ABSTRACT

Title of Document: ADOLESCENTS AND ANTIDEPRESSANTS: ANALYZING A SOCIAL SCIENTIFICCONTROVERSY

Amber Dawn Nelson, M.A. 2007

Directed by: Assistant Professor Laura Mamo, Department of Sociology

This thesis analyzes the scientific controversy over giving antidepressant medications to adolescents as it unfolded in a U.S. Federal Food and Drug Administration (FDA) hearing. Using the FDA hearing held on February 2, 2004, convened in response to a "crisis" evolving around the safety of antidepressant use among adolescents, this paper analyzes the unfolding response. This study utilizes social world's analysis, a qualitative methods approach designed to uncover the multiple stakes and claims of the problem as understood by each person at the hearing. I identified four distinct social worlds: 1) Adolescents, family and friends, 2) Independent professionals, 3) FDA, and 4) FDA-summoned professionals. Findings revealed that 103 actors came together around the crisis and each defined the problem of the controversy through one or more of the following four distinct frames; (1) side effects, (2) data, (3) practices and policies and/or (4) a lack of access to informed choice.

ADOLESCENTS AND ANTIDEPRESSANTS: ANALYZING A SOCIAL SCIENTIFIC CONTROVERSY

By

Amber Dawn Nelson

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Advisory Committee:

Assistant Professor Laura Mamo
Professor Melissa Milkie
Professor Jeffrey Lucas

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"Scientific controversies have long excited both the passion of participants and the interest of social scientists. For researchers into the nature of science, controversies have the advantage that social processes normally hidden in laboratories and offices are brought into open view in a dramatic fashion. Assumptions that are normally implicit are challenged by disputants; routine procedures scrutinized, and weak points in arguments attacked" (Scott, Richards & Martin 1990:474).

Chapter 1. Introduction

A scientific controversy over the connection between antidepressant medication and youth suicide arose in the early years of the 21st century. This controversy revolved around the question of whether or not the use of antidepressant medications in general and Selective Serotonin Reuptake Inhibitors (SSRI's) in particular, have a causal link to suicidal thoughts and behaviors of youth. In December 2003, a government expert panel in the UK declared that all SSRI's except Fluoxetine (Prozac) were contraindicated for prescription to patients younger than 18 (Tonkin & Jureidini 2005), in effect recommending that no youth should be prescribed any SSRI medication except for Prozac. This recommendation in the UK galvanized the American public to similarly weigh the risks and benefits of such medications for youth in the U.S. In response, the Federal Food and Drug Administration (FDA), the regulatory agency of the US, held a joint advisory committee meeting open to the public on February 2, 2004 (Ryan 2005; FDA 2004).[1]

This controversy highlights the uncertainty of scientific knowledge surrounding the crisis of suicide, the use of antidepressants and the very meanings of mental illness

[1] It had been over twelve years since the FDA had convened to address the question of whether Prozac induced suicidality in adults; and the FDA committee members had ruled that there was not enough evidence to take Prozac off the market (Check 2004).

itself. In an attempt to analyze the social process surrounding the pharmaceutical intervention into adolescent mental health, this research study examines social actors who came together at the FDA hearing to provide their interpretations of the problem(s) of the controversy. This study reports the findings from a qualitative analysis of the hearing held in Maryland. Using a situational analysis, I found that each social actor's definition of the problem was shaped by their sociopolitical position and their personal and professional experiences with adolescents and antidepressants.

This research project asked three questions: (1) how do various social actors engaged in this controversy define the problem? (2) What are the sites of ambiguity and contestation that have emerged in the discourse? In other words, what are the areas of the problem or the controversy where different social worlds are able to reach consensus and what are the areas where there is disagreement between social worlds? And (3) what is minimized or missing from each social actor's or social world's depiction of the problem?

I analyzed the adolescent-antidepressant crisis as a controversy in which multiple perspectives came together to define, make claims, and ask for solutions to what is an agreed upon problem, but a problem with uncertainty. It is agreed that certain knowledge does not exist in the case of adolescent SSRI use and that the scientific community must address this uncertainty; however, the source, meaning, and potential responses to this uncertainty are far from agreement. As a result, I examined this controversy as an object around which multiple actors situated in different communities came together in hope of moving towards more certainty. I used the February 2, 2004 FDA proceedings called in response to the escalating uncertainty around the risks and benefits of prescribing

antidepressants to youth as my primary data site. This hearing was important to the development of this controversy because it represented the pinnacle of US state-public-science interaction. I analyzed each speaker and social world's statement as perspectives with specific claims, interests, and stakes in the controversy around which all actors were vested in some way. I then used the answers to these questions to analyze what this tells us about contemporary social constructions of and responses to adolescent mental health and illness.

I identified four distinct social worlds: 1) Family, friends and victims, 2) Independent professional experts, 3) FDA agents and 4) FDA-summoned professional experts (including members of advisory committees). Findings revealed that 103 actors came together around the crisis and each defined the problem of the controversy through one or more of the following four distinct frames; the problem was one of (1) side effects, (2) data, (3) practices and policies and/or (4) a lack of access to informed choice. Following the assertion that all knowledge are contingent and situated (Haraway 1991), I found variety in the definitions of the problem: family social world actors defined the problem as one of material side effects and FDA speakers defined the problem as one of clinical trial data issues. The FDA agents set the terms of the debate, that the question was one of clinical trial data issues. The FDA agents set the terms of the debate, that the question was one of antidepressant risks and benefits and the way to answer it was through statistical analysis of clinical trial data: and the family social world contested these terms through presenting their alternative experiential knowledge of material side effects. Independent professional experts and FDA-summoned professional experts

(advisory committee and other open committee discussion members) contested the FDA agents' terms of debate, mediated conversations, and offered suggestions for change.

Youth, Depression and Pharmaceuticals: The Making of a Controversy

The United States currently has an extremely high prevalence of depression, suicide and antidepressant medication use in adolescents compared to other age groups and time periods, making this controversy unique to this particular sociohistorical junction (Judge & Billick 2004; Rutz, & Wasserman 2004; Scherff, Eckert & Miller 2005; Bucholtz 2002). The median age of onset for any psychiatric disorder is age 16 and a substantial number of people who experience major depression or mood disorders have their first episode before the age of 20 (see Robins, Locke & Reiger 1991; Kessler & Zhao 1999). Depressive symptoms in general have a higher incidence in adolescent and elderly populations compared to other stages in the life course (Weisz and Hawley 2002; Kessler & Zhao 1999; Stockard & O'Brien 2002). The prevalence of depression in youth commonly causes impairment in social functioning and is often associated with an increased risk of suicide-mortality (Ryan 2005). Although not everyone who is suicidal is depressed and not everyone who is depressed becomes suicidal, depression and suicide are often linked (Kircaldy, Eyserick, & Siefen 2004; Delate, Gelenberg, Simmons & Motheral 2004; Cutler, Glaeser & Norberg 2000). Suicide is the third leading cause of death among adolescents 10 to 19 years of age (Weisz and Hawley 2002; Centers for Disease Control, 2002; Anderson & Smith 2003; Berman & Jobes 1995). In 2002, suicide was the second leading cause of death among 12 to 17 year olds in the United States (Macgowan 2004).[2] While these statistics demonstrate that adolescent depression

[2] Although the majority of suicides in the U.S. occur among Caucasian adolescents, the rates among Native American, Hispanic and African American adolescents has been steadily increasing over the past decade

and suicide are important social problems which need addressed, various perspectives exist rendering both the cause of mental illness and the best way to intervene, uncertain.

Contemporary research in mental health studies of adolescent suicide support the notion that there is a strong correlation between the rates of adolescent suicide and sociocontextual issues such as; a lack of family support, school problems and a history of abuse within their family (Murray & Wright 2006). In contrast, some expert science and or medical researchers argue that suicide is the result of the prevalence of depression and other mental health disorders in persons who have not sought treatment. For many psychiatrists, pharmaceutical and medical professionals, depression and the serious risk for suicide it poses for youth is the reason why antidepressants should be prescribed.

According to national estimates, antidepressant use increased 73.4 percent between 1990 and 1995, with the majority of this increase coming from prescriptions of SSRI's (Sleath and Shih 2003).[3] This sharp increase in antidepressant prescription to youth for mental health problems raises concern that their use has outpaced the existing clinical evidence of their efficacy (Shiremen et al. 2002). On average, between 1998 and

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(Rutter & Behrendt 2004). Blacks attempted suicide one-fourth less frequently than white adolescents and completed suicide one-third less (Cutler, Glaeser & Norberg 2000) while suicide is the fourth leading cause of death among Hispanic youth 10 to 19 years of age (Fornos et al. 2005:162), and American Indian/Alaskan Native male adolescents have the highest suicide rates of any demographic grouping (National Adolescent Health Information Center 2006 Fact Sheet on Suicide). Although females attempt suicide 50 percent more than males, they complete the act of suicide six times less frequently (Cutler, Glaeser & Norberg 2000) and rates of suicide are lower for females than males (Stockard & O'Brien 2002). Sexual minority youth (gay, lesbian and bisexual), attempt suicide three times more often than heterosexual youth (Judge & Billick 2004; Rutter 1998). Finally, despite the sex, race, sexual orientation and ethnicity, the economic structure and resources of a youth's family will also determine their susceptibility to being at risk for committing suicide. Adolescents whose families receive welfare are 30 percent more likely to attempt suicide (than adolescent's whose families do not receive welfare) and adolescents who live with a single parent are twice as likely to attempt suicide as those who live with two parents (Cutler, Glaeser & Norberg 2000).

3. A similar estimate found that between 1990 and 1996, the total number of SSRI prescriptions for children and adolescents increased by 69 percent (Shiremen, Olson & Dewan 2002). Finally, a study that evaluated almost a million Medicaid and HMO youths concluded that child and adolescent psychotropic prescription rates nearly tripled since the pre-1990s levels (Zito et al., 2003).

2002, antidepressant prescription among children increased 9.2 percent each year and even more importantly, the largest year-to-year increase was from 2001 to 2002 at 16 percent (Delate et al. 2004). In sum, there has been a sharp increase in antidepressant prescription to children and adolescents since 1990, and this growth is continuing.

Although antidepressant prescriptions have become the dominant medical response to the social problems of adolescent disturbance, there is mixed evidence on the efficacy of antidepressants.[4] Despite the mixed evidence, no clinical trial studies have been designed for the sole purpose of measuring the risk for suicidal thoughts or behaviors or any other serious side effects that antidepressants cause in some patients.

Given the seemingly high rates of depression and suicide, the increase in treatment with SSRIs, and the lack of efficacy in evaluating the success of such treatment, ambiguity has led to controversy. At the center of this controversy are children and adolescents: populations usually deemed vulnerable and in need of protection. It has recently been shown that children and adolescents respond to medications differently than adults, opening up previously taken-for-granted facts about youth and medications (Cohen et al. 2004). This scientific evidence arises as rates of antidepressant use in children and adolescents are increasingly raising significant concern (Brophy 1995).[5] The possibility that SSRIs may worsen youth depression and or

4. Some expert professionals argue the side effects of psychotropic medication for children may actually increase the risk for mania and suicide. In one study that demonstrated efficacy of Prozac (Emslie et al. 1997), it was noted that six percent of the participants dropped out because of manic reactions. If this were extrapolated to the general population, for every 100,000 children taking Prozac, 6,000 would experience this type of serious side effect (Sparks & Duncan 2004:34). Another example is a study of Paroxetine (Paxil), which found that 21 out of 93 (23 percent) of youth taking Paxil reported manic-like symptoms which included hostility, emotional lability and nervousness (Sparks & Duncan 2004).

5. As knowledge about youth and medications continued to develop, so did the skepticism of the decision making process of pharmaceutical companies (Varley 2006) and the FDA. Psychosocial treatment interventions (not pharmaceuticals) are difficult to secure (Cohen et al. 2004; Ryan 2005); and such limited access produces reliance on antidepressant medication as the primary response to youths' psychosocial

facilitate suicidal or homicidal ideation, mania or induce bipolar disorder, is reason enough to de-stabilize buried scientific assumptions in the arenas of scholarship regarding adolescent mental health and illness.

Chapter 2. Symbolic Interactionism, the Sociology of Scientific Knowledge and Western Feminist Epistemology

It is argued that when a social controversy occurs, previously taken-for-granted knowledge as fact becomes disrupted, thereby providing an opening for other (alternative or previously not legitimated) perspectives to emerge. The social process of knowledge construction normally hidden becomes subject to scrutiny. In addition, assumptions embedded in knowledge are revealed for how their perspectives serve as certain forms of knowledge. These ways of constructing, knowing or experiencing can be compatible, contradictory or somewhere in between the assumptions that previously existed. A controversy expands the field by bringing forward multiple social actors and their pluralistic perspectives. To adequately analyze this controversy, I drew on symbolic interactionism, the sociology of scientific knowledge and western feminist epistemology.

Symbolic Interactionism

A premise of symbolic interactionism is that meanings are processual; they are built-up in social interactions. Social processes, not individuals, are the unit of analysis. Social actors are seen as active in the construction of the material and social aspects of their lives, they are not seen as passive beings. As a result, instead of viewing knowledge as fixed or facts, experiences and knowledges are seen as plural. An analysis of social

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disturbances. This reliance on prescription medications may teach youth to solve their emotional and behavioral problems pharmacologically instead of through emotional and social competence such as coping or communication skills (Sondergard et al. 2006).

actors' standpoints allows the often inaccessible experiential knowledge (in this case, of youth and their families), to become visible and be treated equally alongside knowledges of government actors, scientists, doctors and others who also share a stake in the controversy (including working professionals who came to the hearing to voice their specialized concerns).

Following symbolic interactionist theory; if all producers of knowledge and knowledge production are taken seriously as a site for investigation, controversies can be understood as emergent social processes that involve challenges to existing political arrangements; can reveal special interests or hidden assumptions of social actors, and can lead to policy changes (Markle & Peterson 1981). Further, some interactionists examine collective actions characterized by commitments to a common goal, the utilization of shared resources to achieve those goals and the development of shared ideology along the way. Such collective actions, social worlds, are examined rather than individual positions and are understood as a resource for knowledge production. The situated position from which knowledge is constructed does not rely on the idea of individual identity positions. Instead, the situatedness of the group or social world is conceptualized *itself* as a site of knowledge construction.

Using a Symbolic Interactionist perspective, I argue that the FDA hearing and the context surrounding the controversy is not a natural phenomenon, but an emergent social process in which various social worlds come together to negotiate and produce knowledge claims. The crisis of risks and benefits does not reflect physiological facts, nor is it determined by SSRI medications themselves.

The Sociology of Scientific Knowledge

According to the Sociology of Scientific Knowledge (SSK), the study of controversy is an interested project involving the deconstruction of the social aspects of knowledge production (Wright & Treacher 1982). These social aspects of knowledge production include what is politically permissible to talk about or research. Further, social aspects of knowledge production are closely related to how some perspectives or realities are institutionally legitimated or seen as valid while others are seen as less valid. Every controversy over a scientific technology has competing knowledges (or narratives) that emerge from how differentially socially situated people view the problem and how they think it should be addressed. *"Both knowledge claims and value claims shape scientific and technical controversies"* and uncovering both of these types of claims is central to a scientific study of controversy (Markle & Petersen 1981:27). The immediate attention of the nation to this crisis serves as an entry point into studying the multifaceted nature of the controversy and how social actors define or frame the problem differently.

Feminist Epistemology

Feminist epistemology examines knowledge claims as situational, (formed through social locations). Feminist epistemology aims at problematizing how knowledge and "truth" are bound by relations of power that operate in all knowledge contexts. For example, feminist standpoint theory asserts that the experiences or standpoints of lay persons often become excluded, denied or obscured by scientists or other authoritative knowledge producers due to the power relations inherent in any production of knowledge (Hunter 1999). Feminist critiques of science hold that all standpoints are structured by experiences and relations of power within social contexts (Hunter 1999). These critiques

tend to focus on two forms of tacit knowledge that scientific knowledge production/practices obscure (Hunter 1999). First, feminist critiques deconstruct scientific assumptions of objectivity and truth (assumptions such that scientific methods are objective, scientists are autonomous from what they study and scientific language is neutral). Second, feminist critiques interrogate the field of knowledge practices; in particular, the practice of scientific experts effacing or denying the voice of patients (and legitimacy of) or other such marginalized or subjugated persons and their standpoints. Hernstein-Smith (2006:98) argues that the sociological 'symmetry postulate,' as interpreted correctly, implies that there exists no knowledge claim or belief that can be assumed to be inherently valid (as Truth). Feminist epistemologists such as Donna Haraway (1989, 1991 & 1997), Dorothy Smith (1990) and Patricia Collins (1990 & 1998), make interferences into the assumptions of what is considered "scientific" versus "tacit" knowledge(s). Of importance is the power dynamics involved in whose knowledge is deemed legitimate. Feminist standpoint theories argue that the very nature of oppression gives rise to particular experiences and perspectives which provide a distinctive standpoint from which to build theory (see Collins 1990). While Collins locates power and oppression within distinct economic, political and ideological structures, Dorothy Smith uses the term "bifurcated consciousness" to argue that power is located in texts that are disseminated by those who rule in order to maintain their power. Haraway, in contrast, highlights what she terms the ideological god-trick of dominant (especially scientific) knowledges. Haraway implicates the unmasking of the situatedness of knowledges as a political process, one with consequences for the ways in which we imagine whose knowledges and what interests they assert.

The theory/praxis of Haraway, Smith and Collins re-configures the material relations of knowledge production such that the credibility of all constructions of reality are regarded as needful of explanation (Hernstein-Smith 2006). This reconfiguring is not about reordering knowledge producers in an attempt to create a new hierarchy of ideas, but instead, is about democratizing the process of how knowledge is produced, (by whom, and in what knowledge contexts). Feminist epistemology assumes that theory and practice are bound up together and thus produce situated knowledges. This reconfiguring of knowledge as a socially-situated process allows for sociologists to investigate how beliefs about the world are socially shaped, constrained and stabilized (situated), (Hernstein-Smith 2006: 101), despite the nature of the particular locations of both social actors (important public officials or laypersons) and social worlds (organizations, scientific expert disciplines or institutions) whose standpoints are being investigated.

An advantage of using the sociology of scientific knowledge production is that it makes messy social processes problematic instead of taking them for granted. Deconstructing scientific knowledge, sociologically, involves paying attention to the assumptions embedded in scientific knowledge production, including the assumptions about the science or evidence that has led to it (such as the technology of antidepressant medication) being perceived as the right or correct way to solve a problem (adolescent disturbance) (Scott, Richards & Martin 1990).

This sociopolitical crisis allows me as a sociologist to enter into a study of a bounded controversy because it contains conflicting sets of understandings of what the problem is, what is at stake and how the public should respond. One cannot simply make sense of the controversy or the underlying problem(s) without understanding that neither

the issues (for example; whether antidepressants should be prescribed to youth), nor the responses to this issue are given or are one-dimensional. Crisis itself is constituted in the variety of ways social actors define the problem.

