Deriving and Critiquing an Empirically-Derived Framework
for Pharmaceutical Ethics

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ABSTRACT

Background: The pharmaceutical industry has been responsible for major medical advances, but the industry has also been heavily criticized. Such criticisms, and associated regulatory responses, are no doubt often warranted, but do not provide a framework for those who wish to reason systematically about the moral dimensions of drug development. We set out to develop such a framework using Beauchamp and Childress's "four principles" as organizing categories.

Methods: We conducted a qualitative interview study of people working in the "medical affairs" departments of pharmaceutical companies to determine: (1) whether our data could meaningfully be organized under the headings of "autonomy," "beneficence," "non-maleficence," and "justice"; (2) how principles might be expressed in this particular commercial setting; and (3) if these principles are expressed, whether and how competing principles are balanced. We then critiqued these findings using existing normative theory.

Results: Our interviews demonstrated that three of Beauchamp and Childress' four principles were salient to our participants: beneficence, non-maleficence, and justice. Within each of these principles, participants had two broad ethical orientations: an altruistic public focus ("other-ness") and a commitment to their companies ("firm-ness"). Our participants also demonstrated efforts to balance these principles and highlighted the importance of phronesis (or practical wisdom) in balancing and enacting principles. Notably, however, our participants did not spontaneously emphasize the importance of autonomy.

Conclusions: It is possible to use qualitative empirical research, together with normative analysis, to derive a framework for pharmaceutical ethics. We suggest that our framework would be useful for those who wish to reason ethically within, or in collaboration with, the pharmaceutical industry.

Keywords: Empirical ethics, principle-based ethics, pharmaceutical industry, pharmaceutical ethics, qualitative research

INTRODUCTION

The Need for a Framework for Pharmaceutical Ethics

It is widely acknowledged that the pharmaceutical industry has been responsible for many major medical advances, but the industry has also been heavily criticized for (among other things) developing medicines that are likely to be commercially beneficial even if these do not address genuine unmet needs; carrying out research without sufficient concern for the wellbeing of research participants; distorting the design, conduct, interpretation, and presentation of research in order to produce more positive results; overstating the costs involved in research and development in order to over-price medicines; abusing intellectual property laws; and engaging in ethically suspect marketing practices (see e.g., Angell 2004; Elliot 2010). Public trust in the pharmaceutical industry has been shown to be correspondingly low (Brown and Calnan 2012), and many members of the public think that the industry needs to be more heavily regulated (Harris Poll 2010).

It is in this context that the field of "pharmaceutical ethics" has emerged. For the most part, pharmaceutical ethics has been concerned with the ways in which the pharmaceutical industry influences and distorts biomedical research, publication, policymaking, and clinical practice, and the ways in which these distortions can be managed (Lo 2012; Raad and Appelbaum 2012). Ethics has thus contributed to the development of numerous regulations governing, for example, the conduct of clinical research (Califf et al. 2012); marketing practices (Mackenzie et al. 2007; Tabarrok 2009); drug pricing and patenting (Blind 2012); and industry engagement with academic researchers, clinicians, regulators, and funding bodies (DeMartino 2012).

It has been argued recently that pharmaceutical ethics is currently limited in that it focuses too much on professional conflicts of interest and does not make sufficient use of insights from clinical ethics, public health ethics, and business ethics (Brody 2012). One reason for this narrowness of focus might be that, at present, there is no clear framework that can be used by those involved in drug development to think systematically through moral problems as they arise in practice.

A number of ethical frameworks have been developed specifically for those working in, or with, the pharmaceutical industry—such as the set of principles that has been proposed for pharmaceutical physicians who are members of the Faculty of Pharmaceutical Medicine of the Royal College of Physicians of the UK (Bickerstaffe et al. 2006), or those suggested for project collaboration between academics and the pharmaceutical industry (Riis 2012). But these tend to be more rules than general principles, taking the form of statements such as "Pharmaceutical physicians must treat information about patients and research subjects as confidential" (Bickerstaffe et al. 2006), or specific behavioural guides, such as the need to include contractual descriptions of all procedures in academia-industry protocols (Riis 2012). While these rules might be useful behavioural guides, they do not allow for much analytic flexibility or reflection.

