Pharmacovigilance: Watching out for Unexpected Side Effects

Pharmacovigilance can be defined as a set of practices aiming at the detection, understanding, and quantitative assessment of the risks related to the use of drugs in a population and the prevention of consequential adverse effects. In its 2002 report *The Importance of Pharmacovigilance*, the WHO traces the development of these practices back to the thalidomide disaster in 1961 and the subsequent international efforts to address drug safety issues.\(^1\) In this broader understanding of the term, pharmacovigilance refers to any kind of attention that is being paid to adverse drug reactions. However, the term is also used in a more limited way, which—for reasons that will become clear—is closely connected to the latest developments in the history of pharmaceutics, especially to the emergence of patient activism. In this sense, pharmacovigilance exclusively refers to practices of postmarket surveillance.

Arthur Daemmrich’s book *Pharmacopolitics*, a comparative study of drug regulation in the United States and Germany, can be read as a genealogy of two contemporary regulatory regimes, in both of which pharmacovigilance as postmarket surveillance has come to play a very important part. In Germany, physicians have played a predominant role in monitoring and controlling the uses of medicines. Thus the very group of people mostly concerned with drug regulation was also confronted with the effects of drugs already widely distributed. Therefore, the distinction between premarket testing and postmarket surveillance was not as clear-cut as in America. In the United States, not practicing physicians, but a state institution, the Food and Drug Administration (FDA), serves as the gatekeeper to the market. But—at least originally—the FDA lacked mechanisms for paying systematic attention to side effects of drugs it had already approved of. American doctors usually did not report back to the FDA. It dealt with this problem by demanding extensive and time-consuming premarket tests from pharmaceutical companies. In the case of the beta-blocker propanolol, for example, it took its manufacturer Ayerst almost 10 years to get approval.\(^2\) The FDA had gained its power and legitimacy through a number of drug scandals, in which patients had been severely harmed by adverse drug reactions. As a result, it came to see patients as vulnerable subjects in need of protection against industry. This protection was granted by setting up high hurdles to the market. Of course, these measures were criticized from the beginning. The FDA was accused of hampering business interests, slowing down the development of new drugs, and keeping already developed drugs from patients for too long (by the time the FDA approved of a drug, German and other European patients had often already benefited from the substance since a number of years).\(^3\)

However, these attacks only gained momentum in the 1980s when disease-based patient

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\(^1\) WHO, “The Importance of Pharmacovigilance. Safety Monitoring of Medicinal Products,” (World Health Organization, 2002), 5. Whether this origin story will stand up to historical scrutiny remains to be seen. Kees van Grootheest’s first step toward a history of pharmacovigilance suggests that already in the 18th century attention was paid to adverse drug reactions. From his point of view, the thalidomide incident only led to a systematization of the surveillance of pharmacological side effects. Kees van Grootheest, "The Dawn of Pharmacovigilance. An Historical Perspective," *International Journal of Pharmaceutical Medicine* 17, no. 5-6 (2003). The “Pharmacovigilance Timeline” of the West Midlands Centre for Adverse Drug Reaction Reporting in the UK even goes back to the Babylonian Code of Hamurabi in 1780 BC. The Pharmacovigilance Timeline (West Midlands Centre for Adverse Drug Reaction Reporting, [cited 21 July 2005); available from http://www.csmwm.org/timeline.htm. However, from a nominalist perspective these attempts of backdating seem questionable. Whether one likes to speak of pharmacovigilance *avant la lettre* or not, this paper will demonstrate that the observation of adverse drug reactions has undergone significant transformations in the recent past. Unclear where and when the term was introduced!!


\(^3\) Ibid., 29.
organizations—especially the AIDS movement—became increasingly active in the United States (a phenomenon almost absent in Germany where, to this day, patients are primarily represented by doctors or the state). Now patients whom the FDA claimed to protect accused it of withholding life-saving medications from them. Instead of being protected and patronized, they wanted to be given the chance to try out still experimental drugs in an otherwise hopeless situation. Unwilling to bear with the delays caused by the FDA’s due process, AIDS activists began to organize underground tests of new drugs. Eventually the FDA had to give in and made an acceleration of the approval process possible. But the resulting loss of drug safety had to be compensated for. Pharmacovigilance served as a response to this problem: In order to make up for the less rigid premarket tests, doctors and patients as well as the FDA and drug companies had to become more attentive to adverse drug reactions arising after a new drug had entered the marketplace and the clinic.

