Scientific Misconduct as Organizational Deviance

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Although, as Steneck points out in his background report for this meeting, scientific misconduct is usually understood to involve "fabrication, falsification and plagiarism in proposing, conducting or reporting the results of research", human subjects protection cannot be excluded from this agenda. There are two reasons for this. First, it may be argued that research misconduct is in itself a form of human subjects abuse, since people have taken part in procedures that break the contract between researcher and participants by not making a valid contribution to scientific knowledge. Second, as Steneck also notes, integrity is a "measure of the degree to which researchers adhere to the rules or laws, regulations, guidelines and commonly accepted professional codes and norms of their respective research areas." To the extent that human subjects protection is the objective of much of this regulatory framework, we may argue both that researchers who compromise on the truthfulness of their reporting may be more likely to commit other abuses and that the success or failure of strategies for human subjects protection may offer relevant lessons for strategies to limit misconduct.

The death of Jesse Gelsinger in the course of a gene therapy trial at the University of Pennsylvania Institute for Human Gene Therapy (IHGT) in September 1999 has cast a long shadow over the adequacy of the regulatory framework in this area of medical science. It has led to significant restructuring of IHGT, has been used to justify changes in Federal regulatory structures and has provoked a bout of intense internal and external scrutiny of practice in clinical trials throughout the international community. While the narrative of events at IHGT is now reasonably well-established, there is still much to be understood about the reasons for the regulatory breaches brought to light by the subsequent investigations, particularly given the lack of evidence for any causal relationship between these and Gelsinger's death. How significant are the breaches identified? If they are relatively insignificant, have the correct regulatory conclusions been drawn? Will the changes proposed or introduced through the spring and summer of 2000 actually make trials safer, as opposed to satisfying public and political demands that "something be done?"

Traditionally, failures of the kind represented by the Gelsinger case have led to a search for blameworthy individuals, whose errors or omissions produced the negative consequences that have given rise to public scandal. The conventional response has been to call for individual sanctions and a strengthening of regulations or their enforcement. However, social scientists have become increasingly critical of this approach, arguing that organizational failures or misconduct are nowadays rarely the result of individual negligence or deceit. More typically, these failures arise as the unintended consequences of personnel carrying out their routine work under conditions of

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organizational or environmental complexity that fail to give them appropriate feedback on the implications or results. Policy responses that increase complexity may actually further obstruct feedback, or introduce new opportunities for unpredictable system interactions to occur, rather than eliminating those that proved troublesome in the past. This argument, originating with the work of Charles Perrow (1) in the US and Barry Turner (2, 3) in the UK, has been developed over recent years by Diane Vaughan (4, 5) in her studies of the 1977 Ohio Revco Medicaid fraud and the Challenger space shuttle disaster. In the latter, for example, Vaughan shows how the social structure of NASA and its contractors, and the dispersion of information about problems with the O ring seal, allowed correct engineering reasoning to produce advice to launch that had devastating consequences. For present purposes, however, the Revco study may be a more useful model with its deliberate attempt to merge the understandings of social scientists who have studied organizations, regulatory bodies, and white collar crime. How do "respectable folks" end up in situations where they breach regulations intended to keep them honest? Why do organizations fail to prevent this?

This paper falls into three parts. The first briefly reconstructs the Gelsinger case from published sources available over the Internet. (It is not claimed that this is an exhaustive account, given the time and resources available.) Some of the main ideas put forward by Vaughan are then introduced, as a way of thinking about the kind of issues represented by this incident. Finally, these ideas are used to look at the Gelsinger narrative, with some reference to a brief period of participant observation in a British university's genetic science laboratories during summer 2000.