Weber has provided some insight into what a pharmaceutical ethics might look like from the perspective of business ethics (Weber 2006). He has argued that the industry needs to do more than comply with law and regulation, and also focus on fulfilling its responsibilities to stakeholders—particularly avoiding practices that place stakeholders at unnecessary risk of harm. He then suggests a number of specific ethical "responsibilities" such as limiting "gifts" to physicians and providing clear, accurate, and useful information to

doctors and the public. While Weber's framework is richer than the prescriptive rules described above, it still moves very quickly from the general (the need to respect and protect all stakeholders) to the specific (e.g., the need to separate pharmaceutical marketing from continuing medical education) without providing much guidance as to how to generate the specific from the general or how to balance competing commitments to one or more stakeholders.

This lack of a satisfactory framework for ethical reasoning is a problem both for those within the industry, and for those outside the industry, who currently have no framework for engaging with members of industry in shared moral deliberation. While some degree of skepticism about the motives of industry is inevitable and healthy, no one benefits from sustained mistrust, suspicion, and reluctance or inability to engage in shared moral deliberation.

This raises the question: how might we develop an ethical framework that can be used by those working in the pharmaceutical industry and those who need or want to engage with the industry more productively? One framework that has been particularly successful in the biomedical setting is that of "principle-based ethics." In the remainder of this section, we describe principle-based ethics and argue for the value in developing a "principle-based pharmaceutical ethics."

The Success of Principle-Based Biomedical Ethics

Those attempting to resolve morally charged controversies in biomedical research and clinical practice have made good use of a number of normative ethical theories. One normative framework that has been particularly influential in biomedicine has been principle-based ethics (sometimes referred to as "principlism"). The best known version of principle-based ethics is that developed by Beauchamp and Childress, who identified four key guiding principles: respect for autonomy (e.g., allowing people to make informed, uncoerced decisions); beneficence (doing good and preventing harm); non-maleficence (not inflicting harm); and justice (e.g., aiming for a decent minimum of health care for all) (Beauchamp and Childress 2009).

According to Beauchamp and Childress, none of these principles is considered to be foundational, and principle-based ethics is not intended to replace other normative ethical theories. Rather, principles are viewed as four coordinated *prima facie* binding clusters of moral principles, which are part of a framework consisting of principles, rules, rights, virtues, and moral ideals (Beauchamp and Childress 2009). These principles are, by definition, abstract, content-thin and therefore indeterminate on their own in practical situations (Gordon et al. 2011). Beauchamp and Childress have thus described techniques for specifying and enriching abstract principles in particular contexts, and for balancing principles when they conflict (Beauchamp and Childress 2009). Beauchamp and Childress also emphasize the fact that principles are subject to constant, dialectical revision in light of contrary arguments or evidence from particular cases. They invoke the Aristotelian concept of phronesis, or practical wisdom, to describe this dialectical process.

Importantly, Beauchamp and Childress's principles were derived empirically, from a detailed analysis of the considered moral judgments of those attempting to resolve ethical dilemmas in biomedicine, while at the same time drawing upon insights from a cross-

cultural "common morality": "the set of norms shared by all persons committed to morality" (Atkins et al. 2008; Beauchamp and Childress 2009, 3). This method was derived from Rawls' "Wide Reflective Equilibrium" (WRE), a method for developing and justifying principles for a just society which aims for coherence among (1) the particular moral sensibilities and judgments of "competent judges"; (2) reasoning from first principles; and (3) general convictions about, for example, sociology and psychology (Rawls 2001). Although Beauchamp and Childress did not refer explicitly to their approach to deriving principles as "empirical bioethics" they clearly demonstrated the potential for empirical research to contribute not only to resolving specific normative dilemmas, but also to generating and specifying ethical theory.

While Beauchamp and Childress' principles have been highly influential in biomedicine, the principle-based approach has been subject to a number of criticisms. On a practical level, it has been argued that biomedical practitioners and researchers do not actually use principles to analyze ethically challenging situations (Ebbesen and Pedersen 2007). At the meta-ethical level, critics have challenged the idea there is a foundational, globally applicable common morality from which principles can be derived (Gert 2007; Herissone-Kelly 2011; Karlsen and Solbakk 2011; Lee 2010). Others have argued that we need a single, deductively derived, organizing theory, such as Kant's categorical imperative or the Utilitarian principle if principles are to provide a clear guide to action (Lee 2010; Herissone-Kelly 2011; Lee 2010; Strong 2000). At the same time, principle-based ethics has been criticized for being *too* determinate, imposing a rigorous and excessively uniform grid on moral thinking, and being insufficiently attuned to the cognitive and emotional complexities of moral reasoning and decision making (Smith and Dubbink 2011). Each of these criticisms has been countered, but no final resolution has been reached and principle-based ethics remains controversial.

