The pharmaceutical industry and healthcare practitioners: communication, interaction and ethics

A Master's Thesis submitted for the degree of “Master of Business Administration”

supervised by
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Vienna, 30.06.2020
Affidavit

I, RYAN FITZPATRICK, MA, MA, hereby declare

1. that I am the sole author of the present Master’s Thesis, “THE PHARMACEUTICAL INDUSTRY AND HEALTHCARE PRACTITIONERS: COMMUNICATION, INTERACTION AND ETHICS”, 60 pages, bound, and that I have not used any source or tool other than those referenced or any other illicit aid or tool, and

2. that I have not prior to this date submitted the topic of this Master’s Thesis or parts of it in any form for assessment as an examination paper, either in Austria or abroad.

Vienna, 30.06.2020

Signature
Dedication

I would like to dedicate this to my wonderful son, Charlie. And I would like to also say thank you to my family, friends, and work colleagues that have supported me in this endeavour. Equally, I would like to express my gratitude to my dissertation tutor, Prof Tony Warren, for his insight, knowledge and patience. Similarly, I would like to thank the WU and TU for their great MBA programme both on campus and during the educational trips to Harvard, MIT, Colombia and Stanford. The staff have always been professional, friendly and helpful.

Finally, I would also like to thank the healthcare practitioners and the individuals from the pharmaceutical industry that contributed to this thesis with interviews.

Ryan Fitzpatrick
Vienna, 30 June 2020
abstract

This thesis aims to provide an analysis of the relationship between healthcare practitioners (HCPs) that prescribe drugs and how the pharmaceutical (pharma) industry develops and markets medications to influence HCPs. We will employ 9 chapters to breakdown the various ways pharma interacts with HCPs, how and why they do so; and the impact these have on HCPs and the wider ethical and moral consequences for society. The thesis will conclude with recommendations and point to areas that need further research. The chapters will cover the following topics:

- Introduction with clarification and definitions
- Pharma’s hegemony
- Patent protection
- Randomised controlled trials
- Publication of clinical trial data
- How pharma interacts with HCPs
- Ethics, Conflict of Interest and Institutional Corruption
- Summary and Recommendations
- Conclusion

By employing a thematic approach, the author’s research will focus in the main on the United States, as this is where most of the academic research studies has been conducted. It will draw upon primary interviews with pharma and HCPs to elucidate our research findings. A disclaimer: since 2001 I have worked in the medical publishing industry, with firms such as Springer-Verlag and Medscape. Further, as a current business owner of MD Education Limited, a medical publishing firm and an organizer of scientific meetings in Europe and the United States, (see appendix B), I have experienced first-hand the challenges facing healthcare practitioners, the pharma industry and the prism that researching, developing, launching and marketing new drugs entails for all stakeholders.

To summarize, this thesis is intended to encourage and add to the debate concerning the role of how pharma interact with HCPs, to provoke discussion from the theoretical and practical instances documented below and to inspire a similar examination elsewhere.

Keywords: Pharmaceutical industry, ethics, healthcare practitioners, conflict of interest, gifts to physicians, physician-industry relationships, medical ethics.
1. Introduction

Academic debates apropos the pharmaceutical industry (pharma) and their relationship with healthcare practitioners (HCPs) have been raging since the 1980s.⁡ Studies show that the “interaction between pharma and HCPs can influence the prescribing habits of the latter”.³ These interactions lead to a ‘clear conflict of interest that generates a moral, legal and professional dilemma’.⁴ Research has shown profit incentives create an “opportunity for misuse and conflict of interest leading to violation of medical ethics on the part of the physicians”.⁵ This has ramifications for society as a whole. Stark has rightly pointed out that “the societal goal of medicine is to use sound medical science to help people get or be as healthy as possible, even when they have a debilitating chronic disease or they are declining towards death”⁶. With this in mind, could pharma’s interactions with HCPs harm patients, increase costs of healthcare to governments, affect public opinion of the pharma and healthcare industry as a whole and undermine the trust of patients in the integrity of HCPs in the eyes of the public?⁷ What, if any, is the role of HCP/pharma interaction responsible for the legion of financial settlements by pharma to patients and governments? “Between 2009 and 2010, pharma settled for $8.6 billion for cases relating to drug safety issues”.⁸ A cautionary remark: one cannot look at the pharma-HCP relationship through a prism of

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scepticism of a for-profit organization looking to sell their drugs at all costs, as documented by popular media outlets. Indeed, several studies\(^9\) reflect the value that HCPs garner from their interactions with pharma, as do my interviews with HCPs. Nevertheless, governments and regulatory bodies such as the Food and Drug Administration in the United States and the European Medicines Agency in Europe have had to intervene to mitigate against the effects of pharma’s influence on HCPs, seen most notably in 2010 with the Sunshine Act in the United States, which ensured pharma disclose their payments to HCPs over the value of US$10.\(^{10}\) After conducting a reviewing of the literature and drawing on my extensive interactions with pharma and HCPs, I will make recommendations on how conflicts of interest between pharma and HCPs can be made more transparent. Let us commence with a clarification and an overview of the scope of this paper.

1.1 Aim of the thesis

How did the situation arise where pharma can influence an HCP in the prescription of a drug to a patient? And what impact does this have on society? What can be done to mitigate the influence of pharma on HCPs? This thesis will attempt to answer these questions by looking at the academic debates and the history of pharma-HCP interaction from the mid twentieth century. I will attempt to add to the debate by the contribution of interviews and surveys I have conducted with 10 leading clinical experts and 10 pharma senior staff from the US and Europe, (see appendix C). It is worthwhile noting that I work with HCPs and pharma every day in my profession as an owner of a medical publishing company, MD Education Limited\(^{11}\). (Two examples of scientific meetings that MD Education organise in Europe and the United States, and that are funded by pharmaceutical companies, can be found in appendix B.) As such, I have strong personal and professional relationships with pharma personnel and HCPs dating back to more than two decades. To reiterate, my intention is to add to the ongoing research and provide markers where further studies are needed.


\(^{10}\) Silverman E., (2013) Everything you need to know about the Sunshine Act, BMJ; 347 :f4704

\(^{11}\) https://md-education.com/ (accessed June 2020)
1.2 Definition and Clarification:

1.3 Pharma
In this thesis, pharma specifically refers to drug manufacturing companies, and thus excludes medical device and imaging companies.

1.4 HCPs
HCPs refers to only those individuals that prescribe drugs. In medical parlance, ‘physician’, is the preferred term in the United States when referring to an individual that has the authority to prescribe drugs.

1.5 Scope
The lion-share of academic studies surrounding pharma and HCP engagement derives principally from the United States, thanks in the main due to the nature of US medical care for society in contrast to the universal healthcare systems in Europe. Further, studies are lacking in other parts of the world although this is gradually being addressed since 2015 with notable studies in Ethiopia and Lima.\(^\text{12}\) Finally, as mentioned above, my daily work for the last 19 years has been exclusively in the United States and Europe and that is where my interviewees from pharma personnel and HCPs also reside.

1.6 Interaction and Communication
Pharma’s interaction and communication with HCPs encompasses 3 domains and each will be reviewed in this paper:

i. Research projects and clinical trials
ii. Scientific/educational meetings
iii. Pharma sales rep visits to the HCP

Let us now turn to review how the pharmaceutical industry grew into such a behemoth within medicine and how omnipresent its role is in interacting with healthcare practitioners and also the health of the general populace.

\(^{12}\) Patwardhan A., (2016) ibid. Studies surrounding pharma’s interactions with HCPs that are non-physicians, i.e. non-prescribers, “are currently inadequate” p. 2
2. Pharma’s Hegemony

The World Health Organization states “the global pharmaceutical market stands at US$500 billion”.\textsuperscript{13} Pharma’s principle marketing and sales focus is on the US, ‘EU5’, read: Germany, France, Italy, UK and Spain; Japan and China. These countries alone account for over 70\% of total global medicine spending.\textsuperscript{14} To underline, it is no coincidence that most of the academic studies have accordingly been conducted in the United States and Europe.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{Pharma’s medicine spending globally revealing a clear focus on EU5, US, Japan and China\textsuperscript{15}}
\end{figure}

\begin{itemize}
\item \textsuperscript{13} WHO. Trade, foreign policy, diplomacy and health. 2014. Available online: http://www.who.int/trade/glossary/story073/en/. (Accessed May 2020)
\end{itemize}
Table 2. Pharma’s focus on EU5 and US is reflected in the top 10 countries sales revenues.\(^{16}\)

Table 3. 19 out of the 20 top companies by revenue are based in the United States and Europe.\(^{17}\)


Just how much sway does pharma have on our societies? “Between 2009 and 2012, nearly 50% of people in the United States were prescribed a drug. More than one in ten Americans used five or more prescription drugs within a 30-day period”. Alarmingly, “prescription drugs are the 4th leading cause of death and a major cause of hospitalizations”. In short, pharma has a huge sway over the health of our societies.

