Appendix

This appendix provides further details on the arguments succinctly presented through the letter. It is divided into two parts. The first part addresses the legal arguments of the case. The second part focuses on the political aspects of the issue particularly on the impacts of Gilead's SPC on the French healthcare system and on public health policies.

I- Legal arguments

Truvada® (Gilead) is an anti-HIV drug comprised of the combination of Tenofovir Disoproxyl Fumarate (TDF) and Emtricitabine (FTC).

Truvada® was covered until 25 July 2017 by European patent EP0915894. The effects of the patent have been extended by supplementary protection certificates (SPCs) which will expire between 21 and 24 February 2020 depending on the EU member states.

The SPCs are based on European Union marketing authorization EU/1/04/305/001 and on claim 27 of the basic patent, which reads as follows:

"27. A pharmaceutical composition comprising a compound according to any one of claims 1-25 [N.B. tenofovir disoproxil is claimed in claim 25] together with a pharmaceutical carrier and optionally other therapeutic ingredients." (emphasis added).

The main question of law arising from this wording is whether the use of the expression "*other therapeutic ingredients*" to refer to emtricitabine (FTC) is indeed sufficient to protect the TDF/FTC combination pursuant to Article 3(a) of Regulation (EC) No. 469/2009 of the European Parliament and of the Council (hereafter the "Regulation").

This has notably led Justice Arnold of the High Court of England and Wales to request the preliminary ruling at hand on the question of knowing ***"What are the criteria for deciding whether 'the product is protected by a basic patent in force' in Article 3(a) of the SPC Regulation?"***.

The essential case law of the CJEU regarding Article 3(a) of the SPC Regulation as applied to this case, may be summarised as follows:

- C-322/10 (Medeva): "*Article 3(a) of Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products must be interpreted as precluding the competent industrial property office of a Member State from granting a supplementary protection certificate relating to active ingredients which are not **specified** in the wording of the claims of the basic patent relied on in support of the application for such a certificate.*" (Ruling, emphasis added) ;

- C-443/12 (Actavis v. Sanofi): "*It should be recalled that the basic objective of Regulation No 469/2009 is to compensate for the delay to the marketing of what constitutes the **core inventive advance** that is the subject of the basic patent […].*" (paragraph 41 of the Judgment, emphasis added);

- C-493/12 (Eli Lilly): "*Where the active ingredient is covered by a functional formula in the claims of a patent issued by the European Patents Office, Article 3(a) of that regulation does not, in principle, preclude the grant of a supplementary protection certificate for that active ingredient, on condition that it is possible to reach the conclusion on the basis of those claims, interpreted inter alia in the light of the description of the invention, as required by Article 69 of the Convention on the Grant of European Patents and the Protocol on the interpretation of that provision, that the claims relate,* ***implicitly but necessarily and specifically****, to the active ingredient in question, which is a matter to be determined by the referring court.*" (Ruling, emphasis added) ;

In other words, for a product to be protected by a basic patent in force in Article 3(a) of the SPC Regulation both following conditions have to be met:

(i) its active ingredient(s) has (have) to be specified in the wording of the claims or the claims must relate implicitly but necessarily and specifically to the active ingredient(s), **and**
(ii) the product should embody the core inventive advance of the patent.

It is clear that the combination of TDF and FTC (Truvada®) fulfils neither of the two conditions.

(i) Indeed, the TDF/FTC combination can hardly be considered to be **specified** in the wording of the claims, in view of the expression "*and optionally other therapeutic ingredients*" which Gilead alleges would specify emtricitabine (FTC).

It is worth noting in this regard that two requests for preliminary injunctions based of the present SPC have been recently rejected in France (Decision of the High Court of Paris of 5 September 2017) and in Denmark (Decision of the Danish Maritime and Commercial High Court of 26 October 2017) in particular because the SPC appeared invalid in regard of this condition.

(ii) Besides, the core inventive advance of the basic patent clearly relates to tenofovir disoproxil fumarate (TDF) **only**, as can be seen from Example 16, and in no way to a combination of TDF with another compound, let alone with emtricitabine (FTC).

☞ It is particularly revealing in this regard that Gilead filed on 13 January 2004, *i.e*. more than 6 years after the date of filing of the basic patent, a European patent application specifically relating to the combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) (see *e.g*. claim 1 of the granted patent n°EP1583542). In other words, the combination of TDF and FTC forms the alleged core inventive advance of a patent filed more than 6 years after the basic patent.

It would therefore appear contrary to the objective of the Regulation to grant a certificate for a product which was invented **after** the date of filing of the basic patent.

As clear as what the outcome of the case at hand should be, we believe it could still be the occasion for the Court to provide further guidance on these two conditions for future less clear cases:

☞ As the meaning of the terms "*specified*" or "*specifically*" still appears to be debated, it is respectfully suggested that the Court could clarify that these terms mean that no other product than the product for which the marketing authorisation has been granted could be construed as being protected by the claims of the basic patent relied on in support of the application for the certificate.

☞ While the position of the Court on the basic objective of the SPC Regulation, which is to compensate for the delay to the marketing of what constitutes the **core inventive advance** that is the subject of the basic patent, is clear, this position remains an *obiter dictum*. It is therefore respectfully suggested that this position should be reaffirmed in a ruling.

Besides, it is also respectfully suggested that this ruling could be the occasion to define what level of disclosure should be present in the basic patent to establish the core inventive advance of a combination of active ingredients.