Theorizing the Adolescent SSRI Controversy

Following symbolic interactionism, SSK and feminist epistemology, this project examines the historical emergence, social production of knowledge claims, and perspectives of current social actors as part of social worlds (the emphasis here is that their situatedness in a social world shapes their perspective). Together, these inform and shape the ways each understands the "problem" and its necessary solutions. As stated above, symbolic interactionism is a social constructionist perspective emphasizing that meanings arise out of particular social and cultural context, and cannot be separated from them. One variant of this perspective has focused on the social construction of knowledge in general and scientific knowledge in particular. One dominant focus that social studies take regarding scientific knowledge production is the construction of disease itself. In examining depression, I assume the *disorder* itself (depression or another psychiatric diagnosis) is socially constructed such that there can exist multiple knowledges around the diverse phenomena which fall under this rubric. This does not imply that there is no reality in the experiences of those who suffer from psychosocial disturbances that become manifested in various forms of distress, but rather that knowledge about depression or anxiety is differently constructed in the various situations of those who engage it. Depression is real, but it is given meaning through multiple

perspectives; medical, psychiatric and the perspectives of actors who live with depression itself.[6]

A major innovation in the social psychology of health and illness following social constructionism is to bring the perspectives and experiences of patients (persons) forward as valuable knowledge sources. This allows the experiences of adolescents and their families' more equal participation and important consideration in defining adolescent disturbance, antidepressant side effects and other problematic areas of the controversy. Taking this one step forward, it is not only their individual standpoints that are important, but their positions within particular social worlds. Interactionist theories posit that meanings are constructed through human interactions, and thus, constitute a process. Feminist sociological projects which study scientific knowledge production, interrogate how science is produced and then constructed regarding any particular object or

[6] The embodied experience that comes to be depression becomes so because of a process of interactions and discursive constructions—a process that is informed by larger issues of power in society. Psychosocial phenomena that have come to be termed, depression or anxiety, must be sited, defined, categorized and articulated before they come to be what we think of as depression, and each of these is a complex social process including multiple interactions taking place within contexts of power. Knowledge has shifted and transformed over time, both in response to scientific discoveries (themselves the product of complex social processes) as well as changes in the societies in which depression is interrogated as a subject of knowledge production.

> Biological explanations that define mental illnesses as brain diseases legitimize particular constructions of social reality that have great credence in contemporary Western societies. Attributing psychiatric symptoms to depleted levels of serotonin for example, has no more inherent value as a cultural explanation than attributing them to unconscious forces or to demonic possession (Horwitz 2002:9).

Horwitz points out that thinking of mental illness in terms of brain disease or disorder is only one of several possible ways to view mental illness, and has only reached cultural credence in the last few decades. While the current popular social construction of psychosocial disturbance is depression, or anxiety as representing what are considered mental diseases or disorders, this is a potentially invalid way of constructing psychosocial phenomena. Mental phenomena are things of or relating to the mind and the mind is that which is responsible for one's thoughts and feelings (Merriam Webster's Medical Dictionary 2002). Thoughts, feelings and behaviors occur through a social process that is internalized in the individual (Mead 1934). In other words, the mind is not and cannot be confused as being located in the brain because it arises out of the socialization of and relations between individuals within society (Mead 1934). The functioning of individuals directly corresponds to their environment and their relations with others; we are moral and social agents (Szasz 2003), and constructing our problems as mental diseases (that can be located in the brain) defines us as having internal dysfunctions that are asocial, yet we are social beings.

technology of study (in this case, antidepressants and adolescent mental health and illness).

One such project taken in the sociology of scientific knowledge production is a concern with the praxis of various medical and scientific communities and how their science constructs health and illness in society. Clarke, Shim, Fosket, Mamo & Fishman (2003), argue that processes of biomedicalization have come to define and shape health and illness in the 21st century (see also Conrad & Leiter 2004; Horowitz 2002). Biomedicalization, these authors argue, travels culturally (that is, it is no longer contained within the clinic, but has saturated our everyday lives and ways of knowing). Over the course of the past two decades, more areas of our social life have been apportioned under the surveillance of medicine, and are increasingly being defined as connected to or caused by the biology of our bodies (Conrad & Leiter 2004; Horowitz 2002; Clarke et al. 2003). Evidence of this can be seen in popular newspapers, trends of medical and mental health grant monies distributed for research, and the way popular and expert communities construct the etiology of psychosocial disturbances.[7] The term biomedicalization is used to extend medicalization, a term that signifies when previously non-medical phenomena become defined and treated as medical problems (increasingly in terms of disorders and disease) (Conrad & Leiter 2004).

In short, biomedicalization can be equated with the construct of governmentality explosion. Foucault's (1975, 1980) conceptualization of governmentality refers to the

[7] In their study on popular media discourse, Blum and Stracuzzi (2004) found the popular print media largely embraced Prozac and biological psychiatry approvingly. However, in 60 percent of the print media examined, there was some concern mentioned that centered around four themes: (1) overuse of SSRIs for minor stress, (2) use in children, (3) the unknown long-term side effects and (4) the conflicting interests of drug companies. Yet alarmingly, only eight percent of all articles reviewed questioned the corporate interests involved and even this eight percent appeared to trust biomedical practices (Blum & Stracuzzi 2004).

exacting kinds of power that are located within and legitimated by expert knowledges, tactics and discourse (such as psychiatry, pharmacology and pharmaceutical industry advertisements) that simultaneously seek to monitor, measure and normalize individuals and populations. Communities of practice that form out of expert medical knowledges (such as pharmacology experts or pharmaceutical detailers) create new mandates for health and performance in all realms of social functioning and consequently also create new markets for consumption and profit (Clarke et al. 2003). Critics of medicalization and biomedicalization are concerned that the high antidepressant prescription rates are evidence of a changing culture that increasingly defines children's emotions and behaviors as brain disorders or dysfunction and treats them as medical problems. By culture, I mean not only the beliefs and norms of our society, but also our everyday practices. Processes of biomedicalization, while not located in the clinic per se, are nonetheless often contained in meso-level institutional structures. In the case of adolescent health, it would follow that biomedical constructions of medical and mental health problems based on individual biology rather than interactions between the whole individual and his or her social environment have come to dominate.

Central to biomedicalization theory is the assertion that social and cultural factors are effaced in favor of biophysiological explanations which support a particular kind of biological and physiological jurisdiction (not social or cultural or psychological) over the classification and treatments of disease. Similarly, much of the social critique of antidepressants concerns the biomedical model's attribution of behavioral and psychosocial experiences to bio-physiological explanation thereby effacing social and cultural factors. For sociologists, social and cultural factors are recognized as being

entrenched in our everyday lives in a way that they significantly impact both our physical and mental health. While social and biological processes are dynamic constructs that interact and cannot be easily teased apart, the social aspects of our lives should not be repressed or minimized.

For too many psychiatrists, the fact of suffering redefines a problem as medical rather than psychological, social or political. The oppression of women, racism, poverty—many social and economic phenomena—contribute enormously to human suffering. We do not discredit human suffering when we examine underlying societal causes. Instead, we help the individual find a better perspective on [perhaps a better solution to] her [or his] suffering (Breggin 1991:236).

SSRI's treat biophysical phenomena that do not exist for many of the disease entities they are prescribed. Within the medical model, the diagnosis of disorders is based on clinical judgment of how adolescent symptoms of disturbance are indicators for underlying biophysical phenomena. These clinical judgments rely on the expressions of the patient and on the clinician theorizing how symptoms may be the result of biological or chemical deficiencies such as serotonin. The selectivity of serotonin idea is a false conclusion because serotonin nerves spread throughout most of the brain and are involved in multiple functions that challenge popular conceptions of this notion (Breggin 1991). The idea of lower serotonin levels being associated with depression came from pharmaceutical marketing, not psychopharmacological science (Healy 2004a) and some claim that the biomedical theory that distress comes from a chemical imbalance of serotonin in the brain is as narrow as it is outdated (Moynihan and Cassels 2005).

The taken-for-granted fact that depression is a disease or disorder caused by a serotonin deficit is rendered uncertain in this controversy. Despite whether or not scientific evidence exists for the role serotonin has for depression or other mental, emotional and behavioral states, this theory has been highly advertised and presented as fact by professional experts, whose views are legitimated by the media in ways that have created a certain degree of acceptance of this particular construction of distress or disturbance. As a sociologist investigating a controversy embedded in sociopolitical agendas, it is important to make note that there are competing theories of etiology that exist within professional expert and popular discourses, and that expert discourses influence societal responses to bio-psycho-social disturbances.

A psychosocial epidemiological perspective on depression or other disturbances would purport that an adolescents' biological and genetic background is important, but not more so than their family history of depression or poverty or other psychosocial stressors that exist in their environment. For example, social environments encompassing neighborhood instability, unemployment, high rates of poverty, crime and broken families have empirically and consistently been associated with high rates of distress (see Aneshensel and Sucoff 1996; Ross, Reynolds and Geis 2000). Further, the median rates of psychological disturbance in community studies is 36 percent in the lowest social class compared to 9 percent of members in the highest social class, evidencing that levels of distress are intimately connected to an individual's position in the social structure of society (Link & Dohrenwend 1980). Horwitz writes, "There has been a steady rise in depression in subsequent cohorts born over ten year intervals between early and late parts of the 20th century in the United States" (Horwitz 2002:165).

An explosion of rates in depression and anxiety in the last few decades supports a social rather than genetic etiological explanation because families' genes cannot be responsible for this rapid increase, only changing culture and environment can be. Additionally, the most frequent precipitant for entry into mental health treatment is problems with social relationships (see Kadushin 1969; Olfson & Pincus 1994). Finally, rates of the most prevalent disorders (depression, generalized anxiety and substance abuse) all vary widely across social contexts (Horwitz 2002).

Although in the fall of 2004 the FDA made it an objective to use all available data from pharmaceutical clinical trials to assess whether antidepressants increase the risk of suicidal thinking and behaviors in depressed youth, the analysis is significantly limited because none of the randomized studies were originally designed to address the question of side effects, suicidality or how adolescent embodiments fuse with antidepressant medications (Ryan 2005). In other words, the randomized clinical trial studies of antidepressants were not originally designed to investigate the connection between antidepressants and side effects, especially incidents of suicidal or homicidal ideation or behaviors.

Chapter 3. Research Methods and Design

I analyzed the content of the actors' discourse as it was presented in the text document of the FDA Hearing that took place on February 2, 2004. In what follows, I first describe what a social worlds analysis is; including its assumptions and strategies as a particular interpretive orientation to qualitative research. Second, I explicate the steps I used to analyze (code, write memos and interpret) the data (discourse at the hearing). Third, I explain how I came to choose the February 2, 2004 FDA hearing as my site of entry into

studying this controversy and further justify the importance of analyzing this hearing as my primary data source. Finally, I map out the social worlds and actors present in this controversy and give a descriptive introduction of how each of these social world's define the situation of the controversy.

A. Situational Analysis: A Social Worlds Approach to Theory and Method

Theory and methodological tools are deeply imbricated in social world's analysis. Drawing on a constructionist symbolic interaction theory, the analyses of social actors who are engaged in this controversy are analyzed using a modified grounded theory approach, or what Clarke terms Situational Analysis (2005). Situational Analysis (i.e. social worlds) is a set of theoretical and methodological tools based on material social constructionist and feminist standpoint orientations to qualitative research (see Clarke 2005; Casper & Clarke 1998; Clarke & Montini 1993; Clarke 1990).

Clarke provides six guiding methodological strategies in Situational Analysis (2005) that demonstrate how grounded theory can be responsive to different types of data.

(1) Assuming and acknowledging the embodiment and situatedness of all knowledge producers (social actors) and assuming the simultaneous "truths" of multiple knowledges. This assumption or strategy is closely aligned with my research questions because I sought to understand the multiple ways in which various social actors defined the problem (i.e. controversy). This strategy allowed me to discuss multiple versions of reality or the ways different social actors attributed meaning to the practice of treating adolescents with antidepressant medication. Also important to this strategy is for the researcher to look for what is missing from the discourse while attempting to produce new frames for what could or should be known (researched and understood) but is

currently not. This strategy guided me in analyzing content to answer research questions one (how does each social world define the controversy) and two (what is missing from each social worlds depiction of the controversy).

(2) Using the situation of the research phenomenon as the site of analytic grounding. This assumption embraces the notion that perspectives are always partial but that indeed we may learn more from an in-depth analysis of layers of meanings that arise from definition(s) of a particular situation. Important to this approach is the grounding of the situation under analysis (in this case the adolescent-antidepressant controversy) in the particularities of sociohistorical and political context. I grounded my analysis within the larger context of how we as a society are intervening in the mental health and illness of our youth; how we define mental health and illness; what our particular strategies are for intervening and what all of this means for this controversy. Further, I bring contemporary biomedicalization theory and practices to bear on these conversations because they are pertinent to contemporary societal construction and intervention of adolescent mental health and illness.

(3) Shifting from assumptions and representational strategies of simplifying normativities and homogeneity to complexities, differences and heterogeneities. This strategy involves the mapping of social worlds/actors and their positions across the social situation (controversy). This strategy provides new ways of studying relations and seeing variation across the "data" while drawing out the contradictions and ambivalences in the situation and social actors' positions. This strategy is closely related to my second research question in which I attempted to locate the sites of ambiguity, contestation and variation across actors' perspectives in the discourse. In the process of coding my

content, I erred on the side of inclusivity of content and ideas (over counted codes rather than undercounted) to allow for not just similarities or patterns to emerge, but for subtle differences in meaning or the way content was used or structured across social worlds to surface. In other words, I coded liberally so that when a speaker mentioned any discourse related to a data or side effects issue (not just the material aspects, but the statistical aspects of coding and counting and analyzing side effects) was given a color and a count (potentially in multiple colors and counts). The goal here was not to universalize or generalize but to account for plural sources of knowledge or understanding of a single phenomenon.

(4) Asserting the analytic sufficiency of sensitizing concepts and theoretically integrated analytics rather than the pursuit of formal theory. The goal of this strategy was to avoid overgeneralization and abstraction. Instead, I acquired thick description, which refers to the meanings that social actors attribute to the social world they are engaged with to reach a level of specificity of meanings of particular social actor's in particular social contexts. This strategy was somewhat limited in my research given the site of a hearing.

(5) Doing situational analyses throughout the research process, including making situational maps, social worlds maps, and positional maps. The strategy of mapping out social actors was to allow for a new vision of the connections among social actors within the controversy[8]. Part of this work included investigating the professional backgrounds of various social actors and worlds and how they were situated socially or politically with regards to the pharmaceutical industry, expert science disciplines, social movements or other affiliations. Further, I constructed four social worlds from the discourse at the

[8] Appendix A Social Worlds Present at the Hearing

hearing based on what each speaker said about who they were, what their interest in the controversy was and why they came to speak at the hearing.

(6) Turning to discourses—narrative, visual, historical—to expand the domains of social life included in grounded theory research. This strategy is important and serves as additional evidence for why it is important to choose a situation or site of analysis that broadens our possibilities for gaining insights into the various ways social life is experienced. The February 2, 2004 FDA hearing is a perfect site for expanding the domains of what is sociologically known about mental health and illness of adolescents because there are differentially situated actors within this one site who converse with one another around the object (adolescent mental health and the treatment of) of concern. The discourse at the hearing includes both lay and expert articulations of knowledge and therefore allowed for a more expansive construction of the problem because more types of articulations of the controversy were able to be counted as legitimate knowledge sources.

B. Data Source: The Case of the February 2, 2004 FDA Hearing

I chose this particular FDA public hearing to analyze because it represents the pinnacle of US state-public-science interaction around the controversy. This hearing resulted in a vote of the FDA that decided to enforce stricter warning labels being put on antidepressant medications which warn against possible increased risk for suicidal thoughts for the pediatric population while taking these medications, especially in the early stages of treatment. I interpret this particular public hearing as the FDA's primary response to the multiple events that occurred in the transition between the end of the 20th

century into the early 21st century over the controversial nature of the issues involved in adolescent mental health and illness, suicide and treatment.

The diversity of the social actors who were represented and given voice to speak on their positions and experiences related to these issues allowed for heterogeneity and multiple voices and perspectives to be heard. While access to the speaker was still somewhat restricted by the FDA, and the FDA summoned certain kinds of scientific experts more than others (psychiatric and pharmacological instead of mental health professionals or psychologists), persons across disciplinary and professional allegiances were allowed to speak. This public hearing essentially gave anyone in the public engaged in this controversy an opportunity of entry that rarely occurs in medical-scientific negotiations of technologies, interventions and knowledge production (Roth, Dunsby & Bero 2003; Scott, Richards & Martin 1990). Although one has to keep in mind that members of the FDA held more power at the hearing and were given a longer time to voice their professional judgments, access to the microphone was not restricted based on professional allegiances or lay/public positions within the social structure. Instances where lay persons with experiences of psychosocial symptoms are invited to speak publicly of their experiences are rare and are a fruitful site for investigation of alternative ways of understanding the interventions of mental health and illness compared to traditional legitimated ways of understanding these experiences.

C. Coding, Memo Writing and Interpreting Procedures of Content Analysis

Coding

Following principles of the qualitative approaches, grounded theory and situational analysis, I coded, memoed and interpreted the entire text of discourse (Weber 1990).

Before coding, I familiarized myself with the entire document and recognized it as a complete corpus of the situation under investigation (controversy) (Emerson, Fretz & Shaw 1995). After familiarity had been reached, I began the writing of notes (codes) in the margins of the document that signified the ideas, themes, assumptions or issues that emerged from reading the text line-by-line, without paying attention to having any coherence between the codes. This first stage of coding is referred to as open-coding. Open-coding is the tracking, naming or identifying of data through multiple (possibly contradictory) readings or codes (Clarke 2005). In this stage of coding, I asked the data specific and consistent sets of questions, and kept the boundaries of inquiry open in an attempt to prevent alliance with any one standpoint (Berg 1989). For example, during open-coding I investigated the multiple definitions, assumptions and issues for each social actor in a line-by-line coding of the text.

After open-coding was completed, I conducted focused-coding where another line-by-line reading of the text was performed with a focus on particular themes or topics that emerged from open-coding (Emerson et al. 1995). This process of narrowing and focusing within both coding and memo writing continues as a dialectical conversation between the data and the researcher while patterns emerge for interpretation (Emerson 1995). This secondary level of coding that is more focused is also referred to as axial coding (Strauss 1987). This level of coding was performed in a manner such that coding categories were exhaustive and mutually exclusive. My task as a qualitative researcher using an approach of grounded theory/methods was to map out the meaningful relations operating in the social worlds studied and emphasize the hidden processes and meanings that arose from the situational discourse (controversy) (Denzin & Lincoln 1998). From

this process of focused-coding, seven patterned themes emerged from social world's definitions of the problem. Due to project feasibility and theme overlap, three of the seven codes articulated (safety/efficacy concern, conflicts of interest concern and how social world's defined adolescent disturbance differently) were dropped from the final analysis. The four codes which remained were side effects issues, data issues, lack of access to knowledge or informed choice and practices and policies issues.

Memo Writing

Throughout every stage of coding I participated in the practice of writing memos of theoretical ideas that surfaced from my reading of the document. A memo is an exploratory piece of writing that assists the analyst in thinking through interpretive ideas about the codes and data analysis development. Memo writing is a fruitful way to reflect on the coding process. It allows for the analyst to assess the appropriateness of coding categories, see if there are patterns, and intellectual spaces of agreement or disagreement that have surfaced from the content. The process of memo writing occurs throughout the coding process and many of the memos I have written were drawn upon during the stage of writing the final analysis. My memos led me in the direction of bringing biomedicalization theory and practices to bear on my content.