Notwithstanding these ongoing debates, principle-based biomedical ethics remains one of the most influential frameworks for moral reasoning in biomedicine and for teaching bioethics (Ebbesen and Pedersen 2007). For better or worse, principles are enduring, resilient, productive, and adaptive to new situations (Lustig 1992) and, at the very least, provide a valuable heuristic for understanding why biomedicine is as it is (both good and bad), and for justifying—if not determining—decisions and actions in medicine, public health, medical research, health service management, and health policy (Hine 2011).

Given the success of principle-based ethics in other biomedical settings, it seems worth developing a set of principles for pharmaceutical ethics in order to help those in the pharmaceutical industry, and those interacting with the industry, to conceptualize and work through ethical dilemmas that emerge in the context of commercial drug development.

Beauchamp and Childress claim that their principles are derived from a common morality, and therefore are universally applicable to all types of medicine (Herissone-Kelly 2011). Rather, therefore, than starting from scratch and deriving our principles *a priori*, we decided to use Beauchamp and Childress' four principles as an organizing framework for developing a principle-based pharmaceutical ethics.

To develop our framework, we conducted a qualitative interview study of people working in the pharmaceutical industry with a view to determining:

(1) Whether our data could meaningfully be organized under the headings of "autonomy," "beneficence," "non-maleficence," and "justice"

(2) How principles might be expressed in this particular commercial setting and

(3) Whether and how competing principles are balanced to cope with moral conflict.

We chose to focus our analysis on those working in the "medical affairs" departments of pharmaceutical companies (i.e., those responsible for clinical trials, regulatory affairs, and health economics) because they are the groups most likely to participate in policy-related dialogue with clinicians, academic scientists, and regulators.

METHODS

We conducted 15 face-to-face interviews with people working in the medical and drug development departments of nine pharmaceutical companies in Sydney Australia. In Australia, almost all pharmaceutical companies are local subsidiaries of global companies. Our participants represented most of the major companies that have an Australian presence, as well as one manufacturer of generic medicines. We used a purposive sampling procedure to include participants from as many different companies as possible; from a variety of (non-commercial) professional backgrounds, particularly academic research, clinical medicine, and pharmacy; and with a variety of pharmaceutical company roles, including medical director, clinical research manager, regulatory affairs manager, and pricing and reimbursement manager (several participants currently or had previously held more than one of these positions) **[Table 1]**. Interviewees were identified first through organizational websites and the professional contacts of the research team and then via snowball sampling from the initial group. Sixteen people were approached in total and one declined to be interviewed.

Semi-structured interviews were conducted by the first author in late 2011 and early 2012 and lasted approximately one hour each. Interviews were recorded (with interviewees' permission) and transcribed verbatim.

Participants were told that we wanted to hear about the pharmaceutical industry from the perspective of those intimately involved with it and that we were interested in their perspectives and experiences. Participants were first asked to describe, in their own words, their decision to move out of science or clinical practice and into industry and their experiences of making the transition. They were asked how they learned to fulfill their new roles and responsibilities, and whether they had been influenced by any role models. They were asked to describe people they admired and people of whom they disapproved, and to discuss those aspects of their work they found most and least rewarding. Finally, they were asked for their opinions on issues surrounding drug development, such as the globalization of clinical research, the current regulatory and economic environment, and relationships between industry and academia. Through this loosely structured format, participants were able to define and discuss their careers and the process of drug development as they wished.

A number of interesting findings emerged from this phase of the research, including that our participants' discussions were rich in statements about what it means to be "virtuous" and that our participants used a number of psychological strategies to cope with

the tensions inherent in their work. These findings have been published/accepted for publication elsewhere.

We emphasize that at this stage of the research we did not yet know that we would be interested in explicating ethical principles. Our only research question at this stage was: "What matters to those working in the 'medical affairs' departments of pharmaceutical companies?" In this sense our approach was different to that of Beauchamp and Childress, who derived their principles from observing the ways in which people resolved moral dilemmas.

Once we had made the decision to develop a principle-based pharmaceutical ethics using Beauchamp and Childress's four principles as an organizing framework, we then returned to our data and "read for" findings that might fit under the headings of "autonomy," "beneficence," "non-maleficence," and "justice." As mentioned previously, our goal was not so much to "discover" these principles in our data as to confirm their appropriateness as an organizing framework and describe in detail how they played out in the particular context of the pharmaceutical industry.

