BioSocieties (2008), **3**, 355–382 © London School of Economics and Political Science
doi:10.1017/S1745855208006297

Corporate Science and the Husbandry of Scientific and Medical Knowledge by the Pharmaceutical Industry

Alastair Matheson
E-mail: amatheson@blueyonder.co.uk

Abstract
This article analyses the role of the pharmaceutical and medical device industries ('pharma') in the construction of scientific and medical knowledge. Pharma's activities are part of the broader dispositif *of institutions, enterprises, regulations and constituencies within which medical-scientific knowledge is generated, but pharma's contributions exhibit a specific character reflecting commercial pressures. As drug development proceeds, research and marketing activities coalesce around 'product canons' that integrate scientific truth-claims and commercial positioning, generating knowledge with implicit commercial functionality. From this platform, pharma stamps consensus-building 'narratives' into medical-scientific discourse, in which 'problems' arise and are 'solved' by drugs. Concurrently, pharma modulates the structure of discourse and the social networks through which discourse proceeds. Implicit within these activities is a meta-science whose goal is to understand and technologize the operation of science to an external end. This mode of knowledge production can be viewed as a normative transformation of Kuhnian normal science, characterized by the attachment (and at times subordination) of paradigmatic tenets to extrinsic goals; exaggerated control of belief, research and consensus formation; and a capacity for infringement of traditional norms of scientific truthfulness. An International Standard of Integrity in Science would strengthen pharma's contributions to medical and scientific knowledge.*

Keywords Foucault, Kuhn, Marketing, Medicine, Pharmaceutical Industry, Science Studies

Commerce, medicine and science are associated with distinct social networks, discourses, cultures and values: thus, commerce is motivated by profit and medicine by health, while science, ostensibly at least, is conducted to ascertain the truth. This article explores how the pharmaceutical and medical device industries ('pharma') operate at the nexus between these domains to generate scientific knowledge with commercial functionality. The principal focus is on knowledge construction through marketing, but also considered are basic

Alastair Matheson trained in natural sciences and has a PhD in developmental biology. He also holds an MSc in intelligent systems and a diploma in law. He has worked extensively as an analyst, consultant and writer within the pharmaceutical and biotechnology industries, and continues to work within the sector on a freelance basis. He is currently also a Scientific Associate to an international charitable initiative concerned with clinical trials design in oncology. His chief academic interests are in science studies, medical anthropology and the classification of disease.

research, the organization of the pharmaceutical industry, and the interactions between pharma and the institutions of academic science and medicine.

Methodologically, this study relies significantly on auto-ethnography, in the articulating senses distinguished by Reed-Danahay (1997) of the ethnography of one's own group, and autobiographical writing of ethnographic interest. The author has a background in university science, but worked for more than ten years in a variety of roles within the pharmaceutical sector, including strategic analysis, consultancy, medical writing and the formulation of communications programmes, constituting an experience that amounts to what Hayano (1979) terms 'insider status'. A comparable experience, that of a pharmaceutical sales representative, informed the work of Oldani (2004). In addition to personal experience and field notes, the author has made use of commercial documents accumulated during this period, none of which are quoted for reasons of confidentiality; use has also been made of marketing materials acquired during congresses; literature review; website research; and discussions with pharma stakeholders, including participation in meetings convened to discuss the operation and ethics of the pharmaceutical industry. The substantial auto-ethnographic component confers a sense of authenticity on the text, but also involves qualitative observations arising from the direct experience of the author rather than that of informants. Consequently, the study should be considered as complementary to accounts originating 'outside' the industry, such as those of Elliott (2004), Applbaum (2008) and Sismondo (2007a).

Terminology

As shown in Table 1, this article uses the term *core maxims of science* to refer to such things as: a commitment to meticulous observation; to accurate measurement; to logic; to prediction; to reproducibility; to the Baconian, inductive mode of inquiry; to the hypothetico-deductive method. Different fields of natural science, and different individual inquiries, use the core maxims variably, such that one might analogize them to a tool-kit validated by past success and available for all to draw upon.

From the perspective taken in this article, *settled scientific knowledge* is accepted as such by natural scientists because it has been ratified to a substantial degree in terms of the core maxims. In other words, it has been repeatedly observed, measured and documented, shown to be logically consistent with other settled elements of scientific knowledge, tested and used to predict and manipulate the world. There may, however, be no hard demarcations between settled scientific knowledge, working hypothesis, and softer opinion and belief, but more gradual transitions in which successful conjectures are eventually winnowed and codified as settled scientific knowledge.

The article uses the term *working medical knowledge* to describe an amalgam of settled scientific knowledge, tradition, know-how and opinion on which medical practice is based. Working medical knowledge is more heterogeneous and dynamic than settled scientific knowledge, but has greater substance than mere working hypothesis. Since working medical knowledge determines how patients are treated, controlling it is a major objective for pharma.

Table 1. Terminology

Term	Usage
Terms used specifically in this study	
Core maxims of science	Central procedures and values of scientific method, e.g. observation, measurement, logic, testing, reproducibility, induction, falsification. Used differently in different scientific enterprises.
Settled scientific knowledge	Knowledge accepted by scientists as stable and durable on the basis of having satisfied core maxims.
Working medical knowledge	Mixture of settled scientific knowledge, working hypothesis, tradition, authority and opinion, on which everyday clinical practice is based.
'Truthfulness maxim'	Methodological and moral requirement for scientific truthfulness. Requires both honesty and truth-directedness.
'Product canon'	Hybrid commercial/scientific account of a drug by which a company understands its therapeutic role and the surrounding medicine. Basis of product positioning, brand identity and 'drug narratives'.
'Product dogma'	Consolidated, reified form of the 'product canon'; tends to develop with respect to well-established drugs whose usage is stably understood by the company.
'Drug narrative'	Account of the drug and its therapeutic role, in which a drug typically provides the 'solution' to a 'problem'. Elaborates a company's understanding of its drug, and is projected into medical/scientific discourse. Often broken down into a series of 'key messages'.
'Normative science'	Transformation of Kuhnian normal science, characterized by: • Extrinsic (in pharma's case, commercial) goals replace scientific paradigm as the fundamental determinant of activity and exert normative effects; • Exaggerated control of belief, research and communication; • Production of scientific knowledge with an intrinsic functionality in respect of external goals; • Capacity for systematic infringement of the 'truthfulness maxim'.
'Meta science'	Systematic, quasi-scientific programme in which scientific research and discourse are analysed and configured to service external goals.
Terms used within the pharma sector	
KOL	'Key opinion leader'—industry term for a clinician or scientist of high status within a discourse. Also known as 'thought leaders'.
Product positioning	Standard marketing term for the key promotional attributes of a product in pharma, with respect to its clinical role, the commercial environment and competitor products.
Key messages	Systematic set of promotional claims that capture the salient features of a product and its area of use.
Environmental messaging	Claims about the area of medicine in which a product is marketed—frequently these identify 'unmet needs'.
Product messages	Claims about a product—including claims that it meets the 'unmet needs'.

The terms *truthfulness maxim* and *scientific truthfulness* refer to a core maxim of science that comprises both honesty and what might be termed 'truth-directedness'. This is a commitment to, and meticulous pursuit of, scientific truth, as exemplified by core maxims such as accurate observation, reproducibility and exclusion of alternatives.[1] The truthfulness maxim is consistent with Williams' (2002) formulation in which 'Accuracy' and 'Sincerity' are the key features of truthfulness.

The Foucauldian term *dispositif* (Foucault, 1980) is applied herein to the heterogeneous matrix of institutions, constituencies, discourses, regulations, knowledge and assumptions within which medical and scientific knowledge is generated.[2]

Finally, the Kuhnian concept of *normal science* is among those used to analyse pharma's *modus operandi*. Kuhn characterized normal science as 'puzzle solving', pointing out that a puzzle implies 'rules of play', such that normal science has normative features both with regard to the research permitted and the solutions that can be proposed—indeed, the outlines of the solution are generally anticipated in advance (Hoyningen-Huene, 1993; Kuhn, 1962). Thus, while normal science is capable of delivering scientific progress, it has also been criticized for its potential to stifle innovation (Fuller, 2002; Popper, 1970).

The pharma corporation and its satellites

To understand how corporate pharma generates medical and scientific knowledge, a brief overview of the sector is helpful (see Campbell, 2005, for a detailed account). Most major pharmaceutical corporations coordinate their international research and product positioning from a global headquarters, but delegate sales and some marketing to national subsidiaries.[3] Pharma corporations usually organize their activities around disease areas, many of which, such as Pfizer's Neuroscience or AstraZeneca's Cardiovascular group, have subcorporate branding (see AstraZeneca, 2008; Pfizer, 2008). However, individual drugs generally have specific teams allocated to them, and a separate budget.

These drugs are invented in-house, or by smaller companies or university spin-outs, which license or sell to pharma, or are acquired in their entirety. As basic R&D transitions into clinical development, two domains of expertise within the corporation come increasingly into play. *Marketing* experts are involved with traditional promotional activities, including branding, market testing and advertising, while dedicated *medical* experts, including qualified doctors and scientists, are involved in ongoing clinical development, data management, publications and relations with regulators and the medical community. Other

1 The requirement for honesty and truth-directedness is both a moral and methodological aspiration, and applies throughout the scientific process, from preliminary assumptions and postulates through to the communication of results.

2 Foucault (1980: 195) suggested that a *dispositif* is mobilized around a particular urgent need. Three pressing needs are active in this setting—health, knowledge and profit—and it might be considered that three distinct *dispositifs* serve them. In this article, the term *dispositif* is used to refer to the triadic nexus of these three domains, insofar as it impacts on medical-scientific knowledge production.

3 The United States is an important exception, since its market is so large that national franchises often generate research, publications and marketing initiatives on a scale as great as that of international pharma. The internal Japanese market is also distinct from the major Western markets, although several Japanese corporations are key international players also. See Petryna *et al.* (2007) for discussions of global pharmaceuticals.

expertises also have input, including R&D, Regulatory Affairs, Legal and Publications specialists. It is common for there to be cultural differences among these domains, but the resulting structure is robust and flexible, readily melding scientific credibility and commercial imperatives. Also crucial are service companies, including contract research organizations, and publications, 'medical education', public relations and advertising agencies. These companies compete for drug-by-drug contracts. Relations also exist with regulatory and purchasing authorities, and these are generally cordial and constructive. Finally, there are extensive links with academia and the medical profession, discussed in more detail below.