So how did we get into a situation where pharma’s interaction with HCPs influences their prescribing? During the Second World War, science was essential for national military and economic competitiveness. Pharma was touted by governments to assist in the war efforts in both the United States and Europe, and partnerships between government, scientists, universities and pharma grew dramatically. This saw a plethora of novel agents in the 1940s and 1950s with notable developments in antibiotics, antihypertensives, hypoglycaemics, psychotropic drugs and chemotherapy. Most of the clinical trials were run by public sector agencies, such as the national institutes of public health, in collaboration with pharma. In 1951, the Humphrey-Durham Amendments Act in the United States limited the sale of drugs to prescription only by a HCP. The upshot? HCPs were now the target for pharma’s marketing. This is clearly illustrated in the fact that in 2012, knowing the influence that interactions have with HCPs, the pharma industry spent US$89.2 billion, (approximately 60% of their global sales and marketing budget) on promotion, marketing and interactions with HCPs.

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3. Patent Protection

The collaboration between pharma and the public sector that we saw in the 1940s and 1950s has now been replaced by pharma’s dominance over the medicines that are now approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). How did the private sector usurp the public sector in driving the health of society? Rebecca Eisenberg’s research has shown that patent laws effectively “neutered scientific collaboration” between the public and private sector which was replaced instead by “an intellectual property race” between the pharma companies.21

In 1982, the World Trade Organization Trade Related Aspects of Intellectual Property Rights extended patent protection worldwide on patented drugs for 20 years from the date of filing. It takes pharma, on average, “10 years to develop a drug, at a cost of about $1.5bn-$2.5bn, which pharma use to justify the high price of their drugs”.22 A BBC investigation showed that “only 3 out of 10 drugs are profitable, with one of those going on to ‘blockbuster’ status, meaning a turnover of US$1bn sales, per annum”.23 After the drug patent expires, generic versions are available on the market by competitors which are typically 90% cheaper than the original product and sales can be expected to fall by more than 90%.24 As Joshua Owide, the director of healthcare industry dynamics at the prestigious research company, GlobalData, quips, "Unlike other sectors, brand loyalty goes out the window when patents expire" and pharma accordingly market their drugs aggressively to HCPs in this 10 year window of opportunity.25

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4. Randomized Controlled Trials

Governments in Britain and the United States in the 1950s adopted evidence-based medicine with the introduction of randomized controlled trials (RCT). Drugs were tested as they are now: a drug and a placebo are given to the patient. If the new drug is ‘successful’ then it is allowed into use by the FDA and EMA. The 1961 thalidomide scandal put the harmful side effects of drugs into prominent public view, (whereby limbless babies were born to mothers taking drugs during pregnancy), and legislation was enforced that made RCT the only way that drugs could be approved.26

But how do trials get approved by the FDA and EMA? Surprisingly, regulators on both sides of the Atlantic only require two trials to demonstrate statistically significant positive data to grant approval. So we are in a situation whereby a pharma company may be running over 100 clinical trials on one drug but they only have to show data from two studies that the drug is better than a placebo on a drug test or rating scale.27 Healy points out, “it is in the interest of pharma to argue that differences in their drug that may appear to be trivial are in fact substantial and innovative…it’s not the job of a regulator, either the FDA nor EMA, to tell a drug company what it’s business should be.”28 What is most alarming is that due to pharma’s prominence in medicine, it is pharma that provide most of the funding for clinical trials and sponsors the majority of new trials initiated each year.29 Critics say “research-based medicine has become evidence biased medicine”.30

When pharma does not run clinical trials’ themselves they outsource these to Clinical Research Organizations, (CROs). 1982 witnessed the first CRO that was tasked with the job of running clinical trials. By 2018 the “CRO market was valued at US$35.09 billion and expected to reach US$50.65 billion by 2025, and more tellingly, constitute 70% of the

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30 Healy D., (2012) ibid, p. 89
clinical trials undertaken by pharma”. In short, the CROs are exclusively in the pay of pharma. Put bluntly, without pharma the CROs do not exist.

5. Publication of Clinical Trial Data

If a trial is successful, the RCT outcomes are published in scientific journals and incorporated into evidence-based guidelines for the treatment of diseases. The guidelines outline to HCPs what works and what doesn’t. Importantly, these guidelines then become the ‘holy grail’ of what prescribers can and cannot provide to the patient. HCPs, such as Healy, argue, “these guidelines in fact hand medicine over to the drug industry.”

Insurance companies are then ‘trapped’ into reimbursing the cost of the treatment based on the RCT, leading Healy to quip: “patients hospital stays are becoming little more than the institution of a drug treatment regimen”.

RCTs are a logical and prudent development to test new drugs and are generally “valued forms of medical science.” So what’s the problem? The issue, as research has shown, is that the clinical trials that the prescribing guidelines are based on are designed and implemented by pharma or companies that are dependent on pharma money, such as CROs. Moreover, the lead investigators that orchestrate the clinical trials are paid by pharma. And the results of the RCT are written by leading academics, either practising HCPs or researchers, that are also paid by pharma. The findings of the trials are subsequently published in peer-reviewed journals, most of whom are reliant on pharma’s advertising budget in their journals or submission fees. Further, these ‘independent’ articles are ostensibly written by clinical experts associated with the trial to give credibility and gravitas to the paper and thus to pharma. However, research shows these published articles are generally ghost-written by third party agencies, (read: written ‘on song’) and these for-profit agencies are also dependent largely on pharma monies.

The main problem with the RCT is that because pharma funds two thirds of biomedical research they do not publish all of their findings as the data has proprietary value. Pharma can therefore disclose the positive aspects of their trials and omit to show all of the data, including potential harmful negative data. Pharma therefore have a commanding

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33 Healy, D, (2012) Ibid, p.8
position in the realm of clinical trials which remain largely a ‘black box’. Studies have shown, what the findings from the trials do not say, is as important as what they do say, i.e. disclosing harmful side effects. As Light notes: pharma are interested “in designing trials to maximize evidence of effectiveness over placebos and to minimize evidence of adverse reactions”. How the data is created, analysed and disseminated is therefore problematic. Studies clearly show that pharma paid “medical writers, statisticians, and editors add, omit or alter findings when results are written up for publication in leading journals of medical science that become the basis for clinical guidelines and prescribing decisions”.38

As one commentator pointed out: “trials are not only designed for regulatory approval but to test for characteristics that fit company marketing goals and may bear minimal relationship to what some of the drugs most telling effects are”.39

Light goes further, there is evidence that indicates “a hidden business model to develop scores of drugs with few or no clinical advantages over existing ones in order to exploit the broad and long monopoly protections from free-market competition; protections that Congress and society have granted them to support breakthrough research, not market-driven minor variations”.40

As the publication of articles in scientific journals provide the spur for treatment guidelines, this has sparked accusations that pharma is inciting drug consumption by ‘disease mongering’. The work of Getz et al, show that the Guidelines from the European Society of Cardiology on the treatment of hypertension and hypercholesterolaemia have incredibly identified 76% of the adult population of Norway as being at “increased risk”. This ‘disease mongering’ has resulted in what Heath argues is, “a shift of attention from the sick to the well and from the poor to the rich” that can be seen in the debate around the rise of ‘lifestyle’ drugs for contentious ‘new’ diseases such as restless leg syndrome and ADHD.42

39 Healy D., (2012) ibid, p. 204
40 Light D, Lexchin J. Pharmaceutical R&D - what do we get for all that money? BMJ 2012;344:e4348
42 Healy, (2012) ibid, p.108
Moreover, disease mongering is another development by pharma to pressure HCPs to follow the guidelines that pharma have created based upon their data.

Quality control of RCT have also been called into question by studies. The work of Redman highlights the fact that RCTs are now world-wide projects encompassing sometimes over one hundred countries leading her to note: “in a global research world, more than a third of research papers are conducted by authors in several countries raising questions about inconsistencies in research and publishing practices ungoverned by national regulations and practices”. Redman goes on to state: the process of how journals publish articles relating to clinical trials, ensures that “the myth that most science is being produced honestly and with a high degree of quality—and thus is safe for application—is preserved.”

