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EDITORIAL



# Are academia–pharma partnerships essential for novel drug discovery in the time of the COVID-19 pandemic?

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## 1. Introduction

It is tempting to think that the COVID-19 pandemic should provide an optimal opportunity for academic-industry collaborations in developing treatments and vaccines to deal with the deadly outbreak. In this instance, the goal of academia – to advance human health meshes with industry's drive to market therapies that generate large revenues. But even in this case, we are seeing how the interests of industry are starting to predominate. In April 2020, Oxford University announced that it would donate the rights to the coronavirus vaccine that it was developing to any drugmaker, thereby ensuring that treatments to prevent COVID-19 would be available for free or at a low cost to anyone needing them. However, a few weeks later Oxford signed an exclusive vaccine deal with AstraZeneca that gave the company sole marketing rights without any guarantee of low prices. According to Ameet Sarpatwari, an epidemiologist and lawyer at Harvard Medical School 'it is business as usual, where the manufacturers are getting exclusive rights and we are hoping on the basis of public sentiment that they will price their products responsibly'[1]. Perhaps one of the reasons for Oxford's shift is that under its deal it will receive no royalties during the pandemic, but once the pandemic is over, the patents it owns could bring in millions of pounds. AstraZeneca has since said that its vaccine will cost 'a few dollars' a dose but did not specify whether that price will increase once the pandemic is declared over[2].

A similar conflict between public and private values is apparent in the history of the development of remdesivir. Remdesivir was developed with considerable public funding from different United States (US) agencies including the Department of Defense, Centers for Disease Control and Prevention, National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases and the University of North Carolina, through a 6 USD million grant to the university. Public Citizen estimates that over 70 USD million of public money went into the development of the drug [3,4]. However, despite this public investment, Gilead, the company marketing remdesivir, initially attempted to obtain orphan drug status and only withdrew its application in the face of strong public opposition[5]. Gilead is charging US 2,340 USD for a 5-day course of therapy in developed countries (and 3,120 USD for commercial insurers in the US)[6] while an analysis from the independent Institute for Clinical and Economic Review calculates that the price in the US should be 2,470 USD per treatment course for a moderate to severe patient and 70 USD per treatment course for a mild patient[7]. The estimated manufacturing cost of remdesivir is 0.93 USD per dose[8].

## 2. Industry priorities in funding research

It is business as usual – industry's push to find and market drugs that will bring in billions in sales – that largely accounts for the virtual absence of drugs to treat diseases that are predominantly found in low- and middle-income countries. Between 2000 and 2011, there were 336 new chemical entities registered worldwide of which only 4 were approved for neglected diseases and just 1% of the 148,445 clinical trials registered by the end of 2011 were for neglected diseases[9]. The same critique about the absence of new drugs for neglected diseases applies to industry's reluctance to fund research into other important areas. As one example, even the Generating Antibiotics Incentives Now (GAIN) Act in the US that grants 5 years of additional marketing exclusivity for 'qualifying infectious disease products' has not incentivized accelerated antibiotic development[10]. Companies also do not investigate new uses for off-patent drugs since they will not have a monopoly on sales. The funding for the trial showing the benefit of using dexamethasone in COVID-19 patients came from non-industry sources[11]. On-the-other hand, companies are often eager to invest in lucrative therapeutic areas even though the products that result from their research and development offer little to no therapeutic advances[12].

Even when the research efforts of pharmaceutical companies lead to significant therapeutic benefits, these are usually accompanied by significant financial rewards. For example, between 2013 and 2018 revenue to Gilead from sales of its hepatitis C drugs is estimated to have been 58.6 USD billion of which 25.8 USD billion was profit[13]. Vertex, the maker of Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor) the new treatment for cystic fibrosis, earned 420 USD million in

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the first 10 weeks that the drug was on the market in the US [14]. In fairness, it also needs to be acknowledged that skewed research priorities are not exclusive to industry. Moradpour and Hollis show that when research is sponsored by non-industry-funded sources (governments, universities, and foundations) that there is still a bias in favor of diseases that affect wealthy populations[15].

### 2.1. Universities allied for essential medicines

One initiative to counter the bias in industry-funded research at the academic level is the organization Universities Allied for Essential Medicines (UAEM) with chapters in Europe, Latin America and North America. UAEM is a global network of university students who believe that universities have an opportunity and a responsibility to improve global access to public health and necessary medicines. UAEM advocates for universities being part of the solution to the crisis of access to medicines by promoting medical innovation in the public interest to ensure that all people regardless of income can receive affordable medicines and other health-related technologies. Specifically, its three pillars are: 1) to ensure that medicines developed at 'universities are made accessible and affordable to people in resource-limited settings'; 2) to 'dramatically increase publicly funded biomedical research and development for the global health needs of neglected populations'; and 3) to empower students 'to stand at the vanguard of leadership in global health access and innovation, making substantial change at academic institutions'[16].