Chapter 4. Social Worlds Mappings

The FDA hearing was convened on a sunny February morning in 2004, over 300 parents, youth, grandparents, siblings and friends convened to talk to the FDA about the medicine that had contributed to the death of loved ones (Hawthorne 2005). I was not present at the hearing itself, but gathered qualitative and quantitative descriptions from researchers who were present, and from counting the people and speakers on the transcript available

to the public from the FDA's website. There were two panels consisting of 36 expert speakers summoned to advise the FDA along with nine FDA representatives (Hawthorne 2005). In all, there were more than 60 separate public speakers present who had control over the microphone for up to two minutes (Hawthorne 2005). It had been 13 years since the FDA had convened to address the issue of Prozac and suicide. So, who are these social actors who attended the hearing? What were their affiliations and what, for them was the problem in the controversy?[9] Following situational analysis, I first map the positions of the social actors present at the hearing (see Appendix A). I grouped the social actors into four social worlds: the family (N=40), independent professionals (N=23), FDA speakers (N=9) and FDA-summoned experts (N=31).[10]

Adolescents and their Family Social World (N=40)

Over half of sixty public speakers present at the hearing were there because they had lost someone to suicide, homicide or murder that they felt was a result of the adolescent or family member's adverse reactions to an antidepressant medication. More than twenty parents spoke about losing their child, a loss they perceived to be a result of antidepressant medications. Four of these parents spoke on behalf of themselves as parents and as representatives of an organization. Two children were there in response to their parent's suicide. Five adolescents spoke about their experiences taking antidepressant medications, experiences marked by suicidal and or homicidal feelings and behaviors. Two spouses spoke on behalf of the loss of their partners to

[9] Appendix B: Social World's Maps for each of the four main areas of concern for what to each social world was discussed as the 'problem' in the controversy.

[10] At times speakers clearly represented more than one social world. For example, some parents who had lost a child to suicide also were involved in an organization or were a scientist, researcher or doctor. Some of the independent professional experts (professionals who were not invited by the FDA) were also affiliated with academic institutions or research centers but claimed they came because of a need to share their knowledge and experience with the panel, not because of their affiliation with a particular institution or organization.

antidepressant medication and suicide. Finally, two adults spoke about their previous experiences of being on antidepressant medication. It was clear that one of the two speakers was referencing what she went through while on medication from ages 12 to 18.

Independent Professionals (N=23)

There were 23 professionals who came to share their professional expertise at the hearing. These professionals included four lawyers, seven organizational representatives, one retired law officer and sheriff and eleven doctors and or scientists. Independent professionals came to the hearing to share their professional knowledge about the controversy, both as representatives of organizations, and as concerned citizens. For instance, representatives from the Child and Adolescent Bipolar Foundation (CABF), American Academy of Child and Adolescent Psychiatry (AACAP), National Alliance on Mental Illness (NAMI), and the American Psychological Association (APA) (just to name a few), offered their definitions of the controversy at the hearing. Other independent professionals were not affiliated with a professional organization or group, but came to share their experiential knowledge with everyone at the hearing because the controversy was an important concern of theirs (personally and or professionally).

FDA Speakers (N=9)

Thousands and sometimes millions of Americans are affected by technological risk assessments made by the FDA. To begin with clinical testing on any drug, a pharmaceutical company must register it with the FDA. In order to market a drug to the public; the FDA must approve it for safety and effectiveness, and this testing process consists of pharmaceutical clinical trials.[11] From these clinical trials, we get two types of

[11] There are four phases of clinical drug testing. In phase I the drug is given to some human volunteers to establish safe dosage levels and study metabolism and side effect (Relman & Angell 2002). In phase II,

data; data from phase's I-III are considered controlled trial data, while phase IV is known as the post-marketing data consisting of spontaneous reports regarding Adverse Drug Reactions (ADRs) (Relman & Angell 2002). The role of FDA agents is to oversee the drug development process, and ensure that drugs on the marketplace are not toxic or dangerous for human consumption. One reason that products already approved by the FDA as safe can later be found to be unsafe, is that controlled clinical data often requires extrapolation of reliability, validity and statistical significance from the small percentage of people in which the drugs are originally given to (studied in), to the larger population (Abraham & Sheppard 1999). Often, side effects or health risks about medications are not fully discovered until after they are given to the general population. Although the pharmaceutical companies are in charge of monitoring their own products once they are FDA approved, the FDA is ultimately held responsible for keeping unsafe products off the market, and for instituting public warnings or bans on unsafe drugs once they are on the market. In this situation, antidepressants were approved by the FDA, but the safety and effectiveness of antidepressants when taken by children or adolescents, became opened up for debate due to reports of suicidal and homicidal thoughts and behaviors occurring in thousands of adolescents after taking an antidepressant.

There were five FDA staffers present who each gave a presentation on a prepared topic in connection to the problem of addressing the controversy (Laughren, Katz, Murphy, Pfeffer and Hammad). Aside from the five FDA agents who gave

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small clinical trials are conducted that give various doses to patients with semi-relevant medical conditions (Relman & Angell 2002). In phase III, the drug is given to larger numbers of patients and evaluated for safety and effectiveness (Relman & Angell 2002). Total time for phase I through III is on average about six to ten years and only one in five drugs make it through this phase (Relman & Angell 2002). After the approval of the drug if phase III produced favorable results, the company can do phase IV trials in order to have the drug approved for other purposes, and in this phase the *manufacturers* are in charge of monitoring the safety of the drug and reporting adverse drug reactions (Relman & Angell 2002).

presentations, there were two FDA agents who served as chairman (Dr. Rudorfer) and executive secretary (Temple) of the hearing. Finally, there were two professional experts from Columbia University requested by the FDA to speak about Adolescent Suicidality and the Suicidal Reclassification Project, (Dr. David Shaffer and Dr. Kelly Posner respectively). I group these speakers into the FDA social world because they were asked to give presentations on behalf of FDA regulatory science and thus, their standpoints were very different from both the public speakers (limited to two minutes) and the FDA-summoned professional experts who entered dialogue about the controversy only during the open committee discussion at the end of the hearing. Also, Dr. Rudorfer refers to Dr. Posner and Dr. Shaffer as "FDA speakers".[12]

FDA summoned Professional Experts (31)

Out of these 31 FDA-summoned professional experts; seven were members of the Psychopharmacological Drugs Advisory Committee, one was a member of the Anti-Infective Drugs Advisory Committee, 10 were members of the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee, three were consumer representatives (one

[12] Each of these nine speakers had a topic that their presentation was organized to cover. Dr. Katz provided an overview of what he called the background leading to the hearing. His speech (eight pages long) primarily focused on how the FDA came to be concerned with the question of antidepressant side effects, previous action they had taken, and what their current plans were. Dr. Murphy's speech (12 pages long) focused on pediatric depression, therapies for pediatric depression and giving a background on pediatric drug development. Dr. Pfeffer's speech (20 pages long) provided an overview of pediatric depression and how it is a major mental health problem in the United States. Dr. David Shaffer's speech (17 pages long) focused on the topic of suicide and related problems in adolescents. Dr. Thomas Laughren spoke twice. The first time he spoke, (35 pages of speech) the focus was on the regulatory history of antidepressants and suicidality. He also gave an update on what the current plans for re-analysis of the pediatric suicidality data were. The second time he spoke (6 pages of speech), he discussed efficacy data for each of the seven drugs and 15 clinical trials that were being considered as the 'data' or way to answer the antidepressant-suicidality question. Dr. Kelly Posner from Columbia University was summoned by the FDA to describe in detail the 'Suicidality Classification Project' (8 pages of speech). Finally, Dr. Tarek Hammad discussed the plans for analysis of patient level data for the pediatric studies (speech was 11 pages in length). Each of these nine speakers also contributed to the dialogue during the open committee discussion. In order to keep the analysis of social worlds separate, their acts of speech were continuously counted under the FDA speaker social world despite when their speech occurred during the hearing because each of these nine speakers was referred to as an FDA speaker or agent at the hearing.

for each committee) and two were industry representatives (one on each of the larger committees). Along with these 'experts' there were seven Small Group Evaluation (SGE) participants (one who was a patient representative) who had the unique task of voting on any debates, along with one government employee who was a non-voting member.

Chapter 5. Findings: Defining the Problem and Reaching Consensus

These four social worlds came together around a shared concern: the relationship between adolescents, antidepressants and their side effects. Yet the meanings they applied to the social problem varied depending on the situatedness of the social actor speaking. That is, his or her perspective was shaped by their position within one or more social worlds. As a result, in my analysis of defining the social problem, I found that the ways each social world defined the problem or controversy fell into four distinct positions: (1) The problem is one of *Side Effects*, (2) The problem is a *Data Issue*, (3) The problem is a *Practice or Policy Issue* and (4) The problem is one of *Lack of Access to* full disclosure of information, or *knowledge.* Table 1 (see following page) outlines the distribution of category codes that emerged in my analysis.[13]

The numbers in the table are based on the code totals for each of the four social worlds and the number of times they mentioned anything related to side effects, data, practices or policies and access to knowledge. It is important to keep in mind that the family members and independent experts were each only allowed to speak once for up to two minutes while the FDA social actors' speech was not restricted in this way. The

[13] These categories were not coded in a mutually exclusive manner, but were overlapping. In other words, while coding, some passages of text were simultaneously referring to side effects and data issues. In this way, I used a strategy of coding and counting inclusively. While at times the speaker's main point was about data, if that particular speaker was even partially referring to access to clinical trial data as a problem, that passage was color coded and counted under both data and access to knowledge categories.

FDA-summoned experts only spoke during the end of the hearing during the open committee discussion, and while their speech was not timed, they had to negotiate control over the microphone amongst one another and the nine FDA agents who participated in this dialogue.

Table 1: Social World Definitions of the Problem(s) of the Controversy

	Adolescents & Family Members	**Independent Experts**	**FDA Agents**	**FDA-Summoned Experts**	**Totals**
	N=40	*N=23*	*N=9*	*N=36*	
Side Effects	109	39	49	229	**426**
Data Issues	22	54	194	301	**571**
Policies & Practices	50	33	53	160	**296**
Knowledge & Access Issues	54	32	20	93	**199**
Totals	**235**	**158**	**316**	**783**	

In what follows, I discuss each of the four dominant definitions of the problem and the ways each was employed by the actors at the FDA hearing. The FDA-summoned professional experts often summarized the various positions of the other social worlds and thus, their comments reflect the most overlap. If we leave this group out of the analysis for a moment, what emerges most clearly is that family members and FDA advisors define the situation at hand very differently. Adolescents and family members largely define the problem as one of material side effects while FDA members largely define the problem as one of data issues.

Materiality of side effects as the problem of concern

In my analysis of the variety of ways the problem was defined, two clear positions emerged as dominant concerns: family members perceived the problem as one of material

side effects while FDA advisors perceived the problem as one of data issues. These were connected to the perspectives of actors: one determined by experience, the other by scientific knowledge. The independent professional experts and the FDA-summoned professional experts often put the family speakers' experiential knowledge of side effects into conversation with the scientific concerns of the FDA, and they did this by focusing on the following subsequent positions: 1) conflicts of interest, 2) practices and policies and 3) access to knowledge. Further, both the independent professional experts and the FDA summoned professional experts drew on their professional experiences in staking out their claims in the controversy. Yet, if we put analysis of FDA-summoned experts' discourse aside, we see a stark divergence in how social actors socially constructed (defined and understood) problems of the controversy.

First, it was clear that the primary definition of the situation from the perspective of family members was one of side effects. Although adolescents and family members were primarily concerned with conveying their knowledge about how antidepressants caused a multitude of changes of personhood for the individuals who had taken the drug, they also expressed several other problematic concerns regarding side effects.

Subjective experience, often framed as the ways antidepressants were perceived as causing changes in emotional, mental, and behavioral state, was expressed in multiple ways.[14] For example, one boy who was prescribed Effexor for migraine headaches talked

[14] These included akathisia (extreme agitation), becoming overwhelmed with thoughts of suicide, depression, acting irrationally, a loss of inhibitions, a loss of consciousness of activity or behavior or personality changes, hostility and rage toward others, inability to understand or communicate what one is feeling, thinking or doing, psychosis and hallucinations, aggressiveness and more. A majority of these adverse reactions were described as though they were not present in the individual before consuming the antidepressant and were instead the result of SSRI use. In other words, these experiences were "side effects" of the medications themselves.

about how the drug lost its effectiveness after a year so his doctor doubled the dose. Immediately after this increased dosage, he began experiencing adverse reactions.

> For the next nine months, [after an increased dose] my life as I had known it was gone. I thought daily about suicide and hurting myself. I felt void of normal emotions. I was so belligerent, agitated, and filled with hate – hate for my family, my friends, and most of all myself. Rage consumed me. I felt trapped. I said and did things I had never done before and would never do now. I had little control and little inhibition. It was as if I was watching a movie and some villain was destroying all the relationships around me. I spent my time alone and viciously fighting with my parents. They would ask what was wrong and what had happened to me. I could not answer them because I did not know or understand myself. I was terrified (Jame Tierney FDA Hearing 2004:93-94).

Over two-thirds of the members of the family social world spoke in terms of side effects. As illustrated in the words of the boy above, his experience of aggression and suicidal tendencies came after his doctor increased his dose from 75 to 300 milligrams a day. This was a similar narrative offered by adolescents and their family members. Adolescents described their experiences of taking an antidepressant and then shortly after, having suicidal or aggressive thoughts and/or behaviors arise that were not present before taking the medication, or before an increased dosage of an antidepressant medication.

Another adolescent speaking at the hearing described his experiences of being on Paxil and then Effexor after being diagnosed with Social Anxiety Disorder. His family practitioner prescribed him 20 milligrams of Paxil and less than nine months later doubled the dose to 40 milligrams because it had lost its effectiveness. A few months after this, he had the same problem so he was switched to the antidepressant Effexor and

was told to stop taking the Paxil immediately. He was supposed to slowly work his way up to a total of 300 milligrams of Effexor over a three-week period. This is what Corey had to say about his experiences of side effects.

> The day I took the 300 milligrams, I didn't feel very well and I stayed home from school. I went back to sleep and that evening I woke up in a juvenile detention center. Unaware of what I had actually done, I asked one of the members of the juvenile detention center, and I found out that I had taken my high-powered rifle that I use for hunting to my third period class, took 23 of my classmates hostage and one teacher hostage. I spent 14 months in jail, not really knowing why I had been there, not really remembering anything that I had done (Corey Baadsgaard FDA Hearing 2004:90-91).

In this statement, the side effects described included a loss of awareness about or understanding of one's own behaviors, feelings and actions. Similarly, Sara Bostock described how her daughter Cecily acted on the day of her death after she had been taking Paxil for seven days.

> By the day of her death, she was pale, unable to sleep, almost unable to converse, and in a frightened, agitated state, jumping at the slightest noise. That night she got up without turning on any lights, went into our kitchen only 40 feet from where I was half asleep. She stabbed herself twice in the chest with a large chef's knife. The only noise was a slight yelp and a thump when she fell on the floor. . . Her autopsy revealed she had a very high blood level of Paxil, which reflects poor metabolization and is a feature common to many of these suicides.

Once Sara identified her belief that her daughter's behavior was a result of the SSRI Paxil, she continued to describe her perception of the side effects of the medication.

> I believe this induced an intensely dissociative state, perhaps even sleepwalking. . . . The whole regulation of waking, sleeping, dreaming occurs in the brain stem where the serotonin neurons are clustered and where SSRI's are having their impact. . .I believe SSRI's can alter consciousness in some mysterious and

> frightening ways that is not normally seen even in mental illness. I am certain this is what happened to my daughter (Sara Bostock FDA Hearing 2004:101-102).

The passage above complicates the view that depression causes suicide, or that chemical serotonin only affects how sad we feel. This passage portrays a girl suffering, restless, agitated and not metabolizing Paxil well. The way Paxil made Sara Bostock's daughter feel and behave is defined as the problem.

A 14-year-old boy, who committed suicide approximately four weeks after his pediatrician increased his dose of Prozac from 10 to 20 milligrams a day, was also described as having an altered consciousness and conduct after this dosage increase. While the side effects were mostly described as a result of dosage, his mother states that even after the initial dose her son started having strange dreams that affected him in a negative way. To some psychiatrists this may have indicated that her son Jacob did not do well on the SSRI Paxil, but the Williams' family doctor responded by increasing the dosage of Fluoexetine (Prozac).

> Shortly after starting the initial dose, Jacob began to complain of having strange dreams, which he had said were bad. Shortly after the dosage was increased, I began to notice an aggressive behavior, which had not been there before. Jacob also became destructive and destroyed some of his favorite things. His friends would later tell me they had noticed the same behavioral change. He also showed a verbal aggression and short temper, which had not been present before. When questioned about his behavior, he stated I don't know what is making me do this (Terri Williams FDA Hearing 2004:128-129).

The embodied experience of not understanding what was causing one's thoughts, feelings and behaviors to change was an experience shared by several family members as an

important concern of side effects.[15] These examples are by no means exhaustive. They do, however, capture a pattern of understanding from the perspective of family members and patients whose lives were changed and disturbed by antidepressants; this pattern of understanding was that these experiences were the result of medication side effects; they were not present in the individual's themselves. While this is by no means a complete portrayal of all the diverse ways the experiences of side effects were discussed, these quotations reflect the dominance of this perspective among the family social world[16]. Similarly, Independent Professional experts voiced their concerns about the material side effects of antidepressants. These experts' speech often drew upon on their professional experiences with adolescents and or antidepressants.

For example, Rachel Adler, who serves on the board of directors of the Child and Adolescent Bipolar Foundation (CABF), (a parent-led, non-profit organization), presented results of a study CABF conducted where they surveyed 17,000 members and received a 15 percent response (N=2550).

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15 Joe Pittman brought a letter written by his son Christopher to read at the hearing. Christopher Pittman is serving a 30-year sentence for the murder of his two grandparents. His lawyers and supporters were still fighting his sentence with appeals on several grounds with the primary one being that he was tried as an adult despite being only 12 years old when he committed the crime. The defense argued that Christopher was going through withdrawal of Paxil, adjusting to a high dosage of Zoloft and suffered from severe adverse reactions from both of these antidepressants simultaneously. There are several websites that provide information about this case and offer viewers a chance to sign a petition for his appeal to be re-tried; addressed to the Governor of South Carolina where he was sentenced and is incarcerated. The passage below is an excerpt from Christopher's note where he described his side effects.

> I didn't notice a change in my behavior until I was completely off the medication. It made me hate everyone. The smallest things made me blow up, and I started getting into fights, which was not me. I would usually avoid fights. Before the medication, I had only been in two fights my whole life. I just hated the whole world for no apparent reason. A week after the doctor gave me the sample packs; he increased my dosage to 200 milligrams a day. Everything just kept getting worse. Then, I snapped. I took everything out on my grandparents who I loved so very much (Christopher Pittman FDA Hearing 2004:134).

16 As Appendix B reveals, several other concerns regarding side effects were common. These included how autopsies uncovered the deceased had not been metabolizing the drug well, how several of the youth presented family doctors and pediatricians with their side effects yet they were not recognized as side effects, and how families were informed of benefits but were not given all the information the FDA, the pharmaceutical companies or the doctors had about potential risks of serious side effects that could be caused by antidepressants. Several family members called for changes in the prescribing practices related to antidepressants, including things such as mandating full disclosure including written informed consent, increased warning on labels of medication and even a ban of prescribing antidepressants for the pediatric population. Finally, the family social world was commonly concerned with the development of dependence and how antidepressants cause serious withdrawal effects in some people and how this is not being acknowledged by the medical community as it should be.

> We have received favorable comments, but some responses indicate that in some subgroups of children, suicidal ideation and behavior may emerge for the first time or worsen when a child is given an antidepressant. . . For these reasons, CABF urges the FDA to require manufacturers to add a black box warning on the labeling for antidepressants to alert clinicians and parents to the possibility that antidepressants can trigger and worsen suicidality, as well as mania or rapid cycling bipolar disorder in some children. CABF opposes any ban on off-label use of these or other psychiatric medication in children . . . (Rachel Adler FDA Hearing 2004:113-114).

Here Rachel Adler takes a middle of the road position by stating that for some patients, these medications cause suicidal ideation and behavioral side effects, and for others, the medications work well. Yet, she states that while the CABF opposes a ban on the off-label prescription of these medications, because of the seriousness of material side effects, both physicians and parents need better warnings.