Such postmarket surveillance was certainly not a completely new phenomenon. Even after the most rigorous premarket testing drugs had to be watched carefully. When a new drug enters from the controlled experimental conditions of clinical trials into the “real world,” i.e. when it is taken by a larger and more diverse population (including children, old people, people suffering from several diseases at a time, various ethnicities, etc.) and possibly together with other drugs and for a longer period of time than so far tested, so-called unexpected adverse drug reactions are almost to be expected. Pharmacovigilance designates an ethos as well as a set of corresponding practices that are meant to ensure early detection of as well as quick and adequate responses to such unexpected events.

This requires a specific mode of subjectivity that is to be achieved through a certain work on the self. In her article “Expecting the Unexpected—Drug Safety, Pharmacovigilance, and the Prepared Mind,” Anne Trontell writes:

Discovery in an observational science such as pharmacovigilance depends on the capacity to recognize and investigate unexpected clinical events that are manifest once a new drug is in use. The detection of such unanticipated effects hinges on what Pasteur called “the prepared mind.” Trontell refers to a remark the French chemist and microbiologist Louis Pasteur had made in 1854: “In the fields of observation, chance favors the prepared mind.” In order to become aware of something unexpected, to recognize an unexpected event as significant, an observer must be endowed with a sufficiently developed background understanding structuring his or her expectations. He or she has to watch out for disturbing phenomena that do not fit into preconceived categories. It is precisely their unexpectedness, which helps to identify new adverse drug reactions as such:

[R]ecognition is aided by the degree of unexpectedness of the event, given the circumstances of the individual patient, the underlying disease, and background rates of the particular type of event. Highly unusual or infrequent outcomes […] are strong triggers of suspicion about the possible contributing role of a drug.

Registering such unanticipated incidents requires certain technologies of the self, but also a whole scientific and administrative apparatus. The patient needs to watch his body carefully without becoming a hypochondriac; the doctor has to be equally attentive and probing without scaring her patient; she must conscientiously record and transmit any

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6 Trontell, “Expecting the Unexpected,” 1386.
symptom that was neither to be expected from the illness nor as a known side effect from the treatment; the manufacturer has to interpret the data (does it indicate a causal relationship between event and drug use?) and has to weigh the risk of a scandal, claims for damages, and legal sanctions against the substantial sums of money already invested in the development of the new drug; and the FDA must decide on how to respond to alarming reports walking a tightrope between endangering the patients’ health by exposing them to possible side effects and endangering their health by denying them a badly needed treatment. Even though these problems are not brand new, the shortening and deregulation of premarket testing since the 1980s has aggravated them. That is not say that genuinely preventive measures have lost their importance altogether. The identification of pharmacogenetic markers is supposed to allow an assessment of the tolerability of specific drugs in individual patients. And new drugs continue to be tested preclinically as well as in clinical trials before being released. But the decisions of regulatory bodies to approve or prohibit a certain pharmacological agent are now supplemented more strongly by a certain watchfulness exercised once a drug is already in widespread use. This development can be described as a shift in drug safety from prevention (in the strict sense) to vigilance.

This increased watchfulness has been given a form through a number of new practices, tools, and institutions ranging from drug safety databases, data mining algorithms, and causality assessment algorithms to new national and international legal provisions, and the establishment of the WHO’s Uppsala Monitoring Centre collecting and processing adverse drug reaction reports in order to detect early signals of potential drug hazards. This assemblage is still growing. In its 2002 report on pharmacovigilance, the WHO notes:

Within the last decade, there has been a growing awareness that the scope of pharmacovigilance should be extended beyond the strict confines of detecting new signals of safety concerns. Globalization, consumerism, the explosion in free trade and communication across borders, and increasing use of the Internet have resulted in a change in access to all medicinal products and information on them. These changes have given rise to new kinds of safety concerns.

Among those new kinds of safety concerns listed are the illegal sale of medicines and drugs of abuse over the Internet and increasing self-medication practices. The website Erowid (www.erowid.org) can be regarded as a grassroots response to these concerns.

