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Psychiatric Drugging: Forty Years of Pseudo-Science, Self-Interest, and Indifference to Harm

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The "modern" era of psychiatric drug treatment began with the introduction of chlorpromazine into the chaotic mental hospital setting in the 1950s as a new psychotropic agent for controlling excitement, agitation, and aggressivity. In that setting the urgency of management problems operated to shrink the complexity of the patient as a psychosocial being down to specific "symptoms" targeted for chemical subjugation. From this beginning - a chemically produced quieting or "tranquillisation" - there emerged a revitalised psychiatric movement to expand the "strictly medical" understanding and treatment of psychological disturbance that acknowledges no limits. This state of affairs has achieved a position of dominance and respect in the mental health industry, based upon social forces operating within psychiatry as a profession and outside of psychiatry in the larger political-economic realm. The catastrophe of widespread and expanding medically-produced disease has failed to alarm psychiatry into taking stock of the determinants of the catastrophe - indeed the existence and magnitude of the tragedy is barely recognised within psychiatry. This conclusion is illustrated by detailed examination of the psychopharmacologic agents alprazolam (Xanax) and fluoxetine (Prozac).

In 1970, Pierre Deniker, who along with Jean Delay introduced chlorpromazine into psychiatry (in 1952), published a retrospective on the discovery of chlorpromazine and reviewed subsequent progress in psychopharmacologic treatments of "mental disorders." Deniker referred to the use of centrally active drugs to treat mental conditions as providing treatment "in a strictly medical sense," and he clearly regarded this as a triumph for medicine. As to the question of aetiology why is it that the patient has wound up in this unfortunate condition? Deniker takes for granted that this is a puzzle whose solution lies in the realm of conventional medical research into disease causation. Both erroneous ideas - that "functional" psychiatric disorders are in reality due to organic morbidity, and that disturbances in the psychological realm can be successfully treated pharmacologically - can be regarded as the pillar upon which contemporary biopsychiatry rests.

My primary purpose in this paper is to critically examine the latter pillar, that is, the conviction that a happy outcome can result from bypassing the social-interpersonal route of influencing a person's psychological life and substituting direct chemical intervention in neurophysiology. In short, I aim to evaluate the claim that - etiopathogenesis aside - it is simply an empirical fact that

psychiatric patients do benefit from pharmacological treatment, and moreover that the benefits of such treatment definitely outweigh the (organic and psychological) costs. My thesis is that the pharmacological approach must fail in its clinical aims and also damage patients because (a) any drug potent enough to alter psychological life is of necessity toxic and pathogenic, since to be effective it must disrupt normal brain physiology, and (b) the disruption of normal neurophysiological mechanisms, including integrative and homeostatic mechanisms, will eventually exacerbate the original symptomatology or transform it via drug-produced neuropathology.

In the first part of this paper, I illustrate both aspects of the above thesis by reviewing what is known about the effects of "antipsychotic" drugs, since a good deal of the "new" (i.e., post-chlorpromazine) biopsychiatry's reputation rests upon the alleged efficacy of pharmacologic agents designated as "antipsychotic." This review will naturally raise the question of why psychotropic drugs are being advanced ever more vigorously by the profession of psychiatry. The answer to this question will be found outside of scientific reasoning and evidence in sources of influence which shape all large scale social developments. In the second part of the paper, I go over the same ground in even more detail with regard to two recently introduced psychotropic agents (Xanax and Prozac). The second part of the paper will show that the catastrophic consequences of the "antipsychotic" drugs has done nothing to dampen enthusiasm for the "strictly medical" approach to treatment. I do not use the word catastrophe lightly or merely rhetorically. Mosher and Burti (1989), for example, remark that American psychiatry has "created a new species, the tardive dyskinesic" (p. 3; note that Loren Mosher is a former NIMH Chief of the Centre for Studies of Schizophrenia). While "tardive" dyskinesia is so named because this form of neurological motor dysfunction does not typically appear immediately or soon after neuroleptic treatment begins (tardive means "late appearing"), Casey and Keepers (1988) point out that acute motor and mental impairments occur in up to 90% of patients treated with neuroleptics. Such acute neurological syndromes - produced by the "medicine" itself - may then be treated with additional "medication," but even if this does ameliorate the original medication-produced morbidity in some patients, the long-term consequences of adding still other centrally active drugs is unknown and is simply not a topic of investigation.

It might at first glance appear surprising that the "antianxiety" and "antidepressant" drugs have been applied so successfully to patient groups that are in the main less impoverished, stigmatised, and socially degraded than the typical recipient of "antipsychotic" drugs, Although this is indeed a complex topic, I can mention at least two pertinent part-explanations in my introductory remarks: (a) the cultural and professional success of medicine does not actually depend upon the safety and "efficacy of medical treatment (Broadhead and Facchinetti, 1985; Cochrane, 1972; Dubos, 1965; McKeown, 1976; Roper, Winkenwerder, Hackbarth, and Krakauer, 1988; Silverman and Lydecker, 1980); (b) the push from within psychiatry to emphasise drug treatment and the "medical basis" of psychological distress has only been amplified since the introduction

of chlorpromazine into America in 1954 (see ahead).

What Can Be Learned From Forty Years Experience With "Antipsychotic" Drugs

Drug-Produced Effects "On the Side"

Non-medical psychotherapists (such as myself) may find it puzzling how a drug-effect like akathisia (a term used to describe very pronounced drug-produced restlessness and agitation) can be addressed by psychiatrists as a "side effect," and in this manner be virtually dismissed as tangential to the clinical efficacy of a medicine (e.g." chlorpromazine). Although akathisia can vary in severity when it is present, the term is only used to designate a drug-produced neurotoxic effect when the patient is clearly suffering (based upon complaints and/or clinical observation). In fact, akathisia can become so unbearable that it directly precipitates impulsive suicide attempts and successes (Drake and Ehrlich, 1985; Shaw, Mann, Weiden, Sinsheimer, and Brunn, 1986; Shear, Frances, and Weiden, 1983; Van Putten and Marder, 1987). Reading Deniker's 1970 retrospective, in which he makes it clear that parkinsonism, akathisia, akinesia (profound difficulty in initiating movement), and other drug-effects of chlorpromazine were recognised in the early days of its clinical trials, it would appear that a side effect is any drug-effect that does not ameliorate the clinical symptom(s) or sign(s) for which its use is intended. The upshot is that, within the medical framework, a drug like chlorpromazine is considered "effective" for treating (say) psychotic agitation even though it simultaneously produces parkinsonism and other neurological syndromes.

In retrospect, the modern era of psychiatric drugs got off to the worst possible start due to its clinical application in the mental hospital situation and for the purpose of quieting and rendering more tractable severely agitated or violent patients. The urgent need to quiet and render agitated patients more manageable presented an irresistible temptation to reduce the totality of the patient's psychic life, subjectivity, and social functioning to the level of custody (read: becoming less trouble for the custodians) [Elkes and Elkes, 1954; Kalinowsky, 1958; Lehmann; 1955, Lehmann and Hanrahan, 1954]. In those early days there was no talk at all of chlorpromazine, etc. having "antipsychotic" properties - in fact, this was explicitly denied (which of course raises the question of how the very same drugs emerged in the 1960s as "antipsychotics"). Indeed, conditions in the US state mental hospital system were so barbaric (Kiesler and Sibulkin, 1987; Valenstein, 1986), and expectations concerning the fate of hospitalised patients so dismal (Klerman, 1978; NIMH Psychopharmacology Service Centre Collaborative Study Group, 1964), that the discovery of chlorpromazine and related drugs could be likened to the use of morphine in a rough field hospital for severely wounded soldiers. In short, psychological recovery or even substantial improvement was not at issue; at issue was finding some substitute for the straightjacket and equivalent methods, and for the cumbersomeness, morbidity, and mortality that went along with other "somatic" methods of palliation/control available at the time (insulin shock

and coma, metrazol shock, prolonged barbiturate sleep, lobotomy, etc.). This hardly seems an auspicious start for a revolutionary "remedicalization" of psychiatry, since as Scull (1984) rightly points out, at best the new psychotropic agents introduced in the 1950s could accomplish little more than a quieter hospital environment. However, potent political, economic, and professional forces were (and are) at work which seized upon the new "antipsychotic" agents as the basis for expanding pharmacologic treatment to "disorders" that did not even officially exist in the 1950s (see ahead).

As mentioned above, one immediate consequence of treating specific symptoms "in a strictly medical sense" was (and is) that a drug can be regarded as "effective" despite the fact that it simultaneously produces unwanted and even disastrous additional consequences. Unwanted consequences are treated as part of a cost-benefit package that must enter into clinical decisions about the use of any medicinal drug. The "cost" of a drug in terms of its clinical use is obviously a complex matter of judgement. The point I make at this juncture is that the "strictly medical" drug treatment of unruly mental hospital patients did not include any interest at all in the patient's own views on the costs versus the benefits of the treatment. Thus for a long time - and in many ways up to the present - it did not seem at all contradictory (within psychiatric thought) to state that neuroleptics were clinically effective despite producing agitation and anxiety (akathisia), or apathy and indifference, or that they made even simple actions too effortful to attempt, rendered thinking painfully slow and laborious, etc.

The issue of "side effects" still requires further refinement. Although an unwanted effect like parkinsonism or dystonia (painful muscular contractions or spasms) may be identified as a side effect, subjective reactions to adverse drug effects are passed over without recognition or comment. Thus what is absent from psychiatric reports is discussion concerning what it means to patients to find themselves unable to move, to control the shaking of their limbs, to be forced into bizarre postures due to painful muscle contractions, and so on. In short, suffering is excluded from what is recognised as a side effect. Likewise excluded from recognition is the impact that side effects may have on the person's status as a social being, and how impairment in the social-interpersonal realm may act back upon the experience of living (e.g., parkinsonism may impair the ability to swallow, resulting in copious amounts of saliva collecting in the mouth and overflowing in streams from the lips and down the chin). Drug-induced suffering, both the suffering directly produced by the drug itself and the further suffering evoked by the experience of impairment, disability, social stigma etc., are discussed obliquely in terms of how well or not the drug is tolerated, usually in terms of patient compliance. The pervasive phenomenon of poor compliance with neuroleptic medication led directly to the development of new injectable "depot" forms of neuroleptics, a technical advance devised precisely for the purpose of outmanoeuvring subjectivity (meaning that left to their own devices many individuals will not take their medication, usually a decision made on the basis of how the medication makes them feel and the impairments that the medication produces).

Occasional papers which acknowledge an inner world of subjectivity which cannot be dismissed out of hand represent the extreme liberal wing of psychopharmacologic thought (Diamond, 1985, and Van Putten, May, Marder, and Wittman, 1981, can be cited as rarities). Again, concern for the individual's experience as a complex psycho-social being - which would seem, would it not, to be the actual subject matter of psychiatry - is largely eliminated from biomedical treatments. Thus, it has been left to successful litigation to bring the consequences of neuroleptic treatment forcefully to the attention of psychiatry (Brown and Funk, 1986; Deveaugh-Geiss, 1979; Gualtieri and Sprague, 1984).

Psychopharmacologic Treatment Revives the Conviction That What Is Being Treated Is a Medical-Organic Condition

It is also obvious from Deniker's paper that focusing attention on 'symptoms" which most lend themselves to using descriptive language drawn from or inspired by organic medicine ("thought disorder," "pressured speech", "hallucinations," etc.) has the effect of rendering the patient's social history and present social circumstances irrelevant. In this manner the usual fact that virtually nothing is known or understood about the patient's social-psychological history and course of development becomes unproblematic from a practical treatment perspective. That point is made with some candour near the end of the influential 1964 research paper published by the NIMH Psychopharmacology Service Centre Collaborative Study Group, entitled "Phenothiazine Treatment in Acute Schizophrenia." Under the heading "Implications for Public Health Programs," the authors advance the idea that both short and long-term treatment of schizophrenia via phenothiazines eliminates the need for "highly trained" psychotherapy personnel (p. 259). The concluding paragraph is devoted to thanking various private, for-profit pharmaceutical companies for donating the phenothiazines under "investigation." In 1970 Deniker was still willing to acknowledge that successful drug treatment in schizophrenia and other "mental disorders" occurs despite unknown aetiology and pathophysiology. In practice, of course, drug treatment for specific symptoms - the "strictly medical" approach - attracts attention to research into just how and why the drugs produce the psychopharmacological and physiological effects that they do, and also into ever more technical searches for the abnormal physiology assumed to be responsible for the emergence of the symptoms in the first place. At this point, I will simply advance the idea that both from the perspective of the medical-hospital-pharmaceutical industry, as well as the funding and research interests of the biological science community, the conviction that physiological dysfunction is the fundamental case of mental disorder is too valuable to abandon. As a practical matter the "strictly medical" approach to mental disorder - chemical treatment of narrowly defined symptoms and/or signs - dissolves the complexity of what psychopathology is or how it develops by establishing a project that fits into the conventional medical paradigm. This brings us back to the problem at hand - the ensuing epidemic of iatrogenic damage.