Although the independent professionals defined the problem of material side effects with less certainty than adolescents or family members did, independent experts validated the narratives of the family social world by approaching the problem of side effects from their own expert knowledges that were often outside of the quantitative data framework of the FDA. Dr. Donald Marks addressed participants of the hearing as a prescribing physician, a father and as a former associate director and director of clinical research for two multinational pharmaceutical companies. He stated that he came to the hearing because of his belief in the importance of these issues. Dr. Marks stressed that SSRI sales and manufacturing is a serious business comprised of millions of US patients and billions of dollars.

> My experience working for pharmaceutical companies is that any attempt to decrease sales by increasing warnings will be met with severe organized

> resistance. . . The seriousness and severe adverse event effects of SSRI drugs make their use hardly justified in the majority of cases because SSRIs are well known to have limited efficacy over placebo and against non-pharmacologic treatments. There are many studies in the peer reviewed medical literature supporting the causal role of serotonin in disinhibition and violence. My own prescribing experience with SSRI drugs and evaluation of numerous cases referred to me has revealed significant agitation and aggression, akathisia, activation of mania and hypomania, increased depression, serious dependency and withdrawal difficulties, suicidal ideation, and toxic interactions with other drugs. It is important to be aware that these symptoms of SSRI toxicity can be mistaken for the progression of the underlying mental state being treated, leading to the use of more of the same and other offending SSRI drugs rather than to withdrawal of the causative SSRI agent (Dr. Donald Marks FDA Hearing 2004:117-118).

Dr. Marks raises several aspects of the controversy in this passage that are concerns shared by other adolescents, family, friends and independent profession expert social actors at the hearing. One concern that was common among adolescents, family and independent professionals was that the medical community was not informed enough of the potential side effects of antidepressants to recognize the signs of them. Perhaps most importantly, he discusses the uncertainty that surrounds antidepressant efficacy as compared to placebo or other non-pharmacological treatments.

A thorough scientific literature review revealed that treatment efficacy is a significant area of contestation within clinical practice and research. Overall, there are conflicting findings of SSRI efficacy for adolescents in clinical trial studies (Hjalmarsson, Corcos & Jeammet 2005).[17] In general, control conditions such as giving

[17] The first randomized double-blind placebo controlled clinical trial that demonstrated the efficacy of an antidepressant medication (Prozac) for adolescent depression occurred in 1997 and was carried out by Emslie et al. (Varley 2006), and before this study, every other study had not shown efficacy for an antidepressant medication for child and adolescent depression (Birmaher et al. 2003. Tonkin and Jureidini (2005) claim that evidence for SSRI efficacy is disappointing at best. They assert that out of eight published trials, four found no statistically significant advantage for antidepressants

adolescents a sugar-placebo pill for depression have been shown to be as effective at reducing suicidal behaviors as antidepressants have shown to be (Weisz and Hawley 2002), but as a whole, the ratio of potential risk over potential benefit regarding the effectiveness of treatments is complicated for several reasons (Varley 2006).[18] First, there are varying levels of efficacy across different SSRI antidepressants. Efficacy of a particular medication for particular manifestations of distress, disturbance or "disorder" is even more complex. For instance, Ryan (2005) claims that efficacy results for Prozac have been well replicated for the treatment of depression in children but that all other antidepressants have not shown more than one positive study at best.[19] It has been suggested that overall, the benefits of SSRIs have been overestimated and the risks have been underestimated, largely due to the problems with publication bias (Bridge et al. 2005).

Much of the contestation over the effectiveness of treatments stems from the difficulties of scientifically assessing the benefits and risks of pharmacological treatments

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over placebo response for any primary measure, and in addition to the four negative published trials, five unpublished trials have failed to show an advantage for antidepressant over placebo response (Tonkin and Jureidini 2005). Further, a study by Whittington et al. . (2004) found that when comparing published and unpublished data of controlled trials that the risks of SSRIs outweigh the benefits (Papanikolaou et al. 2005). The fact that a majority of negative antidepressant clinical trial results go unpublished is important because it makes the scientific knowledge production around health technologies exclusive to pharmaceutical experts, and this is an important aspect that social actors at the FDA hearing problematized because they claimed it led to a lack of accurate information to parents and doctors about the risks of antidepressant medication (FDA Hearing February 2, 2004).

[18] For instance, while SSRIs are commonly prescribed for all sorts of biopsychosocial disturbances, they have only been tested for efficacy in the pediatric population for Major Depressive Disorder (MDD) (Varley 2006). Olfson et al (2003) argue their study found an inverse relationship between increased rates of antidepressant use and decreased rates of adolescent suicide for those aged 10 to 19. Valuck & Libby (2004) found that treatment with SSRIs was not significantly associated with the risk of suicide attempts. On the other hand, an Australian study of adolescents at age 15 or older found concurrent increases in antidepressant use and suicide (study cited by Bridge et al. 2005). A study by Hawton et al. (2003) of 146,095 adolescents in the United Kingdom found some evidence of an association between SSRI prescription use and non-fatal self harm in adolescents younger than 18 years old.

[19] For instance, there have been three trials for Paroxetine (Paxil) and both of the unpublished trials were negative while the published trial was considered to be negative for the primary outcome measure (Hamilton Depression Rating Scale; HAM-D item), but positive on many secondary outcome measures (Bridge et al. 2005). This is important because although Prozac is the only antidepressant with positive results that have been replicated for treating pediatric or adolescent depression, Paroxetine (Paxil) use increased by 100 percent between 1998 and 2002 and this is why it is important for us to understand how different SSRIs have different rates of efficacy or risk, because in September of 2003, the FDA specifically recommended that Paxil not be prescribed for pediatric depression (Delate et al. 2004). Out of the four clinical trials for Venlafaxine (Effexor XR- two trials) and Mirtazapine (Remeron two trials), all are unpublished and no efficacy was found (Bridge et al. 2005).

in comparison to non-pharmacological treatments. However, any discussion about the best mental health intervention must consider the benefits and risks of all the available treatments if what is sought is an informed choice. Studies evaluating mental health interventions for adolescents have found treatments which addressed the social environment and relationships of youth had greater potency than treatments which focused solely on the teenager (Henggeler et al.1998). This finding makes sense given the previous evidence that social disadvantages and advantages have a profound effect on the causes and consequences of the mental health trajectories of children (McLeod & Shanahan 1993, 1996).

In assessing the efficacy of treatments, Ryan (2005) claims that although Cognitive Behavioral Therapy (CBT) has been proven to be effective in the treatment of child and adolescent depression, it is not always locally available to consumers or necessarily paid for by insurance carriers, so although effective, it can't be thought of as widespread enough to be used as a panacea for adolescent depression. Although many psychotherapeutic approaches have only been studied in adolescents, CBT is claimed to be the most studied psychotherapy for pediatric depression and has demonstrated significant benefits for the pediatric population, even among those with Major Depressive Disorder (MDD) (March et al. 2004). Other psychotherapy scientist reviewers also indicate that there is a growing body of literature suggesting both Interpersonal Therapy (IPT) and CBT are consistently showing positive results of efficacy and effectiveness (Varley 2006).[20] In summary, there is growing evidence in support of both CBT and IPT

[20] For instance, a meta-analysis of CBT conducted by Lewinsohn and Clarke (1999) found that a total of 63 percent of patients improved in clinically significant ways by the end of treatment and similar results have been found in other CBT meta-analyses, but these results are not specific to adolescents with depression (Varley 2006). Further, positive findings for Interpersonal Therapy (IPT) have been demonstrated, showing that a majority of adolescents in the study reported fewer depressive symptoms and maintained improvements in social functioning a year later at follow-up

as efficacious treatments for depressed or psychosocially disturbed adolescents (Brent 2005).

Aside from the contestation of the effectiveness of treatments, there was also significant contestation over what exactly, side effects are, and whether or not they are defined as materially real by doctors and other medical, regulatory and other scientific professionals. Dr. Joseph Glenmullen is a psychiatrist and a clinical instructor of psychiatry at Harvard Medical School and the author of *Prozac Backlash* in which he writes about his experiences with patients becoming suicidal on SSRIs. This is what Dr. Glenmullen had to say about side effects at the hearing.

> I am here at my own expense because there is a specific side effect of SSRIs called akathisia that can make some patients so agitated that they feel death would be a welcome relief. This side effect is so well established that it is clearly described with SSRIs in the Diagnostic and Statistical Manual (DSM), the American Psychiatric Association's Manual. If you look at the transcript of the FDA hearing on this very side effect 10 years ago, you will see the FDA saying repeatedly we don't know what to do, we need more research. It is a tragedy to be here 10 years later and hear the FDA saying the same thing. The industry's response to this side effect has been to blame the underlying psychiatric conditions of patients, to dismiss legitimate medical case reports as anecdotes, and to scare the media away from the subject, claiming that it would frighten patients away from treatment. Indeed, there is a prevailing authoritarian attitude don't warn patients, you might scare them. Well, I prescribe SSRIs and I warn patients, and they are not frightened away from treatment. Let's stop blaming the victims and deal with this very real side effect (Dr. Joseph Glenmullen FDA Hearing 2004:164-165).

(Varley 2006). These same findings were replicated by a larger controlled study where 48 clinically depressed adolescents were found to have improved their interpersonal problem solving skills as well as their functioning, and were rated by their clinicians as less depressed and had met recovery criteria (Varley 2006).

In the passage above, Dr. Glenmullen draws on his own prescribing experiences to concur with the sentiments expressed by Ms. Rachel Adler, Dr. Marks, and other independent professionals whose jobs have caused them to have direct contact with the risks of antidepressants. This common sentiment is one of seeking recognition of the materiality of side effects and their consequences as real. Further, Dr. Glenmullen states that the pharmaceutical companies deny that their products cause these side effects by dismissing these types of experiences as anecdotes. Finally, Dr. Glenmullen raises the important issue of how the FDA, the pharmaceutical companies and the medical community all seem to be more concerned with scaring patients away from treatment than with warning the public of the serious risks of side effects.[21]

Scientific Knowledge Production (Data Issues)

Contesting what counts as a valid knowledge claim

While data issues were not the primary mechanism through which family members presented their definitions of the problem, 9 of the 40 family members spoke about data issues as being important aspects of the controversy. These statements centered on themes of pharmaceutical conflicts of interest between being the researchers, manufacturers and sellers of antidepressants and on how scientific data from clinical trials should not be the only information that is valued in assessing the relationship between antidepressants and their effects in adolescent and child patients.

21 While the FDA members did discuss concerns of side effects, these concerns were not framed as side effects issues. In other words, side effects were discussed as data coding problems, as missing science (data) issues, as lack of clinical trial standardization issues, and more. These concerns are further expressed and presented in the following data section and in the sections where the FDA is in dialogue with committee members at the end of the session. As stated previously, the committee members summoned by the FDA served as mediators of concern between the family, independent and FDA social worlds and the opinions each of these three social worlds had expressed throughout the hearing, and hence, their concerns and mediations of side effects will be discussed in later sections of the analysis.

In contrast to the FDA advisors, the family members are not concerned with how the data can be used to produce scientific analyses, but instead, are concerned that the data is biased because it was not designed or implemented to study side effects issues, and were carried out by researchers who are vested in the study results (drug outcomes). Family members spoke about how pharmaceutical companies fund and carry out their own studies for their own billion dollar drugs and this fact alone makes their data biased. Also, several of the speakers talked about how pharmaceutical companies only publish or report positive studies and keep the failed studies hidden from public access. Further, the pharmaceutical data is charged as being regularly manipulated so as to show results that make their drugs look favorable. A father whose daughter died after taking Zoloft for seven days talks about what he thinks of pharmaceutical relations.

> Suppressing unfavorable data may be legal, but is it ethical? If the trials don't favor a drug, the public never hears of them. Legal maneuverings have thrown out the scientific method. (Tom Woodward FDA Hearing 2004:87).

Speakers of the family social world challenged the FDA on what they count as legitimate knowledge or evidence in determining the nature of the problem in this controversy. A family friend who came to the hearing spoke his opinion of how controlled clinical trial data is what the FDA considers the *right* method to answer the association between antidepressants and side effects.

> What I would like to suggest is behind me is a number of things that do not show up in controlled trial data that need to be heard, that are as important as what can be achieved statistically. I don't think for parents who spend a great deal of time in cemeteries, controlled trial data is as pervasive or persuasive. I do not suggest or believe that everyone here has a negative or grotesque motive or is all greedy. I do think there are legitimate motives here, and I think these things do need to be

> discussed without being incendiary. Nevertheless, it is important to recognize the human dimension here (Mr. Piepenburg FDA Hearing 2004:126).

At this juncture, Mr. Piepenburg stakes the claim that there are different kinds of knowing and understanding phenomena. He contests the FDA's notion that statistical analysis of controlled trial data is the only way one can reach a better understanding about the nature of the relationship between antidepressants and the side effects they produce. The human dimension he privileges is what I analyze to be the social dimension that often becomes erased in constructing and intervening in youths psychosocial disturbances within contemporary biomedical culture.

Related to what knowledge is valued, is the issue of the FDA, the pharmaceutical companies and other FDA summoned researchers labeling family experiences of side effects as anecdotal evidence. There was significant contestation from the family social world about their experiential knowledge being dismissed because it wasn't data. The family and independent social world actors claimed that not all knowledge about the side effects of antidepressants could be understood from analyzing clinical trial data. Here is one more example from a family member who resisted FDA speakers and pharmaceutical company representatives' tactics of calling their experiences and stories anecdotal evidence.

> I am here today to tell you an anecdote. Webster defines an anecdote as a short narrative of an interesting or amusing biographical event, an anecdote or anecdotal. That is the euphemism the manufacturers of Prozac, Paxil, Effexor, and Zoloft use to describe the thousands of reported out of character, violent, homicidal, suicidal events that occur in a vulnerable subset of patients who ingest their SSRI antidepressants. They would have us believe that these are mere coincidences and don't prove anything (Dr. Gary Cheslek FDA Hearing 2004:142-143).

Dr. Cheslek contests the pharmaceutical tactic of labeling victims' stories of antidepressant side effects as anecdotal evidence. Dr. Cheslek was seeking validation for the public's experiences of antidepressant side effects; he was seeking validation from the FDA that first-hand experiences are an important kind of knowledge that deserve to be perceived as legitimate.

The independent experts privileged the experiential wisdom they had each gained from a variety of professions (lawyers, law enforcement, doctors, etc). Their statements contested the FDA by drawing on their expertise to recount the terms of debate the FDA had laid out. The primary area of contestation here was that the current pediatric clinical trials for antidepressants were not qualified to answer questions about the relationship between SSRIs and their potential side effects. In this way, independent professional experts contested the FDA discourse that the clinical trial data of antidepressants in the pediatric population was the correct way to ask and answer questions about the ratio of risks and benefits of SSRIs for adolescents and children. Lawyer Andy Vickery provides an example of this prevailing concern.

> These trials were not designed to detect suicidality; they did not use the Beck Suicide Ideation Scale which would make the kind of refined measurements that the epidemiologist gentlemen who spoke earlier said are needed. They did not use the Barnes Scale as Dr. Mann himself had recommended in a 1991 article to measure treatment emergent akathisia. They weren't designed to answer the problem . . . (Andy Vickery FDA Hearing 2004:109).

Another independent professional stated his opinion about the current clinical trials and their ability to stand as accurate evidence of the association between SSRIs and side effects.

> These results were drawn from studies with design flaws that typically favor the study drug. For example, they frequently exclude placebo responders before random assignment, rely on ratings by clinicians who have a vested interest in the outcome, and are likely to be unblinded by medication side effects. Further, these results are drawn from the published literature which is subject to publication bias and file drawer problems meaning that many studies with negative results do not get published. (Dr.Antonuccio FDA Hearing 2004:80-81).

Dr. Antonuccio contests what the FDA have set as the *right* way to ask and answer questions about the relationship between pediatric use of antidepressants and potential side effects. Further, Dr. Antonuccio makes the claim that clinical trial studies frequently have design flaws and biased results due to the clinicians' conflicts of interest, and this was another dominant concern expressed among both the family and independent professional speakers. For example, Lawrence Diller, a behavioral developmental pediatrician with 26 years experience prescribing psychiatric drugs to children, discussed the current conflict of interest between pharmaceutical companies' research or trial evidence and the profits they gain from their positive studies.

> As a front-line practitioner, I have lost faith in my research academic colleagues to provide me the data information, opinion, and conclusions in an objective and unbiased fashion. I desperately need that information in order to validate and augment the clinical decisions I must make every day on who does and does not get medication. . . I see top research leaders in the field of child psychiatry simultaneously publishing papers in scientific peer-reviewed journals while appearing in press conferences for corporations that have funded the research; which is then reported in the Wall Street Journal. We learn of non-publication agreements of negative finding studies and limited access to raw data that potentially allows for completely different interpretations or conclusions based upon the published information. At this time, the conflict of interest between my academic colleagues and the drug industry rivals that of the stock analysts and the

> brokerage firms. . . I hope there is more government funded research, but as long as I only have research funded or suppressed by drug companies, I will remain quite cautious and hyper-vigilant over what I prescribe the youth of America (Dr. Lawrence Diller FDA Hearing 2004:227).

Dr. Diller points out some of the practices that are controversial about biomedicalization. If during the medicalization era the connections of science and capitalism became more embedded and realized as having specific interests in outcomes, in the biomedicalization era the interests of all parties involved in medical discourse and practices have become less apparent (Clarke et al. 2003). Dr. Diller's claim about the conflicts of interest between academic researchers and the pharmaceutical companies is evidence that in biomedical culture, increasingly; the relations between science and capitalism have become distorted. The best example of this is that pharmaceutical companies hold patents on drugs and are a for-profit industry, yet they hold an enormous influence over the practices and policies of US health care and market their products as necessary and life-saving despite their primary goal being profit. Dr. Diller, other independent professionals and family world speakers contested both the standpoints (terms of debate) and practices and relations of pharmaceutical companies and the FDA through speaking about their own situated experiences.[22]

All of these statements show how the independent professional experts were concerned with data issues, but they showed their concern by contesting the notion that

[22] Independent professionals also contested FDA expressions of the controversy by presenting evidence (peer-reviewed studies, professional documents, letters and more) that showed that both the FDA and the pharmaceutical companies had known about the serious risks of antidepressants for years yet they failed to design and implement good studies or to inform the public. In this way, an important way that the independent professionals defined the problem was in contesting the FDA's claim that the issue of antidepressant side effects had just recently become a concern. One independent professional in particular presented two personal letters and one journal article which exemplified that members of the FDA, American Medical Association (AMA) and the NIMH have known about the risks of antidepressants for years (Rosie Carr Meysenburg FDA Hearing 2004:111-112).

clinical trial data was the right way to better understand the controversy. Further, they used their own alternative or professionally specific knowledges to express their concerns about conflicts of interest inherent in the scientific knowledge production of clinical trial data, and the FDA's conflict of interest in being the regulators of those trials. The standpoints of these independent professionals are corroborated by the scientific literature.

FDA Terms of the Debate

Data issues were the salient theme across all FDA speech acts. Three of the FDA Speakers' presentations focused on pediatric drug development, depression and suicide. These speech acts were counted as data issues because much of what this discourse accomplished was delivering statistics, or what was offered as legitimate knowledge demonstrating that pediatric drug development, depression and suicide are problematic in themselves aside from how these phenomena fit into this controversy.