While some universities have responded positively to UAEM's message, overall only 9 out of 59 American universities[17], 2 out of 15 Canadian universities [18] and 5 out of 25 British universities[19] scored B or better on a combined scale that measures innovation, access, empowerment, and transparency.

### 2.2. Drug development partnerships

The main way that industry has responded to the challenge of developing medicines for neglected diseases has been to combine with academia and others in product development partnerships (PDP), the best known of these probably being Drugs for Neglected Disease initiative (DND*i*). Since 2003, DND*i* has stimulated the development of a new oral treatment for sleeping sickness and developed seven new treatments from existing molecules and recombining drugs to bring better treatments to patients for malaria, Chagas disease, leishmaniasis, and pediatric HIV[20]. The multinational companies that get involved in PDPs tend to focus their efforts on in-kind donations, for example, access to their molecular library or on early-stage research and development, leaving the costly development process to others. Some of the large companies also have an economic motivation for their involvement, as they see some possible commercial value in the form of spin-off research and obtaining exclusive rights to use the research in developed countries[21]. Ownership of patent rights is also an issue in some cases. Although some companies have opted to forgo patents on products that they are involved with, others still plan to apply for patents that may result in restricted access to knowledge and products[22].

## 3. Biases in academia-industry relationships

### 3.1. Funding of clinical research

A Cochrane systematic review examined the results and conclusions of studies with industry funding, including a mix of industry and non-industry funding, versus the outcomes of studies with either non-industry funding, including funding through academic medical centers, and no funding. The conclusion was that 'sponsorship of drug and device studies by the manufacturing company leads to more favorable efficacy results and conclusions than sponsorship by other sources'[23]. The outcomes in favor of industry-funded trials did not result from the usual sources of bias such as lack of randomization or blinding. Instead, drawing on the studies included in their review, the authors speculated that it arose from a variety of factors. Some of those are industry protocols possibly including inferior comparators such as active comparators in inferior doses or placebo controls, that will increase the chance of their product's success. Industry-funded trials may also selectively choose less clinically relevant outcomes as their primary outcome in order to get a higher chance of achieving an effect. There is also the possibility that industry-sponsored studies may be biased in the coding of events and their data analysis; positive results may be selectively reported and published multiple times and whole studies with unfavorable results may not be published. Favorable conclusions in industry-sponsored trials may be reached by over-interpreting results and the use of spin in conclusions. The authors also noted that industry-sponsored studies had less concordance between results and conclusions compared with non-industry-sponsored studies, suggesting that conclusions of industry-sponsored studies are less reliable.

### 3.2. Academic researchers and industry relationships

Life science faculty at American universities were surveyed in 2007 about their relationships with industry. Faculty with industry relationships published significantly more and at a greater rate in the prior 3 years than respondents without industry support and published in journals with a higher impact factor. Overall, 45% of all research funding came from industry for those with industry relationships and when asked how much industry had contributed to their research, 13% responded a 'great extent,' while another 46% responded 'some extent.' 'Faculty members with industry support were also significantly more likely than those without it to report that their choice of research topics had been affected somewhat or greatly by the likelihood that the results would have a commercial application. In addition, those with industrial support were more likely than those without it to report that a publication was delayed by six months or more … or that

the delay was to inhibit the dissemination of undesired results.' These findings are especially concerning since nearly two-thirds of those with a rank of full professor maintained some form of relationship with industry, likely meaning that a group with industry ties had the most say in the direction of research at their institution[24].

Finally, when principal investigators have financial relationships with companies sponsoring trials, the published versions of those trials are more likely to be presented in ways that favor outcomes desired by the sponsor[25].

### 3.3. Academic medical centers and industry relationships

Surveys about the relationship between academic medical centers (AMCs) and industry, admittedly somewhat dated, have revealed a complex pattern of interactions – sometimes restrictive and sometimes lenient. A survey of 107 US medical-school research administrators responsible for negotiating clinical-trial agreements with industry sponsors found that more than 85% reported that they would not approve provisions giving industry sponsors the authority to revise manuscripts or decide whether results should be published. But at the same time, almost a quarter would allow companies to insert their own statistical analyses, half would allow sponsors to draft the manuscript and 80% would permit a provision giving ownership of the research data to the sponsor[26].

A second survey of 86 medical schools found that only 38% had adopted an institutional COI (ICOI) policy applicable to financial interests of the institution. Seventy-eight percent of institutions treated the financial interests held by an institutional research official for a research sponsor or a product that is the subject of research as a potential ICOI. The majority of institutions also adopted organizational structures that separate research responsibility from investment management and from technology transfer responsibility[27]. A total of 459 department chairs from these medical schools were also surveyed and 60% reported having some form of personal relationship with industry, including serving as a consultant, a member of a scientific advisory board, a paid speaker or a member of the board of directors. More than two-thirds of chairs perceived that having a relationship with industry had no effect on their professional activities, but almost three quarters viewed a chairengaging in more than 1 industry-related activity as having a negative impact on a department's ability to conduct independent unbiased research[28].