The upshot is that we have the research, development and marketing apparatus of new drugs developed by pharma and/or dependent on pharma monies. Marc Rodwin, in a seminal paper, illustrated how pharma ‘control’ the following areas:

- Set priorities on drug research and development
- Conduct clinical trials to test whether drugs are safe and effective
- Decide what clinical trial data to disclose to the public
- Monitor post-marketing drug safety
- Supply product information to healthcare practitioners
- Finance continuing medical education and other professional activities.

Light and Lexchin paint a bleak picture about how pharma has engineered a process where they control not only the RCT, the outcomes of the RCT to regulatory bodies but also how publishers are co-dependent on pharma monies and the risk of patients and society as a whole:

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44 Redman B., (2015) ibid, p.8
“researchers, universities, journals of medical science, medical knowledge, physicians, and patients have become dependent on those corporate practices of the pharmaceutical industry that result in distorted medical knowledge and an epidemic of harmful side effects from drugs which usually have few clinical advantages to offset their risks”.

A clear example of the conflict of interest relationship between publishers, researchers and pharma can be seen in the Olivieri affair: the story of the whistle-blower, Nancy Olivieri. It has been called “one of the most important events to occur in research ethics”. When Dr. Olivieri discovered potential side effects with the drugs that she was researching, she decided, rightly so, “to share these findings with drug-trial patients and the scientific community but experienced direct censorship from her corporate sponsor, Apotex. Nevertheless, Olivieri pursued a course of action consistent with the promotion of public health and disclosed her results. Apotex responded by pulling her funding, cancelling her project, and launching a lawsuit against her. Meanwhile, the university dismissed her, and senior hospital staff turned against her”. As Gray notes, the Olivieri case “illustrates the potential for serious problems in the social organization and governance structures involved in a pharmaceutical company’s relationship with a university and its academic researchers”. The message to all universities, research centres, scientists and potential whistle-blowers: pharma call the shots.

Now we have seen the framework of how drugs are trialled and published, let us examine how pharma strategically interact with HCPs.

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50 Gray C., (2013) ibid, p.632
6. How pharma interacts with HCPs

Meetings are central to how pharma and HCPs interact and there are four kinds of meetings that we will explore below. Studies have shown that HCPs enjoy these meetings as it gets the HCPs out of the office, gives them a chance to meet their peers and the meetings are usually held in a plush 4-star hotel or restaurant with food and alcohol.\textsuperscript{51}

6.1 Advisory board meeting. These meetings tend to be a closed community of anywhere between 3 and 30 clinical experts or what pharma term: Key Opinion Leaders (KOLs). The object is to discuss a pharma company’s drug in a competitive landscape vis-a-vis the current drug options on the market. Pharma consider it a SWOT analysis to develop marketing plans. The KOLs are reimbursed for their time, accommodation, travel and entertainment expenses. Currently, pharma pays a KOL anywhere from US$250-450 per hour and the advisory board runs usually from three to eight hours in duration.\textsuperscript{52} In addition to speaker fees, KOLs are also touted for their research skills. Researchers are paid per topic and per case study.\textsuperscript{53} Their remuneration depends on various factors: whether the research is at a global or country level; what the disease area is and how competitive the landscape is. I was informed that a KOL I know personally was paid in excess of US$50,000 for a recent research project for a company developing a new treatment therapy in a niche of haematological malignancies. Industry wide regulations state the accommodation and venue must not be no more than 4 stars or it can be considered a luxury ‘bribe’. These meetings are used as market intelligence by the pharma company and are strictly disseminated internally. They are not for the consumption of a wider audience. Advisory boards are normally conducted extensively before the launch of a product and the focus tends to be on patient case studies, an analysis of the patient data in phase 3 which means pre-market approval from the FDA and the EMA, and advisory boards garner key information for pharma about how HCPs use ‘off-label’ drugs. Off label drugs are “prescriptions which are not approved by the

\textsuperscript{51} Healy, (2012) ibid, p. 139
\textsuperscript{52} These are the fees MD Education pay to KOLs when organising advisory board meetings.
FDA or EMA and in 2014 accounted for nearly 20 percent of all prescriptions garnering US$40 billion in sales”.  

6.2 Continual Medical Education (CME) meeting. According to the Accreditation Council for Continuing Medical Education 2018 annual report, pharmaceutical company contributions totalled $740 million or 28% of continuing medical education (CME) funding in 2018. HCPs must obtain a certain amount of continuing professional education on an annual basis to familiarise themselves with the latest developments in their field. Pharma are therefore strictly forbidden by the FDA and EMA to have any input to the content of accredited meetings. Companies that organise such events, such as MD Education, orchestrate the content, identify the KOL speakers, pay the speaker fees, travel arrangements and food and entertainment. Plus, the organizer must pay for the venue, normally a hotel or exhibition centre, and food and beverages for all attending HCPs. The speakers are chosen on their research expertise, standing amongst their peers, and their presentation skills. Speaker fees start from 1,000 to 10,000 euro for a 30-60 minutes presentation. In turn, each speaker must submit their slide deck for independent review by the organiser. To reiterate, at no point do pharma have a say on content. Funding is garnered by a process of submitting an educational grant request to the pharma companies’ educational online ‘portal’. This development has become apparent since the Sunshine Act of 2010. Prior to the legislation, CME meeting organizers could have direct contact with pharma senior managers and directly request funding either in person meetings or by email. I have been asked by pharma personnel if they could ‘request’ suggestions for topics and ‘recommend’ faculty. This is also reflected in a study by Brody from 2007 that shows pharma companies were asked to become major sponsors of a CME event and in return they would choose the speaker “to represent industry’s interest”. One of the chief reasons why pharma prefer CME

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54 https://www.andruswagstaff.com/blog/big-pharma-has-higher-profit-margins-than-any-other-industry/ (Accessed June 2020)
56 This is the fee MD Education pay to KOLs.
57 See an example of a grant portal from Bristol Myers Squibb: https://www.bms.com/lu/corporate-giving.html (Accessed June 2020)
meetings is not only the credibility of accredited talks but also that during CME presentations KOLs can discuss off-label data.

6.3 Independent Medical Educational (IME) meeting: these meetings are essentially the same as CME meetings, in the sense that they are organised and run by a third-party company, with the caveat that attending clinicians do not receive accreditation for participating in the meeting.

6.4 Promotional meeting: these are pharma run events that are also known as a ‘product theatre’. The value for pharma is they can cherry pick their KOLs and ‘control’ content, including the presentation topics and slides. Promotional talks, however, are limited by the regulatory environment in the United States and Europe by what they can discuss. Namely, HCPs cannot talk about off-label use of their drug to make claims inconsistent with the drug’s approval for marketing. No such regulatory restrictions are in place for CME and IME meetings hence pharma prefer CME and IME meetings to promotional events.

KOLs are a vital component in pharma’s meetings and marketing strategies to HCPs. One study shows “pharma spends 20% of their budget just on identifying and ‘nurturing’ KOLs”. The idea of a KOL, also known as Thought Leaders, derives from Paul Lazarsfeld, who in 1944, devised the term “opinion leader” when researching political views and voting behaviour. The concept was applied to the medical field in 1955 when Katz and Lazarsfeld received funding from Pfizer for a medical study. KOLs are co-opted by pharma to market their products by using their status and standing to disseminate the pharma companies data and to underline the value of their drugs in clinical practice. Physicians, nurses, pharmacists and researches come under the umbrella of KOLs. In short, KOLs are paid by pharma to give talks at scientific meetings, online or in person. KOLs credibility as a bona-fide font of knowledge means they can influence their peers’ opinions and change prescribing habits. The framework for how KOLs are employed by pharma is consistent in the United States and

most of Europe. Smith, in a widespread survey, has shown that KOLs are defined loosely by their influence which can be at a country, continent or global level. Acquiring the ‘correct’ KOL means pharma have an esteemed ally indeed.

The author has worked with over 300 global and European KOLs in his career as an organizer of scientific discussions and he can attest to the lauded status pharma hold these speakers. (See appendix B for an example of two meetings coming in September and November 2020 featuring 40 KOLs in haematology from Europe and the United States). Thus, it is not surprising that a Merck study conducted in 2005 highlighted that scientific meetings chaired by KOLs, rather than pharma personnel, provided nearly double the return on investment when measuring prescriptions habits from the attendance before and after their meetings.