FDA speakers had too many areas of concern regarding data issues to discuss them all, but most of their speech focused on either a quality of clinical trial data component or a re-analysis and reclassification of clinical trial data component. From the very beginning of the trial, the FDA made it clear that their goal was to investigate the relationship between antidepressants and side effects in the pediatric population, and that they perceived the *right* way to assess the nature of this relationship was through controlled clinical trial data. The FDA agents defined the problem, from the very beginning of the hearing, as one of what the controlled clinical trial data could tell them about the nature of the relationship. Dr. Katz opened up the hearing and provided an example of the FDA terms of the debate.

> It is the controlled trial data that we believe is best able to help us provide an adequate answer to this question, but as you have heard, and you will hear throughout today's presentations, we do not believe that this data until now has been provided to us in a way that would permit us to interpret it fully. It should be noted that this view of the data has not been a unanimous one among Agency staff. Some within the Agency have examined the data and concluded the data, as currently submitted, do permit definitive analyses and that these analyses support the conclusion that this class of drugs is associated with a risk of suicidal behavior in pediatric patients (Dr. Katz FDA Hearing 2004:23-24).

Despite some FDA contestation over whether the current clinical trial data shows an increased risk of suicidality with consumption of antidepressants, there was consensus that several data deficiencies had to be dealt with, and these deficiencies were common among much of the FDA and FDA-summoned experts' discourse. Dr. Thomas Laughren explained that the pharmaceutical companies defined and coded their data in two main ways when searching for terms that indicated events of suicidality: 1) possibly suicide related and 2) suicide attempt (Dr. Thomas Laughren FDA Hearing 2004: 241-242). Dr. Laughren also voiced that there were three concerns with the clinical trial cases the FDA received from the above classifications of "suicide attempt" and "possibly suicide related".[23]

In summarizing the concerns of the FDA plans for reclassification and re-analysis, Dr. Laughren asked the committee to comment on the previous three concerns mentioned (case finding, classification approaches and plans for patient level data analysis) as well

23 The first concern is the issue of case finding. This refers to the way the pharmaceutical companies define and search for "cases" or "events" in the data. This was a concern because the clinical trial sponsors defined suicidality and side effects in their own ways, and used varying methodologies to collect and analyze these events. The second concern of the existing controlled clinical trial data deficiencies was how to do a meaningful reclassification of side effects (often referred to as events by FDA speakers). Within this concern, there was the issue of how events coded as suicide attempts varied widely across clinical trial studies and sponsors carrying out the studies. Dr. Laughren noted that some sponsors used a conservative approach towards categorizing events as suicide attempts while others included events that lacked suggestion of self-harm as suicide attempts (Dr. Laughren FDA Hearing 2004:254). The third area of concern was how to go about deciding what to use as the unit of analysis.

as to provide input on how future studies could be designed better and what type of studies would allow for understanding the benefits of these drugs better (such as randomized withdrawal design) (Dr. Thomas Laughren FDA Hearing 2004: 263-264). After Dr. Laughren's speech, Dr. Kelly Posner discussed the plans for reclassification. She stated that a reclassification was needed due to the lack of conceptual clarity about what suicidal behavior means because reliable and valid definitions must be used (FDA Hearing 2004:265). She proposed that the reclassification of suicidality events be grouped into three new categories; suicidal, non-suicidal and indeterminate (Posner FDA Hearing 2004:271), with non-suicidal classifications indicating events where self-injury or mutilation had occurred without suicidal intent, including such things as accidental injuries, akathisia or other psychiatric symptoms, and with the indeterminate category including any event that was hard to classify (Posner FDA Hearing 2004: 272). Following Dr. Posner, Dr. Tarek Hammad discussed FDA plans for reanalysis of pediatric patient data using the classifications that Dr. Posner had just provided.

> The objective of this work is to evaluate the risk of suicidality associated with the use of antidepressants in pediatric patients using the results of the blinded reclassification of cases. . . In this process, we will address the possible sources of imbalance in the data, for example, trial design, duration of exposure, et cetera, and also other potential confounders. . . There are some limitations on the interpretation of data that we should know upfront. . . Now, after everything is said and done, the observed rates will not reflect the actual patients in the general population. Why? Because there are some exclusions in some trials of patients with some baseline suicidality, so the observed rates will not reflect what is going on in real life, and this might hamper our efforts in trying to investigate the risk because it will lead to underestimation in all the arms, so we might not have enough statistical power to be able to detect the actual *thing* [thing means side

> effect such as suicidality here] [italics mine] (Dr. Tarek Hammad FDA Hearing 2004:274 & 284).

In summary, the FDA defined the problem of the hearing as one of investigating the quantifiable or statistical nature of the relationship between antidepressant medications and suicidality, and provided controlled clinical trial data as the framework within which the question could be answered. However, this is not to say that the FDA was oblivious to how clinical trial data was problematic. In Dr. Hammad's statement above, he explicitly informs participants at the hearing that there are several limitations in being able to interpret this data as the answer to the question. As another example, FDA speaker Dr. David Shaffer expressed his concerns of answering questions of suicidality based on the current data.

> A methodological point. Teenagers often conceal ideation and attempts unless they are asked about them directly. Self-report facilitates disclosure. It is my understanding that we are heavily dependent upon event reports in these data, and event reports may be influenced by the mode of elicitation. They are not used with a glossary which precisely defines how things should be classified, so misclassifications can occur. Self-harm is a term that is used by some, but not others in the mental health profession. It is a very heterogeneous descriptor and not all types of self-harm are associated with suicidal intent. There have been no direct studies with frequent and careful measurement examining whether SSRIs increase, decrease or have no effect on suicidal ideation and behavior . . . (Dr. David Shaffer FDA Hearing 2004:75-76).

Dr. Shaffer and Dr. Hammad's remarks about data analysis limitations are important because they demonstrate that even the FDA is struggling to ask and answer a question within a long-established framework. In other words, this controversy unfolded within a long history of scientific expert discourses that hold statistical analysis as the legitimate way to study a social controversy.

What is seen in these FDA statements is that they focused their concerns of the problem on conducting a statistical analysis, whereas each other social world was much more concerned with what had gone wrong in the system that had caused adolescent lives to be put at risk. Each other social world was focused on the overall sociopolitical aspects of the controversy, whereas the FDA was focused on a specific method/approach (science of) to better understanding a drug relationship, not a system or healthcare, or regulatory relationship that was involved in the controversy. FDA articulations were focused on the statistics of data, while other social world articulations were more focused on the overall system in which drug design, production, education and regulation occurred. In summary, while the FDA speakers predominantly focused on the plans for reclassification and re-analysis of clinical trial data, each other social world contested this dominant framework. Each social world responded differently to the terms of debate the FDA had laid out; family members provided an alternative framework of material experiences and fought to have these claims legitimated, while FDA-summoned and independent professional experts served to contest some of the terms of debate and brought ideas from the family and FDA definitions of the problem into conversation with one another.

Debating definitions of the Problem and Reaching Consensus on Plans for Action

FDA-summoned professional experts primarily focused on three areas of concern in responding to the FDA's focus on data issues and families' focus on material side effect issues. One recurrent theme of discourse here was that FDA summoned professional experts lacked confidence in the current controlled clinical trial data's ability to answer

the nature of association between antidepressants and side effects. In other words, several FDA-summoned experts also contested the FDA terms of the debate.

> I have a bit of concern that the study may not answer all of the questions because of the issue that was raised earlier regarding generalizability. These patients may not resemble the patients who are treated with these drugs. They are probably treated in a different way in terms of dose titration in the context of a clinical trial, and in the context of a clinical trial, patients tend to be monitored more carefully, so that perhaps those at highest risk of suicide or suicidal ideation might have been identified earlier with other symptoms and withdrawn from drug or had drug titrated down (Dr. Andrews FDA Hearing 2004:349).

Here, Dr. Andrews expresses his concern over the generalizability of the data being used to study the relationship between antidepressants and side effects in the pediatric population. His concern is founded upon the different social environmental conditions that occur between a clinical trial where the patient is carefully monitored and is less likely to be severely depressed than youth who are prescribed these medications in ordinary or natural life-settings. There are several ways the patients of clinical trials may not resemble the general population, and this is referred to as a generalizability or ecological validity problem. For example, as Dr. Andrews described, during a clinical trial, patients are carefully monitored, have access to professional psychologists (are receiving psychotherapy), are only on one medication at a time, and tend to have fewer psychosocial symptoms than the adolescent in the general population.

Another FDA-summoned expert, Dr. Fink, contested the FDA terms of the debate when he voiced similar concerns about using the current clinical trial data to investigate and answer questions about the relationship between antidepressants and side effects.

> In looking at the questions that are being asked of the committee, we have heard very little about the dataset that is being used. Are the inclusion and exclusion

> criteria for these various studies appropriate in terms of drug history, history of substance abuse, family history of psychiatric diagnoses? Because these were placebo-controlled trials, they probably enrolled less severe disease as evidenced by the lack of completed suicides, and finally, as has been mentioned, there was not need of efficacy. I am concerned that no amount of analyses of a possibly flawed or suboptimal data set will answer the question. If there is shown to be a relationship to suicidality, we may take away drugs that are useful in pediatric depression with different trial designs. If the studies come out negative, we may be falsely reassured. So, I am not sure that these re-analyses are going to answer the question that has been brought forward to the committee by particularly the audience and that maybe we need to start with designing what are the optimal pediatric trials to answer this important issue (Dr. Fink FDA Hearing 2004:294).

Dr. Fink was concerned about the differences between clinical trial context and everyday use of these medications. Along with the uncertainty about the quality of current clinical trial data, some committee speakers held the conviction that it was equally important to implement clinical trials specifically designed for answering questions about antidepressants and side effects in the pediatric population. For instance, Dr. Fost argued that an equally important concern within the controversy was to carry out studies (such as withdrawal studies) that would give more information regarding the benefits of antidepressants. His argument was that withdrawal studies were not very expensive to do (Dr. Fost FDA Hearing 2004: 377). In fact, several FDA summoned experts were concerned with discussing how future clinical trials could better study the relationship in question. Dr. O'Fallon was adamant that future antidepressant studies needed to do more to include youth who were on multiple medications because this was very common in ordinary life settings (FDA Hearing 2004:381-382). Also common in ordinary life settings is the reality that youth regularly experience a wide variety of hard to classify

symptoms (Weisz and Hawley 2002; Horwitz 2002). Comorbidity is when a person has concurrent symptoms of distress, disturbance or disorder (both physical and/or mental) that are perceived as potentially having unrelated etiological pathways (in popular psychiatric or mental health language, this means that youth commonly present symptoms that fall under multiple categories of disorder).

Dr. Katz, of the FDA, responded to these concerns by saying that the FDA had discussed the idea that new studies needed to be designed and implemented but that they didn't know how they could get the studies to be carried out because they were uncertain if they could require the pharmaceutical companies to do them, and funding from the National Institutes of Health (NIH) was too small (Dr. Katz FDA Hearing 2004:312). After much comment on both the deficiencies of current data and how new studies could study side effects better, a significant amount of discussion was dedicated to giving feedback on the planned reclassification and re-analysis project, as had been asked for by the FDA. For example, Dr. Trontell voiced his concerns about the reclassification of categories of side effect events that Dr. Posner had suggested would be used for re-analysis.

> I have a concern, as we have all been discussing, that a very large number of cases may well fall into the indeterminate category using the very clear definitions you laid out for us. Is there any mechanism you can suggest in that category that there might be some classification broadly, you know, low, medium, or high, that might allow some sensitivity analysis? I am a little concerned that data that have been volunteered, you know, since that wasn't a structured inquiry into potential suicidal behavior, might otherwise be lost (Dr. Trontell FDA Hearing 2004:370).

Here, Dr. Trontell focuses on what the proposed reclassification would leave out of the analysis. He notes that youth do not freely disclose suicidal ideation, so if only

classifications of suicidal, non-suicidal and indeterminate were used, it was very likely that the re-analysis would not pick up on instances where suicidal ideation was present without self-harm events and these would be coded under the indeterminate category and bias the findings to show that suicidal thoughts and actions were not present when they actually were. It has been found that a majority of clinical trials rely on a self-reporting system, so if the adolescent does not know how to describe what she or he is feeling, or is too embarrassed to freely disclose their thoughts or feelings, patient knowledge of the medication side effects routinely becomes lost (never recorded, studied, found or reported) (Healy 2004a).

Several speakers were concerned with the project being framed (termed) and thought about as the Suicide Classification Project because suicidality was not the only manifestation of adverse reactions, as repeatedly expressed by the family and independent social worlds. Dr. Chesney discussed his concern with going beyond analyzing only suicidality as the adverse reaction of concern. He noted he had been impressed (learned much from) those who had spoken about stimulation or activation syndrome (FDA Hearing 2004:299). Yet, in determining how the analysts would look for indicators of anxiety or agitation that may serve as a proxy for (or lead to sucidality or homicidality), there was some uncertainty regarding what activation or stimulation (such as an agitation scale) would look like or how it could be defined in a way that analysts could search for it in a clinical trial database, and Dr. Pine was asked to comment on what he knew about the phenomenon of activation stimulation or agitation side effects of medications.

> I think if you look at most of the publications for most of the SSRI trials, you can see relatively broad categories that describe something that people would call

> activation, so, you know, in the original Sertraline (Zoloft) trial, I think it was called hyperactivity. In the Fluvoxamine (Luvox) trial, it was called activation. In the recent Sertraline (Zoloft) trial, I think it was called impulsivity. So, there is a whole range of terms that I think you would have to canvass the field in terms of thinking about what are the most appropriate terms to include, much the way that you have done with suicidal ideation (Dr. Pine FDA Hearing 2004:303).

The committee reached consensus that the planned re-analysis needed to include a search in the pharmaceutical databases of terms that would refer to this activation or stimulation syndrome. In this way, the FDA-summoned experts contested the terms of reclassification and were able to reach consensus with FDA agents that the re-analysis must go beyond investigating presence or absence of suicidality.

Seeking Changes in Practices and Policies

When defining the problems of the controversy in their own terms, family members, independent professionals and FDA summoned experts voiced a common concern about prescribing practices.

> There is a serious problem with the way SSRI medications are being prescribed today and how, in many cases, they can directly cause violence and suicidal behavior in those we love and treasure most, our children. . . We were advised with great authority that Matt was suffering from a chemical imbalance that could be helped by a new, wonderful medication called Zoloft. It was safe, effective, only two minor side effects were cautioned with us – insomnia and indigestion. . . So, Matt's doctor, a man we know through court testimony to have been a well-paid spokesman from Pfizer, gave us Zoloft. He said, 'Take these for a week, call me back when you know how Matt is doing'. Matt didn't have a week (Mark Miller FDA Hearing 2004:88).

What you don't hear in this passage is how the Miller's knew their son was having trouble adjusting to a new school and new friends, and that this social environmental

situation played an important role in his unhappiness, but the Miller's trusted that medical practices and recommendations were safe for their son. However, Mr. Miller made sure to mention that he later found out that his son's doctor had a conflict of interest in prescribing Zoloft, because he was a paid spokesman for Pfizer (the manufacturers of Zoloft). Another father, Todd Shivak, voiced similar concerns about the practices of medical professionals constructing antidepressants as safe drugs that were the right way to intervene.

> As parents, our most important job is to protect our kids. We thought we were doing the right thing. The doctors convinced us that taking these drugs was the only thing we could do for Michael. . . Worse yet, how could all the doctors not recognize what was happening? Michael saw three different social workers, two different psychiatrists, and went through at least four different emergency room psychological evaluations in two different hospitals. We are here to plead that you do something to stop the prescriptions of these drugs, so that no one else has to go through what we are all going through (Todd Shivak FDA Hearing 2004:107-108).

Here Mr. Shivak expressed his frustration with a medical community that failed to recognize his son's adverse reactions to an SSRI. Family members voiced several statements that questioned the taken-for-granted practice of freely distributing antidepressant medication without recognizing side-effects when they did occur.

> My son, Brian Storey, was 17 years old in 1997. Our family doctor diagnosed him with severe depression. He took blood, checked for drugs or medical condition. He found neither. He gave me 14 Zoloft pills and said to come back in two weeks. He never told me they had side effects and he even said if a person is drinking or doing drugs that Zoloft works well with them. Five days later, my son killed a woman… I am praying that you will look at these drugs very closely, and, at the very least, take them out of the hands of pediatricians and GPs. These

> doctors are not psychiatrists, and they do not have the knowledge and experience in treating mentally ill children. My son never had a chance. There are 13 million people on these drugs, 6 to 8 million are children. The question is why are we handing these drugs out like candy, and the answer is $17 billion a year business. It is always about money (Joyce Storey FDA Hearing 2004:91-93).

Both the passage above and the two below point out concerns of a conflict of interest between medical practitioners, FDA and pharmaceutical company practices and policies; especially the conflict between a for-profit industry and the health of the American public. Situating these claims in economic terms, we see that the pharmaceutical industry is the most profitable business in the United States (Public Citizen 2002), and they do use their wealth to secure favorable government policies. Government and political interests are intimately connected to the pharmaceutical industry. For instance, the drug industries comprise the largest portion of lobbyists in Washington DC. According to Public Citizen (a consumer interest group that tracks pharmaceutical corporate affairs), in 2000, the pharmaceutical industry employed 625 lobbyists--more than one lobbyist for each member of congress (Relman & Angell 2002; see http://www.citizen.org/). Despite these sociopolitical facts, family and independent professionals share concerns that the well-being of our youth should be prioritized above the profits of an industry. The social reality is that there exists no organization or entity that has as much power, money or time to invest protecting consumer safety as the pharmaceutical company has to secure business profits.

> We are 100 percent convinced that Zoloft killed our daughter. We are here because we believe the system we have in place is flawed. It is clear that the FDA is a political entity and its leadership has protected the economic interests of the drug industry. Under the Bush Administration, the FDA has placed the interests of the drug industry over protecting the American public. Dr. McClellan

> understands how important political contributions are particularly since his mother has headed up the Republican fund-raising in Texas. Eighty-six percent of the $14 million in political contributions given by drug companies has gone to the Bush Administration Republican candidates –what did Pfizer, Eli Lilly and GlaxoSmithKline Beecham buy? (Tom Woodward FDA Hearing 2004:86-87).

Tom Woodward lost his daughter on her seventh day of taking Zoloft. He was left behind to ask tough questions about the relationships between the pharmaceutical companies, the FDA, and our government. Similarly, Leah Harris, a victim of SSRI side effects, voiced her frustration with the FDA and the pharmaceutical company practices that appear to put the interests of corporate profits over the American public by not informing the medical and public communities of the risks associated with taking SSRIs.

> The FDA must take action now regarding this grave issue of public health. Yes, many people claim to be helped by these drugs, and that is wonderful, but what about those of us who are harmed? Medical professionals and the public must be informed of the very serious risks that are associated with SSRIs. In light of these serious risks, at the very least, isn't it time for the FDA to require the drugs be labeled with clear warnings that might save lives? Such warnings may negatively affect sales, as Dr. Marks referred, which may not please the pharmaceutical industry, but the FDA was created as an independent regulatory agency to serve the interests of the American public, not Big Pharma (Leah Harris FDA Hearing 2004:119-120).

Here, Ms. Harris reminds participants at the hearing that the FDA is supposed to be an independent regulatory agency, yet she casts doubt over whether or not FDA agents' actions are independently serving the American public. Social scientists have studied the relative "independence" of the actions between FDA agents and the products they evaluate, and one such investigation of 18 FDA expert advisory panels found that more than half of the members serving on regulatory panels had direct financial ties to the drug

(and or company) or the topic they were evaluating and were required to make recommendations for (Fontanarosa, Rennie & DeAngelis 2004). In summary, FDA risk assessment and drug regulation is strongly mediated and constructed by sociopolitical judgments, and this was a common claim among adolescents, family and independent professional social actors.[24]

Independent professional experts were similarly concerned about medical doctor's prescribing practices of antidepressant drugs.

