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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:

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

41 The conflict between hydroxychloroquine and remdesivir, started by a publication listing both as
42 treatment candidates (Wang, 2020), has grown considerably, with announcements and counter-
43 announcements as well as contradictory articles (Gautret, 2020) (Gautret, 2020) (Chen, 2020) (Chen,
44 2020) (Huang , 2020) (Tang, 2020) (Mahevas, 2020) (Magagnoli, 2020), which had a significant
45 influence on the share price of the company Gilead Sciences, listed on the NASDAQ (See for example
46 the statement by Anthony Fauci (2) from April 29, 2020, synchronized with an article published in the
47 Lancet at the same time (Wang, 2020)). It therefore seems relevant to us to focus on the links of
48 interest between Gilead Sciences and various opinion leaders, infectious disease physicians in France
49 that are now stakeholders of this health crisis.

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

56

57 **Materiel and methods**

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

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

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

83

84 **Results**

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

90 Gilead Sciences between 2013 and 2019. In all, only 13 doctors out of 98 CMIT members did not
91 receive any benefit, remuneration or agreement from the Gilead Sciences company between 2013 and
92 2019. Among these 13 doctors, 7 were very favorable to the use of hydroxychloroquine, 1 favorable, 1
93 neutral and 4 have not taken a position. On the opposite, among the 13 doctors that received the most
94 important funding from Gilead Sciences, 6 were very unfavorable to the use of hydroxychloroquine, 1
95 unfavorable, 3 neutral and 3 have not taken a position.

96

97 **Discussion**

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

116

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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

236