We drew both on Morse's outline of the cognitive basis of qualitative research (Morse 1994) and on Charmaz's outline of data analysis in grounded theory (Charmaz 2006). This procedure involved initial coding via line-by-line analysis, synthesizing codes into categories until no new codes could be developed from the data, focused coding using these categories, and abstracting into concepts. A coding tree was generated. Throughout the data analysis, a process of constant comparison was employed. Existing codes, categories, and concepts were refined, enriched, and reorganized as new data emerged. Enough material was analyzed to ensure that categories were saturated and all concepts were fully described and well understood. Thematic saturation was reached after approximately eight interviews. Coding was conducted independently by both authors, and agreement was reached on the major themes, categories, and concepts. In each case we asked ourselves whether a particular concept could reasonably be interpreted as an expression of "autonomy," "beneficence," "non-maleficence," or "justice."

The study was approved by the University of New South Wales research ethics committee. All participants signed consent forms and agreed to speak from their own (rather than their company's) perspective.

RESULTS

Our interviews demonstrated that three of Beauchamp and Childress' four principles were salient: "beneficence," "non-maleficence," and "justice." Autonomy was notably absent. We will address this finding (or lack thereof) in the Discussion. Within each of these principles, participants had two broad ethical orientations: an altruistic public focus ("other-ness") and a commitment to their companies ("firm-ness").

Beneficence

Publicly-oriented beneficence

Our participants strongly emphasized the need to be altruistic, idealistic, and committed to the wellbeing of patients and the community. Indeed, this was the most common reason given for choosing to work in the pharmaceutical industry.

> P3: Very often you do know somebody with one of these conditions, and it's a feel good factor that…you can be proud of what you do, feeling like you're contributing to the wellbeing of your fellow humans. Really that's it.

Participants also emphasized the importance of contributing to the development of biomedical scientific knowledge.

> P1 [Explaining why he was drawn to the pharmaceutical industry]: The major revolutions in the 20th Century were largely around the discovery of new therapeutics, most of which were drugs, and so you could be part of change.

Participants acknowledged that there were a number of threats to the pursuit of scientific knowledge in the commercial setting, such as the pressure to produce profitable products.

> P12: The industry overall has become a little bit slack, a little bit too focused on blockbusters, inventing the next atorvastatin rather than inventing the next useful antibiotic, which will only sell for $500 million rather than $500 billion.

But the goal remained nonetheless, and industry was seen to have contributed significantly to bio-scientific knowledge.

> P7: The classic one is cholesterol-lowering—everybody today uses statins … the whole system was discovered by the pharmaceutical industry. This is not statins, this is the enzymes, the enzyme cascade… absolutely 100% discovered by the pharmaceutical industry.

Commercially-oriented beneficence

Commercially-oriented beneficence took two main forms: taking care of one's colleagues, and taking care of the company by being a good team member.

Caring for one's colleagues

In addition to being concerned for the wellbeing of the community at large, our participants emphasized their responsibilities towards their colleagues. It was seen to be important to provide learning opportunities for junior staff and help them to develop their careers.

> P7: [Describing his company]: They are totally, totally focused on getting the right people and then looking after them, making sure they are given satisfying lives, reward them, surround them.

Participants acknowledged that their efforts in this regard could be threatened by forces such as frequent company mergers and lack of mentorship. But the frustration expressed about these forces simply underscored the significance to our participants of looking out for their colleagues.

Working for the good of the team

It was also seen by all of our participants to be crucial to be a good "team player."

> P8 [Re: who is likely to succeed in industry]: you've actually got to be a team player, that's where in my experience a lot of clinicians fall down, they're really used to being single entities. Whereas [company] has [thousands of] employees, it's rare that you actually do anything all by yourself.

This entailed, for example, deferring to group decisions when one did not feel too strongly about one's personal view, and putting the good of the team above one's own personal interests.

> P4 [Describing people of whom she disapproves]: Typically for me, that has been when they are people who have got their own agenda, and really you're part of the machinery to them, or the group is part of the machinery to them. I find that not only disheartening, very disappointing.

Non-maleficence

Publicly-oriented non-maleficence

Our participants were all insistent that, despite their commercial responsibilities, the vast majority of companies and industry employees would prioritize the safety of patients or research participants over any commercial imperatives. Protecting research participants primarily involved monitoring clinical trials extremely carefully and stopping trials if there was any concern about safety, while protection of patients involved not letting unsafe products go to market and withdrawing medicines from the market in the face of safety concerns.

> P10: It was just too difficult a drug to leave on the market as a [disease] drug, when GPs would be managing it. And I think that was a good call, and the company chose to pull it off the market pretty soon after its launch, and I think that was a good call.