> SSRI drugs are mostly prescribed by primary care physicians who have limited time with patients, limited training in childhood and adolescent neuropsychiatry and neuropsychopharmacology, and minimal time to evaluate properly patient suitability and response to pharmacologic versus non-pharmacologic interventions. (Donald Marks FDA Hearing 117-118).

Here, Dr. Marks criticizes the social environmental situation within which he sees most antidepressant medications being prescribed to adolescents. His overall concern was that general practitioners time and training is a poor fit for prescribing interventions for adolescent mental health issues. Another doctor concerned about doctor prescribing practices discussed his concerns. Dr. Thomas Moore represented Drug Safety Research and presented the findings of two studies he completed that raised concerns about current antidepressant prescribing practices.

> The first of those concerns the medical use of these drugs, who are taking them, and the headline finding is that in the four year period from 1998 to 2001, use of antidepressant drugs in children doubled. The second finding is that less than 10 percent of these cases were these drugs being prescribed for FDA-approved use,

[24] Social studies of science have found that regulatory bodies such as the FDA only carry minimal audit functions and in the end, it is the pharmaceutical companies that have the power to decide what clinical trials should be conducted, and these decisions are usually based from maximizing the ways the drug can be marketed (Healy 2004b).

> and the remaining 90 percent of the cases, they were for unapproved use or ones that raised safety concerns. Let me give you some examples of what I found. Among boys 6 to 12 years old, 53 percent of the use was for treating attention deficit or conduct disorders typically in combination with an antipsychotic of a stimulant, such as Ritalin. Now, I know of no scientific evidence that says that combination therapy is effective in these disorders, and I know of no evidence that it is safe either. . . So, what we are seeing is when drugs are ineffective, rather than abandoning them or trying alternatives, doctors increase the dose or combine the drugs in ways, the safety of which we are not aware (Dr. Thomas Moore FDA Hearing 2004:178-179).

Dr. Thomas Moore draws on his research to reveal the uncertainty that surrounds antidepressant prescribing practices and how to intervene in childhood and adolescent disturbances. He raises the importance of the missing scientific knowledge of combination therapies as well as how frequently, in practice, he sees youth prescribed medications for unapproved uses. Other research has showed a substantial number of youth who did not have any psychiatric diagnosis received psychotropic medications (Warner, Pottick & Mujherjee 2004). Consistent with those findings, results from a different study show that nearly 25 percent of adolescents in their sample of new consumers of antidepressants in one year (1997-1998 Ohio Department of Human Services) had not received any diagnosis of mental illness (Shireman, Olson & Dewan 2002). Both studies showed that antidepressants were being used to treat both a wide variety of mental health diagnoses and a large number of youth without any mental health diagnoses at all (Warner et al. 2004; Shireman et al. 2002).[25] These studies lead one to

[25] Further, a review of studies shows that medical practitioners are regularly prescribing combination pharmacotherapy (multiple antidepressants) despite a lack of research supporting this practice (Reed et al. 2004; Crome 2004).

believe that there is significant uncertainty about what antidepressants do, treat, and should be prescribed for (safely, that is).

One of the common reasons cited for why doctors are prescribing antidepressants liberally was that, in practice, they were uninformed of the serious side effects that could occur. Two main explanations were given for why doctors were misinformed about risks of medications. The first reason, cited frequently in the discourse, was the lack of access to clinical trial data. "CABF calls upon the pharmaceutical industry and the National Institutes of Health to make public all safety and efficacy data from unpublished studies in children" (Rachel Adler FDA Hearing 2004:114).

Another reason commonly used to explain why prescribing practices are inadequate has to do with the financial relationships among different social worlds (doctors, pharmaceutical companies, FDA, politicians, researchers, etc). For instance, a few speakers mentioned the possibility that doctors had established financial relationships to pharmaceutical companies in ways that make their practices questionable. It is true that pharmaceutical companies play an ever-increasing role in educating physicians about the safety and intended use of drugs companies sell. Yet, some question why it is that pharmaceutical companies pay for medical *education* out of their *marketing* budgets (Relman & Angell 2002). The largest piece of the drug-marketing budget is spent on drug promotion to doctors; a practice known as detailing (Relman & Angell 2002). One has to ask why there is a need to dispense more than 88,000 sales representatives (detailers) throughout the United States to develop relational ties with doctors and medical research centers if the drugs they are working on distributing are essential for our

lives, and more importantly, how doctor prescribing practices are impacted by pharmaceutical detailers (Relman & Angell 2002).[26]

One independent professional speaker named Dr. Peter Breggin spoke about his research on adverse reactions to antidepressant medications and his prescribing practices. He claimed that he was one of only a handful of experts on these medications in the world who was not involved with the drug industry in some way (Dr. Peter Breggin FDA Hearing 2004:147). Another independent professional speaker expressed her concern over the power of the pharmaceutical companies to influence the way society thinks about and intervenes in social problems (biomedicalization). I refer to Ms. Rider's statement as being concerned about biomedicalization because she expresses her perception of how pharmaceutical companies have *educated* both doctors and the public to believe that mental, emotional and behavioral health issues are caused by biological deficiencies; specifically, she takes issue with the notion that mental health disorders are caused by chemical imbalances in the brain. This is a concern with biomedicalization because in contemporary culture; practices, policies and popularized notions conform to the idea that scientific evidence has proven that depression comes from biological deficiencies, despite that this claim is highly contested by some scientific experts, including some psychiatrists and pharmacologists.

[26] Not only has the pharmaceutical industry been found paying for lunches, elaborate dinners, gas or dispensing out cash per prescription, but several doctors have admitted they have been offered or have received free sporting event tickets, ski resort trips, or just about anything they ask for if they imply they will write more prescriptions of a particular drug (Relman & Angell 2002). Finally, pharmaceutical companies regularly host medical meetings for educational purposes, which have been categorized as "spectacles" and as a "carnival-like scene" and one senior physician described the change of atmosphere at these meetings in the last few decades as one from "sober professionalism" to "trade-show hucksterism" (Relman & Angell 2002: 35).

> We have been educated to believe that mental, emotional, and behavioral disorders are caused by chemical imbalances in the brain. The fact is that this is only theory, and this theory is pushed on us as if it were the absolute truth. The reality is that the best of scientists do not completely understand the complex inner actions of the myriad of chemicals in our brains. Those of us who elect to believe this theory and subject ourselves to treatment become guinea pigs in an ongoing experiment. I know this from personal experience. . . Why do we accept that a drug like penicillin, beneficial as it is for some, can prove fatal for others? We fail to accept that these drugs can have paradoxical effects. These drugs are not safe for everyone. They should be labeled with the strongest of precautions and dispensed only by trained physicians who have time to adequately monitor the patient. Most doctors do not have time for this level of care. Also, patients should be required to sign letters of informed consent (Dawn Rider ASPIRE President FDA Hearing 2004:98-100).

Dawn Rider complicates the popularized biomedical frame while pointing out that even the best scientists are not sure of all the interactions of the chemicals in our brains. The above passage falls under practices and policies because the practice of pharmaceutical companies, several psychiatrists and doctors in contemporary society is to construct and treat psychosocial problems as biological deficiencies. I attribute these practices as being an important part of biomedical culture. Researchers and medical experts do not practice medicine inside of a vacuum; they too are influenced by pharmaceutical advertisements and they conduct research and practice medicine within biomedical culture, not outside of it. In fact, important empirical findings from a community based randomized trial, in which Standardized Patients (SPs) were formally sent into 298 unannounced doctor or physician visits, demonstrated how medical culture and practices have changed due to heavy pharmaceutical advertising (Direct-to-Consumer or DTC advertising was legalized in 1997) (Hollon 2005). In this experimental study, there were six SP roles including the

two clinical diagnoses of major depression or adjustment disorder with depressed mood and there were three prescription request types including: (1) brand-specific, (2) general and (3) none. This study found direct experimental evidence that DTC advertising-driven requests dramatically boost antidepressant prescription (Hollon 2005).[27]

Further, even scientists and doctors themselves are potentially being mis-educated from reading scientific medical journals that have increasingly been found to publish articles that appear to be peer-reviewed and written by well-known experts in the field but instead were ghostwritten by communication agencies (Healy 2004a). Ghostwriting is the practice of someone other than who is credited as the author, actually writing the article or story. This practice is accepted in contemporary publishing due to the notion that the original ideas belonged to the credited author, but someone else wrote them down. However, ghostwriting in scientific journal articles where it is assumed the authors took part in the original research raises ethical quandaries.[28] Despite how many articles are being written by pharmaceutical communications specialists, the direction medical research and science is headed is one of further distancing from primary data analysis. The reason ghostwriting and increasing distance between researcher and scientist from their raw data is problematic, is that we can no longer assume the write-up

[27] Another study that examined the changes and impact of DTC advertising from 1996 to 1999 found that for every 10 percent increase in DTC advertising, drug sales for that class of drugs increased by an average of 1 percent (Kaiser Family Foundation 2003). The Kaiser Foundation then compared these changes on drug spending growth and found that changes in DTC advertising between 1999 and 2000 accounted for 12 percent or 2.6 billion of the total growth in pharmaceutical drug spending in 2000 (Kaiser Family Foundation 2003). To put this in consumer spending terminology, for every dollar spent on DTC advertising in 2000, an additional $4.20 was yielded in pharmaceutical sales for that year (Kaiser Family Foundation 2003). Further, prescription drug spending tripled in the decade transitioning us from the 20th into the 21st century (Kaiser Family Foundation 2003).

[28] Healy himself was given copies of a paper that actually sounded and appeared like a Healy article, but upon making some changes to what was written and sending it back to a pharmaceutical company, all his changes were removed, and he had to advocate getting his name off of the paper. He estimates that up to 50 percent of what we think of as scientific literature in pharmacotherapeutics is being ghostwritten (Healy 2004a).

of results reflects the real data (Healy 2004a). After investigating the SSRI and suicide story, Healy realized that a number of the most prestigious medical journals have published articles full of methodological inadequacies and failed to screen for scientific merit (Healy 2004a).

In contrast to independent professionals at the hearing, FDA speakers were not focused on pointing out the problems of practices or policies, instead, they focused on presenting what some of the current practices and policies were that shape the relations between the FDA and pharmaceutical company product research and development.[29] The FDA did not define the problem of the controversy as a practice or policy issue, but instead focused on policy developments that have furthered scientific and medical knowledge about kids and their reactions to drugs.

First Do No Harm?

FDA summoned professional experts showed significant concern with current practices and policies. Since each of these actors were invited by the FDA to speak of their scientific and or medical expertise, they had several things to say (some which varied from one another) about how they think scientific, regulatory and medical practices

[29] For example, Dr. Dianne Murphy of the FDA spoke at length about the Pediatric Drug Development Program, and much of her speech was focused on explaining all of the Acts that had been passed which had made research on children and drugs possible.

> FDAMA. That is the Food and Drug Administration Modernization Act. This is important because this is the legislative initiative that provided the Agency with the ability to provide an incentive that has been a tremendous – I call it the engine that has really been driving this process for being able to develop information on how to use these products in children. . . Best Pharmaceuticals for Children, renewal of the legislation basically expanding . . . a process which mandates FDA and NIH to work together to develop the same sort of data for products that are older and would not benefit because that was not an area that was not being developed . . .FDA determines what the public health need is and issues a written request defining the studies that they think need to be done, so that we can better understand how to dose children or if it works in children . . . (Dr. Murphy FDA Hearing 2004:28-29).

Dr. Murphy also discussed the PREA legislation which gave FDA the authority to require sponsors to study drugs in children. Further, she noted that much of the drug development and federal mandates that exist have occurred because of tragic adverse reactions that had sparked controversy (Dr. Murphy FDA Hearing 2004:30).

should be improved. For example, Dr. Fost summarized one area of contention in the day's hearing that I found to be an issue of policies and practices because it relates to how scientific controversies having to do with a medication and the public health (such as this one) were responded to by medical, scientific, regulatory and academic communities.

> There have been some comments both in the public session and among the committee and the FDA people that there are two problems here. One is the possibility of causing harm to children by prescribing these drugs that may induce suicide, and the other problem is that we may be scaring people away from prescribing them and there may be inadequate prescribing. That is presented as if they are sort of commensurate or symmetrical, but I think that is not quite right. There is a reason for the first principle of first do no harm. It is almost the whole raison d'etre of the FDA. The reason for that is that it is widely thought that it is more important not to harm people than to fail to help people. . . What is odd about this situation is that we might be doing both. That is, there is not just concern about causing harm to children, but there is tremendous ambiguity about whether anyone is being helped. So, as several people have said, if there is any risk of harm, even if it is a very small risk, it is not worth it if there is nothing on the benefit side (Dr. Fost FDA Hearing 2004:375-376).

Dr. Fost articulated his concern that it had become common medical practice to think of antidepressant medications as a necessary intervention, not an optional intervention. He expressed his disagreement with medical practices that fail to prescribe to the logic of 'first do no harm'. The next passage refers to a similar kind of questioning of how it was that physicians had come to prescribe scientific technologies (medications) so routinely (almost without choice).

> I am struck by the fact that we have so much drug prescription done in a population that the efficacy is not established. I fight that every day in the nursery, to come around and see patients on 10 drugs, of which maybe two have been shown to be effective and trying to withdraw therapy, but it must be . . .a

> large population of children – a lot of the people who spoke this morning, the picture that was presented of their child or someone they knew was not someone who was very, very ill. It was someone who had relatively minor type findings, who were put on these drugs with terrible consequences, and I agree with every speaker who said that something needs to be done to educate practitioners and the public that these things may not be all benign (Dr. Hudak FDA Hearing 2004:364-365).

Here Dr. Hudak discussed how he regularly saw pediatric patients who were overmedicated or who were taking medications in dangerous combinations (medications for which efficacy or safety had not been established through research). Further he reiterates the family social world concern that even the mildly ill were being medicated with antidepressants that had serious risks and should only be used when necessary. Finally, he claims that full disclosure should be required by the FDA and the pharmaceutical companies.

Dr. Fink also discussed his concerns about the medical community practice of prescribing these medications off-label as interventions to all types of problems. Dr. Fink expresses his concern about how in the clinical trial studies designed to assess the relationships between antidepressants and kids, the environmental context of those studies differed greatly from the context out in the public where youth were prescribed these drugs. Both of these concerns were common among FDA summoned professional experts.

> Another sort of global concern – and I think it may be particularly apropos to this class of drugs – is that when these clinical trials are performed, they are usually performed by experts in the field, yet much of the usage today, particularly in the managed care environment, is prescription of these drugs by non-mental health trained professionals. The results of a clinical trial performed by mental health

> professionals where you are already using a highly select audience and highly select practices may bear little relationship to what you see with the drug in use in the real world. From a labeling standpoint, it would make sense potentially to say that at least off-label use of these drugs really should be highly restricted to mental health professionals or make some kind of wording that would imply that, because I think that off-label use of these drugs by non-mental health trained professionals seems to be problematic, and it may well be that much of the placebo effect that we are seeing in the clinical trials is because they are receiving counseling about mental health (Dr. Fink FDA Hearing 2004:340).

Dr. Fink offered his advice on how prescribing practices could be reformed and Dr. McGough disagreed with his recommendation of limiting off-label prescribing rights of antidepressants to professionals trained in mental health care. While consensus was reached that current prescribing practices needed reformed, there was significant contestation among social actors about what these reforms should be. FDA-summoned experts demonstrated this area of contention.

> First, as far as off-label use goes, child psychiatrists could not treat severely ill kids without off-label prescriptions, there is no doubt about that. Secondly, even in the absence of scientific clinical trial evidence, a physician needs to be free in specific instances to choose to take the risk of using a medicine even in the lack of a controlled study. Again, there is no way to meet the needs of these really severe kids without this. To your point, unfortunately, there aren't enough child psychiatrists trained and available to do this, so it is left to other practitioners, and what I was really struck with, hearing the stories this morning, is many of the cases we heard were kids just naively given adult titration regiments at adult doses with no consideration to slow metabolizing, in Caucasian kids particularly, with no concern about the need to monitor for akathisia and early onset activation, so I see we can't restrict non-psychiatrist prescribing, we now have pediatricians, family docs, nurses, psychologists, all of whom will be prescribing these medicines (Dr. McGough FDA Hearing 2004:344-345).

While Dr. McGough acknowledged that current prescribing practices were less than adequate, he felt that clinicians need to have access to prescribe medications off-label and that antidepressant prescription should not be limited to professionals who were trained in mental health care.

After much debate regarding the problems of prescribing practices in the medical community, Dr. Rudorfer, of the FDA, offers what he sees as a potential avenue of change. He shares his ideas about how certain areas of current labeling of antidepressant medication could be taken out and new thoughts could be put in place of them, and how this may help reform overzealous prescribing practices.

> I am wondering if instead we had a statement that encompassed two thoughts, one, that patients should be monitored frequently early in treatment, and two, that any change in behavior, particularly early in treatment, should be reported to the clinician promptly, to avoid getting into issues of causality, which we have not settled since we don't have all the data yet, but I think –correct me if I am wrong, committees –but I think what we are saying is we want to put a speed bump in the road, that, in fact, the sense of the committee is that clinicians should take these medications more seriously, and not dispense them overly liberally with inadequate monitoring (Dr. Rudorfer FDA Hearing 2004:390).

In summary, family, independent professionals and FDA summoned professionals all contested the FDA's position that clinical trial data was the right way to discover the nature of the relationship between antidepressants and side effects in the pediatric population. Further, each of these social worlds had various opinions about how medical, regulatory and pharmaceutical practices needed to be reformed. There was a strong consensus among family members and independent professionals that conflict of interest within pharmaceutical product research and design and between the pharmaceutical industries, the FDA and government politics were contributing factors in this

controversy; particularly the inadequate information provided to parents, the medical and regulatory communities about the ratio of benefits and risks of antidepressant medications. While contestation regarding the data deficiencies of current clinical trial data was not enough to change the way the FDA was planning to respond to the crisis, FDA summoned experts were able to secure agreement that the re-analysis would go beyond investigating indicators of suicidality. Consensus was reached that warning labels on antidepressants would be changed in order to strike a level of seriousness in prescribing physicians who choose to medicate youth with these drugs.

Issues of Power: access to knowledge, information and services

Access to accurate knowledge, information or data was a salient concern for the family, independent and FDA-summoned professional expert social worlds.

I am a parent. It is my right to make an informed decision on behalf of my daughter. You did not allow me to make that informed decision and she was harmed (Lisa Van Syckel FDA Hearing 2004:83).

> In the passage above and the one below, parents express the betrayal they felt not because antidepressant treatment did not work for their child, but because scientific, regulatory and medical communities had more knowledge of the risks of antidepressants than were disclosed to them. This lack of full disclosure was a betrayal of their trust by the medical and regulatory communities in allowing them to make informed decisions. Informed parental consent is only possible as long as full disclosure is made by the pharmaceutical companies, the FDA, and the medical community . . . How come the medical profession doesn't fully disclose the possible harmful and fatal effects of medication as well as watch carefully for diverse effects on its adolescent population? (Lorraine Slater FDA Hearing 2004:123-125).

Here, Lorraine Slater expressed concern about regulatory and medical professionals failing to disclose risks and watch for adverse reactions in their patients. In the passage below, one parent not only feels like he lacked access to knowledge about the risks of antidepressants, but he felt information about risks was explicitly withheld by doctors and pharmaceutical advertisements.

> We were told that antidepressants like Paxil and Zoloft were wonder drugs, that they were safe and effective for children. We were lied to. The pharmaceutical companies have known for years that these drugs could cause suicide in some patients. Why didn't we? (Glenn McIntosh FDA Hearing 2004:131).