The drives which power this distributed system are complex. The goal of revenue generation is refracted through the agendas of different loci and individual motives. No single locus has total knowledge or control over how the system functions, but it is configured to the generation of revenue on a drug-by-drug basis, and this principle directs the capital flows which sustain its operation. However, the system must operate within constraints, both implicit—pharma is an active participant within the wider enterprises and cultures of health and science, and shares many of their norms and conventions—and explicit. In particular, pharma must convince government and regulators to approve clinical trial designs, upgrade their legal definitions of medicines and disease to incorporate their product and its intended use, and product claims and advertising must not exceed the defined indication.[4]

Commercial impacts on data generation

Pharma shapes medical and scientific knowledge both by generating drugs, devices and data, and by contributing to discourse. This article is primarily concerned with discourse, but relevant aspects of data generation are reviewed briefly here.

Inevitably, the direction and volume of pharma research is influenced by market considerations. Emerging drugs must be saleable, and are selected according to the potential market and the expertise of the company as well as their physiological effects. Competitor successes also shape research, frequently leading to classes of drugs sharing the same mode of action. This 'me too' phenomenon is sometimes criticized as a waste of resources (Angell, 2004) but may lead to better tolerated, longer-lasting or more effective drugs, as in the evolution of the ACE inhibitors (Piepho, 2000).

As clinical development proceeds, commercial pressures come into play that remain operative for the commercial life of the product, such that many clinical trials are conducted not merely to assess efficacy and safety, but to secure regulatory approval at the least possible risk, and to bolster marketability. Core aspects of trial design with respect to the choice of comparators, study size and duration, treatment regimens and outcome measures may be impacted, such that results generally favour the sponsored product (Bekelman *et al.,* 2003; Heres *et al.,* 2006; Lexchin *et al.,* 2003; Safer, 2002; Sismondo, 2007b). Independent corroboration is rare, due to both the sheer rate and volume of pharma output, and the

4 There are various pharmaceutical business models; this article focuses on the development of novel products (whether traditional or genomic in origin) for mass sales—this remains the dominant business model of the major Western pharma corporations.

sales-driven design of studies, which neither competitors nor independent scientists have an interest in replicating.

Significantly, however, design bias is hard to identify and most pharma studies are, within their terms of reference, statistically and methodologically robust (Bekelman *et al.*, 2003; Cho and Bero, 1996; Lexchin *et al.*, 2003; Rochon *et al.*, 1994a).[5] Of comparable importance to statistical quality, however, is incisiveness: when a new drug has a strongly beneficial effect, or when research reveals an important new biological mechanism, pharma's contributions to scientific knowledge at the data level are at their most substantive, but when these conditions are not met pharma continues to generate data on a mass scale.[6] Pharma's overall scientific output is of variable quality, incisiveness and pace, and most pharma-generated data, whether important or trivial, have commercial functionality—but such characteristics are arguably inevitable within a market system and do not prevent scientific and medical progress.

The 'product canon', 'product dogmas' and 'drug narratives'

The central issue for this article is not data generation per se, but how pharma understands its data and regulates the understanding of clinicians and scientists. As each promising drug approaches launch, pharma constructs what may be termed a 'product canon', a set of propositions by which it understands its drug, the surrounding biology and the areas of medicine in which it is used (see Table 1, Figure 1). The 'product canon' is based on the clinical properties of the drug and its differentiating features, and may evolve as market opportunities change. It articulates closely with, but is distinct from, the explicit development and marketing goals for the product. It is seldom formalized into a specific, definitive document, but rather finds different and evolving expressions in numerous, mainly internal documents and presentations as the product's life cycle proceeds. It is often formulated and adapted with help from leading medical experts and through consultations with regulatory agencies. It is often also market-tested. Importantly, the emerging canon frequently feeds back into the clinical development programme, such that trials may be designed with the goal of confirming it. The company's vision of its product may thereby become increasingly self-confirming, and the results of trials are considered good if they support or enrich it. Ultimately the canon may harden into a more rigid 'product dogma', a non-pejorative term that emphasizes the paradigmatic status of core propositions.

As the drug approaches the market and commercial objectives are consolidated, the 'product canon' is frequently encapsulated within a concise statement or product profile, and elaborated, often with the help of agencies, into a series of market-driven 'key

5 It is likely that registration trials, which are conducted to support new indications and whose results are submitted to regulatory authorities, are of greater quality than studies conducted solely for marketing purposes, although this conjecture requires confirmation. Equally however, it is likely that registration trials yield unfavourable results more frequently, as in the VALUE and PROVE-IT trials, both of which favoured competitors (Cannon *et al.*, 2004; Julius *et al.*, 2004).

6 Even registration trials may be relatively uninformative, since regulators may be satisfied merely by modest but statistically significant differences or even parity against an existing standard of care, as in the licensing of many recent cancer drugs (Schilsky, 2002). This policy may reduce the incisiveness of research, but helps sustain a viable industry.

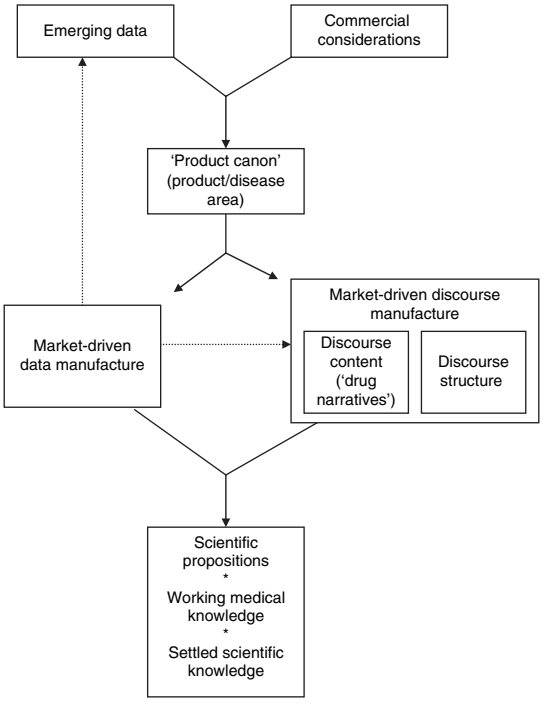

Figure 1. Genesis of the 'product canon' and the ensuing manufacture of scientific data and discourse

messages'. These describe the background area of medicine, why the drug is needed, how it benefits the patient, why it is superior to its competitors and why it is cost-effective. Frequently the 'key messages' form a *narrative* in which a medical 'puzzle' is identified and the drug emerges as the 'solution'. As discussed below, companies seek to stamp 'drug narratives' into the discourse of medicine, such that the 'puzzle' and its 'solution' become widely accepted.

Some within the company's marketing team and hired marketing agencies understand the 'product canon' in terms of brand identity and product positioning, but to others, particularly those with R&D and medical expertise, it may be a matter of considered scientific opinion and paradigmatic commitment. To some, it involves an emotional-intellectual commitment that amounts to faith, such that when conflicting data or a stronger competitor emerge, the threatening new arrival is doubted or scorned; indeed, the reified 'product dogma' may become part of personal identity.

Projecting 'drug narratives' into discourse

There are multiple discourses across the pharma, medical and scientific spheres which intersect, interact, overlap and frequently involve the same individuals, many of whom have compound professional identities: for instance, a pharma employee may be a respected scientist or clinician who participates both in the internal discourses of the company and the public discourses of academia; similarly, a leading clinician may be a paid consultant within

pharma and an advisor within the discourse of the regulatory or reimbursement communities. Even a marketing expert or sales representative is a participant in academic and clinician discourse through attendance at congresses and meetings with clinicians. This article's chief concern is with how, notwithstanding these continuities, the interests and internal discourses of pharma exercise influence on the public discourses dominated by academic science and clinical medicine, which hold the key to the adoption of drugs by regulators, purchasers and prescribing clinicians.

Most overtly, pharma seeks to establish its 'key messages' within working medical knowledge by deploying conventional marketing techniques within a scientific and medical setting, wherein opinion, belief, ontology and values are all targeted.[7] A range of vehicles and media are used, but from the standpoint of scientific knowledge, journal publications are the most important and the steps typically involved are briefly reviewed here. (This account is based on the author's direct experience; see also Healy and Cattell, 2003; Jones, 2003; Sergeant and Eden, 2003; Sismondo, 2007a; Steinman *et al.,* 2006.)

At the outset, an agency with expertise in publications typically collaborates with the pharma company to devise a 'publications plan', usually covering a period of at most a few years. The plan is embedded within the overall development and marketing strategy for the drug. The most important publications for pharma are 'primary manuscripts', which release new clinical trials data. Of almost equal importance are 'secondary manuscripts' containing subsequent analyses, and reviews of the drug and its field of use. Such reviews often dominate publications plans. To create the plan, past publications on the drug and its competitors are reviewed and a 'gap analysis' performed to identify which 'key messages' have been well covered, which need further support and where opportunities lie. A tabulated list of potential titles is then compiled. The list includes reviews focusing on unsolved problems and others with more directly promotional themes. The total number of proposed titles (there may be a handful or several dozen) depends on the budget the company has allocated to the drug, with the total cost of each review typically US$20,000 or greater.

Along with titles, the agency's medical writers draw up justifications for each article to sell the concept within the pharma company. These justifications may be couched overtly in terms of the article's marketing relevance, or more euphemistically in terms of 'medical need' and 'educational value'. Following discussions with the in-house pharma team, more detailed outlines are next developed for approved articles. Around this time 'authors', who are usually leading clinicians (KOLs or 'key opinion leaders'; see below) are approached. Next, the outline (though seldom the 'key messages', which generally remain confidential) is introduced to the 'author' and a manuscript subsequently ghost-written. Some 'authors' take an active role in the process and make changes at the outline and manuscript stages, but at every stage, the manuscript is monitored by the agency and the pharma company to ensure it remains on-message. After pharma sign-off, the 'author' is generally asked to submit to the journal directly to minimize the appearance of pharma involvement, and then receives an 'honorarium'. Increasingly, companies no longer pay 'authors' directly, but reward them intermittently for their interest by providing 'research grants'. Hundreds of reviews are added to the medical-scientific literature each year by this process, and it

7 For a general account of pharmaceutical marketing, see Smith (2008); for a complementary anthropological perspective on the control of 'marketing channels', see Applbaum (2008).

remains an easy task to pilot a commercially driven, authoritatively 'authored' and ghosted review into a respected journal. Stand-alone journal supplements are also used, particularly for papers originating as presentations at sponsored meetings, and these too may be ghost-written. Importantly, however, many publications receiving pharma sponsorship are initiated and controlled by independent academics and are not the result of publications planning; moreover, sponsored publications are frequently of a high scientific standard and educationally valuable, even when originated through the publications planning process.