Longer-Term, Irreversible Drug-Produced Neurological and Psychological Damage

Looking back to the 1950s, it appears that that "new era's" origin in the mental hospital situation, with success defined as the management of patients, in addition to the prevailing nihilism of prognosis (NIMH Psychopharmacology Service Centre Collaborative Study Group, 1964. p. 256), started the path downward to the present predicament. Schizophrenia was treated as if it were a uniformly chronic and deteriorating condition, which made it justifiable in the minds of psychiatrists to apply "heroic" medical measures. The justification for medical treatment with what were clearly neurotoxic substances was no different than the justification for lobotomising the brain or resorting to other heroic (i.e., desperate) medical interventions (see Valenstein, 1986, for a review of pre-chlorpromazine treatments of schizophrenia, especially lobotomy). Nowhere in Deniker's 1970 retrospective does he entertain the possibility that the dismal fate of schizophrenics could in any way be connected to the brutal and inhumane conditions of life to which they were subjected in hospital, although he makes no bones about hospital conditions when he first put chlorpromazine to use. It would seem that only the conviction that schizophrenia (and other conditions) is a disastrous and ineluctably progressive organic disease would allow him to admit the following:

"...it might have been feared that these drugs, whose action compares with that of encephalitis and parkinsonism. might eventually induce irreversible secondary neurological syndromes. Such effects cannot be denied: it has been known for some years that permanent dyskinesia may occur in patients treated with neuroleptics and drugs with neurological activity Finally, in certain predisposed subjects: potent neuroleptics may cause actual "malignant" syndromes with hyperthermia." (p. 163)

This is a staggering admission, but the full implications of it still may not be clear to readers who take "dyskinesia" to refer only to disorders of movement (although, as I have discussed, substantial impairment in this area compromises or even destroys two fundamental dimensions of living: free movement in space, that is, self-controlled locomotion, and control of and feeling at home in one's own body). Deniker is actually admitting that clinical experience with neurological diseases could have predicted the emergence of irreversible neurological syndromes beyond simple disorders of movement. Gualtieri and Barnhill (1988), in the course of discussing tardive dyskinesia among mentally retarded children and adolescents (previously treated with neuroleptics) provide the following comment concerning the long-term consequences: "No disease that afflicts striatal tissue is known to have only motor consequences; Parkinson's disease and Huntingdon's disease are only two examples" (p. 150). In a later paper (1993, p. 105) on the emergence of tardive akathisia in mentally retarded children who have been treated (for "behaviour problems") with neuroleptics, Gualtieri remarks "If behavioural instability and intellectual impairment are inevitably a part of Parkinson's disease, Huntingdon's disease, and Wilson's disease [all progressive diseases of the basal ganglia], should they not also occur in tardive dyskinesia?" This is a rhetorical question answered in the affirmative by his clinical research. To remove all doubt about whether extrapyramidal symptoms observed during the

1950s should have resulted in at least the tentative conclusion on the part of the medical community that neuroleptics would eventually produce wide-ranging mental impairments, I can only cite Deniker's statement that "It was found that neuroleptics could experimentally reproduce almost all symptoms of lethargic encephalitis. . ." (p.160), along with the further statement I have already cited above. These statements show that the clinical course and long-term consequences of the lethargic encephalitis pandemic, which afflicted more than a million people from 1916 to about 1930 (reviewed by Breggin, 1993), were known to Deniker and many psychiatrists and neurologists during the 1950s when neuroleptics were introduced into psychiatry.

The Non-Existent Dimension of "Natural Course" in Psychiatric Thought Concerning the Costs and Benefits of Drug Treatment

A puzzle has emerged from the preceding review of neuroleptic-produced neuropathology and personal suffering. The puzzle is this: How can so much iatrogenic damage be justified? This issue must hinge on the "natural course" of schizophrenia, since on rational grounds only a "natural course" which is more severe, chronic, and unremitting than the consequences of the medications themselves can serve to justify serious and wide-ranging iatrogenic damage which is itself highly prevalent and predictable. A more complete picture of the full damage (costs) produced by psychotropic drug treatment must also include the shift of attention away from the psycho-social origins, development, and consolidation of the person's psychological problems, the downplaying of psycho-social forms of treatment as well as the diversion of funds away from such treatments, the minimisation of current conditions of living in apprehending the person's present psychological state, and the full range of drug-produced physical and mental impairments as undermining the person's capacity to put to good use whatever psychotherapy or social services might remain available. I can provide no rational answer to this puzzle because there does not appear to be one. The drug-treatment literature from the 1950s to the present rarely discusses the issue of "natural course," even when the focus of the discussion is precisely on the severity and prevalence of drug-produced neuropathology. It is simply taken for granted as self-evident that no measures are too extreme (too risky or costly) when it comes to treating schizophrenia. For example, even a 1982 volume of papers devoted to the subject of tardive dyskinesia, under the editorship of a prominent biological psychiatrist (Joseph DeVeaugh-Geiss), fails to discuss the core issue - the severity, chronicity, predictability, and uniformity of the "condition(s)" for which neuroleptics are prescribed. In the preface, DeVeaugh-Geiss presents the dilemma of neuroleptics as a choice between two evils: "the disability of a chronic psychosis or the disability of a treatment-induced movement disorder that is untreatable" (p. vii). No further discussion is offered, which makes it clear that DeVeaugh-Geiss takes for granted both that psychosis is chronic and that no viable treatment possibility other than neuroleptics exists. This inference is further supported in the lead paper (by DeVeaugh-Geiss) of the volume, entitled "Tardive Dyskinesia: Phenomenology, Pathophysiology, and Pharmacology." In the context of discussing other diseases of the basal ganglia along with treatment possibilities, DeVeaugh-Geiss

notes that:

"...most experts agree neuroleptic drugs should be used to reduce movement disorder symptoms in patients with Huntingdon's disease. Whether or not chronic neuroleptic treatment might worsen Huntingdon's disease is unknown at this time, although the theoretical risk exists. The inevitable progression and relatively short course of Huntingdon's disease alters the risk/benefit ratio substantially in favour of using neuroleptics in Huntingdon's disease, as opposed to their use in tardive dyskinesia where the risk may far outweigh the benefit.". (1982b, p. 9)

The above summary of medical treatment considerations crucially misses the real point, which is that neuroleptic-produced tardive dyskinesia is an iatrogenic (medically produced) disease, not an idiopathic (naturally occurring) disease like Huntingdon's disease, and irreversible tardive dyskinesia is iatrogenically created in the treatment of a "condition" which does not inevitably progress, is not uniformly or inevitably chronic, is certainly not a "short course" affair, and may actually improve or remit years or even decades after the patient is first diagnosed, in the complete absence of toxic medication. My point, to reiterate, is that what is at the core of the issue of serious iatrogenic damage - namely the natural course of the disease - is either not discussed or summarily characterised in a manner that is completely erroneous. Further evidence for my contention that the natural course of schizophrenia is a non-issue in the drug-treatment literature is provided in the same volume of papers by George Crane (who deserves much credit for his publications of neuroleptic-produced neuropathologies over the years). In a valuable paper on the long-term effects of neuroleptics on the central nervous system, Crane somewhat obliquely admits that the long-term natural course of schizophrenia is a non-issue in the following manner:

"...The progress of schizophrenia to a defect state of severe mental deterioration [due to long-term neuroleptic treatment) is a slow process. It must be measured in decades rather than years. Longitudinal studies of 20 - or 30 - years' duration have not been made on schizophrenics since drugs were introduced in psychiatry." (1982, p. 80)

Meanwhile, evidence of mental impairments, defects, deficits, and deterioration, as well as physical evidence of CNS pathology, discovered in patients who have not been followed longitudinally in comparison with same-diagnosis patients who have not been treated with neuroleptics (a practically non-existent population in America) is now actually being advanced as evidence that schizophrenia is a brain disease (reviewed in Breggin, 1990). Evidence of neuropathology and/or mental impairment in diagnosed schizophrenics has an ambiguous meaning if such patients have also been subjected to prolonged institutionalisation and/or powerful centrally active drugs. Despite this, both the absence of neuropathological findings in the pre-chlorpromazine era (also reviewed in Breggin, 1990), and the tardive improvement in schizophrenics who have not been treated with neuroleptics (based upon European longitudinal and retrospective studies, M. Bleuler, 1978, in the former case and Ciompi and Muller, 1976, in the latter case; see also Harding, Brooks, Ashikaga, Strauss, and Lenderl, 1987, for a summary of the unique Vermont experiment initiated by George Brooks in 1955) should serve to dampen enthusiasm for the current wave of claims that schizophrenia is a brain disease.

Perhaps it has not escaped the reader's attention that, unlike a real idiopathic neurological disease like Huntingdon's chorea, the "natural course" of schizophrenia has been shunned in the drug-treatment literature. There are several reasons for concluding that there is no natural course of schizophrenia: (a) the precise criteria for "schizophrenia" both continue to change over time and fail to discriminate "schizophrenics" from other patients who present with overlapping symptoms (Carson, 1991; Ciompi, 1984; Fenton, Mosher, and Matthews, 1981; Kirk and Kutchins, 1992; Mirowsky, 1990; Strauss et al., 1979); (b) the natural course of a disease is best reserved for those diseases (like Huntingdon's chorea) which traverse a path of inevitability and virtual invariance in the absence of effective medical (somatic) intervention - in this sense schizophrenia is essentially the antithesis of a disease which follows a natural course (M. Bleuler, 1978; Ciompi and Muller, 1976; Harding et al., 1987; Strauss, 1986; Wing, 1987; the extreme variability in course and outcome, in fact, strongly argues against the view that schizophrenia is at root a neuropathological disease); (c) from the point of diagnosis onward, the course of schizophrenia is responsive to purely social-interpersonal variations in the patient's life (an outstanding example here is Vaughn and Leff, 1976).

Non-Scientific Influences on the Development of Psychiatry Since the Early 1950s

Since there appears to be no rational explanation for the development in psychiatry of routine reliance (both short-term and maintenance) on psychotropic drugs for the treatment of schizophrenia or anything else, it is necessary to turn to considerations external to the facts of "mental illness" and the actual properties and consequences of psychiatric drugs in order to find a way to comprehend the beliefs and practices which have so powerfully established themselves. It hard to see how the drawbacks and perils of psychotropic drug treatment could have been so widely minimised were it not for powerful shaping factors external to psychiatry. It is also hard to see how psychiatric experience with sundry somatic treatments in the pre-chlorpromazine era (Valenstein, 1986) could have failed to induce a more sceptical and cautious attitude within psychiatry where it not for - again - powerful external factors.

The external factors to which I refer are already widely discussed outside of psychiatry. The problem is not to identify or provide evidence for the existence and influence of such factors, but to somehow overcome psychiatry's refusal to seriously consider their impact on theory and practice. Frequently discussed factors include the following:
1. The fiscally determined demise of the old state mental hospital system [Aviram et al., 1976; Brown, 1985; Estes and Harrington, 1981; Estroff, 1981; Gronfrin, 1985; Johnson, 1990; Kiesler and Sibulkin, 1987; Klerman, 1979; Reardon, Rifkin, Schwartz, Myerson, and Siris, 1989; Scull, 1981, 1984; Stone, 1975].
2. The growing competition (economic, ideological, theoretical, etc.) from encroaching professions, which produced the practical necessity to emphasise biomedical treatment possibilities (Breggin, 1991; Cohen, 1993; Garfield, 1986; Halleck, 1971; Menn and Masher,

1982; Mosher and Burti, 1989; Mosher and Menn, 1983; Rothblum et al., 1986; Vega and Murphy, 1990).
3. The desire to re-establish the medical (i.e., organic) definition and understanding of all forms of psychological distress/dysfunction/deviance [in addition to the sources listed under (2), above, see also Coles, 1987; Klerman, 1988a, 1988b].
4. The counter-revolutionary rebound evoked by the anti-psychiatry movement of the 1960s, and by the levelling effects on authority and prestige resulting from multi-disciplinary "teams" in community mental health settings [Kirk and Kutchins, 1992; Mosher and Blirti, 1989; Vega and Murphy, 1990].
5. The development of a massive financial subservience to the pharmaceutical industry. Prominent forms of financial dependence on the pharmaceutical industry include research grants to individual psychiatric investigators inside and outside of the university system, unrestricted grants to the American Psychiatric Association (APA), underwriting of APA conferences, the provision of advertising fees to psychiatric journals, mounting and financing public relations campaigns, gifts, and provision of honorariums and expense money for attending industry-arranged conferences [Breggin, 1991; Coles, 1987; Dumont, 1990; Ghodse and Kahn, 1988; Greenspoon and Hedblom, 1975; Kessler, 1991; Preskorn, 1995; Ross, 1995; Waldron, 1977; Wortis and Stone, 1992].
6. The emergence of harsh cost-containment policies from the commercial insurance industry, necessitated by corporate-sector demands concerning the growing encroachment on profits caused by the cost of (employer paid) medical insurance premiums. The evolution of more restrictive reimbursement policies on the part of the commercial insurance industry emphasized a narrower view of "medical necessity" and appropriate treatment [Chodoff, 1987; Derber, 1984; Kroll and Kirsch, 1978; Kuhl, 1994; Meyer, 1993; Navarro, 1984, Sharfstein, 1987; Wilson, 1993).
7. Budgetary redirection of mental illness - mental illness treatment research provided by the federal government (through NIMH, NIH, ADAMHA, etc.) as part of the overall struggle of the dominant classes to eradicate the dangerously emancipatory concepts, sentiments, and political-organisational thrusts which emerged during the 1960s [Cohen, 1993; Duster, 1984; Halleck, 1971; Humphreys and Rappaport, 1993; Menn and Mosher, 1982; Vega and Murphy, 1990; for a candid discussion of the dangerous emancipatory thrusts of the 1960s from the perspective of political-economic elites, see Crozier, Huntington, and Watanuki, 1975, writing on behalf of the Trilateral Commission; Gusse and Schmacke, 1980, provide a chilling reconstruction of how aligning with power led German psychiatry in the period leading up to the Nazi era into ever more one-dimensional convictions concerning the biological basis of psychological disturbance/deviance and progressively harsher views regarding the uselessness of social-psychological forms of treatment).