To this end, our participants all emphasized that they could and would speak up (at least internally) when the company seemed to be acting in a dangerous manner. In most cases, participants felt that their concerns would be listened to, but they insisted that they

would whistle-blow where necessary and leave a company if they felt ethically compromised.

> P9: If you've got detrimental information, there's an ethical obligation to communicate it internally. Invariably if it's communicated internally, they should be acting. And ultimately if they don't react, people leave and they are whistle blowing.

Commercially-oriented non-maleficence

Harm to patients and research participants were not the only kinds of harm that were salient to our participants. Our participants also felt the need to protect their companies from harm—largely by ensuring that processes did not break down and by protecting the company's reputation.

Preventing failed business processes

Careful preparation for, and oversight of, projects were important ways of preventing a major and costly breakdown in process, such as a failed clinical trial or a delayed regulatory application. Following guidelines closely was another crucial harm-avoidance strategy.

> P15: Companies will interpret [guidelines] usually in a conservative fashion, because understandably … if we get them wrong, our business will fail. If we submit drug marketing applications that the data is considered to be unsuitable because it hasn't been gathered appropriately and we can't demonstrate the quality, we don't have a business.

Preventing criticism

In addition to being concerned about the potential for business processes to break down, our participants emphasized the need to avoid damaging the company's reputation. This entailed vetting any external communications that could paint the company in a bad light and ensuring that the company's communications with other stakeholders were objective and truthful and could not be faulted.

> P1 [Discussing registration applications]: These documents are very, very carefully worded to accurately reflect what the data really means. And one of the motivations in that is that if a pharmaceutical company does not do this, then we are truly open to criticism of the worst kind. And we will be criticized. And so it's not just that people are well meaning. There's a little bit of caution that comes in because of the environment in which we work.

> Participants also described strict rules of engagement with other stakeholders, aimed at avoiding the perception that companies were overstepping their boundaries or trying to put pressure on other agencies.

Justice

Publicly oriented justice

The topic of justice as equitable allocation of resources emerged in several interviews. For the most part, it arose in the context of regretful acknowledgments that the pharmaceutical industry's priorities are often not in accord with the unmet needs of the community.

> P12: The most frustrating thing for me personally is I think industry is becoming far too fixated on making money, and losing sight of what we are really here to do [which] is to provide innovative, high-quality, affordable medicines.

This was in part because of industry's focus on "western diseases" to the exclusion of global health needs and because of the increasing focus on targeted therapies that were beneficial to increasingly small sub-populations and were also more expensive.

> P14: We're focusing on a narrow, narrow population; to generate the return on a narrow population you have to multiply the price, it's a hard reality. And the same hard reality is that individuals can't afford that.

Publicly-oriented justice also comprised issues of "fair play," and our participants emphasized the importance of adhering to regulation, cooperating with other stakeholder groups, and being concerned about the wider effects of one's practices, all for the greater good.

Our participants all went to great pains to describe their conformity with governance at all levels including the law, industry guidelines, and company rules and protocols.

> P12: …we operated in a highly professional way, our goal, not that we don't now, but our goal was always to be very highly compliant, not only with our legal and our industry standards, but from the moral and ethical point of view.

They emphasized the degree to which they cooperate with other stakeholders for the greater good. For example, they saw it as their responsibility to collaborate with regulators in finding ways to improve the system for all concerned, and to respond to crises in such a way that all interests are accommodated.

> P4: I like the whole strategy of okay how can we get the best outcome for everyone, and not make the crisis not be a crisis, but a well-planned, well-organized, so the [regulator] is happy with us, the global [company] is happy with us internally, and I think most importantly the patient is protected, that's the bit I probably enjoy the most.

It was also seen to be important to support academic researchers, consider national resources, and to have a global perspective on the effects of Australian drug development.

> P13: … my feeling was that we, Australia, owe it to our cousins in Asia for example, to bear them in mind when we are making our own decisions, or when we develop

our own processes, because what's good for Australia might have these ripples elsewhere, so we need to be conscious of that.

Commercially-oriented justice

In addition to being concerned about equity and fair play in the public sphere, our participants were frank about their commitment to their shareholders and their desire to be treated fairly by other stakeholders.

Satisfying shareholders

In thinking about resource allocation, our participants very clear about the fact that they worked for companies that had to consider the rights of shareholders as well as those of the public.

> P14: We also have constraints [in] that we get funds from shareholders, and shareholders allocate those funds … we must justify a commercial return commensurate with the rest of our industry, with our past performance, and with other industries as well.

