The liberal state and the rogue agency: FDA's regulation of drugs for mood disorders, 1950s–1970s*

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Abstract

The theory of the liberal state does not generally contemplate the possibility that regulatory agencies will turn into “rogues,” regulating against the interests of their clients and, indeed, the public interest. In the years between circa 1955 and 1975 this seems to have happened to one of the prime regulatory agencies of the US federal government: the Food and Drug Administration (FDA). Intent upon transforming itself from a traditional “cop” agency to a regulatory giant, the FDA campaigned systematically to bring down some safe and effective drugs. This article concentrates on hearings in the area of psychopharmacology regarding several antianxiety drugs, namely meprobamate (Miltown), chlordiazepoxide (Librium) and diazepam (Valium). In addition, from 1967 to 1973 this regulatory vengefulness occurred on a broad scale in the Drug Efficacy Study Implementation (DESI), an administrative exercise that removed from the market almost half of the psychopharmacopoeia. The article explores possible bureaucratic motives for these actions.

1. Introduction

Consider the problem of the liberal state in drug regulation. The whole concept of state control of pharmaceuticals springs from what political scientist Russell Hardin defines as “social liberalism”: a liberalism that gives the strong central state the power to intervene on behalf of those whom capitalism has impoverished and marginalized. Liberalism means the granting of choices, and social welfare liberalism raises the poor, via bureaucratic action, above the poverty line better to choose self-realization.

In the world of drug regulation it is the federal bureaucracy, the Food and Drug Administration (FDA), that is supposed to liberate citizens, not from poverty but from oppression by the pharmaceutical industry, with its toxic and ineffective products.

Hardin asks what it is that keeps social liberalism from being “self-enforcing,” or self-sustaining. Why do these impulses die out? He says, “The resolution of poverty ... [is] not likely to be mutually advantageous for the politically most important groups in liberal societies. [Diminishing poverty does] not serve the interests of ... the politically influential, wealthy entrepreneurial class.”¹

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In the microenvironment of drug regulation – as opposed to the big stage on which Hardin walks his theories – the evil entrepreneurial class becomes the wicked drug companies, striving to upset the happy equilibrium of the interventionist liberal state.

But what if this scenario identifies the wrong villain? What if the real enemy of citizens' access to safe and effective medications is not the wicked pharmaceutical industry but the regulatory bureaucracy itself? The theory of the liberal state has not made due allowance for rogue bureaucracy, bureaucracy that exists to sustain its own power and influence rather than to execute the legislative will of its masters in Congress. Edward Rubin, in his classic 1989 article on how best to realize the legislative will of the “administrative state,” considers federal agencies only as tools of the will of Congress.²

But what if the agencies take on lives of their own, and like the demons unleashed by the Sorcerer's Apprentice, run out of control? What if the liberal state is perverted not by the wealthy and powerful, but by the very agencies it has created to ensure justice, including justice in access to safe and effective pharmaceuticals?

In discussions of regulation of pharmaceuticals within the liberal state over the last hundred years, there have basically been three positions:

1. The official position, namely that regulation exists to improve the ability of citizens to maximize their own pleasure and welfare, defending them from forces that would prey upon them. This is the operative conceit that officials of the Food and Drug Administration (FDA) present in their periodic appearances before Congress. When Commissioner George Larrick testified before the House of Representatives in 1965 on behalf of the expansion of FDA power vis a vis industry, he said, “Mr. Chairman, this hearing being held today is, in a sense, historic. It is the product of two decades of FDA investigation. ... The bill will go far in putting an end to the tragic traffic in human misery. ... We believe it will give us the tools, when supported by adequate appropriations, to adequately deal with the problems which face us.”³ Thus, expansion of Agency power as public service.
2. The progressive position, namely that regulators become the pawns of the regulated and end up advancing the interests of the industries they are supposed to be surveilling. In this model, the industrial establishment ends up controlling their supposed supervisors: the prospect of bureaucrats leaving government for cushy industry jobs, as well as constant political interference, pulls the teeth of the regulatory tigers. Various contributions of Peter Breggin, an antipsychiatry writer, fit this category.⁴ A more sophisticated version emphasizes not a direct “sell-out” but rather “professional closure” – or a community of consensus – among insider experts, industry and regulatory authorities.⁵
3. The “rogue regulator” position, namely that sometimes the regulators turn upon their industrial changelings and beat them up. Far from getting into bed with industry, the regulators challenge and weaken industry, coming out of the fray themselves the victors. In this model, the agencies' imperial ambitions make them subject industry to ever more controls and regulations so that, at the end of

the day, federal power has been vastly expanded on the backs of cowed and complaisant regulatory clients.