Erowid or Post-Black Market Surveillance

Erowid was founded in California in 1995 by two people calling themselves Earth and Fire and is now run by three persons as well as dozens of volunteers. It is a non-commercial organization that has set up an online library providing information about psychoactive plants, chemicals, and related topics. Its more than 30,000 documents range from images, research summaries and abstracts, media articles, experience reports, information on chemistry, dosage, effects, law, health, and drug testing to traditional and spiritual uses of psychoactive compounds. The sources of information Erowid gives access to are diverse spanning from peer reviewed research publications to subjective experience reports by anonymous drug users (critically reviewed and edited by the Erowid team) to fiction. Erowid emphasizes that these

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10 See http://www.who-umc.org/. The FDA runs a similar program called MedWatch: www.fda.gov/medwatch
documents represent multiple viewpoints and conflicting opinions and facts in order “to highlight specific areas of conflict.” The perspectives published on different drugs are positive, neutral, and negative alike. In its mission statement, Erowid stresses differentiation and responsible individual choice:

People are not trained or educated to make informed, rational decisions around managing their own consciousness. […] We believe it is key that people learn to differentiate between different psychoactives based on rational, articulable characteristics, and to understand the uses and risks associated with these substances.

An activist role is decidedly rejected:

The mission of Erowid is explicitly academic and we work to avoid becoming involved in specific legislative or political issues except to comment on factual matters touched on by these issues. While we believe that our work has harm reductive effects in the long term, harm-minimization is not the primary consideration we make when choosing what and how to publish. Erowid is a library. We believe that the creation of this nonpolitical library has desirable effects and is its own political statement.13

These two paragraphs already indicate the core problem raised by the existence of Erowid: the relationship between information on and consumption of psychoactive substances. In the early 1990s, the emergence of the Internet brought about a number of simple underground mailing lists and Internet newsgroups distributing information on psychoactive, especially psychedelic drugs.14 Simultaneously, new types of “recreational drugs”—many of them classified as psychedelics—became available and their consumption increased. Even though different factors have contributed to this phenomenon, the easier accessibility of information on these substances (including instructions on where to find them or how to synthesize them) has contributed significantly to their dissemination.15 Since many of these drugs were new (“designer drugs”) and their effects on humans not well understood yet, the occasional occurrence of dangerous adverse effects was inevitable.16 Critics of Erowid claim that the information presented on the website arouses curiosity and encourages experimentation with illicit drugs, especially among adolescents. They also complain “that the U.S. government, despite extensive and costly efforts, currently does not provide effective alternative sources of information about drugs on the Web, where partisan sites [such as Erowid] still get the attention of both search engines and users.”17 Despite his fierce criticism of Erowid (voiced in The New England Journal of Medicine), the pediatrician Edward Boyer has to admit: "Every physician I know, every law enforcement person I know who wants to find out the very latest in drugs goes to Erowid."18 Thus the information on new illicit drugs provided on the Internet itself seems to work as a genuine pharmakon serving as both poison

13 http://www.erowid.org/general/about/about_faq_vision1.shtml
15 Access to the drugs themselves has also been increased through the Internet as they can be ordered online. Thereby, even brand new or rather exotic substances can be purchased in remote areas without an avantgarde experimental drug scene. Cf. S. Schiavone, "[Illicit market of controlled drugs in Italy: new drugs and trends]," Ann Ist Super Sanita (?), no. 3 (2002). As to the problem of online sales of pharmaceuticals more generally, see B. Arrunada, "Quality safeguards and regulation of online pharmacies," Health Economy 13, no. 4 (2004). B. N. St. George, J. R. Emmanuel, and K. L. Middleton, "Overseas-based online pharmacies: a source of supply for illicit drug users?", The Medical Journal of Australia 180, no. 3 (2004).
17 Edward Boyer, M. Shannon, and P. Hibberd, "Web sites with misinformation about illicit drugs," The New England Journal of Medicine 345, no. 6 (2001): 471. For a description of this controversy, see also Erik Davis, "Don't Get High Without It. The Vaults of Erowid Supplies the Ultimate Trip Buddy: Information," L.A. Weekly (2004). The information provided on the website of the Drug Enforcement Agency (www.usdoj.gov:80/dea) on drugs such as 2C-T-7 or 2C-T-2, for instance, is scarce. Walt Disney’s antidrug website www.freevibe.com designed to reach teenagers in particular has no entries for these substances.
and remedy: It promotes risk-taking behavior, but it also enables drug users to take these risks in a more calculated and responsible manner as well as physicians to treat these users more effectively in the case of severe adverse reactions.\textsuperscript{19}

