Commentary: Epidemiology and the pharmaceutical industry: an inside perspective

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Neil Pearce's impassioned comments on 'Corporate Influences on Epidemiology' are designed to raise awareness of industry activities that he believes 'are major threats to the integrity of the field, and its survival as a scientific discipline'. He argues that 'for every independent epidemiologist studying the side effects of medicines there are several other epidemiologists hired by industry to attack the research and debunk it as "junk science"'. While we recognize his depth of feeling, passion may nurture bias of its own. The relationship between science and industry is complex, and the role of epidemiologists in the pharmaceutical industry is not limited to debunking 'junk science'. Balanced evaluation and discussion are necessary to provide accurate safety information to physicians and patients. Unfortunately, such temperate interchanges rarely make headlines and seldom sell books.

According to Dr Pearce, the tobacco industry, the pharmaceutical industry and all the industries studied by occupational epidemiology should be grouped together as the 'corporate influences' that threaten the discipline of epidemiology. Quite apart from the tobacco industry and smoking-related diseases, the issues related to occupational epidemiology are very different from those related to pharmacoepidemiology, both with respect to regulatory framework and critical methodological challenges. Epidemiology is a core discipline for the development of medicinal products; this is not the case for the tobacco industry or for other industries. Dr Pearce seems deeply aggrieved and doubtless feels justified in pooling together the corporate enemies; however, we suggest that discussion is better served by assessing these very different groups separately. Since we are epidemiologists working within the pharmaceutical industry, our remarks are best confined to our area of expertise: epidemiology in relation to medicinal products.

The role of epidemiology in drug development

Epidemiological investigation has become an essential component in the development of pharmaceutical and biological products. Characterization of target medical conditions with respect to occurrence, natural history, outcomes, related costs and the medical context in which they are managed frequently involves epidemiological analyses. While some of these issues reflect
business needs, most are the direct result of industry’s commitment to understand better at-risk populations coupled with the regulatory requirements regarding information about the effects of medicines. A description of the epidemiology of the target condition, for example, is required as part of ‘Pharmacovigilance Planning’ as agreed by the International Conference on Harmonization3 and incorporated into European legislation on drug approval.9 The new European template for preparing Risk Management Plans also devotes a major section to the ‘Epidemiology of Indication’.5 Similarly, guidelines published by the FDA discuss at length the use of epidemiological approaches to address possible drug-related risks. These guidelines require that the developer of a medicinal product understand and articulate the epidemiological characteristics of the disease being treated, the setting in which the product will be marketed (concurrent morbidity, commonly used medications) and the epidemiology of safety issues that may arise. The pharmaceutical industry is involved with epidemiology as part of its core mission of developing and making available treatments for disease. This has put us in the challenging position of attempting to identify risks, regardless of how small, and to assess them in the face of the benefits of therapy (a task that is distinct from other applied epidemiology fields).

The pharmaceutical industry employs epidemiologists directly and also works with them through a broad range of consultative agreements and collaborations. Highly regulated, the pharmaceutical industry collaborates, not only with academic and government researchers, but also with regulatory authorities around the world. Much of the epidemiologic research undertaken by the pharmaceutical industry is related to regulatory or reimbursement requirements, such as submission of a marketing authorization, compliance with post-marketing requirements or provision of data to support reimbursement decisions. Given these demands, it is the norm for pharmaceutical epidemiologists to work with renowned experts in the field as advisors and consultants. It is not unusual for these experts to be associated with a particular data source that is central to addressing the research question. The membership of the International Society for Pharmacoepidemiology (ISPE), reflects this joint interest. According to the ISPE guidelines, ‘Pharmacoepidemiology is the scientific backbone of therapeutic risk management - the process of assessing a product’s benefits and risks, and developing, implementing, and evaluating strategies to enhance the overall balance of such benefits and risks’. In that context, guidelines have been developed and ratified to assist investigators with issues pertaining to the planning, conduct and evaluation of pharmacoepidemiologic research, including risk management and pharmacoeconomic activities, and to examine the role of epidemiologic studies from the perspectives of both industry and regulatory bodies (http://www.pharmacoepi.org/resources/guidelines_08027.cfm). As with any science, decisions are made in the context of studies that can be challenged by others because of the potential impact of the results.