II- The impacts of Gilead's SPC on the French health system and on public health policies

This part aims at discussing the consequences of this additional form of monopoly rights in terms of economy and public health. It exposes the current state of play with this SPC and its impact on the availability of generic versions of TRUVADA® in France, on the accessibility of a drug critical in the response to HIV, and more generally, on the sustainability of the French healthcare system.

A- Deferred market launches for generic competitors

Gilead applied on 19th July, 2005 for a SPC covering the association with TDF and emtricitabine, in France[1]. Gilead was granted with a patent covering TDF on 25th July, 1997[2] and with a patent for the association on 13th January, 2004[3]. The SPC was granted by the Inpi, the French Institute for Industrial Property, on 29th December, 2006. This SPC came into force when the patent n°EP0915894 on TDF expired, in July 2017. It extends Gilead's exclusivity over TRUVADA® until 21st February, 2020, the expiry date of the SPC. As a consequence, the entry of generics on the market can be delayed. Despite this SPC, Mylan announced last July its decision to launch a generic version of TRUVADA® in France. Likewise, the company Biogaran recently launched a generic version of TRUVADA®. Nevertheless, Gilead's SPC is still in force and the company sued Mylan for infringement of its SPC and asked for a temporary ban of the generics. On 5th September, the judge of the Paris High Court deemed such a ban was not justified given that Gilead's SPC is "in all likelihood invalid" (decision N°RG : 17/57112). Gilead was condemned to pay 100 000 euros for litigation costs. The threat of a lawsuit is real and represents thus a strong legal barrier to the market entry of other generic competitors.

The market entry of generics is critical in terms of drug prices since generic versions are less expensive than the original medicine – especially when there are several sources competing on the market. In France, a box of thirty tablets of TRUVADA® is available for 406, 87 euros. The price of TRUVADA® can be lowered greatly thanks to low-cost generic versions. In France, generic prices are

[1] http://bases-brevets.inpi.fr/en/document-en/FR05C0032.html?p=5&s=1491920536021&cHash=d45d9a132cbc9fe1d705174052f543de
[2] https://register.epo.org/application?number=EP97936257
[3] https://register.epo.org/application?number=EP04701819&tab=main

60% below the price of the original medicine[4]. The generic version marketed by Mylan costs 179, 90 euros. Several competing companies have obtained a MA by the European Medicines Agency (EMA) and could also decide to launch generics on the French market which could make the price decrease even more.[5]

B- A threat for the French healthcare system and for medicine accessibility

1) The impact on French health expenditures

The French healthcare system allows a 100% reimbursement for TRUVADA® in order to ensure equitable access to the medicine to all. The current price of TRUVADA® could have affected French health expenditures and social insurance budgets. Indeed, 64% of HIV-positive people receiving antiretroviral therapy take TRUVADA® for treatment in France which represent 73 440 people[6] and around 3 000 people take it for use in the preventive. Without the recent market entry of generics, the price of TRUVADA® would have challenged the ability of the French system to support this cost. This cost would have been all the more challenging in the coming years since the number of people taking TRUVADA® for PrEP is expected to grow. The total extra cost of TRUVADA® from July 2017 to February 2020 could have reached 815 000 000 euros for Antiretroviral therapy (ART) and PrEP. The market entry of low-cost generics represents thus a sustainable solution for public budgets in France, provided Gilead does not use its SPC as a threat to preclude generic development.

2) A threat for the accessibility of an innovative drug

High prices impact public health budgets which are currently very restricted. The French healthcare system has to cope with growing difficulties to absorb the cost of expensive innovative drugs. These difficulties could lead to questionable choices in terms of access to medicines and public health. In this context, the market entry of generic competitors such as Mylan or Biogaran is of paramount importance to ensure a high scale prevention strategy. Indeed, in order to fight against new HIV infections, the French National Strategy for Sexual Health has planned to broaden progressively the access of PrEP up to 40 000 people in 2020. Without cheaper generics, the additional cost due to Gilead's SPC could have slowed down this policy.

Preventing access to PrEP, a very effective tool of prevention against HIV, would in the end cause other collateral health expenditures. Indeed, depriving people from a means of prevention fosters the risk of new HIV contaminations which represent a higher cost for the healthcare system in terms of long-term treatment and management of the disease.

The current cost of TRUVADA® could also deter other countries from allowing access to PrEP.

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[4] http://www.autoritedelaconcurrence.fr/doc/fiche7_px_medi_juill13.pdf

[5] Emtricitabine/Tenofovir disoproxil Krka, MA 09/12/2016,

Emtricitabine/Tenofovir disoproxil Zentiva, MA 09/11/2016
http://www.ema.europa.eu/ema/index.jsp?curl=pages%2Fmedicines%2Flanding%2Fepar_search.jsp&mid=WC0b01ac058001d124&searchTab=searchByKey&alreadyLoaded=true&isNewQuery=true&status=Authorised&status=Withdrawn&status=Suspended&status=Refused&keyword=tenofovir&keywordSearch=Submit&searchType=name&taxonomyPath=&treeNumber=&searchGenericType=generics

[6] Data from two French cohort studies : FHDH ANRS CO4 et AQUITAINE ANRS CO3

Deprived from this tool of prevention, some people might decide to buy generics abroad, in countries where TRUVADA® is not protected by an SPC. Such practices can foster parallel circuits and two-tier healthcare systems undermining access to medicines to all.

Beyond the example of PrEP, other major health policies can be undermined by questionable monopoly rights which maintain high levels of drug prices. Due to this inflation, health expenditures could be largely redirected on medicine spending at the expense of other priorities such as reshaping the French healthcare system, improving technical facilities or upgrading healthcare providers' wages.