

Regulatory Data Protection

The Issue

Regulatory Data Protection (RDP¹) confers on the holder of a marketing application, for a set period of time, the exclusive use of the proprietary pre-clinical and clinical data that it compiled at significant cost and submitted to the applicable regulatory authority to obtain approval of its product. After the set period of time, generic pharmaceutical companies are then permitted to rely upon the data to obtain approval of their "abbreviated" applications.

Some ask why RDP is needed if patents exist. Others see it as a brake on competition and market access. This paper provides some background on the evolution of RDP and explains why it is so important to the pharmaceutical industry. It also sets out the rationale for why the TRIPs RDP provisions should be interpreted in a robust way and demonstrates how, by protecting the substantial financial investment involved in drug discovery and development, RDP provides incentives to undertake research which is particularly important where patent protection is weak or non-existent.

GSK's Key Messages

- The pharmaceutical industry is virtually unique in its obligation to generate, at risk, a substantial body of data and submit those confidential data to regulatory authorities as part of the product registration process. It submits the data to enable its products to be registered for sale. Governments, therefore, have a responsibility to regulate use of the data in a fair and effective way via strong RDP laws.
- Unlike with patents, enforcement of RDP is the responsibility of governments, not the originators of the data. This obligation represents an important commitment from Governments to support innovation in a spirit of partnership with medical researchers.
- RDP recognises the value and proprietary nature of data submitted to regulatory authorities as part of, and solely for the purpose of, product registration. It also protects (and thus provides incentives for) the substantial financial investment involved in drug discovery and development.
- RDP and patents are two distinct and separate forms of intellectual property protection. A country's intellectual property framework should ensure strong protection for both in order to provide incentives for research and development.
- RDP is of particular significance where strong patent protection for a particular product or indication may not be available, where the patent term has been eroded by a long development phase or where patent enforcement systems are inadequate. Without RDP research might focus only on patentable compounds.

¹ Some refer to RDP as "data exclusivity". RDP should not be confused with protection of personal data under data privacy laws. RDP protects the data generated by the pharmaceutical and agro-chemical industries and is submitted to government authorities in order to obtain marketing approvals for their products. Data *privacy* protects individuals from wrongful disclosure of data relating to them.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

- GSK accepts that, in the interest of facilitating market access of generics at an appropriate time, and the need to avoid repetitive animal testing and human clinical trials, competitors should be able to rely upon the originator's proprietary data for certain types of products. However, such reference to the originator's data should, in fairness, only be permitted *after* expiration of a reasonable period of protection. Direct or indirect reliance upon data *during* the period of protection should be prohibited.
- GSK supports greater transparency of clinical data and has made important commitments in this area. However, it is important that this enhanced transparency does not undermine RDP. Clinical and other data submitted to regulatory authorities must not be used by third parties to gain a license to market a copy of the originator's product.
- TRIPs requires that unpublished data provided to a regulatory authority in order to obtain approval for marketing a pharmaceutical product should be protected against disclosure and unfair commercial use. It does not specify any minimum period of RDP. Many countries offer between 5 and 10 years protection from local approval for new chemical entities (NCEs). GSK supports extending data exclusivity for both NCEs and biopharmaceutical products, plus additional protection for new indications and formulations which require substantial development. We believe this represents a fair reward for the investment and effort involved in generating the data.
- There is no obligation within TRIPs to offer RDP to new indications or formulations for an approved product. However, both the US and EU recognise that RDP is a good way of providing incentives for "the considerable effort" involved in the development of new indications for existing compounds. GSK welcomes this recognition and would like to see it applied globally to all indications, as well as extended to formulations that require a significant investment in additional clinical studies.

BACKGROUND

Definition

The concept behind RDP is that Governments and Regulators should not allow unfair commercial advantage to be taken of the data which a company submits in order to obtain and maintain marketing approval. It prevents competitors or Governments, for a period of time, from using the originator's data by relying on it when seeking or granting approval for a generic copy and thus taking commercial advantage of the expensive investment undertaken by the originator. In this way, it protects (and thus provides incentives for) the substantial financial investment involved in drug discovery, development and regulatory approval.

The data to which protection is extended may include, but is not limited to, the originator's underlying laboratory, pre-clinical and clinical data, including information regarding product indications, efficacy, tolerability, pharmaco-kinetics, drug interactions, side effects, contra-indications, precautions, warnings, adverse effects, dosage and product administration.