Erowid can be interpreted as an assemblage exercising pharmacovigilance in a field that has been excluded from the regulatory regime established by the state. The gradual illegalization of most drugs without acknowledged medical applications (alcohol, tobacco, and coffee being the most prominent exceptions) during the 20\textsuperscript{th} century recreated an uncontrolled drug market. While the FDA evolved as an efficient instrument to standardize manufacture and sale of food and drugs in the corporate world, which depends on licenses, seals of quality, etc., the tightening of regulations also gave birth to a seemingly wild and unregulated zone of collective experimentation.\textsuperscript{20} As its law-abiding counterpart, although at a much slower rate, this sector of clandestine pharmaceutics continuously introduces new—or reintroduces old—drugs to the market. As Philip Jenkins points out, every three to four years a new emerging “drug epidemic” is diagnosed by the Drug Enforcement Agency (DEA) and the media calling for action.\textsuperscript{21} By the mid-1980s, a number of synthetic drugs had already entered the marketplace in waves (methamphetamine, PCP, fentanyl, MDMA). Manufacturers circumvented prohibitive laws by modifying the molecular make-up of their drugs producing substances with effects similar to those of their predecessors, but not covered by drug legislation. The law always lagged behind. In 1986, the Reagan administration responded to the challenge of such “designer drugs” (a term coined around 1980 to designate new synthetic substances serving as “drugs of abuse”\textsuperscript{22}) by establishing a more supple, but highly restrictive legal framework: the Controlled Substance Analogue Enforcement Act. Instead of explicitly listing all substances declared illegal, the so-called Analogs Act anticipated the development of new drugs replacing those prohibited. As administrators were unable to keep up with the flow of new inventions they preemptively illegalized all substances “substantially similar” in structure or action to a controlled substance.\textsuperscript{23} On the black market created by illegalization, Erowid operates as a pharmacovigilance mechanism. Like the WHO’s Uppsala Monitoring Centre and the FDA’s MedWatch, Erowid—among other things—collects and processes data on adverse drug reactions (based on experience reports sent in by the drug users themselves instead of being mediated by physicians—a strategy, which the FDA has taken up in complementary manner since the mid-1980s as well\textsuperscript{24}). Thereby, Erowid establishes a regime of pharmacovigilance within the (virtual) community of experimental drug users. It exercises “postmarket” or rather “post-black market surveillance.”

**Pharmacovigilance as a Mode of Subjectivity**

\textsuperscript{19} This dilemma can be illustrated by the two cases presented by Wax, "Just a Click Away."

\textsuperscript{20} For a different example of how a highly regulated and formal market, the meat market of the European Union, spawns off a black market in postsocialist Poland see Elizabeth Dunn, "Standards and Person-Making in East Central Europe," in Global Assemblages: Technology, Politics, and Ethics as Anthropological Problems, ed. Stephen Collier and Aihwa Ong (London: Blackwell, 2004).


\textsuperscript{22} Ibid., 7.


\textsuperscript{24} Daemmrich, Pharmacopolitics, 137.
However, as there are no preclinical or clinical trials for drugs newly developed in the underground, the boundary between premarket testing and postmarket surveillance is blurred. What might count as a rough functional equivalent to premarket testing though is the controlled and cautious self-experimentation of Alexander and Ann Shulgin. Their books *PIHKAL* and *THIKAL* offer a close-up view on the fine-grained, highly observant attention to drug effects necessary to survive decades of self-experimentation with entirely novel compounds.²⁵ Alexander Shulgin explains his reliance on self-experiments by pointing out that the psychedelic potential of a compound cannot be determined by way of animal testing. Usually, he begins to ingest a new substance at a dose 10 to 50 times less than the known active level of its closest analog. He is well aware of the risk, which he is taking despite his careful proceeding:

> There is no completely safe procedure. Different lines of reasoning may lead to different predictions of a dosage level likely to be inactive in man. A prudent researcher begins his exploration at the lowest level of these. However, there is always the question, “Yes, but what if—?” One can argue AFTER the fact that—in chemist’s jargon—the ethyl group increased the potency over the methyl group because of lipophilicity, or decreased the potency because of ineffective enzymatic demethylation. My decisions, therefore, have had to be a mixture of intuition and probabilities.²⁶

However, Shulgin practices a form of vigilance that serves to anticipate and avoid more serious adverse reactions before they occur at higher dosages. Having lived an “experimental life” par excellence, Shulgin has developed a “prepared mind” merging Pasteur’s preparation for scientific discoveries with the preparation for the early detection of severe side effects of new drugs to which the term refers in the contemporary discourse of pharmacovigilance. In his self-experimentation, Shulgin has learned to exercise pharmacovigilance on a daily level making it his second nature:

> I have discovered that the very few drugs that are active in the human central nervous system which turn out to be dangerous to the investigator at effective dosages, have usually given some preliminary warnings at threshold levels. If you intend to continue being a live, healthy investigator, you get to know those warning signals well, and immediately abandon further investigation of any drug that presents you with one or more of them. In my research, I am usually looking less for indications of danger than for signs that the new drug may have effects that are simply not useful or interesting to me.

