

Regulatory Data Protection

The Issue

The importance of regulatory data protection (RDP¹) is often questioned. Some ask why it is needed if patents exist. Others see it as an unjustifiable 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 where patent protection is weak or non-existent.

GSK's Key Messages

- The pharmaceutical industry is virtually unique in its obligation to submit 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 govern third party access to these data in a fair and effective way via strong RDP laws.
- RDP recognizes the 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. Without RDP, research might focus only on patentable compounds.
- 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.
- GSK accepts that, in the interest of facilitating timely market access and the need to avoid repetitive animal testing and human clinical trials, competitors should be able to refer to the originator's proprietary data which remains on file with regulatory authorities. However, such reference to the originator's data should only be permitted *after* expiration of a reasonable period of protection. Direct or indirect reliance upon confidential data *during* the period of protection should, however, be prohibited.
- 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.

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

- TRIPs requires that regulatory data 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 NCEs. GSK supports a 10 year period plus additional protection for new indications and formulations. We believe this represents a fair return for industry being expected to share our confidential data and a fair reward for the investment and effort involved in collating the data.
- There is no obligation within TRIPs to offer RDP to new indications or formulations. 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.

BACKGROUND

Definition

The concept behind RDP is that it prevents disclosure by Governments and Regulators of the confidential data which a company submits in order to obtain and maintain marketing approval. It also prevents competitors or Governments from relying on the originator's data when seeking or granting approval for a generic alternative 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 and development.

The proprietary data to which protection is extended may include, but is not limited to, the originator's 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. Any data disclosed as part of a patent application or scientific publication is not confidential and therefore not subject to any protection.

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 \$1.2 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 by another means, such as a patent.

RDP v Patent Protection

RDP and patents are two critical intellectual property rights for the pharmaceutical industry; however, they are distinct and separate forms of protection. Key to this distinction is the fact that patent validity is dependent on whether or not there is an invention; patentability has no inherent relationship with the safety, quality and efficacy of the drug as ultimately marketed. This information is established by generation of the data that is subject to RDP. The characteristics which determine patentability may have no bearing on whether a product will come to market. Equally, the proof of safety, quality and efficacy required to market a product is needed irrespective of whether a product is patentable. Protection of one right should not be dependent upon the other as this contravenes TRIPs.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

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 it has been eroded by a long development phase. This may only become clear well into the development phase or after launch of the product.

Implementation of TRIPS Article 39.3

Article 39.3 of TRIPs requires a WTO Member State to protect registration data for NCEs submitted to regulatory authorities against “unfair commercial use and disclosure”, except when necessary to protect the public.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 has been 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 and thereby, play a role in incentivising innovation.

To give practical effect to Article 39.3 WTO members should, in GSK’s view, have laws which include;

- **Non-Disclosure of Data:** Information provided to health authorities in confidence by the owner of the information should be protected against being made public. This, in turn, will help ensure it cannot be unfairly appropriated and used in another country to support a generic application for marketing authorisation in that country.
- **Non-Reliance upon Data:** If a 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. Even once the period of protection has elapsed, regulatory authorities should carefully consider the circumstances under which demonstration of bioequivalence will be sufficient. The confidential data submitted by any R&D based company as part of the product registration process will be specific to their particular product and should really only be relied upon for identical products.

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

Reliance on confidential data for approval of a similar, but not identical, product (for example, a different salt or polymorph) may raise public health concerns.

Indirect Reliance

It is sometimes argued that where an originator does not file a full data package with local authorities, 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 similar 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 even obtained a local approval and the generic company only needs to show that its product is similar to the originator's product which has been 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 data. Therefore there is "indirect reliance" on the data which should not be permitted in the RDP period.

Some also argue that it is permissible to allow approval of a generic product purely on the basis that it is similar to an originator product described in publications (such as medical journals or clinical trials registers). They argue that this is not relying on confidential data. Again, this argument is incorrect. These types of publications summarise the raw and published data that is generated in the development process. Approvals which subsequently rely on these summaries therefore in fact indirectly rely on the confidential data which they summarise. To allow this is unfair commercial use prohibited by TRIPs unless the law provides a sufficient period during which such reliance is not permitted.

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). GSK generally supports a 10 year period of exclusivity. We believe this represents a fair return for industry being expected to share our confidential data and a fair reward for the investment and effort involved in collating the data.

The EU has recently harmonised RDP across Europe by introducing a period of 10 years during which third parties cannot obtain a marketing approval by relying on the originator's data, with the possibility of an extra year's protection for a new use considered to be of "significant medical benefit". This measure should by now have been implemented into Member States' laws. GSK welcomes this new EU approach which harmonises data protection across the European Union where hitherto protection periods varied between 6 and 10 years (depending on the regulatory procedure used).

GSK also welcomes the fact that the EU approach recognises the distinct role of exclusivity and reflects industry's call for 10 years of protection. Other countries, including the USA, should be encouraged to follow the EU's lead.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

It is not acceptable for Governments simply to provide a robust patent system. A country's intellectual property framework should provide for both strong patent protection and strong RDP. In this respect, the five years basic exclusivity offered in the USA, 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.

RDP and Generic Market Entry

The unique position in which the pharmaceutical industry has been placed in being expected to submit confidential data as part of the registration process, is such that the data should never be "made public" (ie. published) by Governments and their agencies even *after* the expiration of the fixed period.

GSK does, however, accept that competitors should be allowed to refer directly or indirectly to proprietary data which remains on file with regulatory authorities *after* the expiration of that period. At that point, generics need only, for example, show bioequivalence of their product to the originator's drug; they do not have to duplicate the extensive tests undertaken by the originator. As a result, the cost of generics is lowered, competition and timely market entry are supported and the proprietary nature of the originator's data is respected.

New Indications and Formulations

Some 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 allowed the development of subsequent valuable indications:

- A medicinal product originally used in second line treatment of metastatic ovarian cancer resistant to platinum-based chemotherapy, subsequently developed as second line treatment of breast cancer, and first line treatment of ovarian cancer, as well as 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, subsequently developed to treat indications such as chronic heart failure (CHF); cardiovascular insufficiencies; cardiac arrhythmias; cardiac symptoms of hyperthyroidism; migraine headaches; prevention of haemorrhage in cirrhosis.

TRIPS Provisions

TRIPS contains no obligation to offer RDP to new indications or formulations. However, both the US and EU increasingly recognise that RDP is a good way of providing incentives for "the considerable effort" involved (TRIPS Article 39.3) 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".

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

As more and more new indications are discovered for existing compounds, RDP will be critical. It could be the only effective means of providing appropriate incentives for some pharmaceutical innovation. By failing to offer some kind of additional incentive for generating data pertaining to the use of drugs in children and the elderly, 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 have no alternative but to 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" (the process of 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 scientific and educational programmes as required by agencies) can be significant. In order to stimulate innovation and investment in the self-medication area, some form of RDP should therefore 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 one year protection period for switches. While GSK welcomes this initiative, we believe further developments are needed (the US, for example, 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 Local Research Companies

The protection afforded unpatented products by RDP could serve as a valuable incentive for fledgling pharmaceutical companies. While they may not have the expertise in discovery research to develop and patent novel compounds, the promise of RDP for new indications and formulations of existing compounds could act as a valuable incentive to secondary research. Given this potential, countries anxious to support and build a viable research base should be encouraged to follow the US and EU's lead in extending RDP to new indications and formulations.

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