This specific example from the Merck study provides an insight into how effective KOL chaired meetings are for pharma in terms of garnering traction to HCPs and communicating findings of RCT. In this instance, Merck asked each participant if they had written new prescriptions for the drug in both the KOL chaired meeting and the pharma personnel chaired meeting. The findings were $623.55 worth of new prescriptions for the KOL presenting versus $165.87 of new prescriptions for the Merck led meeting.

KOLs are accordingly ‘guided’ by pharma or by third party consultancies, including CROs and PR agencies, as to what to emphasise and highlight when giving a presentation. KOLs are therefore the central focus of meetings and they are given slide deck presentations by pharma, produced and ‘on song’ with the messages that pharma want the KOL to get across to fellow prescribers. All of these meetings act as an opportunity for pharma to develop deep-seated and long-term relationships with KOLs. Since the 1990s, pharma have moved away from sales representatives building relationships with prescribers and embraced a new paradigm of ‘covert sales’ viz., Medical Science Liaisons. MSLs are usually medically or

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scientifically educated and act as the pharma conduit for prescribers and KOLs. MSLS build relationships with the HCPs and identify potential or future KOLs and thus play an important role in having ‘offline’ conversations with prescribers that acts as intelligence and market research for pharma.

Aside from monetary incentives, KOLs also receive exposure and status for participating with pharma in their research and talks. With the rise of online educational platforms, physicians can now participate in a video presentation or discussion that is disseminated globally to thousands of their peers. Neutral educational platforms such as Medscape, (https://www.medscape.org/) has over 4 million registered HCPs and provide even more credibility for HCPs than pharmaceutical websites. Incidentally, a study by Landa and Elliott demonstrate HCPs depend on such online educational networks and forums, even though such platforms receive funding from pharma and are used by pharma for direct and indirect marketing purposes.

Most of the latest clinical trial data is unveiled at medical association annual meetings in both the United States and Europe. Each disease area will commonly have one major annual meeting on both sides of the Atlantic and each meeting can anticipate anywhere from 10,000 to 30,000 HCPs over a three-day period depending on the disease area. These medical association meetings, such as the American Society of Clinical Oncology, (ASCO) and the European Society of Medical Oncology, (ESMO), offer CME accreditation for their symposium presentations. A huge revenue earner is the possibility for pharma to have industry supported satellite symposia. The time slot alone for industry symposium this year at ASCO and ESMO varies from US$50,000 to US$150,000. In addition to buying the time slots, pharma has to pay additional fees to organise the meeting, pay speakers honoraria, hire an audio-visual company and provide food and drink to ensure the symposium is comfortable for attendees. In return, ESMO and ASCO will provide a captive audience for the pharma company to attract physicians already attending their meeting to join their

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symposium. Additionally, ESMO and ASCO charge pharma to take exhibition space at their meetings which ranges from US$10,000 to $1,000,000 dollars, depending on the size of the exhibition space and the location to the scientific sessions. In short, the medical associations profit hugely from pharma funding and pharma sponsored events at their annual meetings. During the recent Covid-19 pandemic, the ASCO annual meeting went ahead virtually with over 19,000 oncologists watching online.\(^{71}\) KOLs presenting for pharma sponsored presentations are therefore provided with a global audience of HCPs. As one KOL told me after ASCO, “instead of being in a room of 800 clinicians, I reached over 5,000 fellow colleagues. Who wouldn’t want that kind of exposure?”\(^{72}\) On this point of exposure, in May 2020, MD Education conducted a series of three COVID-19 symposium webinars for Fresenius-Kabi, a nutrition and pharma company. The webinars featured 11 KOLs from 9 countries and were broadcast live for 90 mins and received over 13,000 clinician registrations from 105 countries.\(^{73}\) This kind of global audience and recognition is a key driver for KOL participation in pharma supported educational activities.

The nature of KOL relationships with pharma has led some HCPs to call into question KOL independence. Sismondo, demonstrated that, “most outsiders and many physicians view speaking for pharmaceutical companies negatively”.\(^{74}\) Indeed, such was the outcry over how much influence pharma’s financial payments had on KOLs and HCPs in general, this was a chief reason why the United States passed the Sunshine Act.\(^{75}\) The legislation was enacted to ensure full disclosure to what pharma pay HCPs and to provide patients with better-informed decisions about HCPs to “deter inappropriate financial relationships that may lead to increased healthcare costs”.\(^{76}\) Pharma have to report direct or indirect payments to HCPs of US$10 or more and results are published online. There are some exemptions, including meals, product samples, independent certified and accredited CME meetings and

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\(^{71}\) [https://meetings.asco.org/am/virtual-welcome](https://meetings.asco.org/am/virtual-welcome)  
\(^{72}\) KOL interview with the author  
\(^{73}\) See one of the Fresnius-Kabi online symposium here: [https://md-education.wistia.com/medias/yegr1w151p3](https://md-education.wistia.com/medias/yegr1w151p3)  
\(^{74}\) Sismondo S., (2013) You’re not just a paid monkey reading slides: How key opinion leaders explain and justify their work, Edmond J. Safra Working Papers, No. 26 [http://www.ethics.harvard.edu/lab](http://www.ethics.harvard.edu/lab)  
\(^{76}\) Centers for Medicare and Medicaid Services (2013). Medicare, Medicaid, Children’s Health Insurance Programs: Transparency reports and reporting of physician ownership or investment interests. Federal Register, 78 (27) 9457-9528.
educational materials that directly benefit patients. The Pharma face penalties of up to $1,000,000 for failing to adhere to the Sunshine Act.

In the European Union (EU), there are no laws comparable to the Sunshine Act governing pharma’s promotion and interaction with HCPs. In June 2013, the European Federation of Pharmaceutical Industry Associations (EFPIA) introduced a code of practice on the ‘Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organisations’. The EFPIA Code has improved transparency on pharma payments to HCPs in Europe.

Why did the EFPIA and Congress introduce such measures? Put simply, pharma ‘gifts’ and payments influence prescribing habits. In 2016, a study from ProPublica found that HCPs in five common medical specialities who accepted industry payments in 2014 were “two to three times as likely to prescribe high rates of brand-name drugs compared with others in their speciality”. Perlis’s research shows that amongst those HCPs who received payments, the group receiving larger payments had on average a higher brand-name prescribing rate.

In table 4 below, Lieb has shown that HCP acceptance of monies has a direct effect on prescribing behaviour. Similarly, table 5 shows a much broader study of 342,000 HCPs that “revealed a relationship between the level of payment and the level of prescribing costs per patient”.

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78 See an example of educational materials that pharma purchased from MD Education to provide to hematologists in Austria, Germany, UK, US, Italy and the CEE region. https://md-education.wistia.com/microsites/rz0lbm bv8
Table 4. HCP acceptance of monies and its effects on prescribing. Study by Lieb shows 160 doctors completed an online questionnaire on physician-reported data on the frequency (percentage values in brackets) with which doctors (n = number of reporting physicians for each question) accepted remuneration for interviews, participation in sponsored CME and gifts when they were offered.84

<table>
<thead>
<tr>
<th></th>
<th>Payments for Interviews</th>
<th>Office Stationery</th>
<th>Day-to-Day Items</th>
<th>Drug samples</th>
<th>Dinner Invitations</th>
<th>Sponsored CME</th>
<th>Other*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 159)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>126 (79)</td>
<td>9 (5.7)</td>
<td>42 (26.9)</td>
<td>9 (5.7)</td>
<td>88 (55.3)</td>
<td>62 (39.5)</td>
<td>120 (80.2)</td>
</tr>
<tr>
<td>Rarely</td>
<td>24 (15.1)</td>
<td>39 (25.1)</td>
<td>63 (40.4)</td>
<td>10 (6.3)</td>
<td>55 (34.6)</td>
<td>37 (23.6)</td>
<td>13 (9.6)</td>
</tr>
<tr>
<td>Occasionally</td>
<td>9 (6.0)</td>
<td>59 (37.6)</td>
<td>44 (28.2)</td>
<td>30 (18.9)</td>
<td>16 (10.1)</td>
<td>50 (31.8)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Frequently</td>
<td>0</td>
<td>51 (32)</td>
<td>5 (3.2)</td>
<td>80 (50.3)</td>
<td>0</td>
<td>8 (5.1)</td>
<td>1 (0.7)</td>
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<tr>
<td>Always</td>
<td>0</td>
<td>11 (7)</td>
<td>2 (1.3)</td>
<td>30 (18.9)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Example: textbooks, CME invitations without sponsorship, bottle of wine.