These external factors produced the redefinition of psychological distress/disturbance into more and more narrowly described "syndromes," and promoted a psychopharmacologic nominalism

designed to provide treatment solutions to the "syndromes" classified with drug-treatment in mind. By "nominalism" I mean the practice of creating a name for something mainly on the basis of self-interest rather than on the basis of evidence. What is most real about psychiatric drugs is their toxic and impairing properties, which psychiatry either elides under the guise of side effects or fails to recognise at all. The distinctions made within psychiatry between drugs (anti-anxiety, antidepressant, etc.) are largely self-serving fictions. The great transformation involved in shifting from promoting certain drugs as unusually potent "tranquillisers" to promoting the same drugs as "antipsychotics" is an illustration of nominalism. This transformation has been carried off with the aid of turning a blind eye toward the intricacies of assessing placebo possibilities and to the complexities of distinguishing between impairment and clinical benefits (e.g., failing to press clinical observers into differentiating between drug-produced decrements in disturbing hallucinations vs. drug-produced apathy and muting of mental life generally). Reports in the psychiatric literature that reveal psychopharmacologic classification as nominalism are simply ignored; for example:

1. In a summary paper reviewing ten years of clinical psychiatric experience with depot fluphenazines, Frank J. Ayd, Jr. (1975), a well-known drug treatment advocate, cautions that high-dose therapy should be reserved for patients who "are still reacting [on more customary doses] with affect to their delusions and hallucinations rather than accepting them complacently" (p. 494) - clearly the expected reaction. This does not prevent Ayd later on the same page from referring to depot fluphenazines as "effective antipsychotic agents," although the context seems to make it clear that the drug-effect is far more accurately described as "apathy producing" rather than "antipsychotic."
2. Lerner et al. (1979) report their surprise at discovering that high doses of diazepam (Valium) and haloperidol (Haldol) were not differentially effective in symptom reduction. Each treatment resulted in highly significant improvement. They interpreted their results very cautiously, that is, they did not bring into question whether tranquillisers and antipsychotics are really different.
3. In an extensive review of psychiatric literature concerning neuroleptic treatment for psychosis, Keck, Jr. et al. (1989) attempted to integrate what could be learned about the time course of patient response to antipsychotic medication. Only five studies out of 1300 citations yielded adequate time course data. The interesting finding is that antipsychotic medication was no more effective than placebo, diazepam, or opium powder. The authors discuss their results cautiously, but acknowledge that "Perhaps the early effects [up to four weeks, actually, based upon the data they examined] of antipsychotic drugs are non-specific and are largely the same as those of sedative agents. The success of placebo treatments suggests that early improvements may be largely due to the non-specific effects of hospitalisation or other clinical interventions apart from the specific therapeutic effects of prescribed pharmacologic agents"(p.1291).
4. The effects of neuroleptics on people who have not been given a psychotic diagnosis and who presumably are not mentally ill are apparently the same as on psychiatric patients who have been given a diagnosis of psychosis. Non-psychotic groups include children in residential facilities for the mentally retarded, children in non-residential schools for the mentally retarded, adults in

nursing homes and old-age homes, non-psychiatric medical patients, and normal volunteers. Belmaker and Wald (1977) provide an interesting report concerning their own experience with a single 5-mg intravenous dose of haloperidol. Based upon this experience, these psychiatric researchers were moved to suggest that "neuroleptics may function to restrict cognitive and emotional processes in normals as well as schizophrenics, and thus it is possible that [a neuroleptic] does not specifically antagonise schizophrenic pathology" (pp. 222-223).

The above citations are just the tip of the iceberg. The issue, to repeat, is whether psychiatric classification of psychopharmacologic drugs (antipsychotics, etc.) represents anything more than a self-serving nominalism.

An unusually revealing summary statement concerning the modern effort to refine diagnosis in light of developments in pharmacologic treatment which directly bears on nominalism is provided by one of the elite architects of the new biopsychiatry, Gerald Klerman (1988a) .In this instance Klerman's remarks were offered in the context of introducing papers presented at an international conference on anxiety disorders which took place in Bavaria. Klerman begins his summary by acknowledging that scientific psychiatry's "great leap forward," the DSM-III, has abandoned the traditional psychotic-neurotic dichotomy, as well as unproven conclusions that much psychopathology represented complex lines of development/adaptation to decidedly unfavourable conditions in family life or even more broadly considered social circumstances.

What replaced the pre-DSM-III nosology (Klerman explains) is a new, empirically derived but non-theoretical schema based upon "vigour presenting symptoms" and corresponding categorisation, such as "anxiety disorders" (p. ix). But this official "neo-Kraepelinism" dissolves on the very next page, where Klerman reveals that the new (DSM-III) disorders and categories are actually based upon psychopharmacologic treatment and the presumption of "genetically determined abnormality of CNS chemistry as the predisposition." In addition (p. x), the entire issue of nosology as embodied in the DSM-III is by no means simply a matter of scientific controversy, since it strikes at the heart of interprofessional conflicts between M.D. psychiatrists and Ph.D. psychologists. Interestingly enough, the very first paper in the anthology of papers introduced by Klerman (Wittchen, 1988) reveals that it is completely untenable - as in counterfactual - to split-off anxiety from depression: people who are anxious, have panic attacks, are agoraphobic with or without panic attacks, have "simple" phobias, or are obsessive-compulsive (assessed by the Diagnostic Interview Schedule and/or clinical ratings based upon DSM-III criteria), are also highly likely to reveal depressive signs and symptoms. It would seem that only the prior commitment to a class of "antidepressant" drugs and a class of "antianxiety" drugs makes it necessary to diagnostically separate "anxiety disorders" from "affective disorders," in addition to the presumption (which cannot be empirically supported) that what is actually wrong with the patient is the emotional-cognitive-behavioural consequences of a "genetically determined abnormality of CNS chemistry." In short, all the old burdens of

psychological understanding are wiped away by the expedient of a strictly medical reconstruction of illness and treatment. It also should not he overlooked that such a deconstruction of the person from a unified psycho-social totality into a potential aggregate of narrowly defined syndromes has the consequence of creating a purely fictional theoretical and diagnostic dilemma for (contemporary) psychiatry, namely the vexing issue of co-morbidity.
It is difficult to find support within psychiatry for the discrete syndrome or disorder classification scheme advanced in the DSM-III series and the DSM-IV, even among the architects of the DSMs (Brown, 1987; Frances et al., 1991; Kendell, 1988; Strauss et al., 1979; Terr, 1991; Widiger and Shea, 1991). In practice, clinical signs (impulsivity, delusional thought, etc.) and symptoms (hallucinations, attacks of intense anxiety, dissociative phenomena, etc.) wander across many supposedly discrete syndromes or disorders. No one appears to seriously maintain that any syndrome or disorder presents a distinctive and discrete physiognomy. The continued reassertion of the category system is based upon non-scientific considerations which are nonetheless of great importance to the profession of psychiatry: identification with organic medicine; public relations; billing and reimbursement procedures to and from public and private third party providers; institutional record keeping and budgetary planning; research grant applications and awards from government, private foundations, pharmaceutical companies, etc.; disability and compensation hearings from many sources; multifaceted forensic activities; facilitating the actuarial and epidemiologic calculations of the insurance industry, upon which premium rate-settings are established and costs can be estimated so that a high profit margin is maintained; ideological control of "mental illness" as primarily a problem that fits into conventional medicine, and so forth. Unfortunately, rank and file practitioners across the mental health professions devote much time and effort to teaching and learning how to use the DSMs to identify what the patient "really has." Since everyone in the field must digest and use the DSMs, a very serious impediment to meaningful thought results.

It is now widely acknowledged in the psychiatric literature that the prevalence, seriousness, and variety of neuroleptic-produced side effects is incompatible with continued enthusiasm for using neuroleptics in clinical treatment, This acknowledgement should not be confused, however, with actual prescription practices on the part of psychiatrists. Nor does it lead to renewed interest in social-interpersonal approaches to treatment, or with lessened faith in the organic aetiology and pathogenesis of mental illness, or a more cautious attitude toward the long-term consequences of neurotoxic drugs. It also does not produce a more critical interest in how the private industry-FDA-psychiatric research complex operates to make new drugs available for treatment. In short, the catastrophe of medically-created disease of unprecedented proportion has not produced a critical self-examination on the part of psychiatry as to the ideological, conceptual, financial, and systemic components which in combination produced the catastrophe. I will illustrate this by discussing the introduction of two contemporary drugs into psychiatry, alprazolam (Xanax) and fluoxetine (Prozac).

Learning Nothing From the Past - The Introduction of Xanax and Prozac into Psychiatry

Introduction to the Upjohn Sponsored Studies Resulting in FDA Approval of Alprazolam as a Panic Disorder Treatment

Although it defies all ordinary understanding of bias and conflict of interest, pharmaceutical companies in America are completely in charge of the studies upon which the FDA grants a new drug approval. Congress has considered the possibility of constructing a less flawed method than allowing the sponsoring company itself to design the clinical trials and to select and pay investigators (Braithwaite, 1984), but the logic of U.S. capitalism seems to preclude modifying this arrangement. Successful marketing of a new psychiatric drug depends upon reaching and influencing the only group legally empowered to make the drug directly available to the public, namely physicians. Direct marketing approaches to physicians consist mainly of frequent visits by pharmaceutical "detail" men and women, and (for psychiatric drugs, specifically) the highly sophisticated and expensive ads which appear in psychiatric journals. The journals of course purport to publish disinterested scientific reports, but at the same time both the journals themselves and a substantial percentage of the reports published in them are in fact financially supported by the commercial pharmaceutical industry. Just what the prevailing arrangement means in practice is well illustrated by the Upjohn initiated, sponsored, and controlled clinical studies which resulted in FDA approval for alprazolam as a specific treatment for panic disorder.

The clinical studies which served as the basis of FDA approval for Upjohn's alprazolam as a specific treatment for panic disorder were reported in the Archives of General Psychiatry, Volume 45, May 1988. The introductory overview to the studies is provided by Gerald Klerman, former director of NIMH and ADAMHA. As Breggin (1991) points out, Klerman is quite coy about revealing his link to Upjohn. The reader finds Klerman identified on the bottom of the first page of his article (1988b, p. 407), in the usual space, as associated with the Department of Psychiatry, Cornell University Medical School. But in the body of the paper, under the heading "steering committees of investigators," Klerman reveals that the entire multi-centre, cross-national research project - which he describes as "one of the largest controlled clinical trials in psychiatry" (p. 407) -was under the direction of James H. Coleman of Upjohn's Psychopharmacology Research Unit and one "G.L.K." - himself, of course. At this point the sophisticated reader who has spotted this single, abbreviated, reference to Klerman as actually one of the two people in charge of the entire research project (along with an employee of Upjohn) will also suspect that such a large role for such a prominent person involves a large fee. The text that Klerman provides leaves it entirely up to the reader to guess what the actual financial arrangement might be. According to a telephone interview with Klerman that Breggin summarised in Toxic Psychiatry, Klerman admitted to an "ongoing" relationship with Upjohn since 1982 or 1983, and that he was "hired specifically to help develop the overall package of Xanax studies for FDA approval" (quoted in Breggin, 1991, p. 349).

As Braithwaite (1984) points out, it is certainly possible to imagine an arrangement in which the federal government acts as an intermediary between the sponsoring pharmaceutical company and the clinical investigators. The basic idea would be to sever the direct money-for-services connection between the sponsor and the researchers, as well as severing the development of a long-term, mutually beneficial relationship between pharmaceutical company and allegedly disinterested scientific investigators. As matters stand, the FDA is in the position of relying entirely upon data generated under the direct control of a commercial enterprise single-mindedly fixated on profits (Kessler, Rose, Temple, Schapiro, and Griffin, 1994). The "expert panels" which the FDA may constitute in order to further evaluate the clinical studies directed by the sponsor are themselves composed of researchers accustomed to working for the industry (Pam, 1990). The fact that the Upjohn studies I discuss here resulted in FDA approval should make it clear that the prevailing arrangement is incompatible with public health and safety.

