a generic producer in a country would only be obligated to pay for the fraction of the total costs of the test data that is appropriate for their (likely small) fraction of the total global market for the product.

> For example, if the costs[17] of test data for a particularly drug were $50 million, amortized over five years in equal installments, and the generic producer had sales that were .1% of the **global market** for the product, the pro-rata share of the costs for one year would be as follows:
>
> $50,000,0000 x 1/5 X .001 = $10,000 (a year during 5 years)

If the domestic generic firm's share of the global market is smaller, the contribution will also be smaller.

The proposed cost sharing model has several **advantages**:

- During the period of protection, the test data originators can benefit from reasonable contributions to the costs of the test data.

- There will be less pressure to reward patent owners with strong exclusive rights, because drug developers also benefit from the sharing of costs of test data.

[16] See, for example, the Microgen v. Lonza arbitration Decision (2000) available online at http://www.pesticide.net/x/comp/microgen3.html
[17] Calculated with appropriate adjustments for risk.

- National regulators can avoid the creation of monopolistic situations, and foster competition within the pharmaceutical industry.

- Generic competitors who share costs can enter the market without delay because there is no exclusive marketing period.

- Developing countries' generic companies' contributions will be affordable, because of their small share in worldwide sales.

- The compromise position may be politically easier to sustain than one of no protection of test data.

- It takes into consideration the ethical concerns of duplicating clinical trials, by eliminating the need to duplicate clinical trials.

MODEL LANGUAGE FOR THE COST-SHARING APPROACH[18]

1. Use of or Reliance on Undisclosed Test Data Submitted for Pharmaceutical Approval

Parties shall be permitted to use or rely on undisclosed data submitted by a prior party for the purpose of meeting government requirements for marketing approval of pharmaceuticals, or to have a government agency use or rely on the data. Such right shall be automatic, and is not subject to appeal.

2. Commercial Use of Undisclosed Test Data Submitted for Pharmaceutical Approval

When an agency requires parties, as a condition for the commercial marketing of pharmaceutical products which utilize new chemical entities, to submit undisclosed test or other data, the origination of which involves a considerable effort, the agency shall require subsequent applicants that use or rely upon the originator's data, or have the government use or rely upon such data, for registration of competing products to contribute to the costs of such tests, if the following conditions are met:

a. Marketing approval was obtained within the past five years.

b. Marketing approval was obtained within one year of any foreign approval.

b. The person who seeks contributions to the cost of such tests and data provides the agency with public disclosures of

i. the costs of such tests or data, supported by independent verification,

[18] This is a modified version of proposal earlier proposed by Rob Weissman, as reported in R. Weissman: Data Protection: Options for Implementation. Included in the book: Negotiating Health: Intellectual Property and Access to Medicines, Pedro Roffe, Geoff Tansey, David Vivas-Eugui, Earthscan Publications Ltd. 2006.

ii. a reasonable estimate of the country's likely share of the global market, and
iii. the amount of global revenue the product has generated to date, and in the previous
12 months.

3. Contributions to the cost of tests

a. Pursuant to section 2, parties using or relying, or seeking to have the government use or rely, on data submitted by a previous party shall make reasonable contributions to the costs of such data. The amount of the contribution shall be based upon the payment of a reasonable royalty for the use of the data, or payment of a pro-rata share of the adjusted costs of the data. In the absence of agreement between the parties, the method and amount of payment shall be determined by the agency.

Reasonable royalty. If the reasonable royalty method is selected, the royalty rate should be either a rate agreed to by the parties, or 4 percent of the net sales of the generic product, or a different rate determined by the agency.

Pro-rata share of adjusted costs. If the pro-rata share method is selected, the adjusted cost shall be the actual costs, with reasonable and transparent adjustments for risks involved in clinical trials, based upon evidence of typical success rates, for Phase I, II or III trial. The annual pro-rata share of the adjusted costs shall be one fifth of the total adjusted cost, multiplied by the generic company's percentage share of the global market for the product.

b. There shall be no compensation required where reliance on the data is sought for government or non-commercial purposes.

MORE INFORMATION

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