Table 5. The influence of meals on physicians. In this cross-sectional study of 279,669 physicians, physicians who received a single meal promoting the drug of interest, with a mean value of less than $20, had significantly higher rates of prescribing.85

Unsurprisingly, HCPs and especially KOLs baulk at the suggestion that they are in the throes of pharma’s financial influence. Sismondo’s study of thirteen KOLs and their relationship with pharma captures perfectly the KOL sentiment when one KOL challenged on their role...

of presenting data in exchange for pharma money bristled: “we are not just a paid monkey reading slides.”

Sah and Fugh-Berman have documented that HCPs fail to recognize how susceptible they are to commercial influences due to self-serving bias, rationalization and cognitive dissonance”. Moreover, Sah and Fugh-Berman explore how “gifts make physicians psychologically as well as financially dependent on pharma so that physicians will reciprocate by prescribing a particular drug.” Indeed, the ‘gift-giving culture’ in the United States in the 1990s provided the impetus for Bob Goodman, an American HCP, to create a HCP lobby group called, No Free Lunch, to encourage HCPs to refuse gifts, lunches and ‘free’ products from pharma.

When I questioned KOLs over their relationship with pharma the answers ranged from an agreement that transparency of KOL involvement with pharma was a good thing to incredulousness that KOLs can be even seen to be bribed or in the sway of industry. See appendix for the survey.

“Pharma have a bad reputation in the media but we need them to move science forward.”

“I don’t have any issues with presenting for pharma. People in their academic, ivory towers should grow up!”

A KOL in his eighties told me, “the days of pharma giving us tickets for the opera are long gone. It’s highly regulated now and it is better for everyone.”

A KOL that organises an annual meeting in London told me, “...pharma compliance regulations are so strict now. They (pharma) are not even allowed to support our dinner at

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89 Healy, (2012) ibid, p.51
the House of Commons with the Health Minister anymore. It’s ridiculous. We are clinical experts and only want the best for our patients."

“Come on, is a coffee from Starbucks supposed to bribe me to prescribe a pharma companies drug? It’s laughable.”

“if it’s a new treatment therapy and I can help my patients, some of whom are desperate, then why would I not participate with pharma?”

“I get to meet my fellow colleagues and we always enjoy the face to face interaction and a catch-up. It’s good for everyone that participates in such meetings.”

What are the ethical implications for patients and society knowing that HCPs receive money and gifts from pharma? Let us turn to the academic discussions around corruption and ethics and how these affect the dynamic between pharma and HCPs and their wider repercussions on society.
7. Ethics, Conflict of Interest & Institutional Corruption

Historically, health care has enjoyed a high level of trust compared to other sectors in society. Studies in the United States reveal that rising costs of drugs and the media coverage of pharma drug safety scandals has resulted in “something of a trust crisis.”\(^{90}\) Why is that and where did the public lack of trust in pharma originate?

Studies point to the need to distinguish corruption at the individual and institutional level. Institutional corruption differs from individual corruption. Individual corruption is often illegal forms of corruption and points to the need for different, institutional remedies.\(^{91}\) Institutional corruption is a concept developed by Thompson and Lessig that highlights “legal, systemic, and structural forms of corruption, often not recognized by those involved”.\(^{92}\) What does this mean practically speaking for pharma? Drug safety scandals are a good example of institutional corruption, such as the 1961 thalidomide case and the Merck Pharmaceutical Vioxx scandal of 2004 that resulted in 25 million Americans taking a drug that had substantial heart risks.\(^{93}\) Merck paid over US$5 billion in settlements from 2007-2011.\(^{94}\) See table 6 below for an overview of fines pharma have paid due to drug safety breaches from 2009-2012. The drug safety scandals buttress Light’s argument that “good people, trapped in a corrupt structure, become corrupted as they do their best within the given economic, legal, institutional structure”.\(^{95}\)

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Pharma managers are paid handsomely to get drugs approved but does this mean that corruption is endemic with pharma? More research is needed on this topic but an interesting study from Brown makes an industry analogy for pharma by examining the experience of auditing firms and rating agencies and the egregious role they played in the financial crisis in 2008-2009. Her study asks “if the experience of mortgage firms that

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manipulated financial data provides lessons for creating policies to counter the manipulation of clinical research data by pharma”. 98

Does institutional corruption extend to regulatory bodies, such as the FDA and the EMA? The evidence is damning. Questions about the FDA have been raised since 1992 when the Prescription Drug User Fee Act permitted pharma to pay monies to the FDA, in exchange for expediting the drug approval process, “thereby making the drug industry a major funder of the agency set up to regulate it”. 99 Light’s research shows extensive evidence that the FDA approves many drugs that “do not offer substantial offsetting clinical benefits (about 9 in 10)”, and that leads him to ask: “should the public trust the FDA as much as it does”? 100

In 2007, the American Institute of Medicine criticized the FDA and accused them of “promoting a culture that was more interested in approving new drugs than in carrying out its core mission: protecting the public from unsafe and ineffective products”.

In a revealing examination of drug launches from 1995 to 2010, Light notes that “one in five new drugs approved as safe and effective causes enough serious harm to receive the most severe warning of regulators or be withdrawn altogether. Among priority drugs, reviewed quickly to get them to patients, the probability is one in three.” 101

The latter point is salient and should be heeded by governments currently urging a quick solution to pharma for a vaccine for COVID-19 and thereby trying to expedite the research and development process. Indeed, regarding the role of government in approving new medicine, an interesting study shines a light on the power and influence of pharma lobbying in Congress. 102 In 2005 pharma’s lobbying organization had become the largest in the United

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101 Light, D., (2013) ibid, p.16
States. The grey area of pharma ‘donations’ raises ethical questions and lead one Congressman to sardonically state:

“there is a hairline’s difference [that] separates bribes from contributions.”103

Research has also illustrated that medical associations, such as ASCO and ESMO, are also recipients of pharma funding. As medical associations disseminate guidelines to HCPs this has huge ramifications for medicine because they are becoming “dependent” on pharma funding. Light and Lexchin’s point out: “Historically, these institutions did excellent work without corporate contributions for decades. Now they “can’t live without them” and this self-corrupting perspective affects how patients get diagnosed and treated, as well as how payments and regulations get distorted.”104

Light terms this:

“self-induced institutional corruption, that can occur on either the individual or institutional level. Both can lead to institutionalized practices, rules, laws, and constructions of reality that corrupt the societal mission of the organization”.105

He points out that, “the commercial distortion of professional medical guidelines, key concepts or criteria, and training...constitute institutionalized forms of corruption”.106

Light makes an excellent point when he asks how widely one should “define the range of people or organizations within a given domain of institutional corruption... we need to define the boundaries of institutional corruption and the continuum of corrupt behaviour”.107 More research is needed to define and measure the kinds and degrees of corruption and its size and scope in the pharma industry. In particular, studies are needed regarding those parties that are dependent on pharma money, such as the example of the

105 Light, D., (2013) ibid, p.6
106 Donald W. Light, ibid p.6
107 Light, D., (2013) ibid, p.7
FDA, AMA and medical societies above, and the *degree* of dependency on pharma funds.\textsuperscript{108,109}

Technically speaking, pharma is playing within the rules of regulations and compliance, much like banks were ‘playing the system’ and complying with regulations during the financial crisis of 2008-09. Scholars argue institutional corruption cannot be brought under control by acts of law, as seen with the Sunshine Act. Gustavo Oliveira’s work reveals that corruption is usually a deviation “from a standard of operation but we cannot count as much on the law to provide us the standard, because these deviations are usually legal”.\textsuperscript{110}

In short, pharma will find a way to be ‘play the game’ that is in line with current legal parameters. The example of pharma providing gifts to HCPs of US$10 so they will favour their drugs “can be seen as an instance of increasing profits while respecting the legal framework (even if unethical)....that will ultimately undermine the efficiency of the broader health system.”\textsuperscript{111} Redman goes so far as to say that pharma are “uncontrolled by regulations”.\textsuperscript{112}

The ethical debate regarding pharma and HCP interaction is seen most clearly in the use of what the pharma industry term, off-label drugs. As seen above, in 2014, off-label drugs accounted for nearly 20 percent of all prescriptions garnering US$40 billion in sales.\textsuperscript{113}

Alarmingly, the evidence supporting the efficacy and safety of off-label drugs is not always apparent. This had led one outspoken critic to call for more regulation to ensure safety and efficacy levels are higher and a greater need to track off-label prescriptions “in order to know which patients are affected, to evaluate the risks and benefits, and to know when manufacturers are promoting the practice.”\textsuperscript{114} Rodwin prudentely calls for pharma and the

\textsuperscript{108} Donald W. Light, (2013) ibid p.6

\textsuperscript{109} Studies have also shown the problematic issues surrounding Patient Advocacy Organisations. PAOs accept funding from pharma to finance their activities.