Mr. McIntosh contests the idea that pharmaceutical companies are innocent in not warning about the risks of antidepressant medications. He explicitly blames corporate power for purposefully keeping the American public in the dark by presenting antidepressants as safe wonder drugs.

This next passage offers a similar concern with the public having a lack of access to medical, scientific and regulatory data or information. Mr. Fritz couples his complaints of being left in the dark with suggestions of how this process could be reformed.

> We had no warning of what Zoloft could do to our daughter, but you people, the FDA, certainly did. On October 27th, two weeks before she took her life, you put out a Public Health Advisory and notified physicians about preliminary data from studies suggesting an excess of reported suicidal ideation and suicide attempts for pediatric patients receiving certain of these antidepressant drugs. Why weren't we, the parents of the kids taking Zoloft, notified with this advisory? It is too late for my daughter, but for the FDA to continue to sit on this information and not let the public know the risks associated with these drugs is a gross misuse of power. I am not asking that these drugs be taken off the market. I don't know enough about their safety to recommend that. What I am seeking is that when the drugs

> are prescribed off label, or when drugs are prescribed after an advisory is issued suggesting new adverse side effects, that the FDA make it mandatory that the physicians prescribing such drugs explain in plain English what the risks are and that an informed written consent be received from the parents or the patient's guardian. I hope you will agree that all Americans deserve to know what risks they are assuming when they take medication. I believe that most Americans, including most elected officials, agree with that (Robert Fritz FDA Hearing 2004:148-149).

Here Mr. Fritz expressed his frustration that the health advisory was not enough to adequately inform the public. Another family world speaker, Mr. Routhier, attributes the medical and public communities' lack of accurate information to pharmaceutical industry and FDA practices, and explicitly states he believes these negligent practices were purposeful.

> Do not blame acts of drug-induced psychosis on depression especially when this is happening to people given these drugs for other purposes. It is not only SSRIs. SSRI is a misnomer. None of them are selective to serotonin. When you affect one neurotransmitter, you affect others. Remeron, Serzone, Effexor are not SSRIs. Effexor works on serotonin, norepinephrine, and dopamine, as does Wellbutrin. FDA Med Watch reports hundreds of suicides on Wellbutrin. Wellbutrin is structurally similar to amphetamine and overstimulates many people. . . How many more have to die before something is done? Don't be fooled by manipulated studies. This was whitewashed in 1991, now they are trying to do it again. This happens to adults, as well as children, prescribed for any reason, not just Major Depressive Disorder. My wife was murdered. The FDA is supposed to protect us from these pill pushers (Alan Routhier FDA Hearing 2004:159-160).

In the majority of passages (both those quoted here and those which I had to leave out) the speakers did not blame doctors, they blamed the system within which they were working. While speakers noted the problems with how doctors were prescribing

medications, they also frequently noted how the doctors themselves were ill-informed of both the signs and seriousness of side effects. Pamela Wild's story exemplifies this misinformation. She became very suicidal while on Paxil; she shot herself in the face with a gun, yet she survived. When she had tried to tell her therapist and her doctor how Paxil made her feel, they did not understand or believe it that Paxil was causing her change in mood and behavior. Ms. Wild stated: The side effects I experienced on Paxil, even though I reported them to my doctor, were dismissed because no one was warned that Paxil could cause what I was experiencing (Pamela Wild FDA Hearing 2004:171).

These family members expressed their concern that not only did they lack full disclosure of information, but the medical community did too. They were frustrated that they had been lied to about the safety and efficacy of these drugs by pharmaceutical companies, and that the FDA was aware of the risks and yet failed to inform patients or take regulatory action. Similarly, independent professionals discussed how both the public and physicians lacked access to accurate knowledge and data that would allow them to make informed decisions regarding health care choices.

> The FDA has known for years, but failed to reveal that antidepressants consistently fail to demonstrate a benefit in children. At least 12 of 15 trials failed. The FDA has known and failed to warn physicians and the public that SSRIs increase the risk of suicide and hostility in children. FDA's 1996 Zoloft review found '7-fold greater incidence of suicidality in children treated with Zoloft than adults'. . . The FDA is foot dragging, equivocating, and tinkering with definitions while children are dying. The San Francisco Chronicle reports that the FDA has barred its own medical reviewer who reviewed more than 20 trials involving 4000 children and his findings confirmed the British finding, which is that SSRIs increase the risk of suicide (Vera Sharav FDA Hearing 2004:103-104).

In the passage above, Vera Sharav (on the Board of Directors of the Alliance for Human Research Protection) presented her own evidence that this controversy had not just recently become a concern for the FDA as FDA speakers had claimed. She provides evidence that the FDA had known of a potential problem between antidepressants and the side effect of suicidality since the mid 1990s yet had continuously failed to take action. Several social actors at the hearing claimed that compared to the British Regulatory Branch, the American FDA was failing to take action to keep the public safe. A cross national comparison on clinical risk assessments between the British regulatory commission (MCA) and the FDA found the FDA was much more permissive in its approach to risk assessment and regulation than were the British regulators (Abraham & Sheppard 1999).[30] Karen Barth Menzies, a lawyer who had been working on antidepressant and pharmaceutical liability litigation issues for over 10 years, spoke regarding her professional knowledge of these issues.

> The US Code of Federal Regulations 201.57 mandates that you require the drug companies to warn when there is reasonable evidence, not causation, reasonable evidence of an association of a serious risk. The clinical researchers who did these trials on kids and the drug companies themselves confirmed that there are multiple events of suicidality caused by the drug. The methodology that you are going to be using is designed to explain away those events. Even Dr. Laughren admits in the memo he gave you for this hearing today that there is evidence in these trials of an increased risk of suicidality, reasonable evidence is there. If

30 In particular, American members of the FDA were found to be more "specialist" oriented (psychiatrist and pharmacologist) with a greater potential for group bias of drug benefit over risk based on their specialist backgrounds (Abraham & Sheppard 1999). In contrast, British regulators were more likely to be general public health epidemiological experts with greater distance between their professional interests and the nature of their position as regulators (Abraham & Sheppard 1999). They also found there were several conflicts of interest between current advisors on the FDA at the time of the regulatory assessments and those who were voting members and these analysts concluded that the FDA practices were guided more by political than by scientific climate (Abraham & Sheppard 1999).

> there is reasonable evidence, you must make them warn (Karen Barth Menzies FDA Hearing 2004:172-173).

In this passage Ms. Menzies claims the FDA had been ignoring a federal mandate that required that they make the pharmaceutical companies warn patients if there is reasonable evidence of a serious risk. It was made clear by several FDA speakers throughout the hearing that they were waiting for a causal relationship to be established and that to them, reasonable evidence was not enough.

Daniel Safer, a Professor of Psychiatry and Pediatrics at the University of Maryland in Baltimore discussed the findings of the British Medication Regulatory Agency. He voiced concern about how regulatory agencies appear to lack access to all the data and information from pharmaceutical clinical trials necessary to evaluate the safety of drugs.

> I think the major finding of the British Committee on the Safety of Medicines was that most of the data that they got were unavailable to them prior to the company coming in for an indication, so when they found the data, they were surprised to see that most of the studies were negative or failed for the treatment of depression in children using SSRIs. . . So, I think the focus of the meeting is sort of unfortunate by focusing on suicidality because I think the big issue here is that we don't have access to the data we need from the controlled trials that are simply put in a file drawer by the companies (Daniel Safer M.D. FDA Hearing 2004:161-162).

Dr. Safer's statement indicates that, from the perspectives of FDA agents themselves, regulatory agencies are perceived as lacking the power they need to independently regulate the pharmaceutical companies in an autonomous way.[31] Undeniably, it is the

[31] Research shows that even for clinical trial data analysts, access to the raw data is rare. The loophole with post-marketing data is that pharmaceutical companies are advised to report ADRs to the FDA and public, but are not required by law; therefore we have extensive underreporting of adverse drug reactions that

pharmaceutical companies who hold more power in this controversy than any other social world. It has been said that knowledge is power, and if in this situation the medical profession, the regulatory agency and the public all lack access to full disclosure of pharmaceutical information and raw data, then the pharmaceutical companies have more power of negotiating their stakes and claims in this controversy, and at best this renders some less informed and at worst, renders others able to manipulate "scientific" knowledge.

Related to this issue of power, Dr. Lawrence Greenhill, chair of the American Academy of Child and Adolescent Psychiatry (AACAP), agrees that both professionals and the public need to have access to data from all clinical trials that are carried out.

> . . . I support the mandatory registration of all clinical trials as advocated in JAMA by Dickersin and Rennie in July of 2003. That is because one of the greatest roadblocks to understanding the safety and efficacy of trials is the lack of public access and its disclosure of these data sets due to laws that treat some of the data as proprietary trade secrets. I join my colleagues at Columbia in encouraging the field to carry out further prospective placebo-controlled trials using methods such as we have heard today, the randomized withdrawal discontinuation or challenge—de-challenge (Lawrence Greenhill FDA Hearing 2004:152).

Another member of the AACAP, David Fassler, speaks on behalf of the American Psychiatric Association regarding this same issue of power and knowledge.

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occur after FDA approval, and at worst, this leaves room for massaging and covering up some of the raw data.

> . . . I had accessed the FDA's Adverse Events Database to look at suicides reported on Prozac. As of October 1999, there were over two thousand. The FDA estimated their database picked up only between one and ten percent of serious adverse events. This gives a spread between 20,000 and 200,000 suicides on Prozac. Over a quarter of the accompanying descriptions of the patients' mental state prior to suicide gave clear indicators of akathisia (Healy 2004a:171).

> My name is David Fassler. I am a child and adolescent psychiatrist practicing in Burlington, Vermont. I am speaking today on behalf for the American Psychiatric Association where I serve on the board of trustees. . . We also encourage the FDA to develop mechanisms to enhance access to data from clinical trials including negative trials, as well as unpublished research. We believe that such access would facilitate scientific discussion and dialogue and help physicians and parents make fully informed decisions about treatment options. (David Fassler FDA Hearing 2004:225-227).

In summary, family members, independent professionals and FDA summoned experts questioned the potential conflict of interest underpinning FDA and pharmaceutical relations and how these effect medical and public communities access to information, and therefore, practice. There is strong consensus among these social worlds that the current lack of access to knowledge about risks and benefits, including access to clinical trial data, must change.

FDA summoned professional experts spent considerable time discussing concerns regarding access to information about the potential risks of antidepressant medications. Ms. Bronstein's speech is one example of this.

> If I heard nothing from this morning's testimony, I heard repeatedly that people feel the need for patients and family to have more information than they currently have. I think that is really our responsibility to do something about it whether it is after this meeting or after the summer meeting. I think we need to get something out there that describes akathisia in a way that patients can embrace it and understand it, and family members can watch for this radical change in behavior (Ms. Bronstein FDA Hearing 2004:339).

While several speakers voiced concern about getting more information distributed to the public and patients, there was just as much concern that clinicians themselves needed to

become better informed than they currently were at the time of the hearing. Dr. Irwin provides an example of this type of concern.

> I would argue that the patients may be ahead of the curve than the clinicians are, and I am a person who specializes in caring for adolescents, I run a large adolescent medicine program at the University of California in San Francisco. I would argue that most of the pediatricians who prescribe these agents are not as familiar as the psychiatrists are about the side effects (Dr Irwin FDA Hearing 2004:395-396).

Following Dr. Irwin's lead, pediatrician Dr. Leslie affirms his opinion that pediatricians lack the knowledge they need to prescribe antidepressants adequately. Further, she expresses concern over a different kind of access in the health care system that as a clinician she finds problematic, that of access to intervention choice.

> I wanted to echo what Dr. Irwin was saying as a fellow pediatrician, and also comment that one of the large pressures that many of us in primary care are under is that we cannot access other types of mental health services. There aren't mental health providers to see kids or they are not able to get services through managed care. So, many primary care providers are trying to do what they can to help families and children by giving these medications. So, the other thing we need to do –and I am not sure what the role of the FDA is in this is –demand parity for mental health services (Dr. Leslie FDA Hearing 2004:397).

A suggestion was made by an FDA summoned professional expert that the FDA could help get better information out by sending letters of FDA concern of risks to physicians and parents. It appeared that there was some contestation over this suggestion; one FDA speaker noted that they already dispense health advisory notices on their website, and questioned the purpose of sending out letters. In response to this act of speech, Ms. Griffith explains why for her, health advisories are not enough to adequately inform the

public. Ms. Griffith also discusses how in the American health care system, access to mental health care services is as grave an issue as access to regulatory knowledge.

> I need to clarify, I am not a doctor, I am a consumer, I am a parent, and as a lay person, the most troubling outcome I think of this morning's and this afternoons presentations was the urgency with which this needs to be resolved. . . . My question is what happens then, if there is not enough evidence to make a conclusion, how does the FDA inform the public, because as you say, you put out an advisory on October 27th, which I, as a parent and a consumer, read, found it terribly confusing. It was reported on very contradictorily, and what I am suggesting is I think the FDA is going to have a credibility problem if it does not get out ahead of this with some very public statements about where it is going with these studies and with the data. . . I think that there is a group of people who have not been able to either look at the data or not had access to good therapeutic care, and I think that it is going to become a public relations problem very quickly (Ms. Griffith FDA Hearing 2004:327).

Some of the speakers acknowledged that this hearing has led them to be more informed of the complexity of issues involved in this controversy. Speaking to this effect, Dr. Leslie noted her concern that while she was impressed to see that members of some professional organizations were present at the hearing, there were many other professional organizations whose members were missing from the proceeding. Reaching out to professional organizations on an official level was a concern to Dr. Leslie because many of the members of these organizations are the professionals who prescribe these medications and need to be aware of these issues (FDA Hearing 2004). In attempting to summarize the consensus of the committee discussion for the afternoon, Dr. Rudorfer of the FDA responded to the controversy by creating a plan of FDA action.

> Correct me if I am wrong, committees, but I think our sense is that we would like in the interim [time it takes Columbia and FDA researchers to re-classify and re-

> analyze data] the FDA to go ahead and issue stronger warning indications to clinicians regarding possible risks of these medications, which we don't see as contraindicating their use, but we think such warnings are required to elevate the level of concern and attention that practitioners use in prescribing them (Dr. Rudorfer FDA Hearing 2004:399).

In contrast to the three other social worlds, FDA statements were less focused on how access to information was a problem but did voice concern about the missing science or knowledge regarding kids and medications.[32] However, there was one FDA statement about access to information which provided insight into the relations of power that exist between the FDA and the pharmaceutical companies.

> Often we only got the narratives for the events that the companies had already decided represented the suicidality set, and did not include the exclusions. Often, there was little explanation for why certain events had been excluded or what the criteria had been in excluding events. . . Another problem with these cases is that the majority of them were not well described. We did not have the level of detail in these cases that one would have liked to do a rational classification (Dr. Thomas Laughren FDA 2004: 250 & 254).

This statement shows that the knowledge production of FDA analysts was restricted by both the way the pharmaceutical sponsors carry out (collect) their data and how they submit it to the FDA. This is important because the FDA is commonly thought of as a consumer watchdog, but this is not an accurate perception of the FDA's role. In this particular instance, FDA researchers were limited in their understanding of side effect events that had occurred in these trials because incomplete information was collected and provided to them by pharmaceutical sponsors, which inhibited their ability to make informed decisions.

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32 Missing science, data or knowledge such as information on the discontinuation effects of antidepressants, long-term effects of antidepressants, and lacking dose-range or pharmacokinetic studies were some of these mentions.

In summary, all social worlds present at the hearing recognized that pharmaceutical companies had exclusive rights on their data and the information it held on side effect risks; and this system inhibited regulatory, medical and public communities from making informed decisions about relative risks and benefits of antidepressant medication. Even the FDA, who is the branch of government designed to oversee pharmaceutical affairs has restricted access to pharmaceutical research. No researcher or research organization outside of pharmaceutical companies is able to keep access prohibited to their raw data and yet call their findings *scientific* evidence.

Results of the FDA and Columbia Analysts' Data Reclassification and Re-analysis

The FDA and Columbia data reclassification and re-analysis found there was a 1.8 increased risk for suicidal ideation or suicide attempt in adolescents taking antidepressants in the clinical trial studies (FDA 2004). During advisory committee meetings on September 13 and September 14, FDA-summoned experts concluded that there is a causal link between newer antidepressants and pediatric suicidality (Leslie et al. 2005). It was decided that while this effect was small, it was real, and the FDA advisory committees voted and recommended (15 to 8), the FDA would issue a black box warning label be added to every antidepressant, which became issued in October of 2004 (Varley 2005). On October 15, 2004, the FDA ordered pharmaceutical companies to include package inserts and information sheets to patients who receive antidepressant prescriptions (Leslie et al. 2005). In addition, the FDA completed a patient information guide in February of 2005 that included recommendations to physicians such as weekly face-to-face contact with new patients and diligent observation of clinical worsening (Varley 2005). The American Psychological Association and American Academy of

Child and Adolescent Psychiatry developed a medication guide which recommended patients of antidepressants need comprehensive treatment plans that include psychotherapy, medication or combination of the two therapies. While many FDA advisory committee members commented on the difficulties encountered in gaining access to psychotherapeutic mental health services for some populations, especially those underprivileged or uninsured in the inner cities and rural communities, no formal recommendations were made regarding this important medical practices and policy issue (Leslie et al. 2005).

Chapter 6. Conclusion

This research has demonstrated that when the social perspectives of various actors, embedded in different worlds, are taken into account, a more nuanced picture of a controversy emerges. In general, I found that although agreement existed that interventions are needed for the psychosocial distress (commonly referred to at the hearing as *depression*) of youth, the ratio of risks relative to benefits of SSRI treatment remains somewhat ambiguous. Actors from each social world were uncertain about different aspects of the controversy.[33] To conclude, I return to the three research

[33] A social worlds analysis demonstrated that the family social world is uncertain about pharmaceutical industry and FDA representatives' motives, methods, tactics and techniques used by them in framing and reckoning with the materiality of their experiences of antidepressant side effects. Independent professional experts are similarly uncertain about the background that led to the controversy and many of these professionals were convinced the FDA and had explicitly withheld information and acted socio-politically in favor of pharmaceutical industry profits. On the other hand, FDA agents were uncertain about the materiality of side effects. FDA most commonly referred to side effects as "events" and their language was cautious of believability that medication side effects are casually related to suicidal or homicidal ideations or behaviors. Further, FDA agents are uncertain about how to get better clinical trial studies conducted that purposely study side effects issues; they appeared uncertain about how they could gain the power to require the pharmaceutical companies to carry out new studies of their drugs. The FDA-summoned experts are uncertain about how to analyze imperfect clinical trial data for indicators of suicidality, homicidality, and other serious side effects such as akathisia, activation or stimulation syndrome. FDA-summoned experts are uncertain about whether or not a causal relationship is possible to find in the data. FDA-summoned professionals were uncertain about the best way to improve prescribing practices and how to get more accurate information out to the public and physicians.

questions posed at the beginning of this paper and answer each in turn. I then sketch out implications this research holds for sociological theory.

Research Question 1: Definitions of the problem within the controversy

Social actors and worlds defined the problem in the controversy to be one of side effects, data, practice or policy, and access to knowledge issues. Two dominant positions were articulated. Adolescent patients of antidepressant side effects privileged their material embodiments of medication disturbance, whereas FDA regulators privileged the quantitative aspects of the debate; the *objective* numbers that could be *revealed* through scientific data analysis.

