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***Rapport de Mme Fabienne Keller sur les maladies émergentes infectieuses***

**OBJET : Compte-rendu de l'audition du 4 avril 2012**

**Docteur Soizic Courcier, Directeur Médical et des Affaires Réglementaires du laboratoire GlaxoSmithKline France (GSK) (Marly-le-Roi).**

Le docteur Courcier décrit le laboratoire GSK à la fois comme **un producteur et un inventeur de nouveaux traitements**. Mais le laboratoire s'attache également à favoriser l'accessibilité de ses nouveaux traitements par les populations des pays en développement grâce à des politiques d'accès différenciées. Le docteur Courcier évoque ainsi l'importance majeure des accords de licence volontaires ont été élargis à 69 pays afin que les génériqueurs des pays du Sud puissent développer les traitements de manière autonome. Le laboratoire GSK a également versé un montant de 10 millions de livres sterling à un fond pour l'accès aux soins en plus de ses efforts sur la commercialisation de ses produits.

**Une collaboration très anticipée est la condition indispensable de la réussite des stratégies de surveillance des maladies infectieuses émergentes**. Face à des évolutions pouvant être très rapides - exemple du SRAS -, **le perfectionnement des outils épidémiologiques est indispensable**. Qualifiant l'épisode de la grippe H1N1 « d'exercice pandémique », le docteur Courcier souligne la réactivité des autorités sanitaires et de l' face à cette menace.

Pour autant, **des défaillances subsistent dans le système de surveillance sanitaire français. L'absence d'une base épidémiologique unique est sans doute la principale lacune**. L'organisation actuelle s'appuie sur des structures de référence par maladie **sans véritable coordination** de l'ensemble des données. Selon le docteur Courcier, la France n'a pas pris ce virage épidémiologique alors que la Grande-Bretagne dispose quant à elle d'une base de données unique : le General Practice Research Database (GPRD), devenue *Clinical Practice Research Datalink* depuis le 29 mars 2012. La nécessité de la création d'une base de données unique d'épidémiologie s'ancre dans des préoccupations plus générales. Car la complexité des mécanismes de surveillance sanitaire paraît peu compatible avec la rapidité qui caractérise l'émergence des nouvelles maladies infectieuses. Le développement de la pharmaco-épidémiologie en France et la mise en place de standards méthodologiques de niveau européen et international pour pouvoir accélérer l'innovation thérapeutique en faveur du patient est nécessaire.

S'agissant des perspectives de l'industrie pharmaceutique, le docteur Courcier met en avant les réserves des autorités sanitaires dans leurs relations avec les industriels et il est de ce point de vue souhaitable que s'installe une culture de la transparence. La perception de l'industrie pharmaceutique est actuellement défavorable dans l'opinion après l'affaire dite du Médiator©. Le mouvement de clarification des liens pour prévenir les conflits d'intérêt, qui a été initié par la loi du 29 décembre 2011, permettra de renforcer cette transparence. C'est ainsi que le laboratoire GSK s'attache à séparer ses activités de promotion (marketing) de ses activités d'échanges scientifiques avec les professionnels de santé et l'ensemble des acteurs (ex : associations de patients).

Si les politiques de recherche sont évidemment multiples, le laboratoire GSK s'inscrit néanmoins clairement dans **une stratégie orientée vers les maladies infectieuses émergentes (MIE).** Cette stratégie globale se décline en trois grands axes :

- a) **un axe vaccins** ;
- b) **un axe consacré aux maladies dites négligées** ;
- c) **un axe d'infectiologie et d'antibiothérapie**.

**L'organisation interne de la recherche du laboratoire GSK** s'appuie sur 38 petites unités dont les effectifs sont de 60 à 70 chercheurs par unité. Des plans à trois ans sont fixés définissant des objectifs de recherche qui déterminent le budget triennal des unités et qui garantissent une autonomie de gestion totale de celles-ci. Au terme des trois ans, les résultats de la recherche sont soumis à un comité scientifique composé d'acteurs internes, externes, mais également d'investisseurs.

**Pour expliquer les préoccupations économiques de l'industrie pharmaceutique, l**e docteur Courcier décrit une chronologie-type du développement d'un nouveau médicament autour de trois phases principales : recherche, mise sur le marché, exploitation.

1) **Recherche :**

- recherche préclinique (sur les animaux) ;
- recherche chez l'homme ;
- enregistrement.

Cette période de recherche dure en moyenne **10 ans** et représente un coût d'1 milliard d'euros.