For instance: if I’m trying a new drug at a low dosage level and find myself showing signs of hyper-reflexia, an over-sensitivity to ordinary stimuli—getting jumpy, in plain English—this could be a warning that the drug might, at higher levels, cause convulsions. Convulsants are used in animal research and have their legitimate role in medicine, but they just don’t happen to be my cup of tea. A tendency to drift into reverie might be a warning sign; daydreaming is normal behavior when I’m tired or bored, but not when I’ve just taken a smidgen of a brand new drug and am watching for indications of activity. Or perhaps I become aware that I’ve been falling into brief episodes of sleep—micro-naps. Either of these signs could lead me to suspect that the drug might be a sedative-hypnotic or a narcotic. Such drugs certainly have their place in medicine, but—again—they’re not what I’m looking for.

Once it’s been established that the chosen initial dose has been without effect of any kind, I increase the dosage on alternate days, in increments of about a factor of times two at low levels, and perhaps times one and a half at higher levels.²⁷

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²⁷ Ibid.
encountering indications of imminent harm Alexander Shulgin first asked his wife Ann and then friends to join his self-experimentation. However, he is well aware that a dose, which seemed harmless to his own body, can have very different effects on somebody else.

There is no such thing as safety. Not with drugs and not with anything else. You can only presume relative safety. [...] The most I can ever do in regard to a drug [...] is establish what appears to be a relatively safe level for myself, for my own body and mind, and invite my fellow researchers to sample the sample material at what we decide is a relatively safe level for their particular bodies and nervous systems.28

In an area of research that aims at exploring completely novel drugs and the broad range of “altered states of consciousness,” which they induce, it is not always easy to distinguish between “effects” and “side effects.” The Shulgins describe a group experiment with a drug called 5-TOM, during which one participant lapsed into an alarming state of catatonia being paralyzed and incapable of communicating with his concerned companions. When the drug effect wore off several hours later he reported that he had been “in the most amazing place.” [Exact quote!] One man’s paradisiacal trip can be his friends’ worst nightmare. Consequently, further experimentation with 5-TOM was abandoned.29

From a pharmacological point of view, the validity of such “anecdotal” experience reports produced in this curious kind of “preclinical testing” is limited. The effects and side effects of a new “designer drug” can only be assessed more fully when it is already distributed on the black market being experimented with by a wider population. Here, its consumption does not take place under controlled conditions. This puts users at a serious risk. The psychedelic 2C-T-7, for example, another one of Alexander Shulgin’s creations, caused three deaths in 2000 and 2001. A freelance drug researcher going by the screen-name “Murple” conducted an e-mail survey on Erowid collecting data on side effects, dosage, experiences, etc., from more than 423 people. He or she also used Erowid to publish the results of this study in 2001. Analyzing the cautious self-observations of those who had responded to his survey Murple reached the conclusion that 2C-T-7 as well as its sibling 2C-T-2 have great potential as tools for therapy promoting “very insightful states of mind” and as “spiritual tools, enabling easier access to meditative states.” But Murple also warns that

[along with the potential for benefit, both drugs also present potential risks. This seems especially true for 2C-T-7 [...] used in moderation, both drugs seem to be quite safe. While there have been several serious incidents reported, we need to remember that this represents only a tiny fraction of total uses. There have been fewer than ten incidents of concern, out of thousands of total uses. This record looks even better when considering some of the reckless dosages taken by many people.

The biggest risk of course is that the risk factors are not really known. Until more research is done, it would be wise to proceed carefully.30

By facilitating such post-black market surveillance that integrates a multitude of watchful self-observations Erowid elevates the subjective mode of pharmacovigilance acquired by Shulgin and other members of the experimental drug scene to a collective and pharmacologically more significant level.