The concept of rogue regulator does not originate with the present author but goes back at least to the classic 1934 work of Adolf Berle and Gardiner Means at Columbia University on corporate governance, which argued that corporate management works for itself as much as for stockholders.⁶ On the whole, this rogue regulator model has been deemed an exception to the progressive model of industry controlling the regulators. Yet since the days of Max Weber we have known that regulatory bureaucracies obey an underlying expansionist impulse. The progressive model negates the very existence of this impulse, as the corrupt regulators rush to sell out to their industrial clients. Yet the taste of power may well be more intoxicating than the prospect of attractive jobs after leaving government. Perhaps it is the rogue regulator model that really is the default position, the dynamic that underlies regulatory behavior, and it is the progressive model that represents exceptional, one-off behavior. If so, much of our thinking about the liberal state needs to be recast, for it is not inevitable that those who are regulated control the regulators. And bureaucratic empire building can have results completely counter-productive to the liberal state's professed ambition of creating a policy framework within which the citizens may realize their own goals.

This article argues that between the 1950s and the 1970s, one of the federal government's major regulatory agencies, FDA, followed the rogue regulator model, going after the pharmaceutical industry in a campaign to establish its own predominance in the regulation of drugs. Implicit in this model is the notion of a continuous struggle between the Agency and industry for dominance, and the bureaucrats' determination that the Agency would win. This struggle was not lost on contemporaries. On one occasion, a drug manufacturer warned FDA that, if enforcement against his generic competitors were not relentless, the industry would simply start ignoring the Agency. "Ultimately, FDA would lose control of the marketing of generic drugs across the board," he said.⁷ The bureaucrats would see to it that this did not happen.

We discuss here drugs for mood disorders, one of the major classes of pharmaceutical products, simply because that is where the expertise of the current writer lies.⁸ All the answers to FDA behavior in these years are not yet apparent, but the basic outlines of the story have started to emerge. We cover the period from the 1950s to the mid-1970s, when access to federal archives stops. As further records become available, it remains to be seen whether the "rogue agency" hypothesis laid out here is valid for subsequent decades.

2. Muscle-flexing

The beginning of the story is a psychopharmacological revolution in the 1950s. With the discovery in 1952 of the effectiveness in psychosis of the drug chlorpromazine (Thorazine in the US, Largactil elsewhere), interest quickened in the possibility of using pharmaceuticals to treat what had been considered previously illnesses of the mind, rather than the brain, best addressed with psychotherapy. A vast cornucopia opened, and in the 1950s and -60s dozens

of new agents appeared for the treatment of mood disorders, anxiety, and psychosis. All of these new drugs, of course, had to pass regulatory review.

Before the mid-1950s, FDA had been really small potatoes. Previous commissioners had been “tightfisted with money,” as an Agency insider later put it, reluctant to hire new people “they didn’t think were really up to their standards.” Congress had cut down the Agency budget in the late 1940s, which coasted at around \$5 million — not a lot in federal Washington. Not having enough staff to scrutinize all New Drug Applications (NDAs), me-too products were simply waved through (for every “new drug” with a properly approved NDA there had been 13 without).⁹

Then in the mid-1950s several external events, in particular the Durham–Humphrey Amendments in 1951 and the first Citizens’ Advisory Committee of 1955, mandated a new activism for the Agency. FDA began to receive large increases in appropriations — four-fold between 1955 and 1962. Total Agency staff more than doubled, from 1027 in 1956 to 2412 in 1962.¹⁰

