



Competing interests

Over 150 years ago, I.K. Brunel, Chief Engineer of the Great Western Railway, wrote to oppose the appointment of Government Inspectors of Railways in 1841: “Railway engineers understood very well how to look after the public safety, and putting a person over them must shackle them. They had not only more ability to find out what was necessary than any inspecting officer could have, but they had a greater desire to do it” [1]. In contrast, in our own time, dentists have been criticized for promoting the fluoridation of drinking water supplies, apparently because the widespread fluorosis that results provides a good deal of work for them to do [2].

The *British Medical Journal* defines a competing interest as existing “when professional judgement concerning a primary interest (such as patients’ welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry)”. It seems to be inherent in the nature of what it means to be a professional that what is professed is the primary interest. We must remember that, in Brunel’s day, Britain, leading the world, was just embracing the Industrial Revolution. Mankind stood on the threshold of unprecedented opportunities to master nature. Weir, reviewing this period and what followed, wrote “Beneficial undertakings had been proved profitable” [3]. In other words, primary and secondary interests were found to coincide. No one would have wished to use a faulty railway, hence Brunel’s primary and secondary interests were actually coöperating rather than competing. At about the same time, other professionals (the manufacturers of soda using the Solvay process) were busily massively polluting their environment (with hydrochloric acid). Their primary interest was the manufacture of soda; there was no penalty associated with generating the disamenity of the by-product released into the atmosphere, at least not until the enactment of the Alkali Act in 1863. Then, upon being forced to do something about the hydrochloric acid, the manufacturers found that by collecting it it could also be profitably sold. It could be argued that at no time were there competing interests. By polluting their environment, the manufacturers were not only making themselves unpopular, but also wasting a valuable resource. The proper incorporation of external diseconomies into an economic system was still a subject of discussion 50 years ago [4], and opinion on the matter continues to evolve.

We might be tempted to conclude that, for an entrepreneur or a professional such as a lawyer, engineer or medical doctor, there can be no competing interests because faulty professional work will impact negatively on his or her income. Thomas Bouch did not deliberately

design the first Tay bridge in a faulty manner; he used the best available knowledge of the day. Initially the “beautiful railway bridge of the silv’ry Tay” was a glittering success; Bouch was knighted by Queen Victoria but after the disaster he died a broken man.

Weir, writing a few years after Bouch’s death, already suspected that all was not well: “... It was now assumed that a business, so long as it was profitable, did not require to be proved beneficial” [3]. Our own time has witnessed such extraordinary affairs as the supply of the ADE 651 “bomb detector” to Iraq a few years ago, making a profit of tens of millions of pounds for the British businessman who manufactured it: the devices were deliberately engineered fakes. To understand such events it is not sufficient to suppose that primary and secondary interests were simply interchanged; the manufacturer of the ADE 651 was not merely modestly providing for his family, and the same can be said for NHS dentists earning in excess of half a million pounds per annum; greed becomes the predominant motivating force and it is not clear whether the concept of “competing interests” is applicable.

A colleague recently sent me a paper [5], at the end of which was a substantial list of competing interests: “Jean-Louis Vincent has no conflicts of interest to declare. Matteo Bassetti serves on scientific advisory boards and/or has received funding for research, travel or speaker honoraria for Bayer, Pfizer, MSD, Astellas, Basilea, Tetrphase, Gilead, Novartis, Achaogen, Paretek, Medicine Company, and Angelini. Bruno François is the coordinating principal investigator of an ongoing international phase II trial testing a monoclonal antibody against *S. aureus* to prevent VAP in ICU patients in collaboration with Medimmune, a member of the AstraZeneca group. He has no other conflicts of interest related to this manuscript. George Karam has been a consultant to, and received honoraria from, Merck and Cubist. Jean Chastre has been a consultant to and/or received honoraria from Bayer, Pfizer, Arsanis, Cubist-Merck, Kenta-Aridis, and Medimmune–AstraZeneca. Antoni Torres is on the advisory boards for AstraZeneca, Pfizer, Bayer, and Arsanis. Jason A. Roberts is on the advisory board for Infectopharm (IV fosfomycin) and lectures for MSD (posaconazole). Fabio S. Taccone has no conflicts of interest to declare. Jordi Rello is a consultant/member of the speakers bureau for Assign, Pfizer, Cubist, and Bayer. Thierry Calandra has received consultant income paid to his institution from Merck Sharp & Dohme-Chibret. Daniel De Backer has no conflicts of interest to declare. Tobias Welte has received grants for research from Bayer and Novartis and fees for lectures/for advisory board membership from Bayer, Basilea, AstraZeneca, MSD, and Pfizer. Massimo

Antonelli has received research grants from MSD, Pfizer, Cubist, and Toray and participated in the Advisory board for Basilea and Cubist". Another paper that happened to be on my desk announced "The authors declared that they have no competing interests" [6]. Yet another stated that "GK is a paid employee of Bode Chemie GmbH & Co. KG, Hamburg, Germany" [7]. How is the reader supposed to react to these statements? The Parable of the Electric Irons comes to mind [8]. It seems that the reader is supposed to think that there is the *possibility* that, for example, Bassetti [5] might be tempted to write some text in a way that puts the companies for which he received a financial benefit in a more favourable light than was justified scientifically. It would be hard to find any opportunity for doing so in that particular article, and the same with ref. 7. Presumably GK's co-authors were paid employees of their respective institutions; as I have pointed out elsewhere, this could constitute a real competing interest [9, 10], but academic salaries are never declared. The link between quality of output and income for universities and academic institutes is much less direct than in the case of a company, such as the Great Western Railway, selling a good or service to the public. It follows that the potential for corruption is far more insidious.