Their talk about justice also focused on issues of "fair play" among the various stakeholder groups. For the most part, as described above, they saw themselves, and their companies, as being cooperative players in the drug development process, committed to procedural justice and to cooperation with other stakeholders. In this context, participants were greatly concerned about what they perceived to be ignorance and unwarranted criticism of the industry, inadequate financial support, and unrealistic expectations— namely, a lack of fair play on the part of other stakeholders.

> P6: The pharmaceutical industry in Australia doesn't get the same government support as it does in Switzerland or the UK, because we haven't really got much home-grown industry… So you will find in a lot of countries overseas that actually have R&D based pharmaceutical companies, they treat them better than they do in Australia in terms of government support.

Balancing other-ness and firm-ness

In each of the above domains, a focus on the wellbeing of company and its shareholders (firm-ness) was not seen to be incompatible with concern for the public (other-ness). Indeed, the two were seen to be mutually reinforcing.

> P15: So if they use [the medicine] right — the right patient, the right time — they get much better outcomes and they continue to use it. Doctors have used medications, and [said] 'won't touch that again because I had a patient nearly die.' So you want to make sure those things don't happen, because otherwise it's bad for business and it's bad for patients. But it's bad for both.

Tensions were, however, acknowledged, and it was seen to be necessary to strike a balance (P1) or find a "sweet spot" where both public and commercial goods could be pursued, and where both the public and the company could be protected from harm (P2).

> P1: [Describing a compassionate access scheme]: So that was applying compassion, but it was applying compassion while keeping an eye on the regulatory environment, keeping an eye on the reimbursement environment, keeping an eye on the evidence of the action of this drug in a particular disease, and also looking at what the financial impact might be on an organization that has an obligation to its shareholders, to make sound business decisions.

> P2: I liked the philosophy of the company in terms of being very open … and putting always the patient first … So patient's health, ensuring that's at the forefront, but finding the sweet spot where you can make a buck, and do it ethically with the patient at the forefront. I like that approach.

Importantly, ensuring the wellbeing of patients and the company were seen to be dual responsibilities of those working in medical affairs departments.

> P2: So as a medical person, your responsibility is to make sure the patient is safe, and that the company isn't put at risk and the patients aren't put at risk.

A degree of "wisdom" was seen as necessary to carry out these balancing acts. No matter what the task, it was viewed as crucial to be methodical, objective, and transparent.

> P8: [Re mistakes he has learned from] I think probably maybe…occasionally just getting too enthusiastic and a little bit insular. Because if you live all day every day with 'here's our wonderful new molecule', maybe every so often you just lose balance … I think sometimes you can lose a bit of objectivity because you get very enthusiastic about something.

It was also seen to be necessary to think "strategically" and be able to come up with a variety of solutions to problems.

> P2 [Re who is likely to succeed in industry]: I like the strategic kind of things, I like being able to think creatively and come up with lots of different solutions and different approaches. I like to think through problems … I like[d] the company, I thought it was very strategic, it was sort of change-embraced creativity and innovation.

DISCUSSION

Summary

Our interviews demonstrated that Beauchamp and Childress' principles provide a useful organizing framework for a principle-based pharmaceutical ethics. In aiming for beneficence, non-maleficence, and justice, participants had two broad ethical orientations:

an altruistic public focus ("other-ness") and a commitment to their companies ("firm-ness"). Our participants also demonstrated efforts to balance these principles or to balance other-ness and firm-ness within the principles. We have chosen to view both "other-ness" and "firm-ness" as ethical positions because they each describe a perspective from which to judge acts with moral implications.

Autonomy did not emerge as a salient principle. This may be because participants were being asked to describe their professional lives rather than, for example, how they would conduct a clinical trial. Participants did, however, talk freely about patient welfare without defining what that might mean. We cannot say for certain, therefore, how those working in medical affairs departments of pharmaceutical companies would conceptualize autonomy, only that it did not emerge spontaneously in our loosely structured interviews.

Practical implications

Having described the principles that shape pharmaceutical practice, two questions arise: how might these principles be used to address specific ethical dilemmas in pharmaceutical practice, and how adequate are they as a normative framework? These questions are best answered using a hypothetical, but realistic, case study of a pharmaceutical company with regional offices in a number of small countries:

> Jan is the head of the regional clinical trials division of a major global pharmaceutical company. She has been asked by the head of global clinical trials to conduct a feasibility study in order to determine whether her region would be an appropriate site (among others) for a global clinical trial. Jan notices some inconsistencies in the consent part of the trial protocol that could potentially put research participants at unknown risk because they would not be informed about a rare, but serious, side effect of the trial medication. She wants to raise this issue with the global clinical trials manager, but her company's regional Chief Executive Officer does not want her to do so in case this jeopardizes their chances of being selected as a site for the trial. He is concerned about the trend towards globalization of clinical research, and is worried that their clinical trials division will have to close if trials are sent elsewhere. What should Jan do?