2) Enregistrement et **mise sur le marché :**

Il faut ensuite attendre deux années supplémentaires avant de voir le nouveau médicament arriver sur le marché. On distingue deux procédures d'enregistrement :

- a) la **procédure européenne centralisée** qui est aujourd'hui la voie simple et rapide privilégiée dans une majorité des cas ;
- b) la **procédure décentralisée** : l'autorisation de mise sur le marché (AMM) est d'abord demandée pour un pays et peut ensuite être étendue ultérieurement à d'autres .

Cette période d'enregistrement est suivie de la procédure définissant avec les autorités les conditions de remboursement et de prix

**3) Exploitation :**

La durée moyenne des brevets s'élevant à **20 ans** et les extensions de brevets se limitant à des maladies rares ou aux indications pédicatriques, **le temps d'exploitation effectif du médicament est réduit –**environ huit ans - conduisant à **un retour sur investissement critique** pour le laboratoire.

GLOBAL
PUBLIC POLICY ISSUES
GlaxoSmithKline's Position

# Intellectual Property & Access to Medicines in Developing Countries

## The Issue

Millions of people in developing countries do not have access to even the most basic healthcare services, including safe and effective medicines. This has led to a global healthcare crisis, in which diseases such as HIV/AIDS, tuberculosis (TB) and malaria are spreading in countries that have neither the resources nor the facilities to deal with them.

Poverty is the single biggest barrier to improving healthcare in the developing world. In many countries people do not have enough food, access to a clean water supply, hospitals or clinics in which to receive treatment, and healthcare professionals to care for them.

Nevertheless, there are some who prefer to blame intellectual property, and in particular patents, for the fact that many millions of people are denied access to the medicines they need.

This paper provides some background on the importance of Intellectual Property (IP) to biomedical innovation; addresses some of the accusations around how IP can act as a barrier to access; and sets out the real barriers and possible solutions to the access challenge in developing countries.

## GSK's Position

- Improving healthcare in the developing world presents a complex challenge to the global community. It can only be addressed if the significant barriers that stand in the way of improved access are tackled as a shared responsibility by all sectors of global society - governments, international agencies, charities, academic institutions, the pharmaceutical industry and others.

- GlaxoSmithKline (GSK) is committed to playing a full part in addressing the healthcare challenges of the developing world by taking an innovative, responsible and, above all, sustainable approach. Our core business activity of developing and launching new medicines and vaccines significantly improves health. However, GSK is making a vital contribution to developing country healthcare through action in four areas[1]:

  - preferential pricing of our medicines and vaccines;
  - investing in research and development (R&D) that targets diseases particularly affecting the developing world, including pursuing an open innovation strategy[2];
  - community investment activities and partnerships that foster effective healthcare; and,
  - innovative partnerships and solutions, such as voluntary licensing.

- It is misleading and counter-productive to focus on patents in the access debate. Patent protection stimulates and fundamentally underpins the continued research and development for new and better medicines for diseases including those which occur in the developing world. Without adequate intellectual property protection, the medicines that are needed in the developing world are far less likely to be developed.

[1] For more information, please see *http://www.gsk.com/responsibility/index.htm*
[2] http://www.gsk.com/collaborations/tres-cantos.htm

- The WHO estimates that adequate therapies do not exist for over 70% of the 2,500 currently recognised medical conditions, while many existing therapies could be improved. Market conditions must provide sufficient incentives to encourage the research required to address this need. Patents are a key incentive to the private sector to undertake the cost and risk of pharmaceutical development.

## BACKGROUND

### The Importance of Patents to the Pharmaceutical Industry

Developing an innovative pharmaceutical product or vaccine is a costly and risky activity. It requires:

1. the discovery of active substances suitable for treating or preventing the medical condition
2. developing them into formulations suitable for administration to patients
3. satisfying the regulatory authorities in all countries where the product is to be sold that the product is safe and effective.

Approximately 5-10,000 compounds are synthesised for every one that comes to market. Those that show some type of potential medical activity undergo pre-clinical and, if this is successful, large-scale clinical testing before applications to approve the product are made. Substantial numbers, often thousands, of patients undergo clinical trials. Following approval, post-marketing surveillance of the product is required.

The average cost of bringing a new pharmaceutical product to market has been estimated by Tufts University to be $1.2 billion, including the costs of failure, and only one in three drugs which are brought to market is profitable. Furthermore, approximately 70% of the cost of bringing a product to market arises after discovery of the compound.

### Patent Protection and Pharmaceuticals

Companies would not incur the risk and cost of innovative R&D if, shortly after launch of their products, a cheaper copy could be launched by a competitor who had the competitive advantage of not incurring developing costs and risk and who did not develop the market for the product.