The generation of registration data involves a substantial amount of time and expense for the originator. The entire drug development process from discovery to marketing can take as long as fifteen years and costs on average \$1.3 billion per product. If these data could immediately be shared with or relied upon by third parties, there would be no incentive for a company to generate these data in the first instance, unless the investment in terms of both time and costs were sufficiently protected.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

RDP is Distinct from Patent Protection

RDP and patents are two critical intellectual property rights for the pharmaceutical industry; however, they are distinct and separate forms of protection. Patents protect inventions that meet the criteria for patentability – novelty, utility and obviousness/inventive step. Making an invention, however, is distinct from the enormous scientific work and financial investment to create the data for a pharmaceutical product to demonstrate quality, safety and efficacy to regulatory authorities. This proprietary data is worthy of protection in itself, regardless of whether the product is patentable. It costs no less to develop a non-patented product than a patented one.

RDP is of particular significance where patent protection may not be available, where patent enforcement systems are inadequate, where the patent is weak² or where the patent term has been eroded by a long development phase. This may only become clear well into the development phase or after launch of the product. RDP is, therefore, an incentive for innovation where there is little or no patent protection.

Implementation of TRIPS Article 39.3

Article 39.3 of TRIPs requires a WTO Member State to protect unpublished data relating to pharmaceutical products containing new chemical entities (NCEs)³. An NCE is a regulatory concept and should not be confused with the “novelty” requirement of a patent. Any compound, or combination of compounds, which is approved/ marketed as a pharmaceutical for the first time in the country concerned is a “new chemical entity” for the purpose of protection under TRIPs Article 39.3, irrespective of whether it is “novel” under patent law.

Since January 2000 all WTO member countries – with the exception of the Least Developed Countries – have been required not only to have TRIPs-compliant RDP but also effectively to enforce this protection. Unlike with patents, enforcement of RDP is the responsibility of governments, not the originators of the data. So, even in situations where a patent may exist, during the RDP period, governments must take responsibility for protecting the data by not granting applications for approval which directly or indirectly rely on the originator's data.

Article 39.9 of TRIPs prohibits unfair commercial use of published and unpublished regulatory data. If a third party seeks to rely on an originator's confidential data in obtaining approval to market its product, it makes commercial use of the originator's data. It is necessary to provide for a period during which this is not permitted to prevent free-riding by the third party, which is unfair commercial use. Therefore, marketing approval applications for a product which refer directly or indirectly to the originator's safety and efficacy data should not (for a fixed period of time) be granted by regulatory authorities.

² **Judgment of Jacob J of the English Patents Court in Teva v Merck, 21 January 2003**

“I accordingly hold both patents invalid. I do so with some regret. Merck have only had a few years' exclusive exploitation of alendronate. They must surely have had to make a very considerable investment and incurred considerable risk in bringing it 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 medicines and analogous fields.”

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.”*

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

The data submitted by an innovator company as part of the product registration process will be specific to its particular product and should generally only be relied upon for equivalent products. Reliance on data for approval of a similar, but not identical, product (for example, a different salt or polymorph) may raise public health concerns. In addition, products for which bioequivalence and efficacy cannot be shown by measuring the blood level of the active ingredient, such as inhaled or topically effective products, may require additional clinical testing.

Indirect Reliance

Where an originator does not file a full data package with local authorities, some argue there is no data to protect and it is, therefore, acceptable to allow a generic company to enter the market immediately by showing that its product is equivalent to the originator's. This can happen where, for example, in order to obtain local marketing approval, the originator only needs to show that it has approval to market in another specified country. It can also happen where an originator has not obtained a local approval and the generic company seeks to show that its product is equivalent to the originator's product approved in another country.

This argument is incorrect. In cases such as these, although the local regulatory authority does not examine the originator's data, it relies on the approval by the regulatory authority in another country which has examined the originator's data. This is "indirect reliance" on the innovator's data, and it should not be permitted during the RDP period.

Transparency of Data

Recent transparency initiatives from the EU and elsewhere aimed at increasing access to clinical trial and other data should not undermine RDP. Clinical trial data stored in public databases or published in journals provide a valuable resource for researchers, medical professionals and the public. However, while GSK supports greater transparency of clinical data and has made important commitments in this area, it is important that this enhanced transparency does not undermine RDP. Clinical and other data submitted to regulatory authorities must not be used by third parties to gain a license to market a copy of the originator's product.