The puzzle-solving structure of 'drug narratives'

This section and the next examine how pharmaceutical argument works within medical and scientific discourse. Many of the scientific articles, reviews and symposia cited in these sections involved pharma sponsorship, but no suggestion is made that they or indeed any publications on the drugs mentioned were originated other than from neutral academic interest or involved any marketing considerations. The selected articles are cited because they illustrate the types of content and argument that may be of interest to pharmaceutical marketing, rather than as examples of marketing per se.

Typically, 'drug narratives' weave broad 'environmental messages' together with more specific 'product messages', creating a scenario in which a puzzle arises and is solved by the drug (see Table 2 for examples). 'Creating a perception' of 'unmet need' is a common 'environmental' tactic, particularly when a new drug or indication is planned. For instance, after many years of advocating LDL cholesterol reduction, several companies currently highlight the 'residual risk' left after this has been achieved, that may be treatable by their new lipid-modifying agents (see *Beyond statin therapy,* 2006; *Comprehensive lipid management,* 2006). Highlighting the scale of a problem is a similar tactic: sponsored reviews frequently call attention to the high prevalence or morbidity of conditions such as hypertension, diabetes, obesity and bipolar disorder (Aronne, 2007; Calabrese *et al.,* 2005; Despres, 2006; Mancia, 2005). Of note, these strategies may be deployed as markets change: for instance, Healy (2006a) and Applbaum (2008) have charted the campaign to increase awareness and diagnosis of bipolar disorder in patients formerly considered depressed, generating sales of atypical antipsychotics as the same companies' antidepressants came off patent.

Pharma may also seek to reformulate clinicians' basic understanding of disease if this creates a more compelling 'problem' for the drug to 'solve'. This may involve medicalization—the identification of pathology in what was previously considered the normal range—particularly in psychiatry (Healy, 2004; Lakoff, 2005), but also in other fields. For instance, 'prehypertension' and 'prediabetes' are currently being discussed in cardiology (Del Prato *et al.,* 2007; Ritz, 2006). Importantly, however, 'medicalization' is but one aspect of a varied engagement of pharma with nosology. Pharma may, for instance, seek to expand the range of an existing disease: bipolar disorder is an example, which, with pharma support, is increasingly being identified in children (see Healy, 2006a). Pharma may also seek to reformulate broader conceptualizations of existing diseases. For instance, pharma takes an interest in the concept of the cardiovascular continuum (Dzau, 2005; Schmieder, 2006), which is

Table 2. Selected pharma strategies for moulding discourse content

Discourse contribution	Commercial function	Examples with related content*
Problems/Puzzles		
Highlight emerging therapeutic issues	Prepare/establish new market	• Neuropathic pain (duloxetine)[1] • Sexual side effects of SSRIs (bupropion)[2]
Highlight size of a problem	Prepare/establish new market; increase sales in existing market	• Diabetes/obesity/hypertension epidemics/complications (various CV drugs)[3–5] • Previous under-diagnosis of bipolar disorder (atypical antipsychotics)[6]
Highlight 'unmet need'	Prepare/establish new market	• 'Residual risk' after statin therapy (HDL-raising drugs)[7,8] • Residual risk in diabetics (pioglitazone)[9]
Competitor deficiencies	Differentiation for new entrants; ongoing battles within drug classes	• Target efficacy/safety/tolerability/ convenience/cost (most marketed drugs) • Particularly intense within classes
Nosology		
Expand a disease's range	Obtain new indications; protect patent; open new markets	• Bipolar disorder in children (atypical antipsychotics)[10]
Reformulate current disease	Increase interest in product; provide new rationale for use	• The cardiovascular continuum (various products)[11,12] • Atherothrombosis (clopidogrel)[13]
Promote new diseases	Obtain new indications; protect patent; open new markets	• *Helicobacter pylori* (proton pump inhibitors)[14] • Metabolic syndrome (various products) • 'Prediabetes', 'prehypertension' (various products)[15,16] • Premenstrual dysphoria/obsessive-compulsive disorder (SSRIs)[17,18]
'Solutions'		
Proclaim own benefits/ attack competitors	Build/protect market share	• Most marketed drugs
Highlight new developments/ products	Promote new product	• Inhaled insulin (Exubera®)[19] • Topical calcineurin inhibitors (pimecrolimus, tacrolimus)[20]
Promote new therapeutic concepts	Promote product; obtain endorsement; create market/ build share	• 'OncoSurge' (neoadjuvant oxaliplatin)[21] • Continuous dopaminergic stimulation (entacapone)[22]
Shrink a problem	Reduce unfavourable perceptions	• Statin safety[23] • Cyclosporin-related dyslipidaemia[24]

Omission	Increase likelihood of favourable perceptions	• Data withholding (rofecoxib/paroxetine)[25,26] • Reduced discussion of poorly-responding pathogens (antimicrobials)

* Articles are cited because they illustrate types of content and argument that may be of interest to pharma in the pursuit of the marketing objectives listed, rather than as examples of pharmaceutical marketing per se. It is not suggested that any of the cited articles, or any publications on the drugs listed, were originated other than from neutral academic interest. Whereas the majority of the cited reviews and clinical articles received commercial support with respect to their publication, authorship and/or content, they were authored by unbiased experts and most are of a good scientific standard.

References

1. Thor *et al.* (2007); 2. Stimmel & Gutierrez (2006); 3. Mancia (2005); 4. Despres (2006); 5. Aronne (2007); 6. Calabrese *et al.* (2005); 7. *Beyond statin therapy* (2006); 8. *Comprehensive lipid management* (2006); 9. Schneider (2006); 10. Healy (2006a); 11. Schmieder (2006); 12. Dzau (2005); 13. Leys (2001); 14. Barth & Hahne (2002); 15. Ritz (2006); 16. Del Prato *et al.* (2007, 2005); 17. Steiner & Pearlstein (2000); 18. Cartwright & Hollander, 1998; 19. Scherbaum (2005); 20. Meurer *et al.* (2007); 21. Poston *et al.* (2005); 22. Olanow (2004); 23. McKenney (2005); 24. Moore *et al.* (2001); 25. Matthews & Martinez (2004); 26. Kondro & Sibbald (2004).

consistent with chronic drug intervention strategies and multi-drug portfolios, and atherothrombosis (Leys, 2001), which is commercially useful in the promotion of anti-clotting drugs. Greene (2007) has traced the construction of cardiovascular disease during the successive marketing of Diuril (chlorthiazide), Orinase (tolbutamide) and Mevacor (lovastatin) in the United States since the mid-1950s. More recently, the 'metabolic syndrome' and an alternative construction, 'cardiometabolic risk', have been pursued in cardiovascular and diabetic medicine, with interest from different companies in support of cross-brand initiatives (Metabolic Syndrome Institute, 2008; Sanofi-Aventis, 2006).

'Problems' are complemented by the promotion of drugs as 'solutions'. Compelling data demonstrating that the drug works form the kernel of the 'solution', but there are numerous variants on the theme. Of note, new treatment concepts must be promoted when new drug classes are developed, or novel uses of drugs are proposed. For instance, the concept of continuous dopaminergic stimulation was supported by Novartis in support of its COMT inhibitor, entacapone (Olanow, 2004), and may be of significant therapeutic value in Parkinson's disease. Sanofi-Synthelabo promoted a branded concept, 'OncoSurge', which involves use of their anti-tumour drug oxaliplatin in the neoadjuvant treatment of advanced colorectal cancer (Poston *et al.,* 2005). In many cases, pharma-backed 'problems' and 'solutions' have clear scientific and clinical value alongside commercial utility, although other examples, such as the potential use of low molecular weight heparins in place of warfarin (Camm, 2001), are more exploratory.

Competing narratives

Drugs compete not only on the basis of data, but narrative: the drug whose narrative dominates discourse has the opportunity to prosper in the market. Narrative competition is most apparent within classes of closely related drugs, which share and co-promote a particular problematization of medicine and the general kind of 'solution' required, but contest the details. Thus, the angiotensin receptor blockers (ARBs), a class of well-tolerated blood

pressure drug, promote the idea that antihypertensives should be well tolerated, but compete with regard to efficacy and other differentials. For example, telmisartan's 24-hour half-life is the longest of any ARB, and claimed by the manufacturers to deliver reliable 24-hour blood pressure control (see Micardis, 2008). The 'problem' in blood pressure control is identified as maintaining control in the last 6 hours of the 24-hour dosing interval, a period in which the efficacy of other ARBs might be expected to decline. Several telmisartan clinical trials measure efficacy specifically during the early morning period (reviewed in Giles, 2006), whereas trials with other ARBs assess maximum blood pressure reduction, or average control over 24 hours. Marketing slogans for telmisartan, and presentations at congress symposia, are coordinated with clinical data, with particular emphasis placed on the vulnerability of patients during the early morning hours (see MicardisPlus, 2008). The strategy is scientifically reasonable, and its effect is to reconfigure medical knowledge by means of a puzzle—early morning blood pressure control—and its solution—telmisartan. Competitor ARBs seek to configure medical knowledge in contrasting ways.

Dispelling weaknesses

Quite generally, pharma-sponsored scientific publications and 'medical education' activities give less prominence to a product's weaknesses than an impartial scientist might expect. For instance, the Schering Plough International RespIratory Taskforce (SPIRIT) initiative, on which the author worked and which was devised in support of an antibiotic, ceftibuten, did not give extensive attention to pneumococcal disease, against which ceftibuten had poor activity. The *SPIRIT Bulletin* (1993) took greater interest in pathogens and conditions where the drug was effective, such as *Haemophilus influenzae* and otitis media. In one episode, the agency running the 'medical education' programme had concerns at a meeting in Andalusia, to which many potential prescribers had been flown, that a top clinician not considered a 'friend' of the product but invited for credibility would 'mention the pneumococcus' damagingly during his presentation . He did indeed 'raise the question', but it was felt the episode 'could have been worse'. This example illustrates the sensitivities that surround adverse data, but also medically responsible conduct, since both Schering-Plough and the agency took steps to ensure that a weakness was highlighted by inviting a respected authority likely to criticize the product.