At the conclusion of Klerman's overview, following the reference section, an "Editorial Note" appears in small print from the Editor of the Archives of General Psychiatry, Daniel X. Freedman (on p. 412). The note advises the reader not to be concerned about the fact that he is both the journal's Editor (who decides upon which articles will be accepted for publication) and a consultant to the Upjohn Company for this very study, for which Upjohn paid in order to get FDA approval of its own product. Presumably the reader understands that consultant means a financial arrangement between the Editor and the Upjohn Company. Although Freedman assures the reader that all is well, he does not see fit to explain why the research papers could not have simply been submitted to another journal, a journal whose Editor was not being paid by Upjohn to get FDA approval for alprazolam.

Following Klerman's overview paper, all three subsequent papers which report on different aspects of the alprazolam research acknowledge the sponsorship of the Upjohn Company; the last paper in the series - on discontinuation effects - even lists Carl P. Lewis, M.D., Ph.D., as one of the authors. Lewis is identified as part of Upjohn's Psychopharmacology Research Unit. Klerman admits in his overview that the steering committee (Klerman and J.H. Coleman of Upjohn's Psychopharmacology Research Unit) " ...met frequently to review the protocol, to make amendments as required, to monitor the progress of the study, and to plan for data analysis and for scientific presentation and publication" (1988b, p. 409). This last admission presumably accounts for the overall finding of safety and efficacy, despite the actual data and various important methodological shortcomings (as discussed in part in the long letter to the Editor by Isaac M. Marks and ten other prominent international workers in the field of anxiety disorders). Breggin reports that Marks personally told him that the letter was at first rejected by Archives editor Freedman, its publication was delayed for a year so that its impact was diminished, and finally that Freedman deleted important portions of the letter without permission when he did finally allow its publication (p. 351 of Breggin, 1991; the Marks et al. letter appeared in Archives

of General Psychiatry in 1989, 14 months after the Upjohn sponsored studies were published). The entire project, although sponsored by Upjohn for its own private gain, made extensive and free use of publicly funded academics, medical schools, hospitals, and so forth. This is an illustration of how private, for-profit corporations get costs financed by public funds.

The effect of industry-controlled publications on the integrity of medical journals is lamented by M.N.G. Dukes, Head of The Netherlands' Ministry of Health, Department of Pharmacotherapy, on the occasion of the 1979 Kyoto International Conference Against Drug-Induced Suffering: "...for every one impartial and serious report from a physician recording his observations consciously and in a useful manner there are in the literature some 10 or 20 papers of merely promotional character, written, it is true, by physicians, but commonly ghost-edited and sponsored by the promotional departments of drug companies and published largely (but not exclusively) in second-rank journals. ...One must regard this form of pseudoscientific drug promotion, involving misuse of the medical literature, as one of the bad habits into which the industry has got itself entangled. . . ." (1980, p. 180)
The reader can decide whether these Upjohn initiated, sponsored, designed, and controlled studies constitute "pseudoscientific drug promotion" and a "misuse of the medical literature." The point Dukes makes about pseudoscientific drug promotions being ghost-edited should be modified somewhat for the American scene in psychiatry, where it hardly seems worth the effort to disguise the financial arrangements between drug company and physician.

In the examination of the Upjohn-FDA approval studies which follows I intend as far as possible to stay within the framework of thought advanced by the studies themselves. What I intend to show is that these studies are not merely beset with errors of reasoning and methodology; rather, I wish the reader to consider that these studies are not actually concerned with conducting a sophisticated investigation informed by forty years of clinical research and clinical practice experience with psychotropic drugs. I propose instead that the most sensible and parsimonious way to interpret these studies is to keep in mind what their overall purpose is and the derivative need to put the best face possible on a bad situation, namely treating psychological distress with a sedating, toxic, highly addictive, and dangerous drug. In other words, I will not attempt to ignore the details of the studies by dismissing the whole project out of hand on the grounds that it is absurd to treat psychological distress as a chronic, unremitting, idiopathic somatic disorder like epilepsy or diabetes. In fact, the insistence that panic disorder is an unremitting idiopathic illness turns out to be precisely the justification for the otherwise incomprehensible trivialisation of the problems inherent in prolonged drug treatment, namely side effects (including non-neurological conditions like hepatitis), tolerance, addiction, withdrawal effects, and rebound effects. Since the principal investigators take it for granted (see ahead) that drug treatment is the only viable option for this "chronic, unremitting illness," there is presumably no reason to clarify that rebound and withdrawal effects may operate to produce distress/symptoms despite continuing to take the medication regularly (Ashton, 1991). The "facts" of "mental illness" are used to maximise the

professional position of psychiatry and the profits of the pharmaceutical industry. But at the same time it is important to be aware of just what considerations are completely outside of the project and framework of thought which these studies embody.

1. The assertion that what is being treated with alprazolam (Xanax) is in reality an idiopathic neurophysiological disorder relegates the patient's actual history of loss, threat, abuse, etc. to irrelevance, and likewise moves the patient's present social-interpersonal circumstances into irrelevance. In a 1978 publication, Klerman made it clear that the resurgent neo-Kraepelinian movement held as an axiom that psychiatric disorders were to be regarded as fundamentally organic in terms of etiopathogenesis. At that time he was unable to cite any functional psychiatric disorder which had been shown to even be regularly associated with a demonstrable pathophysiology, much less organic aetiology. In his 1988 overview of the Upjohn sponsored Xanax studies, he was still obliged to admit that no actual evidence of pathophysiology existed in the case of people diagnosed with panic disorder or agoraphobia.
2. The entire issue of what the impact of the psychiatrist's disinterest in the patient's history or present social-interpersonal circumstances might be in the long run has no opportunity to emerge as a clinical dimension. As is customary in psychiatric clinical drug studies, all contact with the patients/subjects is terminated quickly. In these Upjohn sponsored Xanax studies all contact with the patients/subjects ended after 14 weeks.
3. It follows from point one that from a treatment point of view the idea is abandoned that the individual must somehow use the therapist's supportive/interested stance to come to grips with past and present pathogenic influences in order to construct a better life. This is evident from the simple fact that alprazolam treatment is advanced in the same spirit as insulin treatment for diabetes. In short, issues concerning self-alienation and personality defect, which any serious clinical interest will invariably bring into the light, are eclipsed by the task of chemically subduing narrowly described symptoms.
4. Any notions that psychological distress is a sign of past or present disturbing conditions in terms of interpersonal life situations, or that psychological distress in the present has the teleological function of signalling to the social-surround that untoward events are occurring, are likewise abandoned.
5. The complexity of the individual's life from a multifaceted psychosocial functioning perspective is reduced to target symptoms and global self-reports. In short, the problem of assessing the person's psychological status (at any point in time) is treated with the same delicacy as a Gallup poll on U.S. foreign policy. Just what can emerge when the patient is allowed/ encouraged to talk is a primary issue for all research efforts which are concerned with persons as complex psycho-social beings (Kleinman, 1988; Mies, 1983; Mishler et al., 1981; Rubin, 1976; Sennett and Cobb, 1972; Warren, 1988).
6. The inevitable passing of control of affective life from personality resources, interpersonal relations and social circumstances, to the closed circle of drug effects (intended and side), tolerance, addiction, withdrawal, and rebound is conceptually elided, as are the implications of this for the individual's future.

7. The crucial insight that over time the individual may accommodate/ habituate to drug-produced sedation and other forms of mental-behavioural impairment, so that strictly from the perspective of patient complaints a false appearance of relative well-being may he presented, is outside the realm of assessment-evaluation in these studies.

Examination of Klerman's "Overview" of the Upjohn Alprazolam Studies

With the above caveats or reminders in place, I will begin anew with Klerman's overview, with the intention of exposing errors of reasoning, methodological and conceptual problems, and disregard for what is actually known about the dangers of psychotropic drug treatment. Klerman, to recall, is providing a rationale for and summary of the results of the entire project in his overview.

Experimental design. Klerman begins his description by noting that the project compared an 8 week trial of alprazolam against placebo. In their critique letter, Marks et al. (1989) question the point of an 8 week treatment trial in a sample whose mean symptom duration was almost 9 years. This objection requires expansion. First, psychotropic drug research experience over the past forty years has made it abundantly clear that it is thoroughly misleading to compare a biologically active drug with an inert placebo. An intellectually honest study would have included an active placebo group (i.e., a drug which produces subjective effects - like dry mouth - but is not believed to be psychoactive, so as to provide a means of assessing the possible contribution of psychosomatic placebo effects to overall clinical improvement) and another psychotropic drug treatment group. There is simply no other way to ascertain what comparative clinical benefits and costs are produced by the psychopharmacologic action per se of the trial drug in question. It should be noted that in 1991 - that is, after alprazolam was approved by the FDA as a specific treatment for panic disorder - Russel Noyes, Jr., one of the senior researchers in the overall project, reported (Noyes, Garvey, Cook, and Suelzer, 1991) in the context of a further discontinuation study that after an 8 month treatment trial alprazolam and diazepam were not significantly different on two outcome measures of treatment for panic disorder. In fact, On the "mean panic attacks per week" measure diazepam was superior to alprazolam at the .06 level of significance. In all relevant respects diazepam turned out to be the more useful and less dangerous drug, but Noyes and associates did not draw the obvious conclusions from their own data, perhaps because this was another Upjohn financed study. Meanwhile in 1988[b] Klerman can only say that "conventional benzodiazepines have been thought to be ineffective against panic disorder" (p. 408). It remains obvious that it is pointless to compare alprazolam alone to an inert placebo.

Second, an 8 week trial is absurdly short because no one, especially the researchers who designed and conducted the study, intends for alprazolam to be used for only 8 weeks, and therefore the side effects, discontinuance emergent effects, and rebound produced by its expected much longer-

term clinical use cannot be ascertained in what is, after all, the one and only FDA trial conducted. Following FDA approval no further trials or evidence are required, and no regulations are placed upon the drug's clinical use (the commercial importance of this point is brought out by Kessler, Rose, Temple, Schapiro, and Griffin, 1994; note that David A. Kessler is the Head of the FDA). In their reply to the Marks et al. letter, Klerman and the other senior investigators attempt to answer the criticism that alprazolam's purported advantage over placebo during a 4 week period (that is, the period in the 8 week study before the high placebo group drop-out rate made data analysis controversial) is clinically insignificant by admitting that the common pattern for psychopharmacologic treatment is to continue medication for a much longer period, so as to avoid immediate relapse. In fact (1989, same journal) Klerman et al. acknowledge that the actual expected period of use is quite prolonged, even indefinite, given tile "chronic nature of the illness" (p. 672). But in making this admission they simultaneously reveal just how medically irresponsible it is to seek FDA approval based upon an 8-week study.

Third, the absurdly short time frame of the trial does not even provide for an opportunity to determine whether the drug under investigation will sustain an advantage against inert placebo over the course of a clinically more realistic period of time. In fact it is only by blatant data reanalysis that alprazolam appears to produce a clinical advantage against inert placebo over the 8-week trial period (see ahead for more details). A 1992 clinical trial com- paring alprazolam to inert placebo over a 32 week period found no advantage for alprazolam compared to placebo in terms of panic attack frequency and the Hamilton Anxiety Scale (Dager et al., 1992).

Disregard for neurotoxic effects. Under "background" (1988b, pp. 407-408), Klerman refers to "recent research" (no citations) which demonstrated the importance of the gamma-aminobutyric acid (GABA)-benzodiazepine receptor complex in mediating clinical effects. He also states that in 1982 the Upjohn Company initiated research on alprazolam for the purpose of seeking FDA approval. Here two references are cited. One reference turns out to be a 1986 study concerning alprazolam by Leibowitz, Fyer and others. Klerman's reference to the GABA-benzodiazepine receptor complex in all likelihood takes for granted that the journal's readership is largely uninformed concerning the details of neuroanatomy, neurochemistry, neurotransmission, pharmacology, and neuropathology. The limited literature that exists on the prescribing behaviour of psychiatrists (e.g., Seidenberg, 1971; Turner, 1971; Waldron, 1977) indicates that drug advertisements in psychiatric journals are far more determinative for prescribing behaviour than the scientific articles that appear in the same journals. This turns out to be even a more serious issue than meets the eye, since information supplied in the Physicians Desk Reference (PDR), upon which physicians heavily depend, is little more than paid drug advertisements limited only by the feeble influence of the FDA (Johnson, 1980; Waldron, 1977; Wortis and Stone, 1992). Since psychiatric drug advertisements in journals are not all that different than information provided in the PDR or drug inserts supplied by the manufacturer, the only recourse a conscientious practising psychiatrist has is to actually read the voluminous scientific literature

concerning controlled studies. But this is heavily influenced in turn by pharmaceutical industry sponsors, research grants, and the like. Finally, even drug studies that are not compromised directly by financial ties to the drug industry take for granted the project of chemically subduing narrowly defined symptoms, along with the other conceptual-methodological forms of tunnel vision I have described.