\textsuperscript{111} Oliveira G., (2014) ibid., p.11

\textsuperscript{112} Redman B., (2015) *Are the Biomedical Sciences Sliding Toward Institutional Corruption? And Why Didn’t We Notice It?*, Edmond J. Safra Working Papers, No. 59, March 25, p.4

\textsuperscript{113} https://www.andruswagstaff.com/blog/big-pharma-has-higher-profit-margins-than-any-other-industry/

FDA/EMA to conduct awareness campaigns to the general public about off-label drug use and the potential risks.\textsuperscript{115}

The FDA, AMA, medical societies, KOLs, CROs are all beneficiaries of pharma funding. Redman’s research posits that scientific publishers are also “illustrating a number of indicators of institutional corruption that have undermined the aim of science to achieve reliable, quantifiable knowledge”.\textsuperscript{116} Research reveals “as much as 90 percent of the published medical literature” upon which doctors rely is flawed.\textsuperscript{117} And “an estimated 85% of research resources are wasted with false or exaggerated effects”.\textsuperscript{118} The contrast between academic independence and research integrity on the one hand and pharma’s commercial push on the other hand provide problematic issues as the former relies on monies from the latter.\textsuperscript{119}

Ioannidis’ research demonstrates that journal publishers are now dependent on pharma budgets which have undermined scientific integrity because publishers “prioritize significant, novel results, ignoring the responsibility of science to incorporate the lessons of negative findings, and have been insufficiently vigorous in verifying the claims of authors”.

Ioannidis believes the publishing world has not only been subject to corruption from pharma but also in the notion what he terms “science exceptionalism”, and argues the centuries old practice of self-regulation via the peer review process and the widely held belief that ‘false’ science will be identified and corrected has “fed tolerance for the widespread bias in science noted above and for the lack of accountability for obtaining and reporting accurate findings”. Ioannidis states these practices are producing corrupted science and remarks, “the large majority of these practices are not considered illegal or unethical”. Again, pharma is ‘playing the system’. If pharma is orchestrating and manipulating the development of the data by CROs, the publication of the data by journals, the dissemination of guidelines by medical societies and ‘influencing’ Congress and

\textsuperscript{115} Rodwin M., (2013) ibid p.661.
regulatory bodies like the FDA; plus they have developed close relationships with KOLs, who in turn influence the ‘regular’ HCPs in their prescribing decisions, the question is: what is to be done? Let us now turn to recommendations to address these issues.
8. Summary and Recommendations

As we have seen from a review of the academic literature, what stands out is that despite the attempts to mitigate the conflict of interest generated by the interaction between HCP and pharma, problems still persist. Fickweiler’s has shown the need for further studies to examine the depth of interaction between HCPs and pharma. However, what is not disputed is the influence of pharma in the apparatus of approving drugs and rolling them out to a global audience. Pharma’s network of deep-seated relationships with KOLs, their influence on storied journals that publish the scientific data, and the sheer revenues that pharma has to research, develop, garner intelligence from HCPs, market to HCPs globally (and contest legal battles), has eclipsed the work of public sector bodies and has created a situation where governments are dependent on pharma. This can be seen in the clamour by governments for pharma to find a vaccine in the current COVID-19 virus encapsulated perfectly by the bizarre White House conference on 1 May 2020 between President Donald Trump and the CEO of Gilead Sciences, Daniel O’Day, in the hope that a vaccine can be developed in record time.

We will review what action pharma should take firstly by condensing the opinion of scholars and secondly the author will suggest his own recommendations.

As we have seen, academic studies have challenged the belief that the disclosure of financial payments acts as a panacea to cure the ills of conflicts of interest between pharma and HCPs. Although it has been acknowledged that disclosure of funding to organizations and physicians can be beneficial, there are limitations. As Rodwin markedly notes, regulatory moves to mitigate the influence of the pharma industry by making pharma disclose payments and gifts given to HCPs “fails to recede the disproportionate influence of the pharma companies over the production of knowledge”. By production of knowledge, Rodwin is referring to the publishing and RCT apparatus that is heavily funded by pharma.

121 See NBC coverage of the meeting here: https://www.youtube.com/watch?v=HDT7pfmAPl4 (Accessed June 2020)
financing. Table 7 below illustrates Rodwin’s argument that moving away from pharma to government control of RCT would have a positive effect on the pharma industry’s fudging of data.

<table>
<thead>
<tr>
<th>Manufacturer Control</th>
<th>Government Controls →</th>
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<tbody>
<tr>
<td>1. Drug firms conduct clinical trials with little regulation.</td>
<td>2. FDA regulates and oversees clinical trials that drug firms conduct.</td>
</tr>
</tbody>
</table>

Table 7. Rodwin’s recommendations to mitigate against conflict of interest in RCT

Consequently, Redman suggests a root and branch appraisal of the RCT and publishing fields are needed and he calls for

“reproducibility practices; sharing of data, protocols, materials and software; standardization of definitions and analyses; improvement of study design standards; improvement in peer review, reporting and dissemination of research; and better training of the scientific workforce in methods and statistical literacy”.124

To this end, ceasing ghost writing articles of RCT data by pharma or third-party agencies would be beneficial.

Grande suggests having public-funded academic educational programs to replace industry-driven meetings. In reality, pharma is not going to hand over their business to anyone else.

Calls for pharma to be prohibited from meeting HCPs is also not practical in reality. Fickweiler’s studies from 2017 has shown that HCPs want to be kept abreast of latest developments, for their patients and their own curiosity and they like the personal touch from pharma sales reps. Suggestions that the public sector with multi-national bodies such as the European Commission or philanthropic organisations such as Bill Gates Foundation should pick up the baton, rather than relying on pharma, are too simplistic and impractical.

Sismondo argues that the influence of KOLs by pharma can be mitigated by “changing the political economy of medical knowledge by separating pharma research and development from pharma marketing.” He suggests three new approaches to curtail the sway of pharma over KOLs:

- Creating an independent governing body to oversee and conduct clinical trials.
- Separate the research and marketing divisions that pharma currently employ as two separate firms. One would focus on R&D; the other solely on manufacturing and marketing.
- Prohibit or restrict HCPs and researchers from participating in discussions regarding the marketing of drugs.

Miller argues for another type of systemic reform that taps market forces. She posits that we can “develop accreditation, certification, or rating systems that reveal the ethical

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129 Sismondo S., (2013) ibid. p.636
performance of the drug firms to purchasers, investors, employees and regulators. Market forces would then create incentives for drug firms to improve their ethical conduct.”

Miller suggests that ethical rating of drug firms focus on four areas of stakeholder concern:

- Clinical trial design and management
- Dissemination of clinical trial results
- Marketing practices
- The accessibility of medicines.

The author’s suggestions would go further than the above studies have called for. There needs to be a systematic change to tackling the way pharma conducts business and more importantly this needs to be brought into place by governments globally. The author recommends the following changes:

- More research into public trust in pharma would contribute to improving efficiency while protecting the health of the public.

- Punitive legal action is needed to punish pharma that fail to disclose all trial data. For instance, rather than issuing a fine, the author proposes that governments legislate significant such as a moratorium on all business activities for a 12 months period if pharma has not disclosed data that has resulted in harm to patients.

- RCT data should be reviewed by an independent public funded party, a “pharma ombudsman” and not just pharma that has a vested interest in highlighting the benefits of their drug.

- Journals should be prohibited from accepting pharma monies in terms of advertising and in terms of submitting RCT data. Instead, data should be made available online.

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to the general public, i.e. patients and their families and HCPs alike, via a government, (read: not for profit) website.

- KOLs should be capped at what pharma can pay them to mitigate against bias.

- Use of off-label drugs should be suspended and drugs should only be used on patients once the drug has been approved and safety issues have been identified and resolved.

- Medical societies should not be able to receive monies from pharma as it raises clear conflict of interest in terms of pharma funding of annual meetings and creation and distribution of new guidelines. Further research is needed into the relationship between pharma and medical societies.

- Regulatory bodies such as the FDA and EMA should not be allowed to receive monies from pharma.