Gene Therapy at the IHGT

According to an official Food and Drug Administration (FDA) version (6), although gene therapy is an attractive idea, it has been slow to fulfil its theoretical promise. It has proved difficult to package correctly-functioning versions of disease-related genes in a way that allows them both to be delivered into the appropriate cells of a patient and to switch on. US researchers have generally looked to modified adenoviruses as the delivery vehicles, although UK researchers have been more attracted by lipids. The general principles have been known since the 1970's, giving rise to public concern about the possible implications of the release of genetically engineered material. In the US, National Institutes of Health (NIH) established the Recombinant Advisory Committee (RAC) to oversee development. However, RAC's formal powers were limited, and unlicensed experimentation took place as long ago as 1980, although the clinician involved was heavily censured. The first FDA approved trial began in September 1990, to treat an inherited immune disorder, and more than 400 trials are known to have taken place, worldwide, during that decade. However, clinical benefit has been hard to demonstrate. In 1995, Harold Varmus, then Director of NIH, created an ad hoc committee to review NIH investment in a field that seemed to have so much potential and to be realizing so little of it. This committee reviewed more than 100 approved protocols but its report to the RAC meeting in December 1995 underlined the lack of progress and the fundamental scientific problems that remained unsolved.

Coincidentally, the IHGT trial was approved at the same RAC meeting. The trail was intended to investigate possible treatment for a condition known as ornithine transcarboxylase deficiency (OTCD). This condition arises when a baby inherits a broken gene that is needed for the liver to produce an enzyme that breaks down ammonia. The IHGT researchers wanted to package this gene with a modified adenovirus and inject it into the hepatic artery to get the most direct delivery to the liver. Although there were some anxieties expressed about this delivery route, both RAC and FDA eventually agreed to approve the trial. In 1999, Jesse Gelsinger was the eighteenth and final patient to be recruited. Gelsinger was eighteen years old and in good health at the time but could not be described as a healthy teenager. He had a long history of OTCD problems, which had finally been brought under some control by a combination of medications and a highly restricted diet. He received the experimental treatment in September 1999 and died four days later, apparently from an overwhelming immune response to the carrier virus.

The subsequent FDA investigation found a series of regulatory breaches committed by the IHGT (7). Gelsinger had been entered into the trial as a substitute for another volunteer, although his high ammonia levels at the time of treatment should have led to his exclusion. IHGT

had failed to report serious side effects experienced by two previous patients in the trial, and the deaths of two monkeys given similar treatment had not been mentioned to Gelsinger or his father at the time informed consent was obtained. FDA shut down the OTCD trial immediately. FDA Form 483 issued to Dr. James Wilson, IHGT Director, on January 19, 2000, listed a number of concerns, which were summarized in a letter from FDA dated January 21, 2000, as failing to ensure the following:

> conduct of the study in accordance with the clinical protocols that are contained in the IND; obtaining adequate informed consent from subjects prior to participation in a study of an investigational agent or performance of invasive procedures; compliance with reporting protocol changes and adverse events to the responsible IRB; filing of safety reports as outlined in 21 CFR 312.64; and maintenance of complete and accurate records (8).

This letter suspended authorization for all IHGT clinical trials. A nationwide review of other approved trials revealed a high level of under-reporting of serious adverse events and possibly associated deaths. General shortcomings included: eroded adherence to requirements or standards of informed consent; lack of investigator adherence to good clinical practices and current Federal requirements; lack of adequate quality control and quality assurance programs for the gene therapy products used in trials; weak IRB processes; financial conflicts of interest; lack of public access to safety and efficacy data; limited regulatory enforcement options for Federal authorities; inadequate resources for enforcement; scope for improved co-ordination between FDA, NIH and OPRR; and poor understanding by investigators of FDA and NIH roles in gene therapy oversight. Several other trials were suspended for regulatory breaches or because of technical similarities to the OTCD trial. Other funders also suspended trials for review (9).