Often, individual testimonies defined the problem of the controversy in multiple ways because the issues involved are not one-dimensional. The family members, independent professional experts and FDA-summoned experts were concurrently concerned with practice and policy issues as well as what had been a lack of access to full disclosure of the risks of antidepressant medications. The family member and independent professional social worlds related concerns about access to knowledge or information about the risks and benefits of antidepressants to conflicts of interest between regulatory, pharmaceutical and medical social worlds. Family members, victims and independent professional experts expressed that financial and sociopolitical ties between these techno-scientific social worlds contributed to the ways in which parents were being ill-informed of the risks of antidepressants, the ways parents and patients were being uninformed of alternative treatment choices, and of the ways in which both the public and the physicians were largely unaware of the medical signs or symptoms of antidepressant

side effects; that they could occur, or that SSRIs could place adolescents at greater risk for suicidal and or homicidal emotions and behaviors.

Research Question 2: What are the areas of the problem or the controversy where different social worlds are able to reach consensus and what are the areas where there is disagreement between social worlds?

There existed a significant amount of disagreement about what the current clinical trial data was able to show among social actors at the hearing. For example, while Andrew Mosholder and others of the FDA had concluded there was a statistically significant association between antidepressant prescription and increased suicidal ideation and behavior, other FDA agents claimed that pharmaceutical classifications and analyses were not well performed and the data needed to be reclassified and re-analyzed in order to determine the nature of the relationship between SSRIs and side effects. Further, social actors of the family, independent and FDA-summoned professional worlds contested the notion that the proposed clinical trial data were appropriate to use as a source to investigate the relationship between SSRIs and side effects in the pediatric population. However, while there was significant consensus that these data were less than perfect, it was decided during the open committee discussion that the reclassification and re-analysis plan of the FDA would proceed, but there were several suggestions on how the reclassification and re-analysis as had been planned and proposed by FDA and Columbia analysts, needed to be revised.

For instance, it was repeatedly iterated by FDA-summoned professional experts that this data re-analysis needed to go beyond searching for “events” or adverse reactions that indicated the presence or absence of suicidality (variables which expressed the

presence of suicidal ideation or self-harm). Several FDA-summoned professionals had learned from family and independent speakers that violence, inhibition, akathisia, or irritation and restlessness were also common adverse reactions which needed to be analyzed and recognized by the medical community. Hence, FDA-summoned experts were diligent in their dialogue during the open-committee discussion with FDA agents and reached consensus with the FDA that the planned reclassification and re-analysis would go beyond studying events of *suicidality* (acts of suicidal ideation or self-harm). This was a key contribution from family and victim narratives at the hearing because they participated in denaturalizing the taken-for-granted *facts* about adverse reaction *events* (side effects) and the meanings attributed to them.

In other words, the primary FDA response in the acknowledgement of side effects was to construct them either as the result of depression or as a mental illness diagnosis itself; or that side effects resulted from independent or ambiguous events of suicidal ideation or behaviors, and thus, the FDA's plan towards reclassifying and standardizing these *events* was strictly focused on measuring these types of events on a scale of suicidality. Parent, victim and independent professional testimonies were able to destabilize the assumption that side effects were to be defined and measured on a scale of suicidal ideation, or self-harm. Had these parent, victim and independent professional narratives remained absent from this controversy, perhaps the FDA-summoned professionals would not have pushed for data measures or variables such as akathisia or agitation Likert scales to be used as indicators of suicidality, homicidality or simply, presence of serious agitation (often encompassing self-inflicted or other-inflicted rage that manifested in dissimilar ways). Further, if agitation or akathisia is a psychosocial

state associated with causing a person to become homicidal or suicidal, and only suicidal ideation and self harm had been examined in the data, perhaps even more uncertainty would still exist among SSRIs and the wide variety of side effects they can cause. The important thing (according to family and independent professional expert testimonies at the hearing) is that medical, regulatory and pharmaceutical companies recognize the variability of symptoms or forms that antidepressant side effects could take.

Finally, during the open committee discussion, consensus was reached that while Columbia University researchers and the FDA undertakes a reclassification and re-analysis of the clinical trial data, the FDA would require pharmaceutical manufacturers of antidepressants to include stronger warning indications for increased risk of suicidal thoughts and behaviors. While there seemed to be contestation from one FDA speaker about how much distribution of information to physicians and the public was necessary, and why FDA Public Health Advisory Notices did not suffice, overall, most speakers agreed that a lack of access to full disclosure of any potential risks of medications to parents, patients and physicians was an important problem in the controversy which needed to be addressed. Further, family members, independent professionals and several FDA-summoned professionals agreed the FDA should take action to secure public access to all clinical trial data (but this agreement was not corroborated by FDA agents).

Correspondingly, an overall agreement occurred from all social worlds that clinical trial data on antidepressants and children that had been designed and collected up to that point lacked standardization of defining general issues of suicidality and other side effects in meaningful ways, and that this was problematic for quantitative science (data analysis). This limitation of the data made it more apparent that drug sponsors defined

adolescent emotions and behaviors in multiple ways and those clinically meaningful definitions need to be established so in the future the FDA could regulate how these events are being problematized in pharmaceutical product development and research. Most importantly, clearer definitions and measures of antidepressant side effects needed to be established so they would not continue to disappear from the data under other variable categories psychosocial distress or mental illness symptoms.

Further, there was consensus that informed choice about any medical technology for children are currently limited due to a lack of knowledge of side effects, discontinuation issues and dose-range issues (pharmacokinetic data). Overall, this consensus was similar to a consensus made at the 1991 FDA hearing on the issue of Prozac inducing suicidality in adults, the conclusion was that better studies needed to be designed and carried out with the purpose of investigating side effects (specifically, suicidality, yet these studies had yet to be carried out over thirteen years after the 1991 FDA hearing where this consensus was reached).

All social worlds agreed that prescribing practices needed to be reformed, but there was significant contestation about what these reforms should consist of, and these were not social world specific. Some social actors believed antidepressants should be banned for the pediatric population because scientific benefits had not been established. Other social actors disagreed but wanted off-label prescriptions of antidepressants to the pediatric population restricted to clinicians trained in mental health care. This opinion was also contested on the grounds that there are not enough child psychiatrists or mental health professionals available to meet the needs of local communities.

The crux of the prescribing practices debate was the lack of information physicians were giving to parents and patients about the risks of antidepressant medications. The second aspect that was highly criticized was that there was a lack of monitoring of patients who had recently been prescribed these medications. One reason for this agreed upon by all social worlds was that doctors themselves lacked the amount of information about potential risks of side effects. This consensus was reached due to several statements which made it apparent that even when presented with signs of antidepressant adverse reactions, the medical community had not recognized them as such. Another important reason offered for explaining poor prescribing practices was the conflicts of interest inherent in the current pharmaceutical product research and design and the way that detailers disclose (or fail to disclose) information about their products.

Research and discourse at the hearing shows there is widespread concern about the blurred boundaries between whether detailers are acting as pharmaceutical product educators or marketers, and whether or not doctors are fully conscious of this important distinction. In other words, conflicts of interest within and between the pharmaceutical company practices, FDA practices and medical community practices were also cited as evidence for influencing poor prescription practices.

Perhaps one of the most important areas of social world contestation was about what knowledge was considered valid evidence in understanding the association between antidepressants and side effects in youth. While for FDA speakers, the problem could only be answered through statistical analysis of controlled clinical trial data, every other social world was more open to multiple knowledges as valid sources for understanding this relationship (and was more critical of existing clinical trial data being constructed as

the "right" way to investigate the problem). Family members were outraged that their first-hand experiences were considered to be anecdotal evidence, while independent professional speakers appeared to see this label as an FDA and pharmaceutical company tactic of denying the problem of antidepressant side effects.

There was slight contestation between the FDA social world on one hand and the family and independent professional social worlds on the other, about the background leading to the controversy. While the FDA speakers claimed antidepressant side effects issues had recently entered their radar screen, independent professionals and family members cite evidence that both the FDA and the pharmaceutical companies have known since the early to mid 1990s that antidepressants were associated with increased risks for suicidality and other adverse reactions, and had failed to inform or take actions necessary to keep the public safe.

Finally, it became apparent that social actor's definitions of *safe* varied. While for some social actors, to act safely in responding to this controversy meant to proceed in the investigation of the relationship between antidepressants and side effects in a scientifically cautious manor, for others, *safe* was defined as immediately informing the public of any potential concern or suspicion regarding the risks of scientific technologies.

Research Question 3: What is minimized or missing from each social actor's or social world's depiction of the 'problem'?

Overall, there was a lack of alternative constructions of adolescent depression or suicide from FDA and some FDA-summoned professionals. The social construction of disturbance, the idea that depression is not simply caused by an imbalance of chemicals in the brain, but that depression is a form in which distress becomes manifested because

individuals are suffering socially is missing from the majority of FDA and FDA-summoned experts' depictions of the controversy. Depression can be denaturalized from biomedical terminology by thinking of it as a generalized form of communicating social disturbance or distress. If we think about how two persons may both suffer from the same life hardship but one ends up depressed and the other anxious or unable to sleep at night, we can understand how we might be able to construct depression or any other manifestation of distress as a form of communicating a social disturbance. What one social actor called the *human dimension* of side effects, is what is missing from much of the discourse present at the hearing. In other words, there was a lack of consciousness that adolescent disturbance and distress are social problems that form out of interactions between the individual and his or her social, economic, political, psychological and biological circumstances, and that not only one of these circumstances can be singled out in etiological causation or construction of adolescent disturbance.

Narrowly attributing adolescent disturbance (depression, anxiety or other psychosocial manifestations of distress) to a part of an adolescent's biology (the brain) sets up a model or framework that relies on something outside of them as individuals to fix the problem. Reifying our mental environment or our interaction as individuals with our sociopolitical surroundings has serious consequences for knowledge-practices. Our entire consciousness and our practices become co-produced within this biological framework, and as a result, our mental health interventions focus on parts of our selves and our biology, instead of the social relations or environment that is the real *problem* (the problem becomes hidden from consciousness and sight because we are attentive to the parts and not the whole). In summary, few speakers at the hearing acknowledged the

reification of the mind, our humanness, or our mental environment (replacing the mental environment with the brain as the "thing" which holds etiological value in determining adolescent disturbance); and social actors who did recognize this fallacy of thinking were those armed with an alternative way of knowing.

While family social world actors frequently spoke about material side effects, these life experiences were heterogeneously described. Although some FDA-summoned professional experts heard enough side effect disturbance-variance that they lobbied to have the 'Suicidality Reclassification Project' go beyond analyzing data for acts of self harm or suicide, the majority of FDA and other professional experts constructed antidepressant side effects as ambiguous *suicidal events*. The FDA language of referring to side effects or adverse reactions as *events* within the *data*, demonstrated how uncertain they were that these were embodied, material experiences. The language of an *event* has a connotation of an occurrence or a happening, not as though something caused someone to have an embodiment of trauma. Although family members talked about side effects as though they caused significant changes in patients' states of personhood, FDA members talked about side effects as bounded objects, as an incident of self-harm that could be counted. Yet, while the FDA were trying to find a way to quantify these side effect *events*, adolescents who experienced the trauma of side effects, struggled to find words to communicate what the lived reality of experiencing antidepressant side effects is like.

The adolescents who experienced the material embodiments possessed a different kind of knowledge about antidepressant side effects; and this knowledge carried the truth that the embodiment of side effects was a confused awareness about how the antidepressants they were taking were affecting their conscious and unconscious moods

and behaviors. What was missing here is the realization/recognition that adolescent embodied experiences of antidepressant side effects were communicated as entanglements of mental, physical, psychic, social, conscious and unconscious sources of pain and confusion.[34] While the adolescents are framed here by the FDA and other professional experts as disturbed patients, what adolescents articulated about their experiences were technoscientific disturbances that defied the boundaries of social arrangements (norms in culture, including the form and content language) (Orr 2006).

The male adolescent who described feeling like he was in a dream where he and everyone else were just actors in a videogame, articulated a shattered or confused distinction between himself as subject and himself as object. Adolescents struggled to find a new language in which to articulate their traumatic experiences because the biomedical language used by FDA agents to construct adolescent disturbance (depression) or their medication (selectively transmitting serotonin where and when in need) did not fit, it was a different information pattern that was not harmonious with locating the complicated political, technologically enhanced, bio-psychosocial entanglements that were materially experienced. Adolescents and their families continuously articulated that their side effect disturbances did not arise from depression or any other mental illness disorder as was commonly constructed by technoscience experts at the hearing. While adolescent and family voices were heard by the FDA-summoned professionals with regards to the significant variance of experiences antidepressant side effects caused, their source of knowledge remained illegitimate in a knowledge context where only knowledge perceived as "objective science" counts.

34 In Diaries of Panic, Jackie Orr (2006) talks about how experiences of trauma may dislocate the boundaries of how we understand things.

While FDA and FDA-summoned professionals participated in open discussion at the end of the hearing, the "discussion" segment of the hearing was closed off to persons who were least affiliated with the legitimated scientific social world of the FDA. Scientific and other professional experts who were not summoned by the FDA were not allowed participation in open dialogue about the controversy. While it is noticeable and significant that the hearing was open to the standpoints of the public at all, open dialogue between actors and worlds from diverse social and political standpoints, armed with multiple experiences and knowledges, was still missing at the FDA hearing. Members of the public were allowed to speak for two minutes, but social actors from these two social worlds repeatedly stated they did not have enough time to explain what they knew and how they knew it. Perhaps much more understanding could have been reached if more diverse open dialogue had been welcomed by the FDA.

Chapter 7. Implications for Sociological Theory

Theorizing . . . technoscientific transformations of biomedicine requires that their meanings and their material forms and practices, including embodied corporeal transformations and manifestations, be conjointly studied and analyzed as co-constitutive (Clarke et al. 2003).

It was almost a century ago when George Herbert Mead (1934) argued that individuals form their consciousness from the social act, which is a process of social interaction between individuals and their social environment. Drawing on his work, other symbolic interactionists' and feminist theorists' have argued that when the perspectives of social actors are brought forward, the analyst is able to consider the intricacies of the definition of the situation. This is not to render the process of social interaction (situation and definitions of) messy, but it is to open dialogue and discussion across groups,

assumptions, and knowledge sources. The plurality of ideas must come together and become visible if complexity of the social situation and social actor positions is sought.

Opening up what is referred to as "Pandora's box" discourages simplification and the "black-boxing" (Latour & Woolgar 1986; Latour 1987) of knowledge before facts become settled. Scientific claims become "black-boxed" through a process of social groups accepting the claim or concept as an accurate or true portrayal of the way things are (Latour & Woolgar 1986; Latour 1987). Once a scientific concept is black-boxed, it becomes common sense knowledge (a settled fact). SSK, particularly as applied to the technology and science of antidepressants, is engaged in this project of re-opening concepts or claims that have become "black-boxed" such as the safety of SSRIs.

When the FDA called for the hearing in February 2004, the black box of SSRIs as the solution to adolescent disturbance was opened: multiple actors were invited to testify on their understanding of the relationship between SSRIs and adolescent disturbance. In doing so, as this research has shown, adolescent and family narratives about antidepressant side effects destabilized several taken for granted assumptions about the science behind antidepressant medications.

Adolescents, their family and friends, opened up the black-box that existed for many scientific experts about the nature of antidepressant side effects when they did occur, an important of these being the assumption that serious antidepressant side effects are often manifested on a scale of suicidality. Yet, in order for this assumption to be destabilized, first adolescents, their family, friends, and independent professional actors had to destabilize the assumption that adolescent suicides are caused by depression or some other mental illness. Each of these phenomena is multifaceted and has social,

biological and political components. In other words, there were many professional experts at the hearing who spoke against the common scientific *fact* that adolescent suicides are caused by a mental illness. Several adolescents and their family members testified that prior to receiving an antidepressant prescription; they had not suffered from depression, anxiety, restlessness or other non-psychotic symptoms (for example, one adolescent was prescribed an antidepressant for migraine headaches, another for insomnia). The assumption that when serious antidepressant side effects did occur, that they manifested as suicidality was destabilized and opened up for debate by the FDA-summoned professionals after they heard detailed accounts of adolescents who became hyperactive, violent, or lost their inhibitions and conscious control over their thoughts and behaviors after starting an antidepressant or an increased dosage. The debate that ensued at the end of the FDA hearing led to the 'Suicide Reclassification Project' as had been previously planned by the FDA and Columbia professionals to go beyond analyzing events of suicidality in investigating the relationship between adolescent disturbance and antidepressant side effects. Further, it was discovered that doctors themselves were uninformed of the signs or symptoms of antidepressant side effects, and this lack of information rendered medical practices and policies incapable of treating adolescent disturbance responsibly or safely. Scientific and medical experts' assumptions about adolescent disturbance and antidepressant medications, and their interactions, were rendered more uncertain in the contours of this controversy.

This is an epistemological project that investigates how it is that we come to know what we know about adolescent disturbance and antidepressant medications and their side effects. In this controversy, different social worlds have different criteria for what

gets to count as truth claims. For the FDA, quantitative data analysis of clinical trials was the only way to investigate the nature of the relationship between adolescents and antidepressants. Seemingly, adolescent and family narratives of antidepressant side effects were heard by FDA agents, but did not hold credence in determining whether or not antidepressants can cause suicidal or homicidal thoughts or behaviors. For FDA agents, statistical causality was the kind of knowledge that counted as truth. In contrast, adolescents privileged their first-hand experiences of antidepressant side effects but for them, this kind of knowing counted as truth, and for them, pharmaceutical clinical trial data was more suspect to political bias and statistical error (data was not privileged or legitimated as truth for adolescents and their family members who had first-hand experiences of antidepressant side effects).

This project followed the tenets of feminist epistemologists (Smith 1990; Haraway 1991 & Collins 1990), who have theorized knowledge as determined by social positions in power. Feminist epistemology holds that theory/praxis is non-fungible (definition of the situation and the actions of persons in that situation are bound together). In this way, I am extending feminist epistemology (following Foucault) and arguing that knowledge is not determined by, but is produced within discourse.

This is an assertion made by several scholars in the sociology of science. Following, I make the claim that how you define the problem of adolescent disturbance determines the type of intervention or solution that results. While some social worlds defined adolescent disturbance as depression that results from a lack of the chemical serotonin in the brain, others at the hearing defined adolescent disturbance as being the result of various difficult life situations (for instance, moving to a new neighborhood and

school). Both of these types of definitions of the problem lead social worlds down very different ideological paths, and thus, also toward different suggestions for how to "treat" the disturbance. I argue that there is some underlying truth to each of these standpoints, but in society, some perspectives or knowledges have more power or authority to become perceived as truth while others (the non-scientific) are considered suspect.

The social worlds of the FDA, adolescents and their family members, the pharmaceutical company and independent researchers or scientists, are not situated on an even playing field with regards to the production of knowledge. It is the scientific and regulatory expert social worlds in the definition of this situation/problem who have the ruling power to have their definitions institutionally acknowledged, and therefore, have their knowledges or standpoints become black-boxed. The knowledges of pharmaceutical, regulatory and medical communities are perceived as valid because they are alleged scientific, and in Western society, scientific knowledge is what counts as objective truth. Yet, following SSK and feminist theorists' I have demonstrated how the standpoints of all social actors are socio-politically situated and are "partial truths" (Haraway 1991). While every social actor is armed with their own agency to define the controversy, some social worlds or positions have their definitions institutionally legitimated.

The social constructions of both adolescent disturbance and antidepressant medication are an important part of this controversy. Societal constructions of antidepressant medication is bound-up with (co-produced and co-constituted with) the constructions and responses to adolescent disturbance. The nature of how we think about and respond to adolescent disturbance is intimately linked to antidepressant medication

through the widespread cultural production and dissemination of biomedical "regimes of truth". Scientific-medicine, as knowledge/power, produces regimes of truth. Similarly, in their biomedicalization thesis, Clarke et al. (2003) drew on Foucault's concept of "regimes of truth" to demonstrate how specific meso-level institutional processes of knowledge production and dissemination are