Why did the Agency experience this rapid growth? Some of it came from newly mandated congressional programs. The Kefauver–Harris Amendments of 1962, fueled by public concerns over the thalidomide drug scandal, had a huge influence. Congress gave FDA the powers that Agency executives had requested in long Senate hearings. Yet what is striking is the extent to which the Agency chose to devote itself to regulation, by definition a political concept, rather than to science or public education, as well-meaning outside advisers urged. As the Second Citizens Advisory Committee noted in 1962, “These problems in relationships [with other public bodies] seem ... to stem from an emphasis on police power activities, with an apparent lack of genuine desire to cooperate with industry.” The Committee described at FDA “a general negative attitude toward cooperation with other governmental agencies.” Of particular interest was FDA’s hostility toward the pharmaceutical industry: “The Committee wishes to express its particular concern with the current status of FDA–industry relationships. In general, these are found not to be based upon common understanding, trust and respect, but rather upon fear, questioning of basic motives, and lack of opportunity for discussion before drastic action is taken on violations, many of them minor and not related to health hazards.”¹¹

In the Agency’s initial drive for expansion in the late 1950s, it was Congress that gave the FDA its new funding; the Agency’s early growth thus conforms to the Hardin model of federal regulatory agencies carrying out a legislative mandate. Yet during the hearings of Senator Estes Kefauver on pharmaceuticals in 1960–61, the “Young Turks” at FDA – the expansion-driving junior tier of administrators – kept using back channels to get Kefauver’s ear on the inadequacy of Agency powers.¹² It is clear that the drive for new power came internally from Food and Drug. The Agency’s subsequent growth, particularly under the demands of DESI (see below), was thus fueled by self-generated missions, not congressional wishes.

In the area of psychopharmaceuticals, this bureaucratic expansionist impulse drove forward in several ways. As part of its new “expansion program,” in 1957 the Agency began

prosecuting local druggists for dispensing “tranquilizers” without prescriptions, a “Durham–Humphrey” violation.¹³ An above-mentioned junior tier of leadership at FDA ran the various departments. In 1957 this junior tier stepped up its ongoing pressure to make the bromides prescription-only.¹⁴ When George Leong joined the Agency’s Office of Scientific Evaluation he said, “I continually heard – and still hear – people within the agency saying that we are in an adversary arena and have to maintain an adversary role with the industry. As a scientist, this was quite new to me.”¹⁵ These were all straws in the wind. FDA was beginning to picture itself in an epochal struggle with industry for dominance, rather than as a cheerleader for the best drugs.

What completed the conversion of Food and Drug into a hard-charging bureaucracy against the pharmaceutical industry was the arrival in January 1966 of James L. Goddard as Commissioner. Goddard was the first Commissioner from outside FDA. (He previously had been head of the Communicable Disease Center in Atlanta.) Said William Goodrich, FDA general counsel, in a later interview, “He came in with a real stir of activity. He had a speech writer ... who was a very gung-ho sort of a person, somewhat influenced by the public interest movement and somewhat anti-PMA [Pharmaceutical Manufacturers Association] certainly.” Goodrich added, “Goddard was prepared to beat on the industry a little bit, which was what the agency wanted done at that time.”¹⁶

Soon after Goddard arrived, he did several things. “His first step,” said Goodrich, “was to make a bunch of speeches to the various industry groups. They were hard-hitting, mean-spirited speeches. I mean, he in effect called them crooks and said that they were a sick industry.”¹⁷ So it is clear that Goddard’s arrival galvanized the sullen resentment of industry among FDA’s senior management, manifest since the first muscle-flexing of the mid-1950s.

The second thing Goddard did was to single out a few of industry’s favorite drugs and send them to the bottom. These were safe and effective drugs. Marking them for destruction was a power play, not a courageous act of concern for the public health.

3. Taking down meprobamate

In 1962 Congress passed the “Kefauver” amendments to the FDA Act, giving the Agency vast new powers to evaluate new drug applications for efficacy as well as safety (they had received the safety mandate in the Food, Drug and Cosmetic Act of 1938). This touched off a bureaucratic push to scrutinize closely not just every New Drug Application, but to go back and assess the entire pharmacopoeia; initially they looked at only the drugs approved between 1938 and 1962 and later all drugs.