A principle-based ethics approach to solving this dilemma, using the principles derived empirically from our research, would require Jan to balance the communal responsibilities that she owes to the general public (other-ness) against those owed to her company (firm-ness). In this context, she would need to find a balance between publicly oriented non-maleficence (not causing harm to research participants by enrolling them in a potentially dangerous trial) and firm-oriented non-maleficence (not causing harm to the local company by thwarting its chances of being able to conduct the trial). She would also need to consider the tension between publicly oriented non-maleficence and publicly oriented beneficence, because the local population could benefit from being part of a cutting edge trial if it gives them access to, and clinical expertise in relation to, a cutting-edge therapy. The principles of firm-oriented beneficence and justice are also significant here, because Jan wants to keep her clinical research team employed and maximize return to the local company's shareholders.

Because principles are, by definition, abstract and content-thin, Jan would need to specify exactly what each of these principles means in this context, and what each entails in a practical sense. This would help her to determine exactly where the conflicts lie. She would then need to consider her options. These would include (among other things): saying nothing about the inconsistency; immediately reporting the inconsistency to the head of global medical affairs; or discussing with her CEO whether there are other options, such as contacting other regional clinical trials managers (i.e., others competing to host the trial) and sending a joint statement to the global head of clinical research. In considering which option is best, Jan would probably want to choose the approach that best balances competing principles, as it is unlikely in this instance that any single principle would completely trump the others.

If Jan were able to do this, and articulate her reasoning to all other stakeholders, this would be a step in the right direction for pharmaceutical ethics. But the example also illustrates the limitations of relying *only* on those principles that are spontaneously salient to industry employees in a single set of interviews. Most notably, if Jan had used a framework for normative reasoning that drew only on the principles that were emerged empirically in our study, she may not have given sufficient consideration to balancing the liberty of research participants against the benefits to the community of conducting the trial. For this, Jan would have needed to draw on the principle of respect for autonomy—a principle that did not emerge strongly in our data for the reason discussed above.

A framework for normative reasoning that did not have a central place for autonomy would be seriously lacking. While Beauchamp and Childress insisted that none of their principles was more foundational than any other, respect for autonomy has been considered by many to be the cornerstone of biomedical clinical and research ethics—a crucial counterpoint to the paternalism that had arguably dominated medical practice since the time of the Hippocratic Oath. Despite a number of refinements and qualifications, the principle of individual autonomy remains central in debates about, for example, patient rights and consent to medical treatment and research participation (Kerridge et al. 2009), and much of medical ethics remains focused on finding ways to balance individual autonomy against the demands of beneficence, non-maleficence, and justice.

The failure of our participants to spontaneously emphasize autonomy as an ethical principle demonstrates the limitations of using a single empirical study to derive normative theory, and underscores the importance of a "wide reflective equilibrium" in which empirical data of various kinds are combined with existing normative theory to derive a rich and inclusive theory of, for example, pharmaceutical ethics (Daniels 1996; DePaul 2001). While we have focused here on Beaucuchamp and Childress' framework, and identified autonomy as a "missing" element in our empirical data, it would also be important to identify gaps by drawing on other normative theories and ethical reasoning systems such as utilitarianism, virtue ethics, or stakeholder analysis.

Resonance with public health ethics

If we "re-insert" autonomy into our theory of pharmaceutical ethics, then our framework becomes highly resonant with the principles underpinning public health ethics. While public health ethics is centrally concerned with balancing individual liberties and the advancement of health for all, public health ethicists have recognized that this concern is embedded

within a broader commitment to ensuring social justice, removing systematic disadvantage, and mobilizing communities to do so. Health is viewed as a collective, or common good, rather than (just) a property of individuals. As such, public health ethicists have emphasized the importance of principles such as connectedness, solidarity, and communal responsibility (Coughlin 2008).

With this in mind, we would suggest that the production of medicines might be viewed as a public good, and pharmaceutical ethics as a type of public health ethics. Problems in pharmaceutical ethics—as in public health ethics more generally—could therefore be divided into two groups. First, there are those problems that are concerned with the need to balance individual liberties—such as the autonomy of clinical trial participants—against the pursuit of health for all through the development of new medicines. Second, there are problems that are concerned with balancing different kinds of connectedness, solidarity, and communal responsibilities—such as those owed to the general public (other-ness) versus those owed to one's company (firm-ness).

