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TITLE PAGE

Full-length title: Influence of conflicts of interest on public positions in the COVID-19 era, the case of Gilead Sciences

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1 **Abstract**

2 Fundings and gifts from the pharmaceutical industry have an influence on the decisions made by
3 physicians and medical experts. In the context of the COVID-19 epidemic, several treatments are
4 available to treat patients infected with the virus. Some are protected by patents, such as remdesivir,
5 others are not, such as hydroxychloroquine. We wanted to observe the possible correlation between
6 the fact, for an academic doctor in infectious diseases, of having benefited from funding by Gilead
7 Sciences, producer of remdesivir, and the public positions taken by this doctor towards
8 hydroxychloroquine. Our results show a correlation (correlation coefficient = 1) between the amount
9 received from the Gilead Sciences company and public opposition to the use of hydroxychloroquine in
10 France. This should open up the debate on the role of the interest links of doctors with pharmaceutical
11 companies in the medical and scientific public debate.

12 **Introduction**

13 The influence of private interests on scientific research is a well studied research object (Lexchin
14 1993) (Dana, 2003) (Blumenthal, 2004). If the payment of substantial sums is recognized as a source
15 of conflicts of interest, small gifts or meals offered are more tolerated. However, it has been shown
16 that they influence the behavior of those who receive them (Katz, 2003). “There’s no such thing as a
17 free lunch” claimed Nobel Prized Milton Friedman (Friedman, 1975). For example, it has been shown
18 that intense contact with pharmaceutical companies is significantly associated with the prescription of
19 recent drugs (Watkins, 2003), or more expensive drugs when an alternative exists (Sharma, 2018). The
20 low value of these gifts does not take away from their influence: doctors who are offered meals by the
21 pharmaceutical industry prescribe more promoted drugs (Dejong, 2016). The influence of these gifts is
22 not well perceived by doctors, who consider it less influential than what their patients estimate
23 (Gibbons, 1998). Doctors are aware that gifts from industry can influence their colleagues, but few
24 recognize that they can influence them themselves (Steinman, 2001).

25 In France, since Law No. 2011-2012 of December 29, 2011 (1), companies producing or marketing
26 pharmaceutical products are required to make public all the agreements they conclude, in particular
27 with healthcare professionals, as well as the benefits (including meals and the costs paid for attending
28 conferences) and the remuneration they grant them. It is the laboratories which are obliged to declare
29 these payments which show a link of interest. A public site whose consultation is open to the public
30 lists all these declarations: transparence-sante.gouv.fr. Since the start of the Coronavirus epidemics,
31 the public authorities had to push or limit the use of candidate treatments for COVID-19. These
32 decisions have become the subject of public debates, in the written, digital, television and radio press.
33 To inform the debates, infectious disease physicians were asked by the media to give their point of
34 view on the use of the different treatments.

35 Candidate treatments for COVID-19 can be divided into two categories: those that are protected by a
36 patent held by a pharmaceutical company, such as Remdesivir, Kaletra - before Abbvie abandoned its
37 rights to the drug following negative studies on COVID19 (Cao, 2020). Others are generic:

hydroxychloroquine, azithromycin. 39 companies are currently manufacturing hydroxychloroquine (Million, 2020) The choice of the drug by the public authorities therefore translates into a significant gain or loss for the various laboratories which hold the rights to a candidate molecule.

The conflict between hydroxychloroquine and remdesivir, started by a publication listing both as treatment candidates (Wang, 2020), has grown considerably, with announcements and counter-announcements as well as contradictory articles (Gautret, 2020) (Gautret, 2020) (Chen, 2020) (Chen, 2020) (Huang , 2020) (Tang, 2020) (Mahevas, 2020) (Magagnoli, 2020), which had a significant influence on the share price of the company Gilead Sciences, listed on the NASDAQ (See for example the statement by Anthony Fauci (2) from April 29, 2020, synchronized with an article published in the Lancet at the same time (Wang, 2020)). It therefore seems relevant to us to focus on the links of interest between Gilead Sciences and various opinion leaders, infectious disease physicians in France that are now stakeholders of this health crisis.

This debate led us to wonder about the role of pharmaceutical companies in the current therapeutic debate. We particularly question the laboratories that hold rights to a candidate molecule, in particular Gilead Sciences with Remdesivir. Are the medical researchers who have spoken in recent weeks in the debate on the use of hydroxychloroquine in a position of a conflict of interest? This is the question we wanted to answer by studying the links of interest between Gilead Sciences, producer of Remdesivir, and the doctors who took a stand for or against hydroxychloroquine.

Materiel and methods

To establish the list of French academic infectious disease physicians, we used the list of members of CMIT (Council of Teachers in Infectious and Tropical Diseases). In the list we obtained, 98 medical researchers were identified. Public interventions were defined as a direct expression of opinion in a media, academic or not academic. Non-academic newspapers included national newspapers, regional newspapers, television channels, radio channels. For each member of the CMIT, we did a systematic search on Google News to identify press reports containing the word Hydroxychloroquine and quoting

this member of the CMIT. We carefully read their interventions and classified their positioning on a scale of 1 to 5, 1 meaning that they were very unfavorable to the use of hydroxychloroquine, 5 that they were very favorable to it. “Very favorable” was defined as “having expressed a call for generalization of the use of hydroxychloroquine, or reporting a successful use of the treatment in the physician’s facility”. “Favorable” was defined as “having recognized a positive effect of hydroxychloroquine, while waiting for confirmation of results for taking further position”. “Neutral” was defined as “expressing the need for more studies for making any comment of the efficiency of the treatment”. “Unfavorable” was defined as “while still waiting for more results, expressing negative comments about hydroxychloroquine”. “Very unfavourable” was defined as “expression of anger towards the mediatization of hydroxychloroquine, or a strict opposition towards the generalization of the use of hydroxychloroquine”.