Three years later, in 1965, the Drug Abuse Control Amendments gave the Agency additional powers to subject certain pharmaceuticals to special listing on the grounds of addictiveness. Congress had originally envisioned only the barbiturates and amphetamines in this DACA category (narcotics were already regulated). But FDA secured additional authority to designate as “capable of being abused” just about any other drug it wished. It was this latter power, implicitly granted the Agency by Congress rather than explicitly authorized, that gave FDA its tremendous new ability to move against popular drugs and take them out on

the grounds that they were potentially addictive (or capable of producing “dependence,” to use the new buzz word of the World Health Organization in 1964¹⁸). To be sure, the companies had in law the right of requesting hearings, but they would soon have it taken from them in practice.

In January 1966 the new Commissioner, “Go-Go Goddard” as he was called, authorized the take-down of the popular new psychopharmaceutical meprobamate, psychiatry’s first blockbuster drug, which Carter Products had synthesized and was marketing under the brand name Miltown; Wyeth, having bought the license from Carter, was simultaneously bringing it out as Equanil. Launched in 1955, meprobamate was a genuinely safe and effective remedy for nonmelancholic depression and nonpsychotic anxiety, for what used to be called “nervousness.” Evidence of its addictiveness was minimal to non-existent (patients are often reluctant to discontinue many mood, anxiety, and hypnotic drugs). Nonetheless, FDA selected meprobamate for listing as a drug of abuse; it must be said that listing a drug was tantamount to a death sentence for it, given patients’ abhorrence of receiving a drug known to be “addictive.”

The ground had previously been laid for Goddard’s 1966 announcement. In 1963 Arthur Ruskin, director of the Division of New Drugs, told commissioner Larrick that it was high time for a revision of the meprobamate label. (Meprobamate had been in the sights of the second-tier bureaucrats for some time.) Ruskin forwarded a list of 22 purported meprobamate side effects, among which were “fatal suicide attempts,” “withdrawal reactions,” and “addiction, habituation,” as well as “proctitis,” “bronchial spasm” and “hyperthermia.”¹⁹ It is interesting that Ruskin wanted to discuss this with the Commissioner himself, given that sorting out side effects for possible label changes is normally not done at this high a level. Evidently, the FDA second-level had already singled out meprobamate for action.

There was no question of organizing supposedly impartial hearings in a quasi-judicial process intended to get at the truth. As far as FDA was concerned, at the end of the day meprobamate would receive the same status as the barbiturates and amphetamines, becoming a drug identified as a danger to public health and brought under the kind of control reserved for agents deemed addictive, habituating, and intended for use only under very tight restrictions.

Attacking hard was to be the strategy against meprobamate. “We are acutely aware of the necessity for prevailing in the meprobamate hearing,” Kenneth Lennington, at FDA’s Bureau of Regulatory Compliance, told the district offices. The districts were to find “instances in which meprobamate has been involved in complaints, buys not charged. ... In short, we must have a record of instances in which meprobamate was tagged as having been connected with misuse or abuse.”²⁰ The evidence against meprobamate, in other words, lay anything but ready at hand.

In the month before the hearings began, FDA began a frantic search for experts to serve as witnesses for the prosecution. It was the job of FDA officers, like Bennie Moxness at FDA’s Case Review Branch, to locate experts who would declare meprobamate subject to abuse

and a peril to the public health. Moxness phoned Robert Sharoff in the narcotic addiction service of Metropolitan Hospital in New York asking for his views. Unfortunately, “Dr. Sharoff recollects only one case of Meprobamate habituation. ... He does not feel that Meprobamate is a problem insofar as his Service in the Metropolitan Hospital is concerned. He has, therefore, no valid opinion on it.”²¹ The opinions of those who disagreed with the FDA line, in other words, were invalid.

In the meantime, the FDA lawyers who were to argue the case were scrambling to put a credible dossier together. Where could evidence possibly be? They decided to review all 24 meprobamate New Drug Applications (for by that time the drug had appeared in numerous combination products), and see if these NDAs harbored evidence of toxicity that had somehow been missed on the first assessment. Many officers were assigned to this task.²² Bringing down meprobamate was to be a major FDA project.