RDP Periods

Unlike for patents, the period of RDP is not fixed by the TRIPs Agreement. However, most countries which have introduced RDP into their law offer between 5 and 10 years protection from local approval for new chemical entities (NCEs).

The EU has a period of 10 years, during which third parties cannot receive authorisation to market a product for which the marketing approval was obtained by relying on the originator's data. The EU has also allowed for the possibility of an extra year's protection for a new use considered to be of significant clinical benefit in comparison with existing therapies.

The United States has recently introduced a period of 12 years for biological products but only has 5 years for other pharmaceuticals. Recognising the key role that RDP plays in incentivising innovation and thereby supporting public health, GSK would like to see the US increase this 5 year term to at least match the period for biological products.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

A country's intellectual property framework should provide for both strong patent protection and strong RDP. In this respect, the 5 years basic exclusivity offered in the USA for non-biological products is a good example of how an imbalance between patent protection and RDP can work to the possible detriment of innovation and public health. If key patents are challenged after grant and held invalid, the effective period of exclusivity afforded by the US system can be as low as 5 years, substantially less than in the EU. This not only weakens overall incentives to innovate, but also has the potential to focus investment into research areas where commercial risk is lowest, rather than where medical need is greatest.

New Indications and Formulations

Improvements on patented or patent-expired products may not qualify for patent protection. In the absence of some other form of protection, research might, therefore, only be undertaken into "patentable" inventions, rather than into further valuable research on existing products. Detailed below are examples of medicinal products for which RDP provided incentives for the development of subsequent valuable indications:

- A medicinal product originally used in second line treatment of metastatic ovarian cancer resistant to platinum-based chemotherapy was subsequently developed as second line treatment of breast cancer, first line treatment of ovarian cancer, treatment of lung cancer and treatment of Aids-related Kaposi's sarcoma.
- A number of cardioselective β -blockers originally developed to treat arterial hypertension and angina were subsequently developed to treat chronic heart failure (CHF); cardiovascular insufficiencies; cardiac arrhythmias; cardiac symptoms of hyperthyroidism; migraine headaches; and prevention of haemorrhage in cirrhosis.

Both the US and EU increasingly recognise that RDP is a good way of providing incentives for the considerable effort involved in the development of new indications for existing compounds. The US, for example, provides 3 years exclusivity for a new indication (but not **all** indications for the product). Meanwhile, the EU will provide one year for **all** uses of a product - but only when the new indication is deemed to be of "significant medical benefit".

As more new indications are discovered for existing compounds, RDP will be critical for providing appropriate incentives for further pharmaceutical innovation. By failing to offer some kind of additional incentive for generating data pertaining to, for example, new patient populations or indications, governments miss a good opportunity to promote research of potentially great benefit to public health. In the absence of this incentive for further research, doctors may increasingly resort to widespread off-label prescribing of the product. Against this background, countries should be encouraged to follow the EU and US's lead in extending some form of exclusivity for new indications, as well as formulations.

Self-medication / "Switch" Products

Governments and associated funding groups are increasingly considering mechanisms to empower greater patient involvement and self-care within the overall healthcare system. More widespread availability of non-prescription products and, in particular, "switching" from prescription to non-prescription status can be an important tool in this process. However, the investment required to "switch" products (in terms of safety assessment, and scientific and educational programmes required by agencies) can be significant.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

In order to stimulate innovation and investment in the self-medication area, some form of RDP should be extended to the "switch" process. The EU recognised the importance of self-medication within the G10 framework (Recommendation V) and has recently introduced a 1 year protection period for switches. While GSK welcomes this initiative, we believe further developments are needed. The US, in comparison, currently offers up to 3 years RDP for switches. We will, therefore, continue to encourage further efforts in this area, both in the EU and elsewhere.

Support for Smaller Research Companies

The protection afforded unpatented products by RDP could serve as a valuable incentive for fledgling pharmaceutical companies. While they may not yet have the resource or expertise in discovery research to discover and patent novel compounds, the promise of RDP for new indications and formulations of existing compounds could act as a valuable incentive for companies developing an innovative capacity to undertake this type of research. Given this potential, countries anxious to support and build a viable research base should be encouraged to extend RDP to new indications and formulations.

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