Beyond the general pressure to avoid weaknesses, specific scientific difficulties with commercial implications may need to be overcome, for instance as a result of newly identified toxic effects, or critiques from competitors. Examples of the development of narratives to dispel potential weaknesses include the clarification of the risk:benefit profile of intensive statin therapy, and managing the dyslipidaemia associated with cyclosporin treatment (McKenney, 2005; Moore *et al.,* 2001).

More problematically, *omission* of unhelpful data from a narrative may occur (Angell, 2004; Healy, 2004; Kondro and Sibbald, 2004; Matthews and Martinez, 2004; Rennie, 2004). In some cases this may involve never publishing unhelpful data, or publishing only after a delay, although even internal clinical study reports sometimes omit unhelpful analyses (personal observation). Successful industry-sponsored trials are published more rapidly than unsuccessful ones (Hopewell *et al.,* 2007), which may only appear as abstracts or brief papers that omit many details (van Veldhuisen and Poole-Wilson, 2001). Such publication

bias affects independent as much as commercial research (Dickersin, 2005), but specifically commercial considerations may lead to data suppression (Halpern and Berlin, 2005). Rather than suppression, however, unhelpful data may simply not be discussed in subsequent reviews and presentations, thus ceasing to be a significant part of discourse.

Mechanisms of persuasion

Pharma employs a range of mechanisms to persuade prescribers and purchasers to accept 'drug narratives'. As shown in Table 3, the most powerful devices are, first, a 'good story' with logical and empirical consistency and clear clinical benefits, and, second, sheer volume of data, publications and discussion. With regard to the volume of data, *class effects,* which arise when several companies promote drugs of the same kind, are particularly powerful, for much of the data and discussion within a discourse may convey the same basic message through the shared elements of competing narratives. It is likely that effects of this kind have contributed to the commercial success of the ARBs, selective serotonin reuptake inhibitors (SSRIs) and atypical antipsychotics.

Even when a story is both voluble and intrinsically strong, rhetoric is important. 'Drug narratives' are not only scientific arguments, but function also as morality tales in which the scientist, clinician or pharma company is allotted a role analogous to that of protector, sleuth or explorer, and truth and goodness are aligned such that to believe feels like a virtue.[8] From the point of view of scientific knowledge, however, the use of rhetoric within technical language is of particular note. For instance, aliskiren, a new blood pressure drug that is the first renin inhibitor to reach the market, has been characterized in sponsored publications and symposia as a 'direct' renin inhibitor (e.g. Gradman and Traub, 2007). This phrase is reasoned, reflects genuine belief and is likely to become established in the scientific literature, though most of its users will never realize they are being steered towards a specific construction of the renin-angiotensin-aldosterone system and its modulation, in which other drugs, which target different parts of the system, might be construed as being 'indirect', and perhaps therefore in some sense inferior.

Endorsement is also a key mechanism of persuasion. The most important mode of endorsement is by means of authoritative KOLs who 'author' reviews and speak at symposia that market the drug. KOL endorsement has been cited as contributory to the early success of Merck's Vioxx despite cardiovascular concerns (James *et al.*, 2007). Endorsement by a *medical standard* provides a further mechanism of persuasion. The ideal is for a drug to be mentioned in major clinical guidelines or recommended by a purchasing authority—for instance, the recently launched metabolic drug rimonabant has been mentioned in the European Society of Cardiology's guidelines for hypertension (Mancia *et al.*, 2007). Ad hoc quasi-'official' guidelines may also be drawn up with the help of commercial sponsorship. For instance, a number of companies manufacturing LDL cholesterol-lowering drugs financed an initiative on statin safety involving the National Lipid Association of the United

8 Emotional rhetoric is used most strongly, but not exclusively, in advertising. In this setting, one may observe too the regulation of clinician anxiety ('Am I doing the best for my patient?') More general mobilization of health anxieties through direct-to-patient advertising and support of patients' groups may also encourage clinicians to consider narratives as solutions to their patients' problems.

Table 3. Conversion to 'drug narratives': selected mechanisms of persuasion

Mechanism	Features/examples with related content*
Logical/empirical consistency	• Numerous scientifically consistent narratives are often generable, permitting varied positioning for competitors • e.g. different profiles of individual ARBs
Volume of data	• Large number of studies of limited importance overcome scientific principle of reproducibility and improve meta-analyses • Discourse monopolies possible for large drug classes (e.g. ARBs, atypical antipsychotics)
Weight of discourse	• Sheer number of journals and meetings selectively increased by pharma, and populated with its content • Class promotion by several competitors increases collective ability to mould discourse
Authority	• KOLs crucial • Does not require explicit product endorsement to be effective
Establish a standard	• Inclusion in official guidelines—clopidogrel,[1] rimonabant[2] • Backing from quasi-'official' initiatives—statin safety[3] • Create own guidelines—raltitrexed[4]
Different medical values/ meanings	• Emotional appeals to patient care and well-being • Patient quality of life • Cost-effectiveness
Rhetoric	• Compelling/differentiating constructions of disease areas (e.g. 'direct' renin inhibitors)[5] • Exaggeration of benefits or need • Traditions and reliability of the company • 'Drug narratives' as morality tales, in which acceptance/participation is associated with truth and virtue
Incentives to believe	• Money/'honoraria' • Pharma patronage • Potential rewards (e.g. travel to congresses) • Emulation (of KOLs) • Threat (e.g. career prospects for pharma employees) • Loyalty/belonging (e.g. for pharma employees) • Obligation/reciprocity/friendship (e.g. between prescribing doctor and sales representative)
Subterfuge	• Conceal/downplay pharma involvement, e.g. ○ KOLs list all commercial affiliations, not just the salient one ○ Citation of 'unrestricted educational grant' in a footnote ○ In journal supplements, individual articles resemble main-journal articles, are not all peer reviewed and may not highlight pharma involvement ○ Embed pharma-sponsored web content within non-sponsored content

* See note to Table 2.

References

1. Bertrand *et al.* (2002); 2. Mancia *et al.* (2007); 3. International Working Group in Colorectal Cancer (1997); 4. Gradman & Traub (2007); 5. McKenney (2006).

States (McKenney, 2006). An agency, Conexus Health, was also involved. The report emphasized that statins were in general safe. Details of how many dollars individual companies provided, and how the report's content and layout were formulated, are not in the public domain. The report's scientific standards were high and unbiased, but pharma's role in such initiatives requires further ethical and policy research, and greater transparency.

A company may also convene experts on its own initiative to draw up guidelines. For instance, a group of leading oncologists published guidelines for advanced colorectal cancer (International Working Group in Colorectal Cancer, 1997). These guidelines emerged from a meeting convened and financed by raltitrexed's manufacturers. They were ghost-written then reviewed by the company, and included a recommendation for the first-line use of raltitrexed. The resulting guidelines expressed the opinion of the oncologists involved—but would never have existed in the absence of commercial initiative.

Incentives to believe, subterfuge and ambiguity

Beyond rhetoric, pharma may provide prescribers with more tangible incentives to believe its science, such as 'honoraria', rewards or reciprocity towards the sales representative who is a gift-giving friend (see Oldani, 2004). Although not of malign intent, de facto subterfuge, involving the hiding or downplaying of pharma involvement, is also sometimes employed. Many pharma-instigated articles and presentations acknowledge their origins only by means of a footnote citing an 'unrestricted educational grant'. Articles in journal supplements are reported to be of lower scientific quality than those in the parent journal (Cho and Bero, 1996; Rochon *et al.*, 1994b) and may be non-peer-reviewed, yet frequently appear identical to articles in the parent journal, particularly when viewed online or distributed as reprints. Ironically, 'conflict of interest' statements may provide an opportunity for subterfuge, since authors or speakers frequently list all their commercial affiliations, not only the salient ones, obscuring the truth about who is paying for a specific article and implying balance because the author appears to be representing different interests.

Modulation of discourse structure, people and networks

Alongside its contributions to medical-scientific discourse content, pharma regulates discourse structure. It also modulates the people and networks through which discourse proceeds, and the institutional settings in which discourse is grounded and science is done. There is a need for research to clarify these aspects of pharma activity, but some key contours are summarized here (see Table 4; the observations described in this section are made chiefly on the basis of participant observation).

KOLs, societies and congresses

Of considerable importance is the coupled regulation of individuals and interpersonal networks, principally through pharma's cultivation of KOLs. It is reasonable that leading clinicians should advise industry and that pharma should seek their help in educating colleagues, but KOLs are also de facto tools for discourse management. Systems by which KOLs are selected, positioned and used to exert influence are well established—indeed, software for managing KOLs is commercially available (e.g. MDProfile, 2008). KOLs may be constructed and regulated with respect to what they study, where they go, what they say and write, and with whom they interact. Networks among KOLs, and between KOLs and other scientists and clinicians, are influenced by who is invited to sit on advisory boards, supervise clinical trials and speak at meetings. Within the KOL caste there is structure and hierarchy, beginning with new blood and 'rising stars' and culminating with the grandees. KOLs

Table 4. Regulation of discourse structure, people, networks and institutional settings: selected mechanisms

Intervention	Features/comments
People and networks	

KOLs	• Discourse 'sources' defining content through presentations and reviews
	• Regulation of KOLs by pharma includes:
	  ○ Research done (e.g. pharma trials)
	  ○ Papers published; lectures given
	  ○ Congresses visited
	  ○ Contacts with other KOLs

Professional networks	• Construction and manipulation of networks of power/influence/authority
	  ○ Based on KOLs
	  ○ Regulation of KOL–KOL networks (advisory boards, clinical trials meetings)
	  ○ Regulation of KOL hierarchies
	  ○ Regulation of KOL/'rising star' interactions

Professional societies	• Seek to set scientific agenda • Publish journals and in some cases, textbooks • Many leading societies are partly run by pharma KOLs and receive pharma money
Discourse structure	
Congresses	• Focal point for agenda-formation and renewal of networks • Reinforcement of KOL cult • Platform for major results and projection of 'drug narratives' • Conduit for unhelpful results • Congresses receiving pharma funding have better facilities and attract more attendees • Most major medical congresses now heavily dependent on pharma
Peer-reviewed journals	• Many journals dependent on pharma funding

Other print publications	• Blurred border between hard science and infomercial content, e.g.
	  ○ Non peer-reviewed supplements/journals
	  ○ News/features in medical magazines/newspapers
	  ○ 'Independent' promotional magazines soliciting pharma patronage
	  ○ Pharma/agency-published books/magazines/leaflets
	  ○ Sales representatives' briefing materials
	  ○ Advertising

Internet	• Growing importance in medical discourse (e.g. online information, education) • Pharma-shaped expansion of internet services
Education	• Investment in 'continuing medical education' with high promotional content • E.g. satellite symposia and websites
Institutions and settings	
Academic institutions	• Numerous forms of sponsorship/dependency

considered sympathetic to a product are sometimes described as 'friends'; those thought overly anxious to offer endorsement for rewards may be light-heartedly referred to as 'tarts'. Importantly, KOLs are not biased and typically are excellent scientists and clinicians who do not compromise their beliefs, but are approached because their research interests

converge with those of the company. It is through convincing science, not conspicuous marketing, that pharma prefers to engineer commercially productive knowledge.