The hearings began in June 1966 and continued until mid-September. Normally, in discussions of drug safety and efficacy, the evidence is carefully weighed as to the relative benefits of a drug versus its disadvantages. This was not the tack that FDA chose in these hearings. If there were any absolute risk, any risk at all, the drug must be listed as dangerous. As FDA lawyer Walter Byerley argued at the beginning of the hearings, it didn’t really matter if Congress had stipulated “significant” harm as a condition for listing. Harm was harm. “Let’s always remember if you have one out of a million, this may be a low percentage, but for that one it is a hundred per cent, so I can’t agree that the issue should be ‘significant number of individuals were abusing the drug.’”²³

The outcome was really a foregone conclusion. The hearing examiner wrote a report that declared meprobamate a virtual menace to the public health and demanded that it be listed as potentially capable of abuse. With the 1970 Drug Abuse Prevention and Control Act these “listed” drugs became “scheduled” in order of dangerousness, from Schedule I, meaning so dangerous as to have no medical uses, to Schedule IV, meaning, with only slight exaggeration, that one would not become addicted if taking it less than two weeks.²⁴ The meprobamate case played out for years in the appeals courts, and the entire exercise was really a waste of time anyway, because with the launch of the benzodiazepines, Librium in 1960 and Valium in 1963, meprobamate was quickly swamped in the market. But the Agency’s decision to take-down a popular drug as a means of bureaucratic muscle-flexing is interesting: it is a demonstration that the Agency’s core values lay in the area of empire building, even at the cost of public health.

4. DESI

In the Drug Evaluation Study Implementation (DESI) of the years 1968 to 1972 and beyond, the Agency wiped out around half of the American psychopharmacopoeia. This breathtaking piece of bureaucratic imposition grew out of the Kefauver Amendments of 1962, which, as we have seen, gave the Agency the authority to examine all drugs marketed from 1938 to 1962 for efficacy. It became apparent that this mammoth task would have to be farmed out. In June 1966 the National Research Council, which is the operating arm of the National Academy of Sciences, agreed to do it for \$843,000. The NAS/NRC would have their

Division of Medical Sciences conduct a systematic evaluation of all drugs launched in those years. This giant review was known bureaucratically as the Drug Efficacy Study, or DES. Thirty panels were set up, each with six members, mainly academic experts, to evaluate drugs in various areas. The identity of the members was kept secret from the public at the time.

The National Academy of Sciences did not anticipate that they were being turned into the business end of a giant broom intended to sweep away many of the most beloved (and profitable) products of the pharmaceutical industry, in particular the combination treatments that were a mainstay of family medicine. R. Keith Cannan, head of the Division of Medical Sciences at NAS/NRC, said in March 1968, "I have heard it said that the recommendations of the Academy will be that such-and-such drug shall be removed from the market. ... It will be only in that unusual situation in which all claims have been rejected that the Academy's report can be interpreted as a recommendation that the drug should be removed from the market."²⁵ This opinion in retrospect turned out to be either disingenuous or naïve.

On July 6, 1966, FDA published a notice in the *Federal Register* telling companies that wanted to keep their drugs on the market to submit evidence of efficacy. As it turned out, 237 firms sent in information on 2824 drug products, representing around 90% of the drugs commonly marketed in the United States.²⁶

The classification was done along the following lines: effective, probably effective, possibly effective, and ineffective.²⁷ This sounds quite straightforward, but there were two problems:

One, in camera, FDA understood exactly the opposite of what was meant by the categories of "probably" and "possibly." As Herb Ley, director of the FDA's Bureau of Medicine, the head office, casually explained to the Agency's abuse advisory committee, the main categories were "effective, possibly ineffective, and probably ineffective."²⁸ Possibly and probably, therefore, rather than suggesting approval with minor modifications, were death sentences.