A period of freedom from competition from copies is therefore needed to provide the incentive to innovate and reward for innovation. Patents are a vital way of providing this incentive and reward. The period of exclusivity conferred by a patent relates to the specific patented product, not to therapeutic classes, for example. This means that novel products that do not infringe the original patent can still be launched to provide competition. So patented compounds from one company often compete with patented compounds from another, and unpatented (generic) products often compete with patented products.

Patents are granted for products and processes which are new (i.e. not known) and inventive (i.e. not obvious) at the time they are applied for. They give their owner the exclusive right to manufacture and market the product for (usually) 20 years from the date of application. In that 20 years, the innovator can prevent copy products from entering the market (although, as we shall see below, in practice the period of protection is very much shorter for pharmaceuticals.)

GLOBAL
PUBLIC POLICY ISSUES
GlaxoSmithKline's Position

# Compulsory Licenses

## The Issue

Compulsory licenses (CLs) are widely recognised as one of the flexibilities of the TRIPs Agreement. As the access to medicines debate has progressed over the years, it has been argued by some that widespread use of CLs could significantly help to alleviate the access crisis in the developing world. However, as patents are not a barrier to access, undermining their effect via CLs would not help to address the access crisis. If anything, widespread compulsory licensing could exacerbate access problems, as well as undermine the much needed R&D into new vaccines and therapies that society relies on the private sector to undertake.

## GSK's Position

- GSK acknowledges that compulsory licenses (CLs) are one of the flexibilities in TRIPs and that their sparing use can be appropriate. However, as the DG of the WHO, Margaret Chan, acknowledged in January 2007, "*We have to find a right balance for compulsory licenses. We can't be naïve about this. There is no perfect solution for accessing drugs in both quality and quantity*". Compulsory licensing is an option not a solution.

- Systematic use of CLs weakens the intellectual property (IP) system. The IP system underpins the ability of the private sector to undertake the R&D that is essential if we are to see advances in treatments and vaccines for diseases of the developed and developing world. The more the IP system is weakened, the less R&D is likely. Widespread use of CLs may, therefore, contribute to a reduction in R&D.

- Innovative companies are less likely to launch products in markets with weak IP systems as generic companies are more likely to undermine the returns in those markets. Without local launch of the innovative product, generic companies may not be able to obtain "piggy back" approvals to sell their products. And even if they do, they rarely provide the post-launch product support, education and surveillance which innovators provide. Excessive use of CLs may, therefore, deny or delay patients' access to innovative products and undermine the introduction of good quality generic versions in the longer term.

- CLs can reduce incentives for Foreign Direct Investment, including technology transfer. Their excessive use is indicative of a weak intellectual property system generally and can undermine the confidence of foreign investors across all industrial sectors.

- GSK welcomed the 31f Agreement reached by the WTO in December 2005 as a reasonable compromise. It allows for a workable solution for compulsory licensing for export to address healthcare crises, but maintains respect for IP. It strikes a balance in ensuring that GSK and others can invest in R&D for badly needed new vaccines and medicines for patients, whilst allowing countries without manufacturing capacity to receive products produced under a CL in the rare cases where this might be necessary to protect public health.

# GLOBAL
# PUBLIC POLICY ISSUES
## GlaxoSmithKline's Position

**BACKGROUND**

**Compulsory Licensing and TRIPs**

TRIPs provides for minimum global standards of IP protection, including patent protection. These standards are to be introduced at different times, depending on the development classification of countries.

Patents are granted for inventions. They give exclusive rights to manufacture, use and sell the inventive product for a limited time, usually 20 years from the date of filing. The exclusive right given is an incentive to undertake the significant cost and risk associated with innovation and commercial development.

The exclusive rights conferred by patents can be the subject of limitations. For example, use of the invention by a third party without the consent of the patent owner can be authorised by Governments under a CL. CLs are permitted by TRIPs provided certain conditions, specified in Article 31 TRIPs, are complied with.

**Patents and Access to Essential Medicines**

It is misleading and counter-productive to focus on intellectual property protection as a significant barrier to access to medicines in the developing world. The root cause of the inability of developing countries to address their healthcare problems does not lie with the patenting system and their ability or otherwise to grant CLs. More than 95% of drugs on the WHO Essential Drugs List (EDL) are not patent protected and yet the WHO says that one third of the world's population do not have regular access to these drugs. According to the WHO, in the poorer parts of Africa and South-East Asia, 50% of the population lack access to these products. First line treatments for killer diseases like malaria and TB are available as generic products at very low cost, and yet many people are denied access to them. And in India, where for years there were no patents for medicines and where there are numerous generic medicine producers, access to medicines is as big a problem as it is in many parts of Africa. The problem of access to medicines cannot be blamed on patents when the medicines are not patented.