Whose ethics is pharmaceutical ethics?

The case above illustrates how someone working in the pharmaceutical industry might use principle-based ethics to illuminate and help to justify an approach to solving a morally charged problem. But we believe that such an approach could also be used by bioethicists and policy-makers who wish to think about and codify the ways in which industry employees should respond to day-to-day dilemmas. By putting themselves in the shoes of those actually facing such dilemmas, policy-makers would be better positioned to generate nuanced and flexible codes of conduct and regulations.

For those outside the industry to use this kind of thinking in their decisions about pharmaceutical policy, there would need to be a more consistent recognition that the pharmaceutical industry, while clearly responsible for significant wrongdoing, is not inherently evil, and that pharmaceutical policy needs to do more than (just) curtail the industry's power. This does not mean that bioethicists should work within, or consult to, the pharmaceutical industry because this is likely to undermine their credibility as ethicists. When, for example, the company Eli Lilly established a project called the "Values, Ethics & Rationing in Critical Care Task Force," through which they argued that it would be "unethical" not to use its expensive treatment for sepsis, the media picked up on the fact that academic bioethicists were being paid as part of this project and complained—probably rightly in this particular case—that "(t)here is no better way to enlist bioethicists in the cause of consumer capitalism than to convince them they are working for social justice" (Elliott 2003). We believe, therefore, that it is crucial for bioethicists and policymakers to maintain their independence from the pharmaceutical industry, both so that their arguments are convincing, and so that they can switch whenever necessary from a facilitative ("ethics in industry") voice to a critical ("ethics of industry") position.

Limitations and future directions

We have already discussed the problem with using only a single empirical study to derive an ethical framework; in this case it would have led to a discounting of autonomy as an important ethical principle. Our research had a number of other limitations, each of which

points to the need for further research. First, this was a small qualitative study, and we do not know the degree to which our findings are generalizable. Future qualitative research might usefully extend to medical affairs departments in other countries, to commercial departments in pharmaceutical companies (e.g., sales and marketing divisions), and to "parent" companies outside Australia where the commercial ethos may be more entrenched. Second, we cannot make fine distinctions between the sub-groups we studied (e.g., clinical trial managers vs. regulatory affairs managers vs. medical directors). Future research might focus on teasing out differences among these groups.

Third, because we were aiming for maximum variability, we did not limit our focus to those themes that were generalizable across all interviews. Future research could focus on identifying those views that all participants have in common, and on teasing out reasons for differences between participants. Fourth, because the first phase of our research sought emergent findings, we could not know in advance which themes would prove to be most significant and might need "unpacking." Additional studies could pursue more targeted questions with participants about how they specify and balance principles, rather than simply allowing this information to emerge from the data.

Fifth, we acknowledge that it could be argued that our participants were trying to present themselves and their industry work in a more favorable light than is warranted. Triangulation with other methods (e.g., ethnographic observation and quantitative studies of actual industry behaviors) might help to determine the veracity of these accounts. Nonetheless, we believe that *espoused* principles are likely to be significant motivators of future behavior, irrespective of the degree to which they have been put into practice in the past.

Finally, we note that qualitative research provides only one perspective on a complex phenomenon, and that greater understanding of the workings of the pharmaceutical industry would be achieved by combining various qualitative and quantitative methods. Of course, in keeping with the principles of Wide Reflective Equilibrium (Rawls 2001), it is important to treat these principles as tentative, and subject to constant, dialectical, revision in light of contrary arguments or evidence from particular cases.

Conclusion

Society is deeply ambivalent about the pharmaceutical industry. Its presence in society is inevitable because vulnerable people need it and because society now expects and appreciates its products and services. Society acknowledges this by buying its products and supporting the industry through, for example, tax concessions. But the industry is also mistrusted because of its record of episodic maleficence, hypocrisy, and evasion of real justice, and this generates discomfort among all who depend upon it.

There are, however, obviously good and principled people working in the industry. The pharmaceutical company employees in this study already knew a good deal about ethics, but did not have a clear framework for defining or working with the principles they espoused. We have generated, critiqued, and enriched an empirically-derived framework of principles for use in pharmaceutical practice and policy that should assist those—both inside

and outside the industry—who wish to reason more systematically and collaboratively about issues in pharmaceutical ethics.

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