Klerman either is not concerned with or does not expect the readership at large to grasp that it is completely unrealistic to assume that a drug which is physiologically active in the "GABA-benzodiazepine receptor complex" will only be active in this (hypothetical) complex rather than widely active in numerous neurotransmission systems (such as the dopamine-GABA-acetylcholine system). Although much is written in biopsychiatrically oriented and psychopharmacologic drug treatment literature about advances in understanding the brain, the truth is that from a practical perspective (that is, from the perspective of deliberate intervention in brain physiology) the total integrated system of neuroanatomy, neurotransmission, and homeostasis- equilibrium mechanisms is still in what could accurately be called the explorative-speculative stage of knowledge (Heinrichs, 1993; Post, 1992; Stuss and Benson, 1986). Therefore, deliberate interventions in CNS functioning must be regarded as heroic medical practice, a step that can only be justified in the face of demonstrable and serious neuropathology, and in the absence of less risky treatment alternatives. As to the former condition, Klerman himself admits that" ...there is no direct evidence of abnormal biochemistry findings for diazepam receptors in patients with normal or clinical states of anxiety. ..whether or not there are any abnormalities in the [benzodiazepine receptor] complex or in endogenous substances that might interact with the receptor complex during normal anxiety or during clinical states, such as panic disorder and agoraphobia remains uncertain" (p. 411). As for the latter condition, Klerman confesses that the" ...scientific issues [of diagnosis and treatment] are further confounded by professional tensions: most behaviour therapists are Ph.D. psychologists, while most of the proponents of psychopharmacology are M.D. psychiatrists" (1-1. 408).

Just how little concern Klerman has about deliberate interventions in CNS functioning -in the absence, to reiterate, of demonstrable abnormality or pathology -is revealed by the fact that his citation section, although it includes Liebowitz, Fyer et al., 1986, does not draw upon Fyer, Liebowitz et al.'s 1987 alprazolam discontinuation study. In the course of discussing the serious discontinuation (withdrawal) problems encountered in this study, Fyer, Liebowitz et al. draw upon a colleague's speculations as to just how alprazolam use may act to disrupt neurophysiology: Klein has proposed a possible explanation of the rapid panic recurrence and withdrawal symptoms observed during alprazolam discontinuation (personal communication). He speculated that alprazolam exerts its antipanic effect by blocking afferent pathways to the locus ceruleus or other noradrenergic centres. Massive differentiation usually produces receptor hypersensitivity distal to the point of blockage. In this case, discontinuing alprazolam treatment would be expected to leave these hypothetical noradrenergic receptors hypersensitive and prone to over-

response. (p. 307)

The general neural mechanism being calmly discussed above - hypersensitivity - is precisely the mechanism most often advanced in the psychiatric literature for tardive dyskinesia and other late appearing disorders which result from prolonged dopamine receptor blockade caused by neuroleptic drug treatment. The neurological diseases so produced may be irreversible and untreatable (this is the case with non-transitory tardive dyskinesia, and probably other neuroleptic-produced tardive disorders like tardive akathisia, e.g., Gualtieri, 1993). Fyer, Liebowitz et al., in their own paper, appear completely unconcerned about the implications of alprazolam-produced receptor hypersensitivity. Their only comment is that a quick-acting alpha-two agonist such as clonidine might somewhat ameliorate withdrawal symptoms. The first page of this scientific paper, published in the American Journal of Psychiatry, dutifully reports that the research was financed in part by the Upjohn Company. Klerman, who is surely aware of Upjohn sponsored alprazolam research, does not even bother to mention the danger that Fyer, Liebowitz et al. casually dismiss. Needless to say, the design of an 8-week study for FDA approval completely avoids the danger of late-appearing neuropathology. But, of course, as the senior authors admit in their rejoinder to the Marks et al. letter, it is taken for granted that in actual clinical practice alprazolam treatment will be prolonged or indefinite.

The creation of "panic disorder" in DSM-III for Upjohn's alprazolam. Under the major heading "Design of the Cross-national Collaborative Panic Study" (beginning on p. 408), Klerman (1988b) continues to provide "deep back- ground" on the origins and reasons for the cross-national collaborative panic study. Based upon a December 1982 scientific conference on anxiety held in Key Biscayne, Florida, he explains, it was decided to proceed with a series of multicentre clinical trials. Upjohn paid for these multicenter-clinical trials, but Klerman does not inform the reader either who sponsored the Key Biscayne conference or who decided to proceed with the multicenter clinical trials for alprazolam. Klerman's expository style makes no distinctions between Upjohn's commercial interests and the scientific problems and projects facing psychiatry. Evidently there is no difference, if I correctly under- stand the information Klerman provides in this section. That is, the statement that the decision to initiate multicenter alprazolam trials necessitated refinements in diagnosis is followed directly by explaining that a special version of the Structured Clinical Interview (SCID) developed by Sptizer and Williams for DSM-III diagnosis was created for Upjohn's alprazolam trials (the SCID-UP). Further,

"The DSM-Ill classification was modified. and three categories of panic disorder were identified for the research on alprazolam: (1) Panic Disorder Uncomplicated (DSM-III Panic Disorder), (2) Panic Disorder with Limited Phobic Avoidance, and (3) Panic Disorder with Extensive Phobic Avoidance (DSM-III "Agoraphobia with Panic Disorder")". (1988b, p. 408)

Since Klerman specifically states that "Spitzer and Williams had already started to develop a Structured Clinical Interview (SCID) for DSM-III diagnosis, and a special version (SCID-UP) was developed on anxiety disorders" (p. 408), and since DSM-III was published in 1980, the conclusion seems inescapable that the DSM-III panic disorder categories were created for the

purpose of Upjohn's alprazolam clinical trials for FDA approval as a specific treatment for panic disorder. Thus it would seem that Klerman has solid historical and factual reasons for drawing no distinctions between Upjohn's commercial interests and the professional-scientific concerns of psychiatry as they are embodied in the DSM-III.

Disregard for methodological refinements suggested in prior studies and for prior findings of alprazolam-produced EEG abnormalities. Although Klerman describes both phase one of the alprazolam trial (alprazolam versus placebo) and phase two of the alprazolam trial (comparing alprazolam, imipramine, and placebo) under "design" (p. 408), only the useless comparison between alprazolam and placebo served as the basis for FDA approval of alprazolam as a specific treatment for panic disorder. As I discussed earlier, only direct comparison of alprazolam with other benzodiazepines. other classes of psychotropic drugs, a biologically active but not psychotropic placebo, and an inert placebo could provide the necessary minimal conditions for generating useful discriminative information about alprazolam. It is also puzzling why these studies alone served as the basis of FDA approval, since they certainly are not the only studies which used alprazolam for the treatment of panic. A much longer treatment and discontinuance alprazolam-panic study reported in 1987 (Fyer et al., a study partly financed by Upjohn) showed very substantial withdrawal effects, relapse, and rebound. In addition, the Fyer et al. study clearly recognised that its discontinuation data had to be regarded as suspect because of failure to obtain compliance checks (plasma benzodiazepine drug screens) for 10 or 17 subjects. Yet the official Upjohn-FDA approval study repeated the same error. A study published in 1992 which did include such a check found that 23 of 44 alprazolam patients tested positive at the conclusion of the taper (i.e., no authorised alprazolam) versus zero of 17 placebo controls (Dager et al., 1992). The official discontinuance study (Pecknold, Swinson, Kuch, and Lewis, 1988) does not even acknowledge that failure to check compliance with the protocol taper schedule (via plasma screens) is a crucial methodological error. Fyer et al. (1987), directly following their admission that the lack of a compliance check might have substantially compromised the validity of their findings (which were very negative for alprazolam), conclude that it is necessary to directly compare tapering on alprazolam with other drugs, variations in the rate of alprazolam decrease, and the use of adjunctive medication to aid in the (pervasive and serious) consequences of alprazolam withdrawal "before alprazolam's therapeutic role can be fully assessed" (p. 309). None of these necessary steps was taken in the alprazolam-FDA studies. Fyer et al. also report that weekly EEG recordings were completed on 10 of their 17 discontinuance subjects. Of these, two had excessive slowing on one EEG examination. The authors do not state that this is a sign of neuropathology, which it is, nor do they discuss the matter. It is impossible (for me, at least) to tell from their write-up which patients presented this sign and at which point in time - other than the fact that the abnormal EEG readings were obtained at some point in time beyond the planned 30-day taper period, since 13 of the 17 subjects could not endure the planned taper schedule (this includes the two subjects who gave an abnormal EEG reading). It is clear from the text that no long-term neurological follow-ups were conducted. Despite abnormal EEG readings in 2 of 10

alprazolam-treated patients in a pre-"official" Upjohn sponsored FDA-approval study, the "official" discontinuance study (Pecknold et al., 1988) conducted no neurological examinations of any kind. As I have already discussed, these FDA approval-seeking studies simply ignored the organic consequences of long-term alprazolam treatment, although Marks et al. (1989) point out in their critical letter that a literature already existed suggesting ventricular enlargement in patients who were long-term benzodiazepine users.
In spite of clear indications of serious withdrawal effects and/or use-effects (above), Klerman's (1988b) overview of the total project's design (phase one followed by phase two) reveals that -"assuming there would be no problems of safety" (p. 408) - the second phase began in the summer of 1984, although the clinical part of phase one was not even completed until 1985. Since Upjohn employees and paid consultants were in charge of every aspect of this study, it would seem that there was no reason to actually wait for phase one results to emerge before it was deemed safe to go on to phase two.

The Upjohn Sponsored Studies Which Resulted in FDA Approval

I turn now to details of the Upjohn studies themselves as they are presented in three separate papers: efficacy in short-term treatment, patient acceptance, side effects and safety, and discontinuation effects.

Efficacy in short-term treatment (Ballenger et al., 1988). Since this efficacy study compared alprazolam to an inert placebo, it is crucial to clarify just why this experimental design cannot adequately address the issue at hand, which is to assess the clinical benefit(s) produced by the psychopharmacologic action of the drug itself, that is, separated from or unconfounded by other possible contributions to clinical improvement. If this is not accomplished, then there is no way to evaluate just what the clinical costs of the drug are in comparison to its benefits (if there are any benefits over and above other possible sources of contribution to clinical improvement). In psychotropic drug trials, experience (that is, clinical research experience with psychiatric drugs over the past forty years or so) suggests the following sources of (perceived) clinical improvement may be at work in the drug trial:

(a) the clinical benefits produced by the psychopharmacologic activity of the drug itself, acting alone (i.e., aspirin should relieve headache even if the person does not know what the substance is and what it is supposed to accomplish, or even if the person does not realise that medicine has been ingested).
(b) the drug giving-taking interaction, in terms of its psychological impact on the patient (this is the most commonly discussed "placebo" effect).
(c) the biological activities of the drug which are subjectively noticed by the patient but which are not considered part of the pharmacological activity relevant to clinical gain (sedation, ataxia, etc.). Such side effects of the drug may nevertheless instigate a psychosomatic source of clinical

improvement (i.e., a further placebo effect).
(d) the psychological consequences for the patient of being "in treatment" with impressive authorities, in an impressive setting, etc., along with the concerned, interested attention and support of the entire treatment team (i.e., a further placebo effect. A dramatic illustration of just how potent such sources of clinical improvement can be for psychiatric patients was published by Raskis and Smart in 1957; this source of con- founding in psychiatric drug trials is hardly a new idea).
(e) the misperception of clinical improvement (on the part of clinical observers and/or the patients themselves) based upon what are conceived of as unwanted effects of the drug, e.g., mistaking the consequences of drug-produced sedation and amnesia for reduction in panic intensity, frequency, concern, and so on (Fink, 1974, despite being a prominent advocate of electroconvulsive shock treatment, discusses a variety of psychological assessment techniques which all support his own conclusion that the clinical improvement produced by ECT is based upon brain damage and the "euphoric-anosognosic" reactions of some patients to damage. Anosognosia is a term derived from clinical neurology which refers to unawareness of injury or impairment. Breggin (1991) has used Fink's research as part of his own conclusion that the apparent benefits of psychiatric drugs are all based upon damage and impairment. Despite Fink being an ECT advocate, his work shows just how crucial it is to include enough variety of assessment methods to judge whether the observed or reported improvement is not more realistically understood as impairment).

With the above list of possible contributions to (perceived) clinical improvement in mind, it is readily apparent that the design of the alprazolam-panic studies (alprazolam versus placebo) cannot produce any data at all which expose sources (c), (d) and (e), above. In short, the possible contributions to clinical improvement observed in the experimental group (alprazolam) and control group (lactose filler) which may derive from sources (c), (d) and (e) [the latter pertains only to the alprazolam group] remain completely unknown. Thus the degrees of safety and efficacy - upon which FDA approval is supposed to rest - likewise remain unknown at the conclusion of this "controlled" drug trial. I wish to emphasise that my analysis of possible confounding sources of (perceived) clinical improvement in this sort of drug trial is hardly based upon knowledge which I uniquely possess.