Two, FDA did not share with the panels the consequences of a drug's being found "probably" or "possibly": Possibles would have six months to submit new data of efficacy, probables a year, and if the evidence – in the form of controlled clinical trials – did not come in within that time, *the drug would be withdrawn*.²⁹

The work of the panels began in the fall of 1966 and was essentially completed by midsummer of 1968. The panels met periodically, and each considered anywhere from 50 to several hundred drugs. The documentation was often inadequate, and what the panels relied on, basically, was the literature that young doctors from the Public Health Service – doing government rather than military service – had managed to cobble together for them. These little information packets rarely contained proper statistical studies because there weren't any. The panelists also had their personal experience to go on. FDA staffers later complained privately "that the panels' reports are frequently vague and self-contradictory, and that when hard documentation is lacking, they fall back ... on the catch-all phrase 'informed opinion of the panel.'"³⁰

As the psychiatry panel finished its work in 1969, they destroyed a good deal of the nation's psychopharmaceuticals. Of the 60 psychoactive drugs commonly used in psychiatry, internal medicine and family medicine in the 1950s and -60s, the psychiatry panel caused 45% to be withdrawn. That is almost half of the total formulary. To be sure, the single-agent drugs were treated more gingerly: only 34% of them were withdrawn as a result of regulatory action in the following decade. FDA had a particular bias against drug combinations, and 85% of the combinations were removed from the market, an enormous change in therapeutics, given that over half of all drugs sold were combinations.³¹

Yet what is of most interest here is not the work of the psychiatry panel itself, but what the Agency did after the panels had wrapped up. To cope with the mass of NAS/NRC reports, in 1968 the Agency set up a DESI Task Force, the "T" standing for "Implementation," within the Office of Director of the Bureau of Drugs.³²

At first, the pharmaceutical industry was shocked at seeing many profitable agents threatened with disappearance on the grounds that panels of academic experts, more out of personal experience than scientific evidence, thought them unworthy. The quality of the drugs in question seemed to have little to do with it. Ex-commissioner Ley later said, "The issue is not whether the drug is effective" but whether there are controlled trials "to support the claims made for the product." Pharmacologist Louis Lasagna pointed out that most of the antibiotics had had no controlled trials and yet they were still effective!³³

Originally, industry had the right to request hearings, on the model of the meprobamate hearing several years previously. And in October 1969 the Upjohn Company challenged the DESI decision to withdraw a profitable antibiotic combo marketed under the name Panalba. Upjohn lost in court, and the Panalba decision gave FDA the right to decide whether a company's evidence justified the need for a hearing. It was pointless to appeal, because the Agency would grant a hearing only if it decided that the appellant's new data were truly compelling.³⁴ By 1984 only five hearings had been granted.³⁵ There was a suggestion that if a manufacturer made too much trouble, its drug's NDA would simply be withdrawn.³⁶ The FDA's power over the existing drug supply had changed from being mainly advisory, as before 1962, to absolute control.

Such control also included control over the "label," or description of the drug's uses. It was the ability to determine exactly which pharmaceuticals were prescribed for what indications that gave the Agency such awesome new power. (Of course, physicians can prescribe a licensed drug for any indication they wish; yet in litigation such off-label uses would make the prescriber vulnerable.)

This episode strengthens the suspicion of Yale law professor Jerry Marshaw that federal agencies in the liberal state have "moved from a concern for justification and legitimacy into the realm of harassment. Many agencies would certainly relish the opportunity to follow the practice of the disgruntled father who had at least some chance of getting away with an utterance like 'Shut up,' he explained."³⁷ In fact, the Food and Drug equivalent of this was the 1973 Supreme Court decision *Weinberger v. Hynson et al.* which held the Agency was not obliged to grant hearings unless the company's evidence met the Agency's criteria of

“rigorous.”³⁸ Based on the agonies of the Agency in the meprobamate hearings, the bureaucrats had decided the equivalent of “Shut up!” Henceforth, there would be no more hearings. Even the appearance of a judicial check on the Agency’s power vanished.

What is interesting for our story is that the Agency continued to belch forth rulings about drugs that the psychiatry panel of NAS/NRC had never considered. The bureaucrats dropped any pretense of seeking independent expert opinion and merely decided on their own hook whether they wished products to remain on the market. For example, the psychiatry panel had never considered Librium (chlordiazepoxide), the first of the benzodiazepines, marketed in 1960; nor for that matter did they pass judgment on any other benzodiazepine. Yet in 1972, FDA on its own labeled Librax, a combo of chlordiazepoxide and clidinium bromide (an anticholinergic) that Roche had brought in 1965 out for anxiety and gastric distress, only “possibly,” on the logic that Librax was in a NAS-reviewed category.³⁹ So if any NAS/NRC panel had even considered a drug class, the Agency bureaucrats felt free on their own to withdraw members of that class.