In March 2000, FDA and NIH launched a Gene Therapy Trial Monitoring Plan, increasing reporting requirements and requiring researchers to communicate more with each other about safety issues. In May 2000, President Clinton announced plans for legislation to allow FDA to impose civil penalties on researchers and institutions for regulatory violations. In June 2000, the NIH Office for Protection from Research Risks (OPRR), established in 1972, was reconstituted as the Office for Human Research Protections (OHRP), as advised by an NIH review submitted in 1999 before the Gelsinger incident. At the same time, the newly constituted OHRP was given expanded authority and relocated in the Office of the Assistant Secretary for Health in the Department of Health and Human Services (DHHS), placing it closer to the line of direct political authority. The overall response was summarized in evidence to a US Senate Subcommittee on May 25, 2000, under five headings: education and training; informed consent; improved monitoring; conflicts of interest; and civil money penalties. All clinical investigators receiving NIH funds would have to show that they had received appropriate training in research bioethics and human subjects protection, as would Institutional Review Board (IRB) members in their institutions. Audits of informed consent records would be performed and IRBs would be required to monitor informed consent elicitation more closely. Informed consent would have to be re-confirmed after any significant trial event. A wider range of Clinical Trial Monitoring Plans would have to be reviewed by both NIH and local IRBs. Conflict of interest rules for investigators would be reviewed to ensure that research subjects and findings were not manipulated for commercial gain. Finally, as mentioned earlier, legislation would be proposed to allow FDA to levy civil fines for regulatory breaches (9,10).

Meanwhile, IHGT and the University of Pennsylvania had initiated their own actions. IHGT filed a response to FDA Form 483 on February 14, 2000. In contrast to the FDA version, IHGT noted that it had promptly informed FDA, RAC, and the relevant IRB of Jesse Gelsinger's condition and that, in contrast to the FDA version above, IHGT had taken the initiative in suspending the trial. Moreover, IHGT could demonstrate that every trial participant had given informed consent and their eligibility for participation was fully documented. There had been delays of 3-4 months in submitting toxicity information on some early participants, which should have been discussed with FDA before proceeding with the next cohort. Nevertheless, FDA had these reports in its possession for more than six months prior to August 1999 when it approved the trial's continuation for the cohort that included Jesse Gelsinger. IHGT had Standard Operating

Procedures that met the regulatory requirements in force. The study in which two primates had died was unrelated, using different genetic material to treat a different disease. One primate had shown a mild reaction to a viral vector from the same generation but at a much higher dose–seventeen times higher–than in the OTCD trial. Available evidence did not establish any causal link between Gelsinger's plasma ammonia level prior to the infusion and his death (11). FDA reacted critically to the IHGT response. In a Warning Letter on March 3, 2000, there was a parallel exchange over the non-clinical laboratories at IHGT (12).

The University President set up an independent external panel to review IHGT. The panel reported on April 27, 2000 (13). The panel noted the discrepancies between the FDA Form 483 and the IHGT response but disclaimed sufficient regulatory expertise to comment. The panel focused on the operations of IHGT, noting its commitment to good practice and any necessary revision of operating procedures. IHGT had already contracted out the monitoring of its trials to an independent organization. However, the panel noted the growing costs of compliance and the need for the university to invest more resources in this area. The panel made the following recommendations. The university needed better internal monitoring and lower workloads for each of its IRBs. Bioethicists should cease to be involved in operational decision-making but act as consultants to investigators who would be responsible for their own actions. Conflict of interest policies should be reviewed. There should be closer scrutiny of informed consent procedures to ensure compliance with the letter as well as the spirit of FDA regulations. The panel also questioned the lack of continuing review for university institutes, the wisdom of concentrating all gene therapy work in one organization, the training of young clinical investigators in the special issues of investigational drugs, and the desirability of the university itself being simultaneously involved in the production of vectors, research, and the monitoring of standards. The President's response was delivered on May 24, 2000 (14). She announced a new assessment of all clinical trials by the University's Office of Regulatory Affairs (ORA). Where regulatory affairs professionals were not already involved, as in trials sponsored by pharmaceutical companies, the ORA would monitor the trials themselves or recruit external consultants to do so. The IHGT vision of a combined unit for basic, pre-clinical, and clinical work in gene therapy would be abandoned. The Center for Bioethics would become a free-standing department. IRB procedures would be strengthened and given extra resources. Ultimately, principal investigators and research coordinators would require certification before being allowed even to submit protocols to the IRB. The University already restricted investigators from having financial stakes in companies sponsoring trials but would review and strengthen this restriction.