- An independent public sector review of all protagonists that receive pharma monies, including HCPs, CROs, publishers, patient advisory organisations, lobby groups, medical associations. Further, an investigation into the extent these companies or organisations are dependent on pharma money needs to be addressed at the country level.
9. Conclusion

In 2007, a retiring HCP from the UK, Charles Medawar, penned a public letter. In it he raged about the changing nature of medicine and treatment and lambasted against the pernicious influence of pharma and the rise of suspect drug treatments and guidelines before commenting:

“I have spent over thirty years studying the world of medicines, and regret to say that the more I learn, the more shocked I feel. For all the triumphs and miracles, I fear that we are heading blindly in the general direction of Pharmageddon. Pharmageddon is a gold-standard paradox: individually we benefit from some wonderful medicines while, collectively, we are losing sight and sense of health.”

In this thesis, we have seen how pharma communicates and interacts with HCPs and how this has developed from the 1950s. An examination of academic studies has shown the ethical debates surrounding the conflict of interest between pharma and HCPs receiving monies and gifts. We have also seen that the regulatory measures that have been employed to try to mitigate pharma’s influence on HCPs, most notably HCPs and the disclosure of financial payments, has failed to curb pharma’s influence, even recklessness: as seen with the drug safety scandals. We have also seen how the process of obtaining approval for new drugs to regulatory bodies such as the FDA and the EMA has been transformed by the rise of clinical trials and publications of said trials in academic journals. These developments have further cemented pharma’s influence over HCPs with ‘control’ over the guidelines and therefore the process of approving new medicine. Further, directly or indirectly, HCPs, publishing companies, medical associations, CROs, and regulatory bodies have become dependent, partly or fully, on pharma funding. This has created a situation where pharma has an pre-eminent position on all facets within the matrix of research, development, design, marketing, distribution and approval of new drugs. This cartel-like structure needs to be addressed. Further research is needed on the scope and degree of pharma’s interactions with HCPs, and pharma’s interactions with all stakeholders. It is without

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hyperbole to say Medawar’s fear of Pharmageddon, in the control of the health of our nations, is a very apparent likelihood if action is not taken. The author hopes that this thesis has shed some light on the dynamic of the pharma-HCP relationship and has added to the debate.
Bibliography and Suggested Reading


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Appendix A:

List of Abbreviations and Glossary

Physician: Largely US term used for a doctor that prescribes medicine
Prescribing doctor: a doctor or nurse that has the authority to prescribe a drug to a patient
KOL: Key Opinion Leader
EMA: European Medicines Agency
FDA: Food and Drugs Administration
CME: Continuing Medical Education
IME: Independent Medical Education
HCP: Healthcare Practitioner
ESMO: European Society of Medical Oncology
ASCO: American Society of Clinical Oncology
Off-label drugs: prescribing drugs that have not been approved
MSL: Medical Science Liaison
RCT: Randomized Controlled Trials
Appendix B:

Examples of CME meetings

The author of this thesis provides two examples of scientific CME meetings that feature an international faculty of KOLs and funding from pharma. Both meetings are in late 2020 and organized by MD Education, the firm he founded in 2015. (PDFs to be added.)

2020 MPN-MDS European Focus Meeting (page 1 of 2)

Dear Colleagues and Friends,

It is our great pleasure to announce the multisessional online video conference 
MPN-MDS European Focus 2020 that will take place online 
scheduled for September 17-19, 2020.

The online meeting is organized by MD Education, a medical education agency. 
The theme of the online meeting, International Knowledge & Clinical Practice in 2020, reflects the collaboration to advance the research and treatment of patients with MPN & MDS globally.

MPN-MDS European Focus 2020 will be shared online for registered specialists and approximately 25 renowned faculty from the US and Europe. 
The meeting will provide participants with a unique opportunity for sharing knowledge, skills, and experiences. In addition, this activity will provide a platform for networking with many of the world’s leading experts, focusing on reviewing and assessing best practices and state of the art treatments in MDS and MPN.

The online video conference will include presentations, live online discussions, debates with audience interaction, and more.

The Chair of MPN/MDS European Focus 2020 are:

Prof. Dr. Siddhartha Tiwari MD, PhD.
Dr. Siddhartha Tiwari is a Medical Oncologist and Professor in the Department of Medicine at the University of Texas MD Anderson Cancer Center, Houston, Texas. His research focuses on understanding the biology of myeloid malignancies and developing novel therapies for patients with MPN, and he holds membership in the American Society for Clinical Investigation.

Prof. Dr. Alessandro M. Vannucchi MD, PhD.
Dr. Alessandro Vannucchi is an Associate Professor of Hematology, a Head of Center of Research and Innovation of Transplantation in Hematological Malignancies, ASU-Chegg, University of Florence, Italy; Director of the Geneva Foundation for Cancer Research, and Professor of Hematology, University of Florence, Italy; Accl. to 4th Chair of the JNMC; and Principal Investigator of Multiple Myeloma Group, Italy.

It is our pleasure to invite you to participate in this one-of-a-kind event. 
If you would like additional information or have any questions regarding the conference, please email richard.thorpe@mededucation.eu.
# Agenda & Proposed Faculty, September 17-19 2020

## Thursday, September 17

<table>
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<tr>
<th>Time</th>
<th>Session</th>
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<tr>
<td>08:00</td>
<td>Breakfast Symposium</td>
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<tr>
<td>09:00</td>
<td>1. Primer on Epigenetics, Andrei Belesco - University Medical Center Mannheim, Germany</td>
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<tr>
<td>09:30</td>
<td>2. Primer on Mastocytosis, Stéfan Van Sterkenburg - The University of Texas MD Anderson Cancer Center, Houston, United States</td>
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<td>10:00</td>
<td>3. Diagnosis and Therapy of NHL/ALCL, Juan Carlos Gómez-Yúfera - Hematology Department, Methodist University, AIME, Poland</td>
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<td>10:30</td>
<td>Morning Break - Carillon Hall - Tea, Coffee, Fruit and Cold Snacks</td>
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<tr>
<td>11:00</td>
<td>4. Update on CLLM, Eric Tscherg - Centre de Cancérologie Curie-Assistance Publique, France</td>
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<tr>
<td>11:30</td>
<td>5. Primer on overlap MDS/MPN syndromes, Hans-Michael Kleinheisterkamp - University of Erlangen-Nuremberg, Germany</td>
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<td>12:00</td>
<td>Lunch Symposium and Buffet</td>
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<td>13:30</td>
<td>6. My Take on Guidelines and Therapies for ET, Jiri Vlcek - Institute of Hematology and Blood Transfusion, Prague, Czech Republic</td>
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<tr>
<td>14:00</td>
<td>7. My Take on Guidelines and Therapies for PV, Antonina Hatajuk - Hospital Medical University, Rijeka, Croatia</td>
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<td>14:30</td>
<td>8. Update on Management of ET/PV with interferon, Peter Guglielmone - The medical University of Vienna, Austria</td>
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<tr>
<td>15:00</td>
<td>Afternoon Break - Carillon Hall - Tea, Coffee, Fruit and Cold Snacks</td>
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<tr>
<td>15:30</td>
<td>9. Update on Management of ET/PV with ruxolitinib, Jean-Jacques Kürstner - Clinical Investigation Center, Saint Louis Hospital, Paris, France</td>
</tr>
<tr>
<td>16:00</td>
<td>10. Diagnosis and Therapy of Pre-Blastic Myelofibrosis, Tiziano Rambaldi - Foundation of Clinical Research IRCCS Istituto Nazionale dei Tumori, Milano, Italy</td>
</tr>
<tr>
<td>16:30</td>
<td>Oral presentation of best abstracts</td>
</tr>
<tr>
<td>17:00</td>
<td>Dinner Symposium</td>
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## Friday, September 18