Under the cover of DESI, Agency administrators went to the psychopharmacological drug stock and began removing items that struck them, as individuals, as questionable. All of this occurred without legal protection for industry, now unable to appeal except with evidence of new, expensive controlled trials. (To further pour vinegar into the wound, many of the controlled trials of these years were meaningless because they enrolled too few patients. Being thus “underpowered,” they were unable to detect small but important differences between drug and placebo. As a result, many effective drugs were sent to the bottom on the grounds of being “inert” when in reality the trial itself was riddled with so-called “type II error”: inability to detect a difference because of small sample size.⁴⁰)

In DESI as a whole, FDA removed many more drugs than it ever let on. In an unpublished assessment in 1978, Robert Temple, then acting director of the Office of Drug Research, said that only 12% of the drugs the panels reviewed were found effective for all indications and another 47% found effective for some of the claimed indications. That is 59% of the total drug supply in 1968 that somehow survived.

Yet here is the problematic aspect: of the remaining 41% originally considered “ineffective,” “possibly,” or “probably,” only an eighth ultimately won upgrades to effective. Many of those original possibilities and probables resulted from panel dynamics rather than from a genuine lack of efficacy. Yet few of the less than effective drugs were ever rescued. As Temple put it, “The 18 years of effort to upgrade less than effective products by the sponsors have resulted in a total, as of January [1984], of 214 upgradings, about 15% of the nearly 1400 products that were considered less than effective.”⁴¹ To the knowledge of the present author, this statistic was never made public. It is a testimony to the sacking of the nation’s drug supply that half of it was eliminated by a bureaucratic machine running out of control. Psychopharmacology was no less affected than other areas.

5. Conclusion

DESI greatly advanced the conversion of Food and Drug from a sleepy little cop agency into a bureaucratic powerhouse whose main *raison d'être* was power itself. In these years FDA began learning how effectively to lobby Congress in order to garner ever larger appropriations, a skill that any inside-the-Beltway operator must possess. In 1969, for example, the normally secretive Agency somehow leaked an internal draft report to the press. Said the insider-newsletter *The Pink Sheet*, "Speculation was that the 'final draft report' of the study group was deliberately leaked by the agency to UPI with a view toward national publicity and congressional hearings to point up the need for more money and manpower for the agency. If that was the aim, the immediate result was a whopping success." Paul Rogers, chair of the House Health Subcommittee, immediately focused committee deliberations on FDA's needs. *The Pink Sheet*: "The agency's topside is belatedly recognizing that going through official administrative budget channels is not necessarily the only way to get more funds for essential programs."⁴²

In the conversion of a public authority to an anti-public rogue agency, an essential step is regulation for its own sake, to the exclusion of the ultimate public good or even common sense. The FDA that plunged into DESI showed ample evidence of this essential quality. In 1969 Congressional counsel James Duffy asked Jerome Levine, an administrator at a sister federal agency, the National Institute for Mental Health, somewhat rhetorically, "If I discovered alcohol today ... would it be classed as a psychotropic drug?" Levine said of FDA's probable response, "Yes, it would, and it probably wouldn't be allowed on the market because it causes damage to the liver."⁴³

It is possible that some of the anti-public features that characterize a rogue agency started to soften in the 1970s, when a new generation of bureaucratic leaders arrived such as Robert Temple, Paul Leber, and Richard Crout. Looking back in 1973, Leon Goldberg, professor of pharmacology at Emory University, called the pre-1970 FDA "a sort of fiefdom in which no one could tell them anything." Goldberg said, "It is not such a closed society anymore."⁴⁴

Maybe, and maybe not. This application of the theory of the liberal state to a major regulatory agency is not necessarily invalidated even if Food and Drug has somehow become gentler and more caring. Possibly these big agencies drift in and out of phase, depending on circumstances.⁴⁵

A final question: how could Big Pharma have permitted this to happen? The pharmaceutical industry is not without allies in Congress, and a wealthy lobby, called in those days the Pharmaceutical Manufacturers Association (PMA), militated on industry's behalf. How could such tough guys have permitted a bunch of pencil-necks to beat them up? Who was watching the watchers?