By the expository technique of separating efficacy from unwanted or adverse side effects (each examined in separate articles), the clinical benefits derived from alprazolam treatment are presented as if they were cost-free. Despite the frequently repeated conclusion by Ballenger et al. that alprazolam treatment is rapidly effective and safe, the actual data themselves tell a different story. The most consistent and important finding of this study - the authors' own commentary to the contrary - is the rapid rate of improvement of the placebo group. Even during the first four weeks of treatment (before the high placebo-group drop-out rate began), where statistically significant differences favour alprazolam over placebo, it is nevertheless the case that the

magnitude of difference is small and what remains most striking is the degree to which the placebo group has improved relative to baseline (especially in view of an average duration of illness of approximately 9 years). By week 8 (again, a very short time period), examining the data that actually exist rather than the imaginary data (see ahead) that Ballenger et al. advance as most important, there are practically no benefits from alprazolam compared to placebo: no significant difference between the two groups in total panic attacks per week, spontaneous panic attacks per week, situational panic attacks per week (Table 2, p. 416); percent of patients panic free (neither type present), percent of patients free from situational panic attacks (Table 3, p. 416); mean ratings of disability in work, in social and leisure time, and in family and home (Table 6, p. 418).

The placebo group's improvement is actually the most important finding of this study since (a) it 'indicates that whatever it is the subjects suffer from can be modified in a clinically beneficial direction without recourse to a highly addictive drug with unknown but suspect long-term consequences, and (b) it indicates that largely unknown and unexamined social-interpersonal aspects of the total research study situation exert potent effects that operate in the direction of clinical gains. Since these purely social-interpersonal sources of clinical gains operated in the absence of any formal psychotherapy arrangement (which the research design strictly prohibited), the most responsible conclusion (scientifically and medically) should have been to channel future efforts in the direction of refining treatment techniques that do not require drugs. Of course, as Klerman admitted in the overview, such a conclusion directly implicates professional tensions between M.D. psychiatrists and other treatment professions, in addition to the self-evident point that Upjohn is hardly amenable to the conclusion that drugs are unnecessary for treatment. These studies are for the purpose, after all, of obtaining FDA approval for Upjohn's alprazolam. As a general observation, I can state that placebo effects are consistently strong and effective, and this fact -as well as what it implies about the putative organic basis of "mental disorders" - is systematically elided in the psychiatric literature, which almost uniformly regards placebo effects as an annoyance in the task of demonstrating the efficacy of the drug at hand (Kleinman, 1988; Ross, 1995). Just to cite one important example, the efficacy and promise of "placebo" effects should have been, but of course was not, the major conclusion of the 1964 NIMH collaborative research study regarding phenothiazine treatment in acute schizophrenia, based upon how much the placebo group improved in the absence of any attempt to provide psychological treatment or to upgrade the social conditions of life in-hospital.

Placebo effects are potent and ubiquitous in medicine (Dinnerstein, Lowenthal, and Blitz, 1966; Kleinman, 1988; Ross, 1995), Since psychiatric drugs are toxic in clinical dosages (whatever additional clinical benefits may also be produced), their clinical use demands a methodologically sound demonstration that no extant non-drug treatment can provide substantial clinical benefits (the Upjohn alprazolam studies of course did not include any non-drug treatment other than placebo).

I have already suggested that a broad reading of the psychiatric drug treatment research literature reveals that (inactive!) placebo effects are consistent and strong, A clever confirmation of this conclusion in the area of antidepressant medication has recently been provided by Greenberg, Bornstein, Greenberg, and Fisher (1992), Their demonstration depends upon the reanalysis of drug studies which, at the time they were conducted, used both an inactive placebo group and an established antidepressant medication group (imipramine or amitriptyline) to establish by comparison the clinical advantage of a newer antidepressant drug (amoxapine, maprotiline, or trazadone), Greenberg et al, reasoned as follows: (a) the attempt to provide support for a new antidepressant drug (the point of the research effort) indicated lessened vested interest in the other medication on the part of the researchers, (b) the use of an older antidepressant medication and a newer antidepressant drug in the same study made it more difficult for the researchers to recognise who was on which drug or placebo (i.e. to penetrate the double blind research design), (c) using only patient self-ratings for the reanalysis rather than researcher interview methods of assessment (i.e. the Hamilton Rating Scale for Depression) further deprived the researchers of an opportunity to penetrate the double blind on the basis of familiar side effects described by patients during the course of the interview, In short, studies which used both an inactive placebo group and a standard antidepressant medication group for the purpose of showing the clinical advantage of a new drug provided the opportunity to re-evaluate the effectiveness of standard antidepressants versus placebo when the vested interest (Greenberg et al's term) had moved on to some new drug, The reanalysis of such data revealed that patient ratings concerning the antidepressant effect of the standard antidepressant medications were no different than for the inert placebos,

A major issue for analysing the results of the 8 week trial comparing alprazolam to placebo was that only 56% of placebo patients who completed the first three weeks of the trial remained in the study by week 8, Ballenger et al "solve" this problem by using the data obtained on the placebo subjects at the end of week 3 and who subsequently dropped out in place of the non-existent data for weeks 4, 5, 6, 7, and 8:

"As has become the standard method in such situations, we also analysed the "end point data" from all evaluated patients, using the week eight data when they were present and the last available value carried forward when they were not" (p.416)

In other words, 44% of the data for week 8, in what the authors called the end point analysis, actually were not obtained during week 8 but sometime before week 8, since from week 3 to week eight 44% of the placebo group dropped out of the study. It is this end point data - 44% of which are simply imaginary - that Ballenger et al. repeatedly urge the reader to regard as the real findings of the study. The reader has no way of knowing until and unless the Marks et al. letter is examined, which was published more than a year later, that the research subjects were told that they could drop out of the study and receive alternative active treatment (1989, p. 668) if they

wished. Marks et al. further reveal in the letter that, according to a personal communication from R.P Swinson, M.D. at the Toronto site (May 10, 1988), research personnel who were retrospectively asked to guess which patients were on placebo and which on alprazolam were 90% correct. Marks et al. therefore conjecture that prescribers and raters who were not actually blind may have encouraged dropouts. This is a quite different conjecture about the high drop out rate than the one proposed by Ballenger et al., who suggest the high placebo drop out rate was produced by the ineffectiveness of the (inert) placebo. Ballenger et al. also do not recognise that symptom relief based upon sedation and mental impairment (the alprazolam group) does not have the same meaning and significance as symptom relief in the absence of sedation and mental impairment (the placebo group, see ahead).

The proposal on the part of Ballenger et al. that the high placebo group attrition rate shows the ineffectiveness of placebo effects requires further consideration. What is ultimately at stake here from the perspective of practical treatment possibilities is the idea that many people who suffer panic attacks will not benefit from non-pharmacologic treatment (although it is equally clear that many will benefit, and the authors do not seem interested in how to make the relevant discrimination). Of course the placebo group was not receiving any specific treatment, but it is nevertheless useful for drug proponents to show that the social-psychological aspects of placebo treatment provide little benefits. There is actually a very compelling additional explanation for the high placebo group drop out rate (that is, in addition to prescribers and raters not being blind as to which subjects were receiving placebo in conjunction with subjects being informed that they could drop out and receive "alternative active treatment"). The additional compelling explanation for the high placebo group attrition amounts to this: a substantial but not precisely determinable proportion of the placebo group was with drawing from one or more benzodiazepines (Xanax and/or Valium) during the course of the 8 week study. This completely changes the understanding of the drop out rate: from the "ineffectiveness" of placebo to intolerance of benzodiazepine withdrawal.

The evidence for the alternative explanation is provided by the researchers, although they fail to apply the information to the issue of placebo group attrition. To begin with, subjects were accepted for the study despite being on "psychoactive medication" (p. 414). Following acceptance to the study, subjects were instructed to discontinue psychoactive medication for a 7-day period. This instruction therefore initiated a convoluted issue of who did and did not comply and the consequences (for understanding what happened to the placebo group) of compliance and non-compliance. Following the initial drug-free week, a second drug-free week was designated as the pre-treatment, baseline week. The same convoluted issue of compliance-non-compliance pertains here. As a biochemical check of compliance, plasma measures of alprazolam (Xanax), diazepam (Valium), and desmethyldiazepam (the principal metabolite of diazepam) were obtained during the baseline week, and again during weeks 3 and 8. During what was supposed to be the second successive drug-free week (the baseline week), 25% of the placebo group had measurable plasma levels of a benzodiazepine (1.6% measurable plasma levels of alprazolam

plus 23.4% measurable plasma levels of desmethyldiazepam). Even at week 8, of the placebo group subjects who remained in the placebo group, 12.3% had measurable plasma levels of a benzodiazepine (all the foregoing figures come from Table 7, p. 419). The upshot is that the placebo group was actually a mixture of people withdrawing from benzodiazepines, those surreptitiously taking a benzodiazepine, and those not previously on a benzodiazepine and who complied with the protocol. It is not known "who was who," but it is clear that some placebo subjects were withdrawing from a benzodiazepine during the 8 week study period, and it is clear that the placebo group as a whole emerged as an unknown mixture of different treatments.

Patient acceptance, side effects, and safety (Noyes et al., 1988) .The question of whether a drug can be used safely as medication is obviously a core component of what the FDA is supposed to evaluate. The issue facing the FDA was not whether alprazolam should or should not be made available for physicians to prescribe, since alprazolam was already an approved medication. The issue rather was whether or not the agency should extend its imprimatur to alprazolam as a specific treatment for panic disorder. The FDA realised that approval would result both in enhanced credibility for the disorder itself, a diagnostic entity which owed its existence in large measure to Upjohn's efforts, and in a massive upsurge in Xanax (alprazolam) prescribing. (1)

Upjohn's own researchers in this matter, namely Noyes et al. (1988), repeatedly state that high doses of alprazolam produced few side effects, but Marks et al. (1989) point out in their critical letter that "the data suggest otherwise" (p. 619). The manner in which Noyes et al. compare frequency of adverse effects in the alprazolam group to frequency of adverse effects in the placebo group is misleading, since it gives the impression that the pharmacologically inert placebo (lactose filler) produced much the same "side effect profile" as high doses of alprazolam. A more realistic treatment concerning the side effects of lactose filler for this placebo group would address both temporal variations in the original symptom complex (fatigue, etc.), and the commonplace. drug study phenomenon that the placebo group tends to mimic the active drug treatment group in terms of nature and time course of side effects (Fisher and Greenberg, 1993, discuss the latter point in terms of "penetrability" of the standard "double blind" arrangement).

In addition, Noyes et al. do not consider the possibility that reduction in reporting some adverse effects on the part of the alprazolam group over the 8 week active drug treatment period may be due to the development of lessened self-awareness and self-monitoring, which are common consequences of neurological injury (Dinnerstein, Lowenthal, and Blitz, 1996; Lindstrom, 1977; Morrow, Ryan, Hodgson, and Robin, 1990; Streufort and Gengo, 1993; Stuss and Benson, 1986; Summerfield, 1978). It is necessary to investigate whether some symptom reduction due to the clinical use of a neurotoxic agent is part of a larger clinical picture of neurological morbidity as Fink (1974) has done, that is, to apply multiple assessment methods which challenge a broad spectrum of cognitive-perceptual capacities. Nothing of this nature was attempted by Noyes et al. As I have pointed out previously, it is characteristic of psychiatric clinical drug studies to simply

ignore the complexity of psychological life.

Noyes et al. report that "only" 10 of the 263 alprazolam treated patients (about 4%) developed "serious or unexpected" reactions. Three subjects became severely intoxicated on only l or 2 mg of drug. One subject became "completely amnestic" for a 2 day interval on 6 mg daily. Aggressive or violent behaviour was reported by one subject on 4 mg daily; although this subject had not, according to the authors, behaved in this manner before receiving alprazolam, he was retrospectively judged to have an unstable personality disorder. Two subjects became manic, although neither had a history of mania. Two subjects developed alprazolam-produced hepatitis. Noyes et al. do not explain how such reactions - produced at a rate of about 4 in 100 - are compatible with consistently describing alprazolam as "safe." They also do not discuss the fact that in actual clinical practice it is not likely that most patients will meet once a week (as in the research study) with a psychiatrist for the purpose of carefully reviewing alprazolam-produced reactions. Although the authors note that "[symptom checklist] items reflecting cognitive impairment were more often reported by subjects taking alprazolam" (p. 425), and also that "the effects of benzodiazepines on memory are well known" (p. 427), they do not appear to consider this cognitive impairment a serious side effect, nor do they consider its effects on total psycho-social functioning. As previously discussed, this series of studies does not consider the organic and mental/behavioural consequences of long-term drug use at all, although long-term use is exactly what is expected in terms of treatment.

Discontinuation effects (Pecknold, Swinson, Kuch, and Lewis, 1988). The most glaringly irresponsible aspect of these Upjohn sponsored research reports is the manner in which the topic of discontinuation is handled. Although the Ballenger et al. (1988) paper reports on "efficacy in short-term treatment" (8 weeks), short-term treatment is not the expected use for alprazolam in the treatment of panic disorder. Klerman and the other senior investigators make this point clear in their 1989 response to the Marks et al. (1989) critical letter in Archives of General Psychiatry. In the response to Marks et al. they admit that it is in fact expected that alprazolam will be used in the treatment of panic disorder "indefinitely," due to the "chronic nature of the illness" (p. 672). In short, the discontinuation data derived on the basis of 8 weeks use is simply a sham, since the investigators are perfectly well aware that this time period does not represent how alprazolam will be used in clinical practice.