Drugs Futures 2025

Instead of a minister concerned with science the British government employs a Chief

28 Ibid., 156.
29 Ibid., 345-357.
Scientific Adviser who is not a politician, but a supposedly independent scientist. Currently, the chemistry professor Sir David King serves as the voice of science in Tony Blair’s cabinet. As head of the Office of Science and Technology King is also running the Office’s Foresight program. Its aim to “to produce challenging visions of the future in order to ensure effective strategies now.” Next to projects exploring the potential risks of flooding up to 80 years in the future, future risks of “cyber crimes,” and new and emerging infectious diseases the Foresight program has also conducted a project to address the question: “How can we manage the use of psychoactive substances in the future to best advantage for the individual, the community and society?” In his foreword to the Foresight report “Drugs Futures 2025?,” King states:

The greatest changes we will see in the twenty first century may be brought to us through developments in our understanding of the brain. These advances may offer revolutionary treatments for the brain […]. Anything we take can have unexpected and unwanted effects. Just as we may see new advances in the treatment of addiction, we could also see continuing use of existing and novel 'recreational' drugs. These drugs bring with them the potential for considerable harm with significant potential negative impact on individuals, families and communities. This is not a future we want to fall into unprepared.

Even though King points to the “potential for considerable harm” of new “recreational drugs,” the assumptions underlying the Foresight report differ significantly from those inspiring the ongoing “War on Drugs” and the resulting Analogs Act in the United States. The constant invention and consumption of new psychotropic compounds for non-medical purposes is taken for granted. Tightening regulations or even illegalization are considered as a last resort, but cannot guarantee security. In fact, they entail their own risks: “If management of the use of a specific substance is tightened, users may try to find a way around the change, which can lead to other forms of harm.” Lack of quality controls on the black market, high prices leading to drug-related crime, unhygienic conditions of drug administration, etc. put drug users and their fellow citizens at risk. Instead of advocating prohibition as the panacea for all drug problems the Foresight report suggests that promoting individual responsibility is as important as policy decisions. Accepting that the use of drugs old and new cannot be prevented it points to the positive potential of their continuous development and improvement:

New types of so-called 'recreational' psychoactive substances are being developed:

— Scientists have been able to separate the effect of one psychoactive substance from its addictive properties. This could pave the way to non-addictive 'recreational' drugs, but as with any new substance the risks will need to be assessed also.

— A psychoactive substance has been developed that reduces the side-effects of 'recreational' drugs. Such compounds might allow users to shape their drug experience.

— Scientists believe that they could produce a 'recreational' substance with similar effects to alcohol but fewer harms.

The tone of the report oscillates between visionary optimism and concern: “We are on the verge of a revolution in the specificity and function of the psychoactive substances available to us. […] The challenge is that every advance will bring risks, so there are no easy choices.” In tune with this diagnosis—“there are no easy choices”—Foresight refrains from advocating a particular course of action. Nor does it attempt to forecast the future. Instead Foresight presents four fictional socio-economic scenarios ranging from a Brave New World-like year 2025 to an extreme prohibitionist situation and from an economically highly restrained health care system significantly cutting down drug prescriptions to a world of small

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31 Foresight, "Drugs Futures 2025?," (London: Office of Science and Technology, 2005), 3 (Executive Summary and Overview).
32 Ibid., 1 (Executive Summary and Overview).
33 Ibid., 8 (Executive Summary and Overview).
34 Ibid., 4 (Executive Summary and Overview).
manufacturers using open-source technologies to quickly create customized precision treatments matching individual disease profiles. These scenarios are neither presented as true predictions nor as desirable utopias. Instead they are supposed to serve as bases of workshop sessions with upwards of twelve participants who can employ the scenarios in different ways (“gaming,” “windtunneling,” “reverse engineering”). These imagined futures are treated as exercises helping policy makers to develop a particular kind of future-orientation, which is meant to improve their planning in the present.

However, Foresight does not presume that the future of drug use can be completely determined by policy decisions. Too many unknown factors are involved to guarantee a certain outcome. The report repeatedly emphasizes the uncertainty of the future. Therefore, what is more important than planning is to be watchful and to ensure the capability of dynamic responses to newly emerging threats to the population.

It will always be important to respond quickly to new harmful patterns of use of 'recreational' drugs, ideally to allow intervention before those patterns become embedded in culture. Developing mechanisms which can look for and identify harmful new patterns early will be important to achieve this, as will the creation of a dynamic regulatory structure that can be adjusted as clear new evidence emerges.

“Mechanisms which can look for and identify harmful new patterns” of drug use can be regarded as expansions of institutionalized pharmacovigilance. In the realm of non-medical drug use, applications are not primarily (if at all) determined by professional advice. Hence, surveillance of new drugs and their side effects needs to be complemented by observations of their uses.