Undoubtedly there is a problem with sponsorship. Michael Rutter and colleagues published a book called *Fifteen Thousand Hours* [11], which essentially contained the results of an investigation into the value of schools that was sponsored by the education ministry of the British government. The conclusion was that schools made a very valuable contribution to education. The schools investigated were state schools financed by the education ministry. Hence, the report provided a pleasant pat on the back for the ministry, and became far better known than the damning criticisms of the study (essentially methodological flaws invalidated the conclusion) published in the following year by Heath and Clifford [12]. More recent cases are "ClimateGate" and aircraft cabin air contamination. There have been several experimental investigations of the latter, mostly sponsored by governments [9]. Vakas' finding was that "key industry, government and regulatory stakeholders have shown significant bias in recognizing and responding to the health and safety issues of cabin contamination" [13]. The fact that a university carried out an investigation has provided no protection against such bias creeping in, for reasons variously connected with the movement sometimes called "post-modern university" or "post-normal science" [14]. Science is indeed "in crisis" because of sponsorship [15,

16], but the source of the sponsorship does not seem to make a difference. Even if there is no sponsorship, "There is no cost to getting things wrong, the cost is not getting them published".¹ With open access, the barrier to not getting something published has become very low [17].² Academic pressures are now as invidious as commercial ones. The latter have become more complex and institutionalized than mere sponsorship. Pharmaceutical companies employ "medical science liaisons" (MSLs) whose job it is to influence "key opinion leaders" (KOL), which may include medical practitioners, in matters such as "off-label" use of manufactured drugs. Given such pervasive interaction, Stelfox et al.'s findings that "authors who supported the use of calcium-channel antagonists were significantly more likely than neutral or critical authors to have financial relationships with manufacturers of calcium-channel antagonists" [18] might well originate in subconscious bias [19].

In 1980 Altmann reprehended badly planned (due to ignorance of statistics) clinical trials as unethical [20]. The badness nowadays may well be deliberately engineered (at the level of design, execution or reporting) in order to provide support (especially for medicinal drugs, but other issues such as climate change are also affected) for a predesired outcome. Competing, or conflict of, interest occupies increasing attention as a topic in itself [21]. The approach proposed in ref. 21 amounts to a methodology for computing the bias engendered by the conflict or competition and then, presumably, modifying assertions made in a paper accordingly. If no modifying is needed (as appears to be the case in, e.g., refs 5 and 7) does that mean that the "competing interests" statements are, in fact, superfluous? Buenz gives an admirably succinct expression of the actual state of affairs: "Industry and its employees have a common goal—to develop a saleable product [which] means that there is little individual incentive in industry to fabricate data: drugs developed from flawed preclinical results, for example, are doomed to fail expensive multi-centre clinical trials [whereas] irreproducibility in academic research is all too common" [22]. Admittedly this does not consider the temptation towards bias in advocating "off-label" use, which does not require clinical trials. Nor does it consider the case of the individual consultant: "Should a principal or client wish to think that black is white, don't disillusion him—you might lose a fee! What the French call *prévenance* held precedence over a hammered-out truth" [23]. It is, however, sobering to reflect that the Academy, far from offering an institutional environment

¹ Quoted in ref. 16.

² Because of the conflict of interest of the publisher inherent in accepting "article processing charges" (APC) [17].

bolstering the ethos of disinterested investigation, actually strongly promotes bias—or an unethical indifference to irreproducibility—because of the revenue-gathering priority of most academic institutions nowadays [9,14].³

The bottom line must always be the personal integrity of the individual scientist [24]. It is his or her reputation that is on the line. As Richard Ernst has pointed out, “The most important virtue or value in science is honesty and self-criticism”.⁴ As long as those virtues remain intact, one may have confidence in the research output of the scientist, whatever his or her affiliation. This does not, course, mean that that output is “infallible”, whatever that may mean. The design, execution and interpretation of experiments, and the formulation of theory, is constantly undergoing improvement. Hence, rather than a public registry with “the ability to automatically generate conflicts of interest statements for use in published articles” [21], an assessment of each co-author’s integrity would be more practically useful, perhaps even a self-assessment.⁵ This approach does not appear to be incompatible with Michael Polanyi’s view that “into every act of knowing there enters a tacit and passionate contribution of the person knowing what is being known, and that this coefficient is no mere imperfection, but a necessary component of all knowledge” [26].

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³ Which, if unmodifiable, might even make continuing membership of the institution untenable.

⁴ Quoted in ref. 24. Richard Feynman has expressed similar sentiments [25].

⁵ A “venality index” would, perhaps, be more realizable and serve the same purpose. Such indexes do not obviate the responsibility of the recipient of such information to make his or her own assessment of its validity.