### Pharmaceutical industry standards on study conduct and quality

As part of the critique of epidemiology in relationship to pharmaceutical products, epidemiologists who work for or receive funding from industry are routinely accused by certain critics of bias in their work; such critics assume per force that a financial relationship with industry will corrupt study conduct. These critics ignore, or perhaps are unaware of, the degree to which industry-sponsored research involving human subjects (and also animals) is subject to very elaborate and strict sets of controls and standards. Industry research is continuously auditable both internally and by regulatory agencies; unannounced inspections are the norm. Computer systems are subject to costly and elaborate validation requirements. Because the results of pharmaceutical industry research bear directly on patient well-being, expectations for quality and documentation are in an order of magnitude above those that are the norm for academic researchers and often require substantial additional support.7

While potential bias based on presumed financial conflicts of interest is easily identified and quantified, the pressures on academic researchers are more subtle. Professional pressures such as tenure and the need to publish might well affect the perspectives of academic scientists.8 An anti-industry stance could be placed in the service of career development.

### Challenges in the interpretation of pharmacoepidemiologic research

Dr Pearce charges industry with discrediting academic studies that question drug safety by labelling them ‘junk science’. However, academic origins are not sufficient proof of objectivity or scientific rigor, and examples of flawed academic epidemiological science are as readily identifiable as bad examples of industry-funded science.9 In pharmacoepidemiology, issues of confounding by indication are fundamental concerns and to raise them does not constitute an inappropriate area of discussion or an accusation of ‘junk science’.

Moreover, while medical journals have often been accused of being influenced by industry advertising, many journals evince a level of skepticism that borders on a pronounced bias against industry.10 This double standard is one that has led to the stipulation that industry-sponsored research be required to have a
non-industry statistical reviewer (http://jama.ama-assn.org/cgi/content/full/286/10/1232).

Pharmacoepidemiological research is undertaken in the face of considerable limitations in the nature, quality and completeness of much of the information analysed. Study design and analytic methods attempt to compensate for the inherent limitations of the data. The potential for variability in interpretation of findings exists and the perspective and emphasis of the interpreter can shape interpretation. Regardless of the motivations that may be at play, an adherence to rigorous scientific principles and a commitment to patient safety should always inform epidemiological studies, academic or industry-funded. If the health of the patient is truly what motivates both industry and the academy, then academic studies and industry studies should not find themselves so often at odds. Unbiased scientific evaluation will be more easily achieved if multiple viewpoints in the service of the same goal are considered.

True, there have been instances in which corporate entities have demonstrated less-than-optimal behaviour, but academic and government institutions have also suffered from breakdowns in standards. The pharmaceutical industry is subject to rigorous regulatory review and systems designed on the principle of verification; much non-industry research is accepted on the basis of trust. Industry is also working with the regulatory authorities to increase industry accountability through measures designed to strengthen the drug regulatory framework. This is not a contradiction. In the United States of America, the Institute of Medicine of the National Academy of Sciences has emphasized the degree to which the credibility of the FDA and that of the pharmaceutical industry are intimately entwined. 11

The contribution of epidemiology, particularly pharmacoepidemiology, to drug development continues to increase in importance and be recognized by all stakeholders—including regulators. As the ability to link large sets of health information becomes increasingly feasible technologically, defining the principles for their use becomes a prerequisite for their productive utilization. Thoughtful consideration of the concerns of various parties along with mutual respect is necessary and required. As industry and academia strive to make drugs safer for patients, scientific inquiry should be guided by sound principles. No one can benefit from science or rhetoric that serves simply to further private agendas.

References
7 International Conference on Harmonization. Guideline for Good Clinical Practice: E6 R1.