At the time of writing (October 2000), a number of loose ends remained, particularly the final determination of FDA's response to IHGT and University of Pennsylvania's actions and the nature of any new legislation. However, there is no doubt that the Gelsinger case has come to be seen as iconic of problems in the regulation of scientific research and of public and political mistrust of this process, not just in the US but also in the UK and other countries with advanced levels of science. The regulatory and institutional responses will be widely studied. How much faith should we place in them?

Understanding Organizational Misconduct

Over the last thirty years, researchers in the fields of law and society and of organizational studies have become increasingly sceptical about the effectiveness of regulatory interventions as incentives for corporate bodies to act in a lawful fashion. Vaughan has summed up the alternative as a view that organizational misconduct is produced by social structure:

> By social structure, I mean (1) the stable characteristics in American society that form the environment in which organizations conduct their business activities: sets of social relations, laws, norms, groups, institutions; and (2) the stable characteristics of organizations themselves: internal structure, processes, and the nature of transactions. (4, p. 54)

Vaughan elaborates on a model first suggested by Merton (15) that locates the incentives for deviant action in the tension between cultural goals of economic success and social structures that limit access to legitimate means for achieving these goals. Merton set out a range of possible responses, but the one that interests Vaughan is "innovation". This is the attempt to achieve the valued goals by expedient but

prohibited means, justified on the basis that the unequal access to legitimate means compromises the norms that distinguish legitimacy from illegitimacy. If this distinction is perceived to be arbitrary or discriminatory, then it may fail to command moral respect. In the context of science, for example, Barber and colleagues (16) showed that those most likely to cheat on the norms of the professional community were those who felt unjustly treated in their careers. Vaughan notes that Merton focused mainly on the impact of the tension between culturally valued goals and social structures for individuals in lower social classes. However, Vaughan argues that this approach is at least as well suited to the analysis of organizations, which may be more strongly driven than individuals by the requirements of profit-maximization but where competition undercuts the force of norms. The processes of change that are the dynamic of a market economy continually challenge the normative order of that economy. The formalization of norms into law has limited effectiveness. Legal responses to "innovation" occur after the event and are skewed by the extent to which both rules and their enforcement rest on negotiations between regulatory agencies and the firms they regulate (17).

As Vaughan points out, unlawful behavior cannot be explained solely in terms of these social structural tensions. Opportunities must arise that offer the possibility of unlawful acts and the regulatory environment must be such that there is a reasonable chance of escaping sanctions. Vaughan points to the processes, structures, and transactions of modern complex organizations as the sources of opportunity. As the literature on white-collar crime shows, these create the conditions for individuals to act illegitimately: her claim is that they also make organizational misconduct possible. Organizational processes create a moral and intellectual world for members, encouraging them to identify with the organization and its goals. The survival of one becomes linked to the survival of the other. Those most exposed to temptation are those in the subunits most relevant to the resource or profit-seeking goals, with information linking subunit performance to the achievement of those goals and some responsibility for that achievement. Their choices reflect their awareness of the organization's relative rewards for achievement and its sanctions for illegality and of the structural visibility of their actions. Complex organizations multiply opportunities for misconduct through their structural differentiation and task segregation.