Professional societies seek to set the scientific and clinical agenda for their discourses. They also provide services and educational programmes, publish guidelines, journals and websites, give prizes (frequently to their own grandees) and organize congresses. Some, such as the European Society of Cardiology (ESC), have begun to participate in the authorship of textbooks (e.g. Priori and Zipes, 2006). Most major European and American professional medical societies receive money from pharma for activities such as the annual congress, and are frequently led and have their agendas set by the same KOLs who chair pharma trials, 'author' pharma-funded review articles and speak at pharma satellite symposia.

The official meetings of professional societies are major events within academic discourses. Pharma-sponsored meetings are likely to be bigger and attract more attendees, although pharma funding may also shift the weight and topics of discussion, especially in the 'satellite' programme. Many major congresses are dependent on pharma with regard to their format, logistics and even attendance—thousands of doctors are often flown in, fed and accommodated at pharma expense. Congresses also reinforce the cult of prestige that surrounds KOLs, for instance through the allocation of more ostentatious identity badges to 'faculty' and officers of the society, many of whom are KOLs, and, as at the ESC congress, the creation of VIP areas where only the select may go. It is not yet clear, however, how far relations with pharma shape the scientific agendas of professional societies or the content of their meetings and publications, and further studies are necessary, focusing in particular on governing committees.

Publications, the internet and medical education

Most medical journals are heavily dependent on pharma funding, principally through advertising (Smith, 2005), and this inflates the number of journals and publications in areas of interest to pharma. The sheer volume of pharma-funded publications, and the use of KOLs as 'authors' to give authority to this output, are in themselves modulations of discourse structure. It has been estimated that two-thirds to three-quarters of the trials published in *Annals of Internal Medicine, Journal of the American Medical Association,* the *Lancet* and *New England Journal of Medicine* are pharma-funded (Egger *et al.,* 2001). There are no definitive measures of the total number of ghost-written reviews, although they appear to be disproportionately represented in 'high-impact' journals (Healy and Cattell, 2003).

Internet-based resources are growing in importance within medical discourse (e.g. http://www.theheart.org; http://www.cmeinstitute.com; http://www.medscape.com). Websites provide an excellent medium for the projection of 'drug narratives', both through company-developed sites and independent sites whose content can be purchased or sponsored, and at present are also a major conduit for the CME (continuing medical education) industry (e.g. http://www.cmeplanet.com).

Modulation of institutional settings

Although not discussed in detail here, pharma also inhabits and shapes the institutions in which discourses and social-professional networks are grounded. Pharma's input may support important research, but it may also have the capacity to constrain, direct or shift the

balance of medical-scientific knowledge (see di Norcia, 2003 and Yang, 2004, for discussions of the impact of corporate funding at Berkeley and the University of Toronto).[9]

Pharma within the *dispositif* of medical-scientific knowledge production

From a holistic perspective, the activities of pharma can be situated within the wider *dispositif* of institutions, programmes, regulations and discourses within which multiple constituencies jointly contribute to the generation, structure and usage of medical and scientific knowledge. The varied constituencies of commerce, science, health and governmental regulation are heterogeneous internally, but nonetheless broadly distinguishable with respect to their agendas and perceptions, their representations of truth and the functionalities they attach to knowledge.

Corporate 'meta-science'

Successful pharmaceutical development and marketing requires that within this setting, solutions emerge to a higher-order or meta-puzzle: how to configure scientific research and discourse in such a way that it delivers a sales-supporting output. In this sense, pharma's contributions to science across many levels can be viewed as products of an emerging 'meta-science' whose goal is to understand and technologize the operation of science itself to an external end. Currently, such a 'meta-science' should be understood as an implicit rather than an overt undertaking, for notwithstanding the rationality of drug development and individual marketing initiatives, there is no plan or integrated programme for its evolution on the broadest scale, but rather a quasi-Darwinian process whereby innovations that enhance profitability are retained and replicated by other companies.[10] Of note, 'meta-science' is not an activity of commerce alone, but is engaged in overtly or implicitly by all constituencies within the overall *dispositif*.

Normalcy and normativity: a Kuhnian perspective

Pharma's contribution to knowledge production is rendered distinctive by the importance of commercial drives, whose effect can usefully be summarized in relation to Kuhnian normal science. Kuhn (1977) highlighted the 'essential tension' between tradition and innovation, but although pharma science is often highly innovative, its commercial character can also lead to rigidity and normativity. As in Kuhnian normal science, belief, commitment and an intolerance of alternative viewpoints are typical, but in pharma science the fundamental determinant of output is not the commercially adapted but scientifically codified 'product canon', but the requirement for profitability the 'canon' serves. This requirement may inculcate with exaggerated force among a drug's supporters the belief and expectation that it is, and must be shown to be, beneficial. Individual pharma companies seek to establish dominance for their

9 Ziman (2003) has raised concerns about the transformation by commerce of academic science, whereby values and goals associated with commerce are blended with those of non-instrumental research.

10 As pharma's capacity for configuring science becomes more systematic and scientific, such activities are likely to become more declarative in character. In the terminology adopted by Applbaum (2008), this process can also be interpreted as part of the increasing control by pharma of 'marketing channels' which evolve to achieve a more productive alignment of demand and supply.

own narrative maps, a process Healy (2006b) has described as 'manufacturing consensus', although it is not apparent how the techniques used by pharma differ, other than in their scale, systematic nature and penetrativeness, from those of traditional science—indeed, pharma's activities may help clarify the more general structure and modes of modulation of medical-scientific discourse. It is notable, however, that pharma's contributions to discourse can lead it to nurture 'soft' knowledge and opinion, delaying its winnowing into more settled scientific knowledge by focusing on investigations which, not atypically for Kuhnian normal science, are designed merely to confirm and expand existing suppositions rather than address fundamental questions. Studies that might point directly to fundamental weaknesses and failings, or to the superiority of alternatives, are often eschewed in favour of more anodyne investigations that seek to establish some minor but marketable benefit. The result is that, despite an abundance of information, uncertainties do not merely persist within clinical medicine but are husbanded, while communications programmes and authoritative voices are deployed to preserve the power of the narrative. Kuhn took the contestable view that normal science delivers obvious progress (1962: 163), and that research 'moves fastest and penetrates most deeply when using the tools provided by the paradigm' (1962: 76). But in pharma science it is revenue generation that is most accelerated, such that in some instances it is appropriate to view settled scientific knowledge as a residue rather than an objective of discourse, left behind when the voice of commerce has moved on.

The structure of knowledge within the dispositif

The truth-claims arising from the pharma programme can be viewed as an engineered mesh of puzzle/solution narratives that is both simplified and reified in comparison with the puzzle/solution knowledge maps of Kuhnian normal science. A truth-claim such as 'there is a clinically important surge of blood pressure in the early morning hours' might be subjected to more extensive research, achieve justification on the basis of stronger evidence and finally gain particular salience at the expense of other truth-claims, not only because it is probably true, but because it received commercial support. More extended narrative constructions based on successful truth-claims gain salience accordingly. Yet successful truth-claims and narrative constructions have multiple functionalities: this particular claim's significance for science relates to human physiology and circadian rhythm, for medicine it relates to cardiovascular risk and its management, while for commerce it provides 'leverage' for a particular drug.[11] Converts to truth-claims inevitably give support to all these functions.[12]

11 Biological metaphors are useful for illustrating the compound functionality of pharma-influenced truth-claims. If, for instance, the knowledge generated within this setting were to be analogized in terms of anatomy and morphogenesis, then distinct anatomies would be required with respect to settled scientific knowledge and working medical knowledge; furthermore, within each setting, different and at times conflicting *functional* anatomies would be possible according to the constituency being served, or controlled. Finally, if one considers the notion that key truth-claims become constrained and acquire paradigmatic status because they are fixed to external goals, such fixed points may also at a more holistic level be viewed as *chaismata* or points of attachment, cross-over and interchange between the discourses of commerce, medicine and science. (The term *chiasma* refers in biology to a point of attachment and cross-over, for instance with respect to the optic nerves or chromosomal recombination.)

12 Nonetheless, the relationship between constituencies and the meanings of truth-claims within them is not symmetrical, and thus 'a particular discourse can figure at one time as the programme of an institution, and at another it can function as a means of justifying or masking a practice which itself remains silent' (Foucault, 1980: 194).

The problem of truthfulness

While most pharma science is accurate and much is excellent, the status of traditional scientific norms of truth is complex, and there is an intrinsic potential to compromise the maxim of scientific truthfulness. This is a consequence both of the normative power of the 'product canon'—and the drive for sales that stands behind it—and of cultural differences between pharma and academia with respect to the values by which knowledge is constructed. At every point, from study selection through design and methodology, data analysis and the projection of 'drug narratives', the choice exists to select the option likely to yield the 'best' data or argument—where 'best' relates not to truth, but to the beautification of the product. Outright scientific falsifications or conscious deceptions are rare, however, and violations of the 'truthfulness maxim' are often subtle, with no clear boundaries between contributions that disinterested observers might consider scientifically and clinically valid, those in which arguments and data are configured in a distorted way, and those that are misleading or false. Moreover, even if the 'truthfulness maxim' is breached it remains possible for scientific progress to be made and new treatments devised.