It should not be imagined that benzodiazepine addiction (alprazolam is a benzodiazepine, like Valium and Halcion) is merely an inconvenience. The major danger is that acute psychological and physical adverse effects may accrue over time, evolving into a tortured and severely impaired existence for the chronic user. Attempts to reduce the dosage or to discontinue completely may not be an option due to the severity of rebound and withdrawal reactions (Ashton, 1984, 1986, 1987, 1991). Although the present group of subjects (for the Pecknold et al. discontinuation study) reported a long history of panic attacks, no evidence is presented which suggests that the

emergence of panic episodes necessarily or usually heralds chronicity. Even when episodes of panic do become chronic, alprazolam (all benzodiazepines) causes too many severe adverse effects to be used as a long-term treatment. I have already observed that the placebo group improved substantially over the 8 week period of placebo-taking in spite of the fact that no deliberate form of treatment for this group was permitted by the research design. In a subsequent investigation instigated by these Upjohn-FDA approval studies, Marks et al. {1993) have shown that a psychological form of treatment can achieve clinically beneficial results without exposing patients to adverse drug effects and addiction. Note that by 1988 the State regulatory body in Britain, the Committee on the Safety of Medicines, had taken the step of officially warning all doctors that benzodiazepines should only be used on a short-term basis {Committee on the Safety of Medicines, 1988; Gabe, 1994). By contrast, in 1989 Klerman et al. acknowledge that they expect alprazolam to be used "indefinitely" in the treatment of panic disorder. It cannot be overlooked in this regard that in Britain a large part of the entire organisation of medicine is removed from private capital accumulation by virtue of the National Health Service.

On the basis of internal FDA documents obtained through use of the Freedom of Information Act, I can state that the FDA was so concerned about adverse long-term effects and addiction that it took the unprecedented step of extracting a commitment from Upjohn to conduct post-marketing, long-term dose-response and withdrawal studies by 1992 {letter from Robert Temple, M.D., of the Office of Drug Evaluation 1, to J.R. Assenzo, Ph.D., Upjohn Company, dated November 6, 1990). In the letter from Dr. Temple, Dr. Assenzo is reminded that Upjohn is required to comply under FDA regulations concerning a New Drug Approval. In response to my specific inquiry to the FDA concerning these required studies by Upjohn, I received a letter {dated June 15, 1995) which simply stated that the FDA has no documents "responsive to your request."

With regard to the Pecknold et al. {1988) study, the results following 8 weeks of alprazolam treatment or placebo by 4 weeks of taper and then 2 further weeks of no drug or placebo are discussed under three headings: relapse, rebound, and withdrawal syndrome.

Relapse data can be summarised straightforwardly. The alprazolam patients swiftly relapsed while the placebo group continued to improve during the taper period and the post-taper period or held more or less steady during this period {depending on the symptom or measure). The authors attempt to minimise the significance of the relapse data by pointing out that by the end of week 2 of the post-taper period the alprazolam patients who were still left in the discontinuation study had more or less achieved parity with the placebo group. But it isn't too difficult for the careful reader to discern how misleading it is to present the last post-taper week data in such a manner, for by this point only 33 alprazolam treatment patients out of the original 59 who began the taper were still left in the study, the rest having fled back to alprazolam because they could not endure the combined consequences of relapse, rebound, and withdrawal {note again that the placebo

group did not relapse, nor did it suffer drug-produced rebound effects and other drug-discontinuation effects, that is, withdrawal syndrome). It is also necessary to once again recall that no plasma screenings were conducted to check on compliance during taper and post-taper, so that it is legitimate to be sceptical about the extent to which the alprazolam patients who had not officially given up the attempt to withdraw actually complied with the protocol. As mentioned above in connection with Klerman's overview paper, a 1992 study (Dager et al.) which did conduct plasma checks on compliance found evidence of non-compliance in 23 of 44 alprazolam-treated patients.

The rebound effects for the alprazolam group are striking: of the 16 patients who were identified as suffering rebound panic, 4 reported more than 50 panic attacks per week during their worst week, and 8 reported from 6 to 36 attacks per week. This contrasts to the group's (N=59) baseline average number of panic attacks per week of 6.61 (Table 1, p. 432). Of the 8 alprazolam patients identified as suffering rebound anxiety, 3 had scores on the HAM-A exceeding 40 points (the baseline average for the alprazolam treated group was 23.86). Since rebound scores can only be obtained for patients who continue on taper or later on zero dose post-taper, patients who terminated discontinuation and relieved their withdrawal suffering by taking alprazolam could not be counted in terms of rebound. Inspection of week by week numbers in the alprazolam group during discontinuation (Table 1, p. 432) supports this interpretation. If this is correct, then patients who could not tolerate discontinuation did not figure into the data on rebound (this would mean that 26 of 59 patients in the alprazolam group did not figure into the rebound data by the second post-taper week). Again, no plasma level check was conducted to ensure that the rest had actually tapered to zero and remained at zero during the two post-taper weeks.

Pecknold et al. begin their report on "the withdrawal syndrome" by stating that no serious or life-threatening symptoms were observed, that in no case was the withdrawal syndrome incapacitating, and that of the 21 patients (of 59 who originally began withdrawal) in the alprazolam group identified as suffering withdrawal symptoms, symptoms were considered minimal for 8, mild for 7, moderate for 6, and severe for none. Withdrawal symptoms included confusion, clouded sensorium, heightened sensory perception, dysosmia (abnormality in taste and smell), paresthesias (tingling), muscle cramps, muscle twitch, blurred vision, diarrhoea, decreased appetite, and weight loss. The authors admit that the experimenter-created checklist limits what counts as a withdrawal symptom, and that the experimenter-created demand that subjects report at least four simultaneous symptoms in any given week to qualify as suffering from withdrawal syndrome may have operated to underestimate the true prevalence of withdrawal syndrome. There is no recognition or discussion of the fact that the alprazolam group's rapid flight back to alprazolam-taking obviously results in underestimation of the withdrawal syndrome. The importance of the limited checklist is borne out in a later discontinuation study by Noyes et al. (1991), who found that "Perhaps the most distinctive [withdrawal symptoms] were the unusual or distorted perceptions reported. ...These included a feeling of movement when there was none and

the perception that body parts had become separated from the rest of the body. Also reported were sensations of floating and falling, shimmering vision, and faulty depth perception" (p. 522). Of course by the 1991 report FDA approval was not at issue, as it was in Pecknold et al.'s 1988 presentation of findings (recall that Noyes is the first author of the 1988 report in this series on side effects and safety).

Although Pecknold et al. state that no patient suffered a severe withdrawal reaction, no information is actually provided as to how withdrawal syndromes were differentiated into minimal, mild, moderate, or severe. Likewise, no method of evaluation is presented as the basis of the conclusion that no patient was "incapacitated," or even just what the authors mean by this term. This conclusion is all the more suspect because the authors insist on discussing relapse, rebound, and withdrawal separately, as if these discontinuation phenomena were not happening simultaneously to the same person. Recall that 4 of the "non-incapacitated" subjects suffered more than 50 panic attacks during their worst discontinuation week.

Since the placebo group is not actually withdrawing from anything, the comparison of the placebo group's withdrawal symptoms with the alprazolam group's withdrawal symptoms does more to obscure than to enlighten the consequences of discontinuation for the alprazolam group. The experimental design could have included somewhat different time lines for taper and discontinuation within the total pool of alprazolam patients. In this manner dose-reduction and discontinuation-emergent effects could have been more credibly observed, eliminating at one stroke the confusing issue of symptom overlap with the placebo group. Given the seriousness of rebound and withdrawal effects for patient well-being (the two terms actually refer to the same physiological process), it is difficult to think of a higher priority for obtaining valid data in the overall research design. This is all the more pressing because regular daily use of alprazolam does not obviate rebound/withdrawal effects, since the biological activity of the drug initiates compensatory physiological reactions which result in such effects as the drug is metabolised (Ashton, 1991),

Prozac -A Further Illustration of Psychiatric Irresponsibility, Commitment to Invasive Medical Treatment, and the "Safety" Provided By the FDA

Many of the themes I have discussed above are also well illustrated in a recent clinical report concerning fluoxetine (Prozac)-produced akathisia (Lipinski, Mallya, Zimmerman, and Pope, 1989). Since financial support for this study was supplied by public funds (U.S. Public Health Service grants from NIMH), the obligation to act responsibly in the public interest is all the more pressing, although licensed physicians should not require additional incentive to act responsibly in the public interest, as the only justification for restrictive legislation on the part of the state (i. e., licensing) is the public interest (certainly not the interests of the profession or the pharmaceutical industry).

It is clear from details provided in the text that Lipinski et al. had been supplied with fluoxetine by Lilly Laboratories and were using it clinically on the basis of FDA permission (for "compassionate use") for some time before FDA approval of fluoxetine as a treatment for depression was granted in 1988. It therefore seems self-evident that it was incumbent on the authors to bring their clinical observations of fluoxetine-produced akathisia to the attention of the FDA before fluoxetine received FDA approval, but there is no suggestion that this was done or even attempted in the report, which was not even submitted for publication to the Journal of Clinical Psychiatry until July 6, 1988. This obligation was all the more pressing since, as reported on page 340, the authors had no expectation (based obviously upon information provided by the manufacturer, Lilly Laboratories) that fluoxetine would produce akathisia and therefore did not even look for this adverse effect until it was recognised by a psychiatric nurse (one of the eventual authors, Paula Zimmerman, R.N.). Apparently the drug insert information for fluoxetine as of the submission date of the paper (July 6, 1988, six months after fluoxetine had been marketed as an FDA approved antidepressant) still provided no information concerning its akathisia-producing properties. Based upon their own clinical assessments of fluoxetine-produced akathisia on 20 patients, the authors estimate that the prevalence rate for fluoxetine-produced akathisia is from 9.8% to 25%. However, they immediately add that "only a properly designed prospective study with adequate numbers of subjects can answer this question" (p. 340). But, of course, Lipinski et al. fail to suggest that fluoxetine should not have been approved for marketing while the prevalence rate was unknown, nor do they suggest that fluoxetine should not be used widely (as it was and is) while its akathisia-producing prevalence rate remains unknown. The authors are apparently content to allow the true prevalence rate to emerge slowly on the basis of clinical reports seeping into the literature over years or decades. Meanwhile, this adverse effect is treated with a variety of ameliorative drugs (e.g., propranolol and/or a benzodiazepine), and with no concern for long-term neurological damage and irreversible tardive neuropathologies (tardive dyskinesia seems especially likely, given fluoxetine's effects on dopamine neurotransmission). Lipinski et al.'s briefly stated observation that patients who developed akathisia due to fluoxetine "suffered greatly" (p. 340) is unusual in the psychiatric literature, although it in no way influences their thoughts about its continued use.

The notion of compassionate use of a non-FDA approved drug has a special meaning within the medical-pharmaceutical-FDA network. The FDA has the authority to permit non-approved drugs to be used by physicians if the FDA can be persuaded that evidence exists which suggests possible patient benefit - thus compassionate use. In the present case it can be seen how the commitment on the part of psychiatry to drug treatment converges with the interest of pharmaceutical companies in marketing profitable new drugs. Both interests lead to a specific outcome, namely clinical trials with experimental drugs on human subjects. It is by no means clear to me how experimental drugs should be tested on humans under the best of conditions. It is clear that under prevailing conditions the pharmaceutical industry and the psychiatric profession need to be constantly testing new drugs. There is little incentive to realistically think-through

what informed consent is supposed to mean to people who agree to take experimental drugs. Under extant legal authority the FDA cannot even oblige pharmaceutical companies to divulge all they really know about an experimental drug's effects on laboratory animals, on the grounds (according to the pharmaceutical industry) that such disclosure would required surrendering "trade secrets" (Dukes, 1980; Johnson, 1980). Since nothing prevents the federal government from granting the FDA such authority, the limitations imposed upon the FDA's ability to protect the public suggests that its real (as opposed to nominal) purpose is to protect and advance the pecuniary aims of the industry it is supposed to regulate (Berman, 1978; Navarro, 1976). I do not wish to move my critique of scientific psychiatry too far afield, but it is simply impossible to advance an intelligent discussion of psychiatric drugs without bringing in drugs as business and the relation of business to government. This does make the topic more complicated, but ignoring these complications has a high cost - to scholars of course, but more importantly to people who wind up taking the drugs.

It should be emphasized that reports concerning adverse effects of psychopharmacologic treatment seep very slowly into the psychiatric literature. Major problems exist in the area of psychiatric undereducation concerning the existence and recognition of adverse effects and in the area of clinical non-recognition or mis-diagnosis of adverse effects (Dixon, Weiden, Frances, and Rapkin, 1989; Van Putten and Marder, 1987; Weiden, Mann, Haas, Mattson, and Frances, 1987). The upshot is that psychiatric opinion regarding the range and prevalence of a drug's adverse effects must be regarded with great scepticism. Dixon et al. (1989) report that their examination of the curricula of five local psychiatric residency programs revealed that on average only 0.5 hours was spent specifically on neuroleptic-produced neurological syndromes during the course of the entire program. Brown and Funk (1986) provide an important discussion of medical reluctance to recognise iatrogenic illness.