The Limits of Vigilance

Vigilance has recently become a key element of different security apparatuses that are meant to protect populations from terrorism, biohazards, natural catastrophes, or drugs. In his 1977/78 course “Securité, Territoire, Population,” Michel Foucault outlined the concept of security in opposition to discipline and law. The law constitutes a purely negative form of normativity, which prohibits certain acts on a certain territory, e.g. the manufacture and sale of particular drugs in the United States. Discipline ideally aims at a continuous panoptic observation of individuals responding even to minute deviations from a norm by disciplinary measures. Close monitoring of all people having to do with illicit substances can serve as an example: Drug scenes are infiltrated by undercover narcotics officers; dealers are prosecuted; potential consumers are tested for drug use; pharmaceutical companies and scientists are granted revocable licenses for handling and/or producing certain substances while being subject to regular supervision. However, total control of all citizens has remained a totalitarian utopia. Despite the establishment of a massive juridico-disciplinary apparatus the “War on Drugs” has failed to effectively repress drug trafficking and consumption in the United States (in fact, cocaine prices declined continuously during the 1980s indicating a growing availability of the drug). As neither proscriptions nor the surveillance of individuals guaranteed the desired outcomes, a third strategy was developed. The emergence of security as a form of government can be interpreted as a response to the limits of legal and disciplinary means. Here, the aim of total control is replaced by the modulation of a pre-existing milieu in order to regulate a population at large. While discipline is based on sustained interventions

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36 Ibid., 8 (Executive Summary and Overview).
security adopts—at least to a certain extent—a *laisser faire* attitude only intervening as a last resort and after observation and evaluation of the specific tendencies of a given situation.\(^{37}\)

The tension between these different strategies plays a prominent role in the Foresight report. In the discussion of a number of choices the UK will have to consider with respect to its policy concerning “recreational” psychoactive substances, one of the options presented is to

> Seek to identify as early as possible any emerging threats, including new drugs, new modes of delivery or new cultures of harmful use. While there is value in knowing what is on the horizon, it is difficult to know which emerging issues will be important and how to respond in order to dampen rather than fuel the problem.

or to

> Wait until significant problems emerge and then focus resources on those issues. This risks allowing harmful use to become embedded in society and making it more difficult to respond.\(^{38}\)

What is at stake here is the right balance between discipline and security. Both strategies are based on vigilance, i.e. surveillance of certain trends and events in the population. However, the first option emphasizes early and continuous intervention (discipline) while the second one advocates a sustained state of vigilance, in which action is taken only occasionally to (re-) direct the population into a desired direction (security).

In both cases, vigilance serves as a key element of government. However, vigilance cannot be exercised effectively in a top-down manner only. In the role of a panoptic observer, the state would be overstrained. After the terror attacks on the public transport system in London in 2005, the BBC repeatedly asked British citizens to be “vigilant” and to report any suspicious activity or items to the police. In order to work vigilance requires the cooperation of the citizenry, i.e. a self-observation of and by the population (and even when helped by the population the police had to work at the very limit of its forces to follow up every hint). This, in turn, requires the formation of vigilance as a mode of subjectivity, which is inseparable from the formation of individual responsibility.

One important way of reaching this goal is the distribution of information—be it police portraits or basic medical and pharmacological knowledge, which allows consumers of new drugs to recognize, evaluate, and report unexpected side effects. This is the strategy pursued by Erowid: The website provides a detailed account of the effects of a wide range of psychoactive substances based on scientific literature as well as experience reports. To prevent the reader from acquiring a false sense of safety, information on every drug is accompanied by the warning:

> Every individual reacts differently to every chemical. Know your Body – Know your Mind – Know your Substance – Know your Source. Erowid’s dosage information is a summary of data gathered from users, research, and other resources and should not be construed as recommendations. Individuals can respond differently to the same dosage. What is safe for one can be deadly for another.\(^{39}\)

A responsible user will approach a new drug cautiously and report back any untoward events to Erowid to inform future users of the drug about potential risks. Vigilance is based on such an exchange between vigilant individuals and centralized organizations, which collect, process, and distribute information—returning the results of their analyses to the watchful

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\(^{38}\) Foresight, "Foresight," 10 (Executive Summary and Overview).

\(^{39}\) For example, at http://www.erowid.org/chemicals/2ct7/2ct7_dose.shtml
citizenry, which originally provided the raw data. But, in this case, information does not only serve to spread knowledge, but also to raise awareness.