Nineteen of the 47 largest pharmaceutical companies, as of 2012, had at least 1 board member who concurrently held a leadership position at an AMC, including 16 of 17 United States-based companies. Eighteen industry board members held 21 clinical or administrative leadership positions including 2 university presidents, 6 deans and 7 clinical department chairs or center directors[29].

Finally, Rochon and colleagues collected institution-level financial COI (FCOI) policies from all 16 Canadian academic medical centers (16 medical schools and 47 teaching hospitals as well as their 16 partner universities). Nine universities, 9 medical schools, and 15 teaching hospitals responded that they had no policies on institutional FCOI. The existing policies were evaluated as to whether they dealt with 16 core standard items such as royalties from sale of the investigational product that is the subject of research, the requirement of disclosure/reporting of institutional COI and the rebuttable presumption against the conduct of human subject research when institutional level FCOI exists. On average, individual policies contained just 20% of these items and no individual policy contained more than 65%[30].

## 4. Expert opinion

Relationships between academia and the pharmaceutical industry are fraught with the potential for biases, in the choice of topics that are examined and in the results and conclusions from that research. Ideally, in my opinion, research into vaccines and treatments for COVID-19 should shift to public funding and independent conduct and analysis of research. This change should be a goal informed by the recommendations found in the World Health Organization report 'Research and development to meet health needs in developing countries: strengthening global financing and coordination'[31].

A crisis such as the COVID-19 pandemic presents an opportunity to fundamentally rethink current research paradigms, but we cannot be naïve about the efforts that it will take to change the way that medical research is conducted, nor about the political and economic shifts necessary to attain the conditions where those changes are possible. In the meantime, the world is facing the most deadly infectious disease outbreak in over 100 years and action cannot wait for what might happen in the indeterminate future. Therefore, we need to work with prevailing structures when it comes to containing the effects of COVID-19 and make use of industry expertise, but within strict boundaries.

To start with, governments and other non-industry funders need to define their own research priorities and not just rely on those from the pharmaceutical industry. These may include looking at repurposing low-cost existing generic drugs as has already been the case with dexamethasone. Research funding that governments give out to all parties, including industry, should include provisions mandating that any eventual therapies be made available at prices that are affordable in low- and middle-income countries. Governments should also seriously consider funding product development partnerships which might be especially receptive to looking at repurposing older medicines.

Academic medical centers should take on board the messages from UAEM and license or sell intellectual property rights or products developed through research on their campuses only on the condition that prices are affordable in low- and middle-income countries. They should also strengthen their COI policies, or enact them where they are absent, and ensure that faculty members conducting research with industry strictly adhere to those policies with significant penalties for those who do not.

COVID-19 is a threat to the entire world and dealing with it will require the knowledge and expertise of all parties but the guiding principle must be public health not private profit.