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>08:00</td>
<td>Breakfast Symposium</td>
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<tr>
<td>09:00</td>
<td>11. Prognostication for Primary and Secondary Myelofibrosis, Patrizia Giglio-Menni - University of Florence, Italy</td>
</tr>
<tr>
<td>09:30</td>
<td>12. When and how to Start Ruxolitinib for Myelofibrosis (goals of therapy), Martin Göhringhoffmüller - Johannes-Ewering-Breiden-Medizin, Germany</td>
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<tr>
<td>10:00</td>
<td>13. Management of Side Effects and Loss of Response to Ruxolitinib (progression), Lucia Marasca - MD Anderson Cancer Center, Houston, United States</td>
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<tr>
<td>10:30</td>
<td>Morning Break - Carillon Hall - Tea, Coffee, Fruit and Cold Snacks</td>
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<tr>
<td>11:00</td>
<td>14. Transplantation for Myelofibrosis, Donald McLlwain - Guy’s and St. Thomas’ NHS Foundation Trust, London, United Kingdom</td>
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<tr>
<td>11:30</td>
<td>15. Novel agents for Myelofibrosis, Alessandro Vannucchi - University of Florence, Italy</td>
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<tr>
<td>12:00</td>
<td>Lunch Symposium and Buffet</td>
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<tr>
<td>13:30</td>
<td>16. Prognostication in MDS, Valeria Santoro - University of Genova, Italy</td>
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<tr>
<td>14:00</td>
<td>17. Optimal Management of Low Risk MDS in Everyday Practice, Peter Rönniy - University Hospital Oulu, Finland</td>
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<tr>
<td>14:30</td>
<td>18. Optimal Management of High Risk MDS in Everyday Practice, Aurélien Chuvik-Kittang - Sankt-Anna Hospital, Aarhus, Denmark</td>
</tr>
<tr>
<td>15:00</td>
<td>Afternoon Break - Carillon Hall - Tea, Coffee, Fruit and Cold Snacks</td>
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<tr>
<td>15:30</td>
<td>19. Novel Agents for MDS, Pierre Frick-Rousset - Marseille Cancer, France</td>
</tr>
<tr>
<td>16:00</td>
<td>20. Transplantation for MDS, Elisabeth Yatsco-Ngilla - University Hospital Laie, France</td>
</tr>
<tr>
<td>16:30</td>
<td>Oral presentation of best abstracts</td>
</tr>
<tr>
<td>17:00</td>
<td>Dinner Symposium</td>
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## Saturday, September 19

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>08:00</td>
<td>Breakfast Symposium</td>
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<tr>
<td>09:00</td>
<td>21. How to Manage Post MDS vs. Post MPN AML, Maria Teresa Visco - University of Ancona, Italy</td>
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<tr>
<td>09:30</td>
<td>22. FLT3 Inhibitors for AML and Beyond, Glauciano Marcielli - University of Bologna, Italy</td>
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<tr>
<td>10:00</td>
<td>23. Bcl-2 Inhibition for AML and Beyond, Paula Montesinos - Hospital Universitario Arnau de Vilanova, Spain</td>
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<tr>
<td>10:30</td>
<td>Morning Break - Carillon Hall - Tea, Coffee, Fruit and Cold Snacks</td>
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<tr>
<td>11:00</td>
<td>24. IDH Inhibitors for AML and Beyond, Stéphane De Botton - Institut de Cancérologie Gustave-Roussy, France</td>
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<tr>
<td>11:30</td>
<td>25. Other Novel Therapies for AML, Thomas Pillot - University Hospital and University of Bern, Switzerland</td>
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<tr>
<td>12:00</td>
<td>Oral presentation of best abstracts</td>
</tr>
<tr>
<td>12:30</td>
<td>Lunch Symposium and Buffet</td>
</tr>
<tr>
<td>14:00</td>
<td>Thank you and Farewell</td>
</tr>
</tbody>
</table>
Dear Colleagues and Friends,

It is our great pleasure to announce the international congress MPN-MDS US Focus 2020, that will take place at the La Jolla Hotel, Torrey Pines San Diego, California, USA, scheduled for November 5-7, 2020.

The meeting is organized by MD Education, a British medical education agency.

The theme of the meeting, International Knowledge & Clinical Practice in MPN, reflects the collaboration to advance the research and treatment of patients with MPN worldwide.

MPN-MDS US Focus 2020 will host nearly 500 delegates and experts mainly from the UK and Europe. The meeting will provide participants with a unique opportunity to share knowledge, skills, and experiences. In addition, this activity will provide a platform for networking with many of the world's leading experts, focusing on reviewing and assessing best practices and state of the art treatments in MDS and MPN.

The meeting program will include presentations, roundtable discussions, debates, workshops, participation atSabina sessions, poster sessions, and a number of interesting social events. The theme of MPN-MDS US Focus 2020 is:  

It is our pleasure to invite you to participate in this one-of-a-kind event. If you would like additional information or have any questions regarding the conference, please email MD@education.eu.
2020 MPN-MDS United States Focus Meeting (page 2 of 2)

MPN-MDS US Focus 2020

Suggested Faculty, November 5-7 2020

Thursday, September 5
8:30  Registration
12:00 Lunch time
14:00  Primer on eosinophilia, Jochen Götze
14:00  Primer on mastocytosis, Claudia Urban
15:00  Diagnosis and therapy of CML, Oana Bucuta
An update on CML, E. Paethen
16:00  Coffee break
16:15 Non-PV erythromelalgia, Joseph Provenza
My take on guidelines and therapies for IF, Jerry Spinak
My take on platelets and therapies for PV, Howard Taylor
17:30  Oral presentation of best abstracts
18:30 Dinner

Friday, September 6
7:30  Breakfast
Morning Symposium
10:00 Update on management of ET/PPV with interferon, Richard Silver
Update on management of ET/PPV with ruxolitinib, Uriel Versoever
11:00 Management of side effects and loss of response
for ruxolitinib (progressions), Martin Bose
When and how to start ruxolitinib for MF (goals of therapy), Jaggi Rampal
12:00 Lunch time
14:00  Lunchtime Symposium
15:00  Diagnosis and therapy of prefibrotic MF, Laura Michaels
Navigating preprogression for primary and secondary myelofibrosis, Robert Kenta
16:00  Coffee break
16:15  Transplant for MF, Jonathan Deeg
Novel agents for MF, John Warnakulasuriya
Progression in MF, Rafael Sáez
17:30  Oral presentation of best abstracts
18:30 Dinner

Saturday, September 7
7:30  Breakfast
Morning Symposium
10:00  Optimal management of low risk MDS in everyday practice, Ilene Papoquet
Optimal management of high risk MDS in everyday practice, Tony Stock
11:00 Novel agents for MDS, Guillermo Garcia-Manero
Transplant for MDS, Yolanda Navarrete
12:00  Lunch time
14:00 Lunch Symposium
15:00 How to manage post MDS vs post PMN AML, Sagnik Dasgupta
Other novel therapies for AML (EFSK, Molsk, etc), Selma Lager
16:00  Coffee break
16:15 FLT3 inhibitors for AML and beyond, Estela Wang
BCL-2 inhibition for AML and beyond, Cherie Bresne
IDH inhibitors for AML and beyond, Matthias Ohnke
17:30  Oral presentation of best abstracts
18:30 Dinner
Appendix C:

Interview Questions: KOLs have asked to keep their names confidential.

Key Opinion Leaders

1. What do you think is the role of pharma in society? Please elaborate.
2. Do you interact with pharma online or in person? If so, how?
3. Do you receive gifts from pharma?
4. Do you feel pharma have too much influence on HCPs prescribing habits?
5. Is more transparency needed on pharma marketing spend and RCT trial findings?

KOLs

1. Prof A, Heamatology HCP, Guys and St Thomas' Hospital, London
2. Prof B, Heamatology HCP, AKH Hospital, Vienna
3. Prof C, Heamatology HCP, MD Anderson Cancer Hospital, Houston
4. Prof D, Heamatology HCP, Saint Louis Hospital, Paris
5. Prof E, Heamatology HCP, University of Florence, Italy
6. Prof F, Heamatology HCP, University Hospital Bratislava
7. Prof G, Heamatology HCP, University Hospital of Ulm
8. Prof I, Heamatology HCP, Southampton University Hospital
Interview Questions: Pharma personnel have asked to keep their names confidential.

Pharma Management Personnel

1. What do you think is the role of pharma in society? Please elaborate.
2. Does your organization interact with KOLs online or in person? If so, how?
3. Do you give gifts to KOLs?
4. Do you feel pharma have too much influence on HCPs prescribing habits?
5. Is more transparency needed on pharma marketing spend and RCT trial findings?

Pharma Management Personnel

1. Product Manager Oncology, Novartis
   UK
2. Product Manager Rheumatology, Roche
   UK
3. Product Manager Haematology,
   Celgene US
4. Medical Director, Roche Switzerland
5. Medical Director, Celltrion Netherlands
6. Commercial Director, Celltrion UK
7. Commercial Director, Pfizer Global
8. Medical Director Nutrition, Fresenius-Kabi Germany
9. Product Manager Oncology, Roche
   Belgium
10. Product Manager Gastroenterology,
    Takeda Czech Republic