Such dissemination of vigilance in a population is an element in a strategy of governing a world too complex for legal and disciplinary measures alone. As a whole an alert population can observe more than the most hypertrophied police state. The abundance of information registered is counterbalanced by moderation on the level of intervention. Reacting to every single clue would bind too many capacities. However, there is also a limit to vigilance. Attention is a scarce resource, too. It has to be focused. Paying attention to too many things at a time would result in excessive demands on the observer. When being prescribed a new antibiotic, most consumers do not have enough time and knowledge to conduct the kind of research scientifically literate members of the experimental drug scene engage in when trying out a new drug. Most patients need to trust their doctor, who, in turn, needs to trust the FDA or other national and supranational regulatory bodies. Trust is a key element of an economy of attention. As Niklas Luhmann has argued, trust serves as an alternative strategy of dealing with complexity. 40

The history of the FDA can be read as a construction of a regulatory apparatus in response to a series of drug scandals involving acetanilide in 1906, sulfanilamide in 1937, and thalidomide in 1961. 41 The agency employed disciplinary and juridical measures to control the products legally available to the population. Thereby, it rebuilt trust in medicines. The emergence of pharmacovigilance added elements of security to this apparatus. Its reform due to the liberalization of the review process of new drug applications in response to AIDS activism in the 1980s assigned an important role to pharmacovigilance. However, in the meanwhile the situation has changed again. In 1992, the US government and the pharmaceutical industry reached an agreement that the industry would pay money to the FDA, which the FDA had to use to hire more drug reviewers and speed up the review process. This deal seemed to help everybody: Neither patients nor companies would not have to wait unduly while the FDA had a bigger budget and staff at its disposal. Subsequently, it managed to half its review times. However, post-approval monitoring of drug side effects is not in the interest of pharmaceutical companies. The 1992 agreement brought about a situation in which the agency had to shift money out of its postmarket surveillance programs into new drug reviews to satisfy the requirements of the agreement and industry demands. 42 The resulting cutback of pharmacovigilance led to the two latest drug scandals and the current reconfiguration of the drug safety system in the United States. In the early 2000s, the discovery of an antidepressant-induced increase in suicide rate among teenagers as well as an increase of heart attacks and strokes due to COX-2 inhibitors such as Vioxx put the FDA under severe political pressure. It had taken the agency four years to demonstrate that those taking Vioxx were suffering disproportionately from heart attacks. Consequently, the FDA was accused of having failed to protect the population against drug dangers. It responded to this criticism by tightening its regulations. The requirements for both pre- and postmarket testing have been raised significantly.

For drugs approved in the first half of 2005, the average time from application to approval was 29 months, compared with an average of 16 months for drugs approved in the first half of 2004. And the F.D.A. is more often asking that drug makers study the safety of their medicines after they are approved. 43

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It has also been discussed whether drug makers will have to pay for independent continuing post-approval surveillance of their products. Here, stricter regulations and an increase of pharmacovigilance have been used in order to restore trust in drugs—and the FDA. Hence, vigilance cannot only serve as an alternative to trust, but also as its basis.

But the FDA’s second strategy of responding to its critics runs counter to this restoration of trust. To avoid being blamed for unexpected adverse drug reactions the FDA has begun to issue warnings even if there is no clear evidence. Its new commissioner Lester Crawford said that the agency could no longer wait until risk information is proved but must communicate its uncertainty to the public. Often it does so by advising patients to speak to their doctors about questionable medications. But, as one medical practitioner put it, “the physicians don’t know what to tell the patients, either.” And a colleague of his added: “They’re just passing the blame onto the physician. […] They’re just trying to say that they warned us.”

In the case of the experimental drug scene assembling around Erowid and the creations of the Shulgins or the desperate AIDS patients participating in underground drug trials in the 1980s, it is undisputed who is taking responsibility: It is the consumers themselves who are willing to take the risk of ingesting drugs not well known. In the public medical system, the situation seems more controversial. While consumers, for the most part, are regarded as medically and pharmacologically illiterate and—in the Kantian sense—immature, those producing, regulating, and prescribing drugs are passing the bug to each other. However, in the management of an uncertain future, someone needs to take over responsibility. How the four parties involved (pharmaceutical industry, regulatory agencies, doctors, and patients) will redistribute accountability will significantly shape the forms pharmacovigilance will take in the future.

44 Harris, "At F.D.A., Strong Drug Ties and Less Monitoring."
45 Harris, "F.D.A. Responds to Criticism With New Caution."
LITERATURE