The simple answer is that industry's influence is capable of being overpowered by public hysteria. At each major expansion of Agency power, there has been a drug scare, an alarm of sufficient proportion to stampede Congress into action and cast aside industry objections. The original Food, Drug, and Cosmetic Act in 1938, which gave the Agency authority to scrutinize drugs for safety, was ushered in with a drug scare over the "Elixir of

Sulfanilamide,” a drug suspended in a toxic solution of diethylene glycol.⁴⁶ The legislation that Estes Kefauver was about to draft on pharmaceutical pricing looked dead in the water until the thalidomide scandal broke in 1961–62.⁴⁷ The Kefauver–Harris Amendments to the FDC Act passed both houses of Congress unanimously. Finally, at this writing (June 2007) a major new expansion of Agency power looms as the regulatory community is convulsed over Vioxx, a Merck painkiller that evidently causes rare but serious cardiac side effects. No industry, however powerful, could stand against such tides.

Yet even between such convulsions, in the years under discussion the pharmaceutical industry proved surprisingly ineffective in resisting these depredations upon its interests. How is the theory of the liberal state to account for this impotence against a rogue body? FDA may be different from other regulators, such as the Department of Agriculture or the Federal Trade Commission, in that after 1962 it really did have its clients in a potential death grip. FTC could not put a major television network out of business with a single regulatory decision, but FDA could – and can – with a negative decision about a New Drug Application (always a close call), or with the judgment that a slow trickle of adverse-effect reports constitutes reason for a drug’s withdrawal. In an industry that came increasingly to depend on blockbuster drugs for survival, a bureaucratic shake of the head could mean the difference between life and death. Under these circumstances, it makes little sense to talk of “industry’s power over FDA,” for the power gradient runs in exactly the opposite direction.

Perhaps the general implication for the liberal state is that whenever the power gradient is this uneven, regulators might turn into rogues who put their own institutional imperatives before the common good. That a big cog in the federal wheel such as FDA was capable of antagonizing the public interest in preserving useful drugs of demonstrated validity shows that liberal-state theory must somehow accommodate itself to rogue agencies. Or accept that all big regulatory powerhouses harbor the capacity within them of becoming rogues.

What policy changes suggest themselves from this analysis? Two brief points:

1. FDA today justifies its awesome power as “protecting the public from harm.” Yet protection from harm must be weighed against the public interest in the development of effective new drugs for the future. As William Wardell, a pharmacologist at the University of Rochester, shrewdly observed in 1973, “In terms of drugs, the patient’s immediate need is for a highly effective drug that has an acceptable degree of risk for its likely benefit. ... The patient also has a longer-term but equally important need: the development of new therapies and the safe, more effective use of old therapies. These are the two primary needs of the patient and thus are the goals that the regulatory system should aim at.” Wardell believed that as a result of Kefauver–Harris and FDA power, “the cost-benefit ‘thermostat’ of society’s attitude toward therapeutic drugs has been set too far in the direction of minimizing harm rather than maximizing benefits to the patient.”⁴⁸

Indeed, today the suffocating restrictions on drug trials currently in place have the stated purpose of protecting subjects in these trials from risk and safeguarding the public from side effects once the drug is launched. But this

anxious monitoring of risk sends to the bottom many drugs of great therapeutic promise as soon as company executives learn of a side-effects profile in any way adverse. This is a false balancing of benefit to millions versus one-in-a-thousand risks to a few. The scales are so heavily weighted against industry because FDA politically cannot tolerate the screams from Congress and the media about “dangerous drugs” and “inadequate oversight” that inevitably are prompted by public interest groups. The behemoth the Agency has become it destabilizes easily in rough water.

2. Perhaps it is time to transfer the approval of new drugs from the Agency to another health body, such as the National Institutes of Health, which is less of a sharp-elbows bureaucratic player and more science-driven. It is almost unthinkable that NIH would have hesitated with the “Plan B” birth control pill in the way that Food and Drug did,⁴⁹ simply because NIH still speaks the language of science rather than politics. And giving such crucial power as drug approval to a thoroughly politicized agency such as FDA is almost a guarantee that licensing decisions will continue to be made for the wrong reasons. The interest of the public that inhabits the liberal state is clear here.

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