When subtle violations or distortions of the 'truthfulness maxim' do occur, they are often not the result of conspiracy or intent, but arise simply from an accumulation of selective or biased constructions, both within the process of generating data and argument, and across the modular structure of the pharmaceutical corporation and its satellite agencies. Within the corporation, the perspective of medical experts is closer to that of non-commercial science, whereas that of marketing specialists is more amenable to exaggeration, while legal experts have the 'duty' of protecting the company's interests and may help restrict the release of data. External marketing agencies also help shape 'key messages', shifting responsibility from the company itself. There may be hidden ceilings within corporations above which hard choices are nakedly made, but it is primarily by processing nascent knowledge through a variety of subcultures and agendas that the distinctive commercial-scientific character of pharma's output is distilled.

Compound identities, belief, faith and compromise

Individual beliefs, faiths and compromises are instrumental in this process, as are the compound identities of individuals who participate within different discourses. Pharma internalizes its narratives and commits itself to them, such that, to many employees, the underlying commercial calculations and goals become merely implicit, or detached from the scientific contemplation of the drug, permitting a 'double-think' in which scientific commitment and commercial knowingness exist in parallel. Importantly, the scale of individual compromises is typically small, both inside and outside the pharma company, and they may be made for such reasons as friendship, ease, complacency, duty, reward and threat. Thus it seems a trivial matter to a KOL to accept a 'research grant' to 'author' a web-based 'educational' package with promotional content, or a college to grant CME points to a symposium, or a journal to accept a ghost-written but interesting publication, or for medical staff within pharma to shift position subtly to accommodate the understandable concerns of marketing colleagues. Genuine belief in 'product canons' may in any case cloud objectivity, much as faith conditions perceptions of any theory, while individuals who are aware they are making compromises may become habituated and cease to reflect on their conduct,

or employ the common tactic of fashioning rationalizations for their behaviour. Thus, medical staff within pharma believe what they say about their drugs, and have the data to prove it; they might allow commercially unhelpful data to be omitted because a colleague suggests this is 'not the right publication'; or they might congratulate themselves for being ethical by including it, when an equally strong incentive is the opprobrium that might ensue if an omission were exposed. Hence, by working with transitive concepts and data that retain continuity with good science, by means of heterogeneous subcultures, through multiple belongings and the interweaving of discourses, through the power of belief and by requiring only modest and easily accommodated individual compromises, the pharma system readily conducts clinical research and generates narratives within which commercial pressures can shape the objective truth-claims of science.[13]

An International Standard of Integrity in Science

Various initiatives are in progress with regard to relations between pharma and medicine (Brennan *et al.,* 2006; Coleman *et al.,* 2006; Hopewell *et al.,* 2008; International Committee of Medical Journal Editors, 2006; Laine *et al.,* 2007). A further useful development would be the establishment of an International Standard of Integrity in Science. The Standard would be formulated by leading journals, professional societies, CME accreditation bodies and teaching institutions. World Health Organization involvement should also be considered. Journals, institutions, CME bodies, websites, professional associations, congresses and symposia applying the standard would be asked to reproduce its logo at the head of each publication or initiative.

Two notable features of the proposed Standard are, first, that it would involve joint action between the leading journals, professional societies and teaching institutions, as joint custodians of medical-scientific knowledge; and, second, that it would have global reach. Journals, societies, websites and institutions which did not apply the standard could readily be identified, whereas those adopting the logo would benefit from enhanced credibility.

The Standard's content would require careful discussion. A commitment against commercial bias in the framing and content or scientific articles is desirable, but free thinking and space for dissent should take precedent. One key goal should be to improve commercial transparency. This is a wider matter than the probity of the author; indeed, Cain and colleagues (2005) have pointed out that disclosure of 'conflicts of interest' is not a panacea, and may make claims appear more credible or encourage disclosing authors to be more biased. Disclosure should therefore not merely be author-focused, but set out the background and rationale of any publication in which commerce was involved. This should include: which company financed the publication; which specific drugs were being promoted, highlighting the lead drug; if the KOL was receiving payment directly and/or in kind, or had any

13 Interestingly however, it is the author's impression that even such seemingly trivial personal compromises involve subtle transformations. The KOLs who benefit from the system appear sated and replete, for the culture of professional medicine has been aligned with pharma assistance to accord them status, although one may detect on occasion a trace of willed self-assurance in their bearing; but the ghost-writers who fashion their words sometimes seem weathered by years of selling their identities, and may come to look faded—almost, ironically, as if they were slowly becoming ghosts. These varied effects merit further anthropological study.

financial relationship with the sponsors; what input there was regarding title, content and structure from pharma or agencies; and if the project was instigated at the behest of a pharma company or agency. Ideally, financial details should also be included. There should be explicit notification of all details in a format comparable to 'black box warnings' on prescribing information leaflets, prominently situated at the beginning or end of the article. The abstract too should list key details, since abstracts are often viewed online in the absence of the full paper. Speakers at congress satellites should be required to draw stepwise attention to each point, rather than briefly showing a slide listing all their commercial relationships. Employers should be encouraged not to accept CME points that did not meet the requirements of the Standard.

Discussion

This closing section considers further aspects of the Kuhnian analysis of pharma science, then turns to some implications for scientific knowledge.

'Normative science'

In Kuhnian terms two problematical features that may occur in pharma science are, first, the attachment, and at times subordination, of paradigmatic propositions to external objectives—in this case revenue generation—that have normative implications for output; and, second and in consequence, the compromising of standards of scientific truthfulness to a greater degree than in traditional academic science. These features originate in tensions inherent within Kuhnian normal science, but may be diagnostic of a distinct mode of knowledge production that can, in contrast to Kuhnian normal science, be termed *normative science*.[14]

Comparative studies in the agricultural, food, chemical, tobacco and other industries might clarify the extent of this mode of knowledge production within the corporate section—a 'normative corporate science'. Beyond the corporate sphere, the role played by the profit motive is likely to be replaced by different drives. The activities of the Creationist and 'intelligent design' communities might, for instance, be characterized as 'normative religious science', in which paradigmatic formulations and research programmes exist to validate theological doctrines.

The Kuhnian analysis also raises the question of scientific revolutions within the corporate sector. Local paradigms rise and fall regularly in pharma much as they do in biology, and their passing may be attended by disbelief and dismay among their adherents. Local paradigms based on drugs may, however, be swept away with greater speed than traditional Kuhnian local paradigms, when sales collapse. Indeed, market performance might be considered the measure of a corporate science paradigm's vitality. The demise of Merck's Vioxx (James *et al.,* 2007) can be seen as a collapse of a local paradigm, while Pfizer's Celebrex, a product in the same class, survived on the basis of continued marketing and KOL support,

14 The term 'normative science' has previously been proposed in a very similar sense by Lackey (2004) in the context of the science/policy interface, to refer to science conducted to serve a particular class of often-tacit objectives. The term 'normal corporate science' was also considered to describe the activities examined in this article, but discarded as it failed to clarify the distinction from normal science as envisaged by Kuhn. Traditionally, the term 'normative sciences' has referred to the disciplines of ethics, aesthetics and logic.

and better data (McGettigan and Henry, 2006). We are unlikely, however, ever to see the collapse of pharmaceutical or biomechanistic logic as a whole, although in other corporate settings such disjunctures may occur.[15] Of note, the revolution in molecular genetics is feeding through into new medicines and agriproducts without major discontinuities in the organization or values of these business sectors.[16]

Pharma and scientific knowledge

While the establishment of a more scientific basis for medicine is to be welcomed, it must be acknowledged that this is proceeding to at least some degree on pharma terms. Pharma's influence within the overall *dispositif* of biomedical knowledge production is pervasive, reaching beyond research per se into the networks, institutions, cultures and mind-sets of academic medicine and science—though many within these communities may be but dimly aware of such influence. Pharma's contribution to medical-scientific knowledge is manifest on many levels, including the dominance of the biomechanistic model of human health, the choice of what problems are investigated, the drugs themselves and associated clinical and mechanistic research, and the way specific aspects of human biology, pathology and medicine are constructed. Different companies compete over the details, and a narrative may prosper on the basis of KOL authority yet impart a permanent cast on settled scientific knowledge. Shapin's (1994) analysis of science in terms of the social status of the scientists making the truth-claims is clearly apposite in this setting. If Hacking (1999) is correct that the directions knowledge takes in its evolution might close forever other possible accounts of the world, then emerging drugs and commercial drives may prove to have lasting effects on human self-understanding. From pharma's perspective, the trajectory of scientific knowledge may be partially contingent with respect to the possibilities human biology affords, but it is non-contingent with respect to market potential. Lakoff (2005) and Greene (2007) have suggested that disease classification is driven increasingly by the reported effects of drugs, but a fuller statement would be that our conceptualizations of drugs and diseases are adjusted each to the other, with human biology and market potential jointly arbitrating the negotiation within a legalistic regulatory framework.

Pharma's contributions to scientific knowledge are further complicated by its complex relationship with norms of scientific truthfulness. Rare but highly publicized episodes of deception, fabrication or cover-up should be understood not as freak occurrences, but

15 Steve Fuller (personal communication) has suggested that 'Schumpeter's entrepreneur who ''creatively destroys'' markets is like a scientific revolutionary: Thus, Henry Ford is like Newton who radically revises the transport market with the introduction of the mass produced automobile.' However, while such seismic shifts may have occurred with respect to technology and the logistics of production, it is debatable whether any have yet been bound up with fundamental changes in scientific knowledge.