The real reason for inadequate access to essential medicines lies not with patents, but with a lack of funding, a lack of political will and inadequate healthcare infrastructure.

**The Importance of Strong IP to the Pharmaceutical Industry**

Strong patent protection is needed to incentivise the high risk and high cost of developing new pharmaceuticals as it creates the conditions under which industry can generate the returns needed to fund R&D. The cost, time and risk involved bringing a product to market is huge:

- Safety and efficacy requirements mean it takes between 8 and 12 years to bring a product to market, and the vast majority of this time passes while the 20 year patent term is running. Returns on the investment, therefore, usually only begin relatively late in the patent term, thus reducing the effective period of patent protection in which adequate returns can be obtained.
- For every 10,000 compounds that are tested for pharmaceutical activity, only 3 reach the market. And only one in every 3 drugs which reach the market is profitable.
- It costs on average almost $1.3 billion on research and development to bring a drug to market

Although the public sector has a crucial role to play in the initial discovery of some drugs, most are invented by the private sector. Further, the post-invention proof of safety and efficacy (by far the most expensive and risky part of the development process) is almost without exception undertaken by, and at the risk to and cost of, the private sector.

Drugs are generally easy and cheap to copy. Industry estimates suggest that it usually costs less than $2 million, including cost of capital employed, to bring a copy product to market. Generic companies generally (and understandably) focus their efforts on copying very successful innovative drugs at the end of patent protection. Therefore, companies which do not bear the risk and cost of drug development can, without doubt, sell drugs at a profit more cheaply than those that do incur the risk and cost of development.

**CLs and Access to Innovative Medicines**

To create a market for a product in a particular country involves cost and effort. If an innovator believes that a CL will be granted once the market has been created, it might not launch its product at all or might delay launch. In such cases, patients in the country concerned are deprived of the innovative product either altogether or temporarily.

Further, in some countries, it is only possible to launch generic products if there is a local approval of the innovative product which the generic company can "piggy back" on. The generic company may have to show that its product is essentially similar to the locally marketed innovative product. If the innovative company does not register its own product for launch, launch of a generic product might be prevented or delayed.

**CLs and Local Health Infrastructure**

CLs reduce the profitability of the local operating companies of innovative pharmaceutical organisations, particularly in developing countries where the commercial environment for companies is already challenging. Innovative companies provide employment, medical services and product support to these markets. It is innovative companies who educate local medical staff about the benefits and dangers of the products concerned and thereby contribute to the local health infrastructure, particularly in the poorest countries. These services are rarely provided to any significant degree by generic companies. CL, therefore, risks undermining local infrastructure in these markets.

**The Doha Declaration and 31f**

In recent years, there has been one issue relating to Article 31 of TRIPS which has attracted considerable attention, namely the requirement in Article 31f that any production under a compulsory licence should be *predominantly* for the *domestic* market. That meant that country A could not issue a CL only to supply country B. So if country B had no capacity to manufacture pharmaceuticals, it may not be able to take advantage of the compulsory licensing safeguards in TRIPS.

In December 2005, the 149 countries of the WTO reached a consensus regarding how to amend the TRIPs Agreement to allow the granting of CLs to address the needs of countries with inadequate manufacturing capacity. The amendment permitted the granting of CLs for export to countries in response to requests from another country providing that, amongst other issues, adequate measures were undertaken to prevent diversion of the product to other (more lucrative) countries/markets.

Some argue that the 31f Agreement created a number of obstacles that poor countries and generic manufacturers would find difficult to overcome. Indeed, many point to the lack of CLs issued under the

Agreement since 2003 as evidence of its ineffectiveness. Clearly, however, the WTO's 149 country membership would not have agreed to the proposal if it had been overly bureaucratic. Furthermore, the Agreement's provisions, such as the anti-diversion measures, actually act *in full accordance with* the interests of poor countries by ensuring that badly needed medicines are not diverted to wealthier markets.

The fact that the 31f Agreement has not been used more often is because:

1. The main problem of lack of access is not related to IP, so an IP-based (CL) solution will not provide the answer;
2. Most essential medicines are not patented, therefore, no license is required to manufacture them. Where some essential medicines do have patents, voluntary licences have already been granted to generic companies;
3. Countries wishing to import generic versions of patented medicines can do so from India without needing a CL to export because the majority of medicines are not patented in India; and
4. Evidence suggests that developed world generic companies may not be able to compete on a cost basis with those in the developing world.

**Revised: August 2011**