The result is what Vaughan terms "authority leakage", the loss of capacity for internal control. The actions of subunits may become effectively invisible, particularly where they involve specialized knowledge that is not shared elsewhere in the organization. A rational process of internal censorship designed to match upward information flows to the processing capacity of senior managers, obscures misconduct, and diffuses personal responsibility. Finally, the nature of transactions both provides legitimate opportunities for illegitimate behavior, and further minimizes the risk of detection and sanctioning. Transactions between complex organizations have four distinguishing characteristics: formalization; complex processing and recording methods; reliance on trust; and general rather than specific monitoring procedures. Because of the difficulty of monitoring each individual transaction, organizations tend to rely on signals that can be manipulated to present an appearance of legitimacy to outside observers, whether transaction partners or regulators.

Vaughan discusses the particular example of Medicaid fraud where determinations of eligibility for participation tend to rest on data submitted by would-be service providers. The complexity of the government paperwork and the lack of resources for verification create conditions where willful misrepresentation can occur. This also indicates a problem of system interface, where the culture and structure of two organizations, in this case government bureaucracies and relatively small for-profit enterprises, conflict. If these cannot be brought into alignment, one or both organizations may choose unlawful actions as a means of achieving their goals. Vaughan notes how Revco executives felt justified in false billing the Ohio Welfare Department for an amount equal to the claims for payment that had been denied on what Revco felt to be excessively bureaucratic grounds. The Welfare Department wanted Revco to internalize a government agency culture that Revco found incompatible with a private, for-profit enterprise.

Regulating Science

Vaughan's analysis of the Revco case focuses on

the potential sources of misconduct in profit-seeking organizations, although she makes some suggestions about its possible relevance to other sorts of enterprise. Scientific research organizations have some peculiar features, and may vary somewhat according to whether they are in universities, not-for-profit corporations, or commercial companies. However, it is arguable that, whether or not scientists are overtly engaged in profit-seeking, the incentives that they face are functionally equivalent. Profit, as Vaughan notes, is merely the most obvious indicator of an organization's success in locating and securing resources for its operations and survival. Scientific work depends upon flows of grant and contract income which, in turn, depend upon the production of results which lead to further income flows. These may derive from patentable innovations or from peer esteem, which leads to publication in high-quality journals, professional networking opportunities and so on. For the individual scientist, personal rewards may be symbolic rather than material, but these virtual profits are converted into economic resources for the research organization (18). Science is reward-driven in the same way as other enterprises and, as elsewhere, a failure to win rewards leads to bankruptcy, whether personal or corporate. In the British university department that I studied, for example, laboratories began almost literally as shells, which faculty were expected to equip for both the capital and consumable needs of their research through their income-generating activities. A run of unsuccessful grant applications could lead to a downward spiral where the investigator simply ran out of resources. The department claimed to be unusual in having an internal taxation system that could provide some support for a member in this position, at least for a period, in the hope that their luck would turn. This was said to be unpopular with funders who would have preferred to see a purer market system with no socialization of resources.

If this leads us to accept that Vaughan's analysis could be broadly applicable, we also need to acknowledge that there may be some differences between scientific research organizations and other kinds of enterprise. The most important may be the way in which the problems of the reactive nature of regulation are accentuated by the defining characteristic of science, namely its engagement with uncertainty. Regulation is an institutionalized means of managing risk. It can work reasonably effectively in mature environments where risks are well-understood. In many engineering situations, for example, there is a recognizable cycle of risk and regulation. A new technology generates a number of accidents that lead to a definition of hazards and a regulatory response that produces a safe environment until the next significant change in technology comes along. Although there are also routines in scientific research, science is ultimately about pushing into the unknown and taking unknowable risks. A regulatory regime that prevented all risk would prevent all scientific innovation. However, to the extent that contemporary societies have a low tolerance for risk, there is an inherent tension for regulators between the demand that risk be averted and the functioning of the regulated enterprise at all. A level of regulation that stifles enterprise is not in the regulators' interest any more than a failure to regulate sufficiently that leads to legitimacy problems with the public or the political system. In any clinical trial, participants assume some measure of risk: regulators may do their best to manage this, but it cannot be eliminated because of the variability of human response and possible interactions with other idiosyncratic features of the participant's biology or environment. The question is whether participants are adequately informed about this risk and compensated for adverse outcomes. If the risks were eliminated, so would be the possibility of discovery. Regulators must always trail behind and the letter of regulation can never be more than a partial solution to the management of risk.