16 Kuhnian normal science has previously been contrasted by Ravetz and others (*Futures*, 1999) with a state of 'post-normal science', in which 'uncertainty' and 'urgency' require decisions to be made in the absence of settled scientific knowledge. Some advocates of 'post-normal science' have called for an 'extended peer community' to be involved in science. However, this article takes the view that traditional scientific method is not in crisis, and what difficulties prevail at present lie rather with its control. It is through the role played by communities such as pharma that scientific output can become vulnerable—indeed, uncertainty itself may be systematically sustained and managed by pharma. The involvement of any community in scientific practice is likely bring its own issues, and favourable conditions of knowledge production will always be difficult to define and enforce within the overall *dispositif*. Ironically, medicine itself (when operating free of undue commercial or governmental distortion) represents one model of how science might be benignly directed and brought into policy for a social good.

sporadic bucklings of a system which moves knowledge tectonically in the interests of shareholder value. Milder breaches of the truthfulness maxim do not prevent pharma science from deepening human understanding or improving health, but should be resisted—not least, to counter a trend in which uncertainties are systematically managed and accounts of reality constructed not out of verisimilitude but in order to exercise power—in pharma's case, with a view to driving sales.[17]

These concerns also relate to the concept of 'biopower' (Foucault, 1978). Rabinow and Rose (2006) suggest that biopower involves one or more 'truth discourses' about the 'vital' character of human beings; a set of authorities with the status and expertise to pronounce on the truth; strategies for modulating collective existence in the name of life and health; and modes of subjectification, in which individuals 'work on themselves' in the name of individual or collective life or health. Pharma activity articulates with all four of these dimensions, and requires further exploration in this context, both with respect to knowledge production and the wider cultural regulation of anxieties and sensibilities in relation to health. Of note, pharma's role within 'truth discourses' may be coloured by its utilization of managed uncertainty and its multiple, competing accounts of disease and treatment: the plurality, uncertainty and contestation of truth within the pharma sector may perhaps be viewed as part of a broader plurality of discourses through which individuals may become subjectified, extending beyond the maps of pharma through those of biology, conventional and alternative medicine.

All modes of science evolve, and the mode based on the development by major corporations of mass-selling drugs and devices is not exempt. Failing a regular stream of new 'blockbusters' the scale of pharma involvement with medical discourse may decline, while ongoing research may also create a more personalized medicine, in which more customized interventions emerge, each for relatively few patients. What is likely, however, is that medical-scientific discourse and knowledge construction will continue to be shaped by commercial interests, and that truthfulness will remain a problematical concept and point of vulnerability. Careful policy studies are required to help science both corporate and academic remain vibrant, incisive and free.

Acknowledgements

I am grateful to several anonymous industry stakeholders for discussions during the development of this project. I thank Carl Elliott, Michael Oldani and Kal Applbaum for stimulating discussions, and David Healy, Steve Fuller, Sergio Sismondo and Ian Hacking for helpful suggestions.

17 Although sales are the goal, power relations among pharma, clinicians and patients are all inevitably modulated. Metaphors of proprietorship and control are part of the standard vocabulary of pharma in this regard, and not considered to have sinister implications: one corporation recently engaged in a cross-brand initiative that in the words of a former executive would help enable the company 'to own the metabolic syndrome patient' (see LinkedIn.com, 2008). Whereas this article has focused on scientific knowledge construction, a related account might address the regulation of knowledge and power fields across pharma, scientists, clinicians and the general public.

References

Angell, M. (2004). *The truth about drug companies: How they deceive us and what to do about it*. New York: Random House.

Applbaum, K. (2008). Where demand meets supply: Comorbidity and channel stabilization in the creation of a psychopharmaceutical blockbuster. Unpublished manuscript presented at the London School of Economics, 11 January.

Aronne, L. J. (2007). Therapeutic options for modifying cardiometabolic risk factors. *American Journal of Medicine, 120* (3 Supplement 1), S26–34.

AstraZeneca (2008). AstraZeneca Cardiovascular division, URL (accessed May 2008): http://www.astrazenecacardiovascular.com

Barth, J., & Hahne, W. (2002). Review article: Rabeprazole-based therapy in Helicobacter pylori eradication. *Alimentary Pharmacology & Therapeutics, 16* (Supplement 1), 31–33.

Bekelman, J.E., Li, Y., & Gross, C.P. (2003). Scope and impact of financial conflicts of interest in biomedical research: A systematic review. *Journal of the American Medical Association 289*, 454–469.

Bertrand, M.E., Simoons, M.L., Fox, K.A., Wallentin, L.C., Hamm, C.W., McFadden, E. *et al.* (2002). Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *European Heart Journal, 23*, 1809–1840.

Beyond statin therapy: How to address the high short-term remaining risk in secondary prevention? (2006). Satellite symposium (Merck KGaA), World Congress of Cardiology, Barcelona, Spain, 2 September.

Brennan, T.A., Rothman, D.J., Blank, L., Blumenthal, D., Chimonas, S.C., Cohen, J.J. *et al.* (2006). Health industry practices that create conflicts of interest: A policy proposal for academic medical centers. *Journal of the American Medical Association, 295*, 429–433.

Cain, D.M., Loewenstein, G., & Moore, D.A. (2005). The dirt on coming clean: Perverse effects of disclosing conflicts of interest. *Journal of Legal Studies, 34*, 1–25.

Calabrese, J.R., Elhaj, O., Gajwani, P., & Gao, K. (2005). Clinical highlights in bipolar depression: Focus on atypical antipsychotics. *Journal of Clinical Psychiatry, 66* (Supplement 5), 26–33.

Camm, A.J. (2001). Atrial fibrillation: Is there a role for low-molecular-weight heparin? *Clinical Cardiology, 24* (3 Supplement), 15–19.

Campbell, J. (2005). *Understanding pharma: A primer on how pharmaceutical companies really work*. Raleigh, NC: Pharmaceutical Institute.

Cannon, C.P., Braunwald, E., McCabe, C.H., Rader, D.J., Rouleau, J.L., Belder, R. *et al.* (2004). Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *New England Journal of Medicine, 350*, 1495–1504.

Cartwright, C., & Hollander, E. (1998). SSRIs in the treatment of obsessive-compulsive disorder. *Depression and Anxiety, 8* (Supplement 1), 105–113.

Cho, M.K., & Bero, L.A. (1996). The quality of drug studies published in symposium proceedings. *Annals of Internal Medicine, 124*, 485–489.

Coleman, D.L., Kazdin, A.E., Miller, L.A., Morrow, J.S., & Udelsman, R. (2006). Guidelines for interactions between clinical faculty and the pharmaceutical industry: One medical school's approach. *Academic Medicine, 81*, 154–160.

Comprehensive lipid management: Managing patients beyond LDL-C (2006). Satellite symposium (sponsored by MSD), World Congress of Cardiology, Barcelona, Spain, 5 September.

Del Prato, S., Bianchi, C., Miccoli, R., & Penno, G. (2007). Pharmacological intervention in prediabetes: Considering the risks and benefits. *Diabetes, Obesity and Metabolism, 9* (Supplement 1), 17–22.

Despres, J.P. (2006). Intra-abdominal obesity: An untreated risk factor for type 2 diabetes and cardiovascular disease. *Journal of Endocrinological Investigation, 29* (3 Supplement), 77–82.

Di Norcia, V. (2003). The Olivieri Report—A compelling study of the growing tensions in clinical research. *Science and Engineering Ethics, 9*, 125–132.

Dickersin, K. (2005). Publication bias: Recognizing the problem, understanding its origins and scope, and preventing harm. In H.R. Rothstein, A.J. Sutton, & M. Borentein (Eds.), *Publication bias in meta-analysis: Prevention, assessment and adjustments*, 11–34. Chichester: John Wiley.

Dzau, V. (2005). The cardiovascular continuum and renin-angiotensin-aldosterone system blockade. *Hypertension, 23* (Supplement 1), S9–S17.

Egger, M., Bartlett, C., & Juni, P. (2001). Are randomised controlled trials in the *BMJ* different? *British Medical Journal, 323*, 1253.

Elliott, C. (2004). Pharma goes to the laundry: Public relations and the business of medical education. *Hastings Center Report, 34*, 18–23.

Foucault, M. (1978). *The history of sexuality, vol. 1: An introduction*. New York: Random House.

Foucault, M. (1980). The confession of the flesh. In M. Foucault (C. Gordon, Ed.), *Power/knowledge: Selected interviews and other writings*, 194–228. Brighton: Harvester Press.

Fuller, S. (2002). *Thomas Kuhn: A philosophical history for our times*. Chicago: U Chicago Press.

Futures (1999). Special Issue: Post-normal science. *Futures, 31*(7).

Giles, T.D. (2006). Circadian rhythm of blood pressure and the relation to cardiovascular events. *Journal of Hypertension, 24* (2 Supplement), S11–S16.

Gradman, A.H., & Traub, D. (2007). The efficacy of aliskiren, a direct renin inhibitor, in the treatment of hypertension. *Reviews in Cardiovascular Medicine, 8* (Supplement 2), S22–S30.

Greene, J.A. (2007). *Prescribing by numbers: Drugs and the definition of disease*. Baltimore, MD: Johns Hopkins UP.

Hacking, I. (1999). The Social Construction of What? Cambridge: Harvard UP.

Halpern, S.D., & Berlin, J.A. (2005). Beyond conventional publication bias: Other determinants of data suppression. In H.R. Rothstein, A.J. Sutton, & M. Borenstein (Eds.), *Publication bias in meta-analysis: Prevention, assessment and adjustments*, 303–318. Chichester: John Wiley.

Hayano, D.E. (1979). Auto-ethnography: Paradigms, problems and prospects. *Human Organization, 38*, 99–104.

Healy, D., & Cattell, D. (2003). Interface between authorship, industry and science in the domain of therapeutics. *British Journal of Psychiatry, 183*, 22–27.

Healy, D. (2004). Shaping the intimate: Influences on the experience of everyday nerves. *Social Studies of Science, 34*, 219–245.

Healy, D. (2006a). The latest mania: Selling bipolar disorder. *PLoS Medicine, 3*, e185.

Healy, D. (2006b). Manufacturing consensus. *Culture, Medicine and Psychiatry, 30*, 135–156.

Heres, S., Davis, J., Maino, K., Jetzinger, E., Kissling, W., & Leucht, S. (2006). Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: An exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. *American Journal of Psychiatry, 163*, 185–194.

Hopewell, S., Clarke, M., Stewart, L., & Tierney, J. (2007). Time to publication for results of clinical trials. *Cochrane Database of Systematic Reviews 18*(2), MR000011.

Hopewell, S., Clarke, M., Moher, D., Wager, E., Middleton, P., Altman, D.G. et al. (2008). CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet, 371*, 281–283.

Hoyningen-Huene, P. (1993). *Reconstructing scientific revolutions: Thomas S. Kuhn's philosophy of science*. Chicago: U Chicago Press.

International Committee of Medical Journal Editors. (2006). Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication. URL (accessed September 2006): http://www.icmje.org

International Working Group in Colorectal Cancer. (1997). An international, multidisciplinary approach to the management of advanced colorectal cancer. *European Journal of Surgical Oncology, 23* (Supplement A), 1–66.