Lipinski et al., present five clinical cases for the purpose of illustrating the phenomenology and time course of fluoxetine-produced akathisia. These five cases are described as representative (1989, p. 340), and indeed they are, not merely of fluoxetine-produced akathisia, but of the entire tragedy of treating psychological distress "in a strictly medical sense."

It will suffice to summarise and comment upon only two of the cases:
Case one. Miss A was hospitalised at the Mailman Research Centre, McLean Hospital, when she was 18 years old. She is described by the authors as "well" until the "onset of typical depressive symptoms" 18 months earlier. She is further described as developing severe obsessions, including fear of contamination and compulsive rituals, approximately six months after the onset of depression. Since the authors had clearly met Miss A for the first time when she entered McLean Hospital, the question arises as to how they knew she was well until the onset of typical depressive symptoms 18 months earlier. If such a retrospective judgement can be plausibly made, it would have to depend upon a great deal of information, much of which could only come in the

form of self-disclosure from the client herself. The authors present no basis for their description of the client prior to her appearance at McLean Hospital. There is certainly nothing in their report which suggests that their description was based upon a prolonged and in-depth exploration of the patient's life from her own point of view. The reader is certainly curious as to what events, conditions, or circumstances might have contributed to the sudden emergence of Miss A's depression, but Lipinski et al.'s write-up does not address this.
It might be argued, I believe disingenuously, that the report is essentially an adverse-drug reaction notification, and therefore not the place to discuss the origin of Miss A's outbreak of symptoms. Such an argument would entirely miss the point of describing Miss A as well until the outbreak of symptoms when she was approximately 16~years old, since this characterisation simply dismisses as irrelevant the vast psychiatric clinical research literature which indicates that it is preposterous to expect the emergence of such serious symptomatology in someone who in reality enjoyed a benign course of psychological development (e.g., Bryer, Nelson, Miller, and Krol, 1987; Fontana, 1985; Goodwin, 1985; Gunderson and Chu, 1993; Pribor and Dinwiddie, 1992; Rose, Peabody, and Stratigeas, 1991; Terr. 1991). The description of Miss A as well up to the recent past is a deliberate advancement of biopsychiatric theory, which, as Klerman (1978) made explicit in anticipation of the DSM-III, regards psychological development as irrelevant to both diagnosis and etiopathogenesis. In short, Lipinski et al.'s credulity regarding Miss A's psychological history represents the paradigm shift within psychiatry's ruling elites during the past 25 years - from the psycho-social framework of thought to the biopsychiatry-neo-Kraepelinian framework of thought (Wilson, 1993). It is the self-confident (if largely tacit) reliance on the latter framework which spares Lipinski et al. any need to justify "treating" Miss A with what is manifestly a neurotoxic chemical substance, or to comment on the fact that during the past 18 months she had been already treated with alprazolam, amitriptyline, lithium, perphenazine, and pimozide.

If any thought was given to the possibility that Miss A might first and above all need her treatment professionals to seriously inquire into the conditions of living which prevailed at the time of her outbreak, or that she might improve with proper psycho-social care, or that her psychological condition in the present might be hopelessly confounded by drug interaction effects, side effects, and withdrawal effects, it certainly does not appear in the summary of her case. Instead, Miss A was at once treated at McLean with a non-FDA approved drug about which little was known. On treatment day 5 she reported severe anxiety and displayed typical signs of akathisia. Since she was being treated in a research centre, fluoxetine was not discontinued. Rather, a beta-adrenergic receptor antagonist (propranolol) was added to her drug regimen to ameliorate her fluoxetine-produced akathisia.

If the treatment 'professionals at McLean had any concern that adding another centrally active drug to what had already shown itself to be a neurotoxic substance (fluoxetine) might further disrupt Miss A's neurophysiology - especially in the long-run -it likewise failed to appear in the

write-up. It cannot be overemphasised that the long-term consequences of fluoxetine in combination with propanol are unknown. Psychiatric drug research simply does not address itself in any planned (prospective or retrospective) manner to the issue of long-term consequences (e.g., Crane, 1982). Reports in the psychiatric literature on adverse consequences are not based upon long-term follow-up studies -such studies do not exist. Nevertheless, it can be surmised from other sources that long-term exposure to neurotoxic chemicals leads eventually to serious organic and psychological morbidity (Lindstrom, 1977; Morrow, Ryan, Hodgson, and Robin, 1990; Streufort and Gengo, 1993; Summerfield, 1978). Recall that Miss A was only 16 and a half when she began to be exposed to neurotoxic "medications." Psychiatric drug research and clinical practice seems -incredibly -indifferent to the long-term consequences of centrally active drugs.

Case four. Ms. D is a 35 year old woman with a five year history of progressively worsening Obsessive Compulsive Disorder "refractory to treatment with several antidepressants and ECT" (Lipinski et al., 1989, p. 340). At admission to McLean, she was receiving trazodone 600 mg/day. She also displayed mild jerking movements in all extremities, diagnosed as myoclonus. This reveals that her CNS had already been damaged, a state of affairs Lipinski et al. are willing to attribute to her history of exposure to several antidepressants and to ECT. It is therefore obvious that the long-range outlook for Ms. D must emphasise protecting her from further CNS assault. Nevertheless, three days after discontinuation with trazodone she was placed on 20 mg/ day of fluoxetine. Within 12 hours she developed signs of akathisia - an unmistakable sign of neurological disturbance. Furthermore, her myoclonic symptoms had become more severe. Treatment with 60 mg/day of propranolol (another centrally active drug) produced remission of symptoms of akathisia, but the myoclonic symptoms continued. Lipinski et al. do not reveal how they could discern that the subjective symptoms of akathisia (anxiety, tension, restlessness, agitation) had remitted while the symptoms of Obsessive Compulsive Disorder and depression, which overlap to a substantial degree, still required treatments with fluoxetine. In the general discussion section, the authors admit that akathisia persisted for more than a year in the case of one patient (unidentified), but they do not explain how this might be compatible with overall clinical gain produced by treatment with fluoxetine.

The entire tone of this report takes it for granted that psychological symptomatology indicates in-hospital treatment with an experimental neurotoxic agent. In this regard it is necessary to point out that most of the money spent on "mental health treatment episodes" in this country is for in-patient treatment (approximately 82%, according to Kiesler and Simpkins, 1993), and that reimbursement policies on the part of both the federal government and the commercial insurance industry actively discourage out-patient care (Brown, 1985; Kiesler, 1992; Kiesler and Sibulkin, 1987). This means that - contrary to what Kiesler and Sibulkin (1987) regard as popular opinion, even among many mental health professionals - psychiatry as a profession is tied to the medical hospital setting, regardless of how counterproductive it is to treat psychological disturbance as a medical condition which requires hospitalisation and conventional medical treatment (drugs).

Perhaps the most poignant spokesperson on the issue of using drugs as treatment is Loren Mosher, former NIMH Chief of the Centre for Studies of Schizophrenia and founder of the Soteria House project in San Jose, California, a non-hospital, primarily non-drug facility for the treatment of persons newly diagnosed as schizophrenic. Despite the well-documented success of this project over a ten year period, funding by NIMH and other sources was ultimately terminated. Mosher has been remarkably candid concerning the reasons for the demise of the Soteria project, namely its manifest threat to the hospital-psychiatry-pharmaceutical industry (an excellent and brief summary of treatment findings regarding the Soteria project as well as non-scientific and non-treatment reasons for its demise is provided by Mosher and Menn, 1983). Certainly the vigorous promotion of biopsychiatry (both in terms of cause of psychological disturbance and in terms of treatment of psychological disturbance) drains interest, energy, and resources away from practical responses to the roots and manifestations of psychological damage. In terms of the origins and development of psychological disturbance, what is most important is to limit the individual's exposure to pathogenic conditions of life. Since treatment professionals have little to gain by prevention, minimal professional thought is devoted to this area (Kleinman, 1988). Thus psychiatry, like American medicine generally, is fixated upon diagnosis and treatment (Hurowitz, 1993). Unfortunately, medical treatment for the already sick remains problematic in all areas of medicine, but perhaps nowhere more conspicuously than in psychiatry. In terms of treatment, it is first of all imperative to acknowledge that by the time a person has become a "patient," a good deal of damage has already been done. Practically speaking, this means that conditions of healing must be made available for prolonged periods if there is to be a realistic hope of substantial and sustained improvement. Although it is appealing to suppose that the means (i.e., psychotropic drugs and/or ECT) exist to apply a purely technological relief from psychological disturbance, I hope that 1 have provided reasons for concluding that this does not in fact constitute a viable route for healing or even palliation.

Conclusions

In the preceding pages I have discussed the following points concerning the past forty years of psychiatry's attempt to treat psychological distress in a strictly medical sense:
1. Psychopharmacologic treatment research has in effect created a fabulous beast - a person who is simultaneously better or improved under one heading of a research report and suffering from \V hat may be disastrous side effects under another heading of the same report. The way is prepared for this purely rhetorical outcome by construing the seamless totality of the patient's psychological distress/disturbance/dysfunction in terms of narrowly defined target symptoms, and thereby creating a problem and task that fits into a medical framework of thought and action. In this manner the consequences of the "medicine" in terms of its effect on the target symptoms can he regarded as independent from its other consequences, and the idea that the patient is an actual person whose life-as-a-whole is completely integrated as a unified totality is dispensed

with. It is only by defining target symptoms narrowly that it is conceivable even to discuss the relative efficacy of psychopharmacology and psychotherapy, since the psychiatrically reconstructed task is indifferent to how the target symptoms are subdued, the suffering and disability produced by adverse drug effects, and the long-term (unexamined) organic and psychological consequences of treatment with centrally active chemicals.

2. The reconstructed task of pharmacologically subduing narrowly defined target symptoms operates to render irrelevant both the patient's past (in terms of conditions of life and resultant course of psychological development); and present conditions of life. Pragmatically, the functional imperatives of the medical-hospital-pharmaceutical industry and the funding needs and research interests of the biological science community make the conviction that "mental disorder" fundamentally derives from organic abnormality too valuable to abandon.

3. It has been known for many decades that neuroleptics produce not only irreversible movement disorders, but also as a consequence of their widespread pathophysiological effects in the brain, eventually produce mental-emotional-behavioural impairments. The idea that any class of psychoactive drug has only limited action that is restricted to specific anatomical sites and specific neurotransmission systems is a fiction that ignores what is actually known about the total anatomy and integrated functioning of the brain.

4. The issue of the costs and risks connected to the clinical use of a drug is a complex matter which involves both the natural course of an illness as well as patient evaluation of the overall burdens imposed by the illness compared to the overall burdens imposed by the medications (among other considerations). The overall burdens imposed by the medications is a massively under- developed topic in psychiatry, which is subject to the usual medical reluctance to recognise iatrogenic illness and the insidious deforming consequences of competitive pressure exerted by the encroaching non-medical treatment professions. As for the natural course of "psychiatric illnesses," psychiatric reliance on drug treatment has enormously underplayed the actual variability in severity and degree of distress/impairment across persons and over time intrapersonally, the responsiveness of any "mental disorder" to variations in social-interpersonal-material conditions of life, and the con- founding consequences of many drugs and drug combinations over time.

5. The commitment to psychopharmacologic treatment can be adequately understood only by including potent external (i.e., non-scientific) influences on the development of psychiatry as a discipline and a profession in the post World War II era, not the least of which has been the competition posed by the emergence of encroaching professions.

6. Potent external (i.e., non-scientific) influences have acted to move psychiatry into ever more vigorous assertions of the organic roots of "mental disorder" and into a corresponding

psychopharmacologic nominalism for treatment purposes.

7. The catastrophe of medically-created illness of unprecedented proportions on the part of psychiatry from the 1950s to the present (which far exceeds its record of multiple "shock" therapies, psychosurgeries, muscle relaxants, amphetamines, and barbiturates} has not produced a critical self-examination within psychiatry of the ideological, conceptual, financial, professional, and systemic factors which in combination produced the catastrophe.

8. My contention that for all practical purposes nothing of value has been learned from the catastrophe of the past forty years on the part of psychiatry is illustrated in detail by examining the recent introduction of two psychopharmacologic agents: alprazolam (Xanax) and fluoxetine (Prozac).

9. The most important lesson produced by the past forty years of psychopharmacologic research with respect to the theoretical understanding of psychopathology and practical lines of treatment alike is the potent and consistent placebo effects which this literature has inadvertently uncovered.

10. The entire question of the safety and efficacy of a psychotropic drug for either acute or prolonged treatment must be removed from the pharmaceutical industry-psychiatry-FDA cabal (Mosher and Burti, 1989, use this term - a strong word coming from someone - Mosher - who was [to repeat] NIMH's Chief of the Centre for Studies of Schizophrenia). Each arm of this cabal is irretrievably compromised - although in the case of the giant, for-profit pharmaceutical companies there is no realistic expectation in the first place that they would place public good above profit maximisation. The condition of genuine neutrality is an absolute minimum for trustworthy research and policy making. Any suggestion for reform which does not recognise this principle is thoroughly in bad faith.

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(1) I have drawn upon internal FDA documents concerning alprazolam obtained under the Freedom of Information Act as the basis for the foregoing remarks.