If the effectiveness of regulation is necessarily limited, we may need to look more closely at the social norms of research organizations and the structures in which they are embedded (19). The university department that I studied was a relatively compact physical group, where the principal investigators had offices in the corner of the laboratories in which their postdocs, research assistants, technicians, and graduate students worked. Laboratory work was highly visible to colleagues. There was also an active tradition of seminars, journal clubs, gathering for coffee and lunch breaks, and departmentally-based socializing. This facilitated the development of a departmental culture, although it did not prevent perceptible differences emerging in the climate of different faculty member's laboratories. Clinical trials,

however, as the Gelsinger documents clearly show, tend to have a much longer chain of command, which makes important parts of the process substantially invisible to principal investigators.

The scale and complexity of the clinical trial process has generated an increasingly intricate division of labor. At the top are the principal investigators (PIs), whose strategic vision and social networks are crucial to generating the flow of resources that keep the enterprise going. In the middle are the trial managers and coordinators who keep the process on track. Patients, however, actually have direct contact with much lower level people who obtain informed consent, administer the interventions, and collect the test data on the results. The "hired hand" problem has long been recognized by those social sciences that make extensive use of survey techniques (20). How do you guarantee that low-level workers doing rather mundane jobs do not simply make up data or ignore the code book when entering it? Computerized interview techniques have reduced the opportunities for misconduct, but it has historically been a considerable challenge to the management processes of survey organizations. It represents the same problem of authority leakage and internal censorship that Vaughan describes. Structural differentiation and task segregation make operational performance invisible to senior managers. Whatever performance or quality standards are set, managers are unable to follow them through. At the same time, information from lower-level personnel is censored as it rises to match the capacity of supervisors and managers to handle it.

Various solutions have been tried, two of which are worth further discussion here. One is more detailed organizational rule-making to try to govern lower-level personnel by command and control methods. The result of this is usually to reduce further commitment to organizational goals and to sacrifice the potential gains from a degree of flexibility at the point of operational activity. If we take the specific example of informed consent, this has become the subject of increasingly elaborated procedural rules. Consent may now be deemed to be informed only if it is in accordance with these rules, something that may account for the discrepancy in view between FDA and IHGT. FDA finds that the paperwork is not in order, while IHGT claims that, although not recognized by the FDA, adequate documentation for consent does exist. However, the elicitation of consent is also a difficult interactional task. How do you ask someone voluntarily to assume a risk that can be broadly described but is ultimately unknowable until after the event. Lower-level personnel charged with the execution of the task tend to deal with this by a measure of improvisation. They seek to comply with the spirit of the regulation rather than the letter.

The result is a degree of variance that is hard to reconcile with the command and control approach. Both the University of Pennsylvania and FDA seem to have responded by trying to toughen the regime. Indeed there are even proposals that IRB members should monitor the consent process by direct observation. The problem would seem to be that you could reduce the process to a script, force the consent-takers to read the script aloud to the patient by recording or observing them, as in call centers, and then discover either that hardly anyone is willing to volunteer, because the process has been made regulator-friendly rather than user friendly, or that consent is formal rather than substantive and that patients who experience adverse outcomes can still reasonably claim to have been deceived or not to have understood the nature, purpose, and risk/benefit ratio of the trial.