James, M.J., Cook-Johnson, R.J., & Cleland, L.G. (2007). Selective COX-2 inhibitors, eicosanoid synthesis and clinical outcomes: A case study of system failure. *Lipids, 42*, 779–785.

Jones, J. (2003). Sponsored publications. *Pharmaceutical Marketing, August* (Supplement: Practical Guide to Medical Publishing), 10–11.

Julius, S., Kjeldsen, S.E., Weber, M., Brunner, H.R., Ekman, S., Hansson, L. et al. (2004). Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: The VALUE randomised trial. *Lancet, 363*, 2022–2031.

Kondro, W., & Sibbald, B. (2004). Drug company experts advised staff to withhold data about SSRI use in children. *Canadian Medical Association Journal, 170*, 783.

Kuhn, T.S. (1962). *The structure of scientific revolutions*. Chicago: U Chicago Press.

Kuhn, T.S. (1977). The essential tension: Tradition and innovation in scientific research? In T.S. Kuhn *The essential tension: Selected studies in scientific tradition and change*, 225–239. Chicago: U Chicago Press.

Lackey, R.T. (2004). Normative science. *Fisheries, 29*, 38–39.

Laine, C., Horton, R., DeAngelis, C.D., Drazen, J.M., Frizelle, F.A., Godlee, F. *et al.* (2007). Clinical trial registration: Looking back and moving ahead. *Lancet, 369*, 1909–1911.

Lakoff, A. (2005). *Pharmaceutical reason: Knowledge and value in global psychiatry*. Cambridge: Cambridge UP.

Lexchin, J., Bero, L.A., Djulbegovic, B., & Clark, O. (2003). Pharmaceutical industry sponsorship and research outcome and quality. *British Medical Journal, 326*, 1167–1170.

Leys, D. (2001). Atherothrombosis: A major health burden. *Cerebrovascular Disease, 11* (Supplement 2), 1–4.

LinkedIn.com (2008). Joseph Medel, Managing Consultant—BioStrategies Group. URL (accessed May 2008): http://www.linkedin.com/in/medeljj

Mancia, G. (2005). The association of hypertension and diabetes: Prevalence, cardiovascular risk and protection by blood pressure reduction. *Acta Diabetologica, 42* (Supplement 1), S17–S25.

Mancia, G., De Backer, G., Dominiczak, A., Cifkova, R., Fagard, R., Germano, G. *et al.* (2007). 2007 Guidelines for the Management of Arterial Hypertension. *Journal of Hypertension, 25*, 1105–87.

Matthews, A.W., & Martinez, B. (2004). Emails suggest Merck knew Vioxx's dangers at early stage. *Wall Street Journal,* 1 November: A1.

McGettigan, P., & Henry, D. (2006). Cardiovascular risk and inhibition of cyclooxygenase: A systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *Journal of the American Medical Association, 296*, 1633–1644.

McKenney, J.M. (2005). Pharmacologic options for aggressive low-density lipoprotein cholesterol lowering: Benefits versus risks. *American Journal of Cardiology, 96*(4A), 60E–66E.

McKenney, J.M. (Ed.) (2006). A symposium: Report of the National Lipid Association's Statin Safety Task Force. *American Journal of Cardiology, 97* (Supplement 8A), 1C–97C.

MDProfile (2008). URL (accessed May 2008): http://www.emed-media.com

Metabolic Syndrome Institute. (Sponsored by an unrestricted educational grant from Solvay Pharmaceuticals and Abbott Laboratories). URL (accessed May 2008): http://www.metabolic-syndrome-institute.org

Meurer, M., Lubbe, J., Kapp, A., & Schneider, D. (2007). The role of pimecrolimus cream 1% (Elidel) in managing adult atopic eczema. *Dermatology, 215* (Supplement 1), 18–26.

Micardis (2008). URL (accessed May 2008): http://www.micardis.com/com/Home/About/index.jsp

MicardisPlus (2008). Additional power including the early morning danger zone. Advertisement reproduced by HealthyScepticism.org, URL (accessed May 2008): http://www.healthyskepticism.org/adwatch/au/2004/micardis.php

Moore, R., Hernandez, D., & Valantine, H. (2001). Calcineurin inhibitors and post-transplant hyperlipidaemias. *Drug Safety, 24*, 755–756.

Olanow, C.W. (Ed.) (2004). Levodopa, COMT inhibition and continuous dopaminergic stimulation. *Neurology, 62* (1 Supplement 1).

Oldani, M.J. (2004). Thick prescriptions: Toward an interpretation of pharmaceutical sales practices. *Medical Anthropology Quarterly, 18*, 325–356.

Petryna, A., Lakoff, A., & Kleinman, A. (Eds.) (2007). *Global pharmaceuticals: Ethics, markets, practices*. Durham, NC: Duke UP.

Pfizer 2008. Pfizer Neuroscience logo. URL (accessed May 2008): http://www.aocn.com.sg/images/Logo_Pfizer-Neuroscience-Lo.gif

Piepho, R.W. (2000). Overview of the angiotensin-converting-enzyme inhibitors. *American Journal of Health-Syst Pharmacy, 57* (Supplement 1), S3–S7.

Popper, K. (1970). Normal science and its dangers. In I. Lakatos, & A., Musgrave (Eds.) *Criticism and the growth of knowledge*, 51–58. Cambridge: Cambridge UP.

Poston, G.J., Adam, R., Alberts, S., Curley, S., Figueras, J., Haller, D. *et al.* (2005). OncoSurge: A strategy for improving resectability with curative intent in metastatic colorectal cancer. *Journal of Clinical Oncology, 23*, 7125–7134.

Priori, S.G., & Zipes, D.P. (2006). *Sudden cardiac death: A handbook for clinical practice*. ESC Education Series. Oxford: Blackwell.

Rabinow, P., & Rose, N. (2006). Biopower today. *BioSocieties, 1*, 195–217

Reed-Danahay, D.E. (1997). Introduction. In D.E. Reed-Danahay (Ed.), *Auto/ethnography: Rewriting the self and the social*, 1–17. Oxford: Berg.

Rennie, D. (2004). Trial registration: A great idea switches from ignored to irresistible. *Journal of the American Medical Association, 292*, 1359–1362.

Ritz, E. (2006). Total cardiovascular risk management. *American Journal of Cardiology, 100* (3 Supplement), S53–S60.

Rochon, P.A., Gurwitz, J.H., Simms, R.W., Fortin, P.R., Felson, D.T., Minaker, K.L. *et al.* (1994a). A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Archives of Internal Medicine, 154*, 157–163.

Rochon, P.A., Gurwitz, J.H., Cheung, M., Hayes, J.A., & Chalmers, T.C. (1994b). Evaluating the quality of articles published in journal supplements compared with the quality of those published in the parent journal. *Journal of the American Medical Association, 272*, 108–113.

Safer, D. (2002). Design and reporting modifications in industry-sponsored comparative psychopharmacology trials. *Journal of Nervous and Mental Disease, 190*, 583–592.

Sanofi-Aventis (2006). *Annual report*. URL (accessed May 2008): http://en.sanofi-aventis.com/Images/sanofi_ra06_en_tcm24-17381.pdf

Scherbaum, W.A. (2005). Unlocking the opportunity of tight glycaemic control: Inhaled insulin: clinical efficacy. *Diabetes, Obesity and Metabolism, 7* (Supplement 1), S9–S13.

Schilsky, R.L. (2002). End points in cancer clinical trials and the drug approval process. *Clinical Cancer Research, 8*, 935–938.

Schmieder, R.E. (2006). Endothelial dysfunction: How can one intervene at the beginning of the cardiovascular continuum? *Journal of Hypertension, 24* (2 Supplement), S31–S35.

Schneider, C.A. (2006). Improving macrovascular outcomes in type 2 diabetes: Outcome studies in cardiovascular risk and metabolic control. *Current Medical Research and Opinion, 22* (Supplement 2), S15–S26.

Sergeant, E., & Eden, A. (2003). Challenging publication planning. *Pharmaceutical Marketing,* August (Supplement: Practical Guide to Medical Publishing), 6–8.

Shapin, S. (1994). *A social history of truth*. Chicago: U Chicago Press.

Sismondo, S. (2007a). Ghost management: How much of the medical literature is shaped behind the scenes by the pharmaceutical industry? *PLoS Medicine, 4*, e286.

Sismondo, S. (2007b). Pharmaceutical company funding and its consequences: A qualitative systematic review. *Contemporary Clinical Trials, 29*(2), 109–113

Smith, M.C. (Ed.) (2008). *Principles of pharmaceutical marketing.* Philadelphia: Lee & Febiger.

Smith, R. (2005). Medical journals are an extension of the marketing arm of pharmaceutical companies. *PLoS Medicine, 2*, e138.

SPIRIT Bulletin (1993). Egham: Medical Action Communications.

Steiner, M., & Pearlstein, T. (2000). Premenstrual dysphoria and the serotonin system: Pathophysiology and treatment. *Journal of Clinical Psychiatry, 61* (Supplement 12), 17–21.

Steinman, M.A., Bero, L.A., Chren, M.M., & Landefeld, C.S. (2006). Narrative review: The promotion of gabapentin: an analysis of internal industry documents. *Annals of Internal Medicine, 145*, 284–293.

Stimmel, G.L., & Gutierrez, M.A. (2006). Sexual dysfunction and psychotropic medications. *CNS Spectrums, 11* (8 Supplement 9), 24–30.

Thor, K.B., Kirby, M., & Viktrup, L. (2007). Serotonin and noradrenaline involvement in urinary incontinence, depression and pain: Scientific basis for overlapping clinical efficacy from a single drug, duloxetine. *International Journal of Clinical Practice, 61*, 1349–1355.

van Veldhuisen, D.J., & Poole-Wilson, P.A. (2001). The underreporting of results and possible mechanisms of 'negative' drug trials in patients with chronic heart failure. *International Journal of Cardiology, 80*, 19–27.

Williams, B. (2002). *Truth and truthfulness: An essay in genealogy*. Princeton, NJ: Princeton UP.

Yang, S. (2004). Novartis agreement became 'lightning rod' for debate. *Berkleyan,* 2 September. URL (accessed August 2007): http://www.berkeley.edu/news/berkeleyan/2004/09/02_novartis.shtml

Ziman, J. (2003). Non-instrumental roles of science. *Science and Engineering Ethics, 9*, 17–27.