Using the eurofordocs.fr website which aggregates the data from the transparence-sante.gouv.fr website, we listed the links of interest with the Gilead Sciences laboratory of all CMIT members, as well as their links of interest with all companies subject to the declaration on the Transparency Health platform. We finally established the average of the sums received from Gilead Sciences for each of the categories of researchers established by their positioning with respect to hydroxychloroquine; similarly, we have averaged the amounts received by all reporting companies. We performed a Spearman correlation test to explore the relation between position towards hydroxychloroquine and funding received by Gilead Sciences.

Results

A total of € 678,527 was paid by the company Gilead Sciences, manufacturer of Remdesivir in 7 years, to doctors who are members of CMIT (Table 1). This represents an average of € 6,924 per doctor. All reporting companies combined, a total of € 4,603,098 was paid to CMIT physicians between 2013 and 2019 (Table 2). There is a strict correlation (Spearman test, $p=0,017$) between the position of doctors towards hydroxychloroquine and the average amount paid to them by the company

Gilead Sciences between 2013 and 2019. In all, only 13 doctors out of 98 CMIT members did not receive any benefit, remuneration or agreement from the Gilead Sciences company between 2013 and 2019. Among these 13 doctors, 7 were very favorable to the use of hydroxychloroquine, 1 favorable, 1 neutral and 4 have not taken a position. On the opposite, among the 13 doctors that received the most important funding from Gilead Sciences, 6 were very unfavorable to the use of hydroxychloroquine, 1 unfavorable, 3 neutral and 3 have not taken a position.

Discussion

In this short work, we wanted to observe the influence of conflicts of interest, in the time of COVID was confirmed. Not surprisingly, we have shown a correlation but we have been impressed by the level of correlation, which is perhaps one of the explanations for the violence of the debate that has taken place concerning the use of hydroxychloroquine. None of the studies involving Remdesivir (Wang, 2020) or Lopinavir/Ritonavir (Cao, 2020) could show any effectiveness of these drugs in the could show effectiveness in the prevention of mortality or the reduction, and reduction of the the viral load of COVID-19, whereas 4 studies have now shown significant differences on: clinical course, radiological course, mortality, viral load (Million, 2020) (Yu, 2020) (Huang, 2020) (Membrillo de Novales, 2020). In addition, the issue of conflict of interest goes beyond that of practitioners, and also undoubtedly affects publishers and conference organizers, who also have links of interest with the most dynamic pharmaceutical manufacturers. The COVID crisis will make it possible to re-analyze many things, including the issue of conflicts of interest, a problem which is absolutely not resolved in many countries of the world, including France. It does not concern only doctors, this matter also concerns publishers and organizers of medical events, who are subject to the same types of financial conflicts. It is interesting to notice that major measures have been taken in France to fight conflicts of interest in politics, including mandatory declarations of patrimony during the course of the mandates of representatives to a national authority (HATVP), such measures have not been taken in the medical field.

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232 **Table 1: Links of interest with Gilead Sciences between 2013 and 2019 depending on the position**
233 **towards hydroxychloroquine (HCQ)**

| Position towards HCQ | Number | Average (€) | Median (€) | Extreme – (€) | Extreme + (€) |
|-----------------------|-----------|-------------|-------------|---------------|---------------|
| Very favorable | 8 | 52 | 0 | 0 | 417 |
| Favorable | 6 | 1524 | 1208 | 0 | 4773 |
| Neutral | 14 | 9729 | 2729 | 0 | 48006 |
| Unfavorable | 7 | 11085 | 10547 | 234 | 31731 |
| Very Unfavorable | 9 | 24048 | 26950 | 122 | 52812 |
| Did not take position | 54 | 4421 | 2143 | 0 | 36706 |
| TOTAL | 98 | 6924 | 2188 | 0 | 52812 |

234 **Table 2: Links of interest with pharmaceutical companies between 2013 and 2019 depending on**
235 **the position towards hydroxychloroquine (HCQ)**

| Position towards HCQ | Number | Average (€) | Median (€) | Extreme – (€) | Extreme + (€) |
|-----------------------|-----------|--------------|--------------|---------------|---------------|
| Very favorable | 8 | 6649 | 1558 | 42 | 30875 |
| Favorable | 6 | 10913 | 9999 | 42 | 24840 |
| Neutral | 14 | 62858 | 26339 | 585 | 291755 |
| Unfavorable | 7 | 61519 | 57529 | 11842 | 100358 |
| Very Unfavorable | 9 | 157939 | 130250 | 7498 | 543673 |
| Did not take position | 54 | 32451 | 19766 | 0 | 241267 |
| TOTAL | 98 | 46970 | 21978 | 0 | 543673 |

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