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## References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Hancock J Oxford's COVID vaccine deal with AstraZeneca raises concerns about access and pricing. Fortune; 2020 [cited 2020 Sep 13]. Available from: https://fortune.com/2020/08/24/oxford-astrazeneca-covid-vaccine-deal-pricing-profit-concerns/
2. Reuters Staff. Factbox: AstraZeneca's potential coronavirus vaccine; 2020 [cited 2020 Sep 14]. Available from: https://www.reuters.com/article/us-health-coronavirus-astrazeneca-factbo/factbox-astrazenecas-potential-coronavirus-vaccine-idUSKBN25L1OH
3. The Real Story of Remdesivir. Public Citizen; 2020 May 7 [cited 2020 Nov 27]. Available from: https://www.citizen.org/article/the-real-story-of-remdesivir/
4. Access challenges to COVID-19 therapeutic candidates. MSF Access Campaign; 2020 Aug 24 [cited 2020 Nov 27]. Available from: https://msfaccess.org/sites/default/files/2020-09/MSF-AC_COVID_Rx_briefing-doc_Ed02-20200824_0.pdf
   • **Analyzes the main access challenges associated with selected priority therapeutic candidates for COVID-19 treatment.**
5. Mancini D, Kuchler H, Stacey K. Gliead asks to rescind special status for potential coronavirus drug. Financial Times. 2020 Mar 25.
6. Herper M. Gilead announces long-awaited price for Covid-19 drug remdesivir. STAT; 2020 [cited 2020 Nov 27]. Available from: https://www.statnews.com/2020/06/29/gilead-announces-remdesivir-price-covid-19/
7. Campbell J, Whittington M, Rind D, et al. Alternative pricing models for remdesivir and other potential treatments for COVID-19. Inst Clin Econ Rev. 2020 Nov 10.
8. Hill A, Wang J, Levi J, et al. Minimum costs to manufacture new treatments for COVID-19. J Virus Erad. 2020;6(2):61–69.
   • **Demonstrates that COVID-19 therapies can be manufactured at very low and affordable costs.**
9. Pedrique B, Strub-Wourgaft N, Some C, et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. Lancet Glob Health. 2013;1:e371–79.
   •• **Provides concrete data to show the bias against developing new treatments for neglected diseases.**
10. Outterson K, Powers J, Daniel G, et al. Repairing the broken market for antibiotic innovation. Health Affairs. 2015;34(2):277–285.
11. The Recovery Collaborative Group. Dexamethasone in hospitalized patients with COVID-19 - preliminary report. N Engl J Med. 2020;383:2030–2040.
12. Angell M. The truth about the drug companies: how they deceive us and what to do about it. New York: Random House; 2004.
   •• **A seminal work by a former editor-in-chief of the New England Journal of Medicine that makes the case for a major reform in the way in which the pharmaceutical industry operates.**
13. hep Coalition. Hepatitis C cure, sofosbuvir, turns 5 years old: the vast majority of people still have not been treated; 2018 [cited 2020 Nov 25]. Available from: https://hepcoalition.org/news/press-releases/article/hepatitis-c-cure-sofosbuvir-turns-5-years-old-the-vast-majority-of-people-still
14. Bell J. Vertex's drug launch hits new heights, but further growth could be harder to find. Biopharmadive; 2020 Apr 30 [cited 2020 Nov 25]. Available from: https://www.biopharmadive.com/news/vertex-trikafta-drug-launch-new-heights-growth/577107/
15. Moradpour J, Hollis A. Patient income and health innovation. Health Econ. 2020;29:1795–1803.
16. Our Work. UAEM: Universities Allied for Essential Medicines; 2020 [cited 2020 Sep 13]. Available from: https://www.uaem.org/our_work
17. University Report Card: Global Equity in Biomedical Research. UAEM: Universities Allied for Essential Medicines; 2015 [cited 2020 Sep 13]. Available from: https://globalhealthgrades.org
18. University report card 2017: global equity in biomedical research. UAEM: Universities Allied for Essential Medicines; 2017 [cited 2020 Sep 13]. Available from: https://canada.globalhealthgrades.org
19. University global health research: league table. UAEM: Universities Allied for Essential Medicines and Medsin UK; [cited 2020 Sep 13]. Available from: https://globalhealthgrades.org.uk
20. Drugs for Neglected Diseases initiative. Treatments delivered; [cited 2020 Aug 30]. Available from: https://dndi.org/research-development/treatments-delivered/
21. Commission on Intellectual Property Rights: Innovation and Public Health. Public health innovation and intellectual property rights. Geneva: World Health Organization; 2006.
   • **Discusses the limitations of using intellectual property rights as an incentive for research into new treatments.**
22. Fiestas HV. Investing for life: meeting poor people's needs for access to medicines through responsible business practices. Oxfam International; 2007.
23. Lundh A, Lexchin J, Mintzes B, et al. Industry sponsorship and research outcomes. Cochrane Database Syst Rev. 2017. (2. Art. No.: MR000033).
   •• **Shows the effects of different types of sponsorship on the results and conclusions of clinical research.**
24. Zinner D, Bolcic-Jankovic D, Clarridge B, et al. Participation of academic scientists in relationships with industry. Health Affairs. 2009;28(6):1814–1825.
25. Ahn R, Woodbridge A, Abraham A, et al. Financial ties of principal investigators and randomized controlled trial outcomes: cross sectional study. BMJ. 2017;356:i6770.
   •• **Examines the effects of COI on trial outcomes.**

26. Mello M, Clarridge B, Studdert D. Academic medical centers' standards for clinical trial agreements with industry. N Engl J Med. 2005;352:2202–2210.
27. Ehringhaus S, Weissman J, Sears J, et al. Responses of medical schools to institutional conflicts of interest. JAMA. 2008;299:665–671.
28. Campbell E, Weissman J, Ehringhaus S, et al. Institutional academic-industry relationships. JAMA. 2007;298(15):1779–1786.
29. Anderson T, Dave S, Good C, et al. Academic medical center leadership on pharmaceutical company boards of directors. JAMA. 2014;311(13):1353–1355.
• **Shows the relationship between the leadership in academic medical centres and the largest pharmaceutical companies.**
30. Rochon P, Sekeres M, Lexchin J, et al. Institutional financial conflicts of interest policies at Canadian academic health science centres: a national survey. Open Med. 2010;4:E134–E38.
31. Consultative Expert Working Group on Research and Development: Financing and Coordination. Research and development to meet health needs in developing countries: strengthening global financing and coordination. Geneva; 2012.