In effect, this reproduces the Revco problems of the organizational interface between a Federal regulatory bureaucracy and, in this case, the professional traditions of university science. Traditionally, universities have been federations, or even confederations, of professionals, with a high degree of internal autonomy and limited collective responsibility. Although this model has come under some pressures from demands for greater social accountability in recent years, these have been opposed by the encouragement of entrepreneurial science. The difficulties of raising student fee income to a level where salaries competitive with the general commercialization of professions (21-23) can be paid have been met by a shift in culture that allows those who can to top up their incomes with consultancy earnings and stakes in spin-off companies. Although academics may be able to raise their market price by trading on their university's reputation, they are simultaneously less constrained by the university's employment discipline, since their salary may be a relatively small proportion of their income. This poses a

considerable management problem for universities, since bureaucratization may cost them faculty whose presence is crucial to their general competitive position. The University of Pennsylvania, for example, proposes to introduce certification for PIs: if this is perceived as burdensome, the result may be that the university loses star talent to less intrusive competitors.

The result, as is evident from the FDA response to the Gelsinger events, is often a division of rules into those taken seriously and those on the book but disregarded unless something goes wrong and a source of sanctioning is required. There is a hierarchy of rules, some of which "really" matter and some of which are there for use only if needed. The IHGT/FDA clashes seem to suggest that something similar has happened. Having complied with what IHGT seems to have been led to understand were the "important" rules, it clearly feels aggrieved that the FDA inspection has produced an exhaustive list of breaches, arguably to cover the agency's own collusion in the procedures at the Institute. One might note particularly the counter-charge that FDA had been in possession of toxicity reports on earlier trial participants for six months without comment before approving the recruitment for the final cohort that included Gelsinger.

When bureaucratic command-and-control fails to defend the organization from regulatory pressures or liability suits, one response can be its replacement by a network of outsourced sub-contractors, as the University of Pennsylvania seems to envisage. PIs or research organizations lay off the risk by sub-contracting the work through contracts that specify performance and quality but locate the responsibility outside the core business. The difficulty with this model is that exhaustive performance contracts are essentially impossible to write and that further incentives for misconduct tend to be created. If a sub-contractor is required to deliver a certain number of patients and associated paperwork for a fixed price, they clearly have reason to see where corners can be cut. The PI sacrifices control over data quality and, to some extent, ethics in favor of protection from the professional or legal implications of failing to control either personally, provided that there are adequate risk-shifting clauses in the original contract. It is, however, probably naive to assume that such risk-shifting will be an effective defense, particularly given the tendency of US courts to look behind the letter of such contracts to the responsibility of those issuing them to audit the performance of contractors. The growing liability of hospitals for the acts of physicians afforded admitting privileges is an obvious parallel. The result is likely to be an organizational internalization of law, as the alternative to bureaucratization, with PIs required to attend to the compliance of the documentation of their work with the forms of private rather than public law (24). It is simply a different kind of interface problem.

Ultimately, there is probably no substitute for the more active engagement of PIs with their projects and methods of countering authority leakage and internal censorship. The paradox is that the enhanced systems of scrutiny, whether bureaucratic or legal, will tend to make this more difficult by enhancing the competing calls on this pool of senior investigators to participate in peer oversight of others. To the extent that their time is drawn into this system, by the sorts of measures that FDA envisions in terms of more frequent sharing of trial experiences or the expansion of IRB membership to spread workload and allow more intensive scrutiny of proposals, then the problem that internal censorship solves will grow worse. Internal censorship, remember, is the solution to the limited time and attention that senior organizational actors can give to any particular problem. If time becomes more restricted, then censorship will increase. The FDA's measures may mean that PIs become much better informed about other people's problems and less well informed about their own. Which is most likely to contribute to safer research for human subjects?

This is obviously a brief account of a complex story that is still some way from completion. It is also heavily reliant on the public record and would obviously benefit from interview data of the kind that Vaughan had access to in her work. However, it may serve to exemplify an approach to the study of scientific misconduct and, in particular, to illustrate some of the very real difficulties of imposing a strong external regulatory regime on practice. The issues of compliance that arose in the human subjects protection of Jesse Gelsinger are immediately parallel to those that arise in controlling falsification, fabrication, and plagiarism, which also are compromised by the structural and cultural problems that lead to

authority leakage and internal censorship. It is only by recognizing and engaging with these underlying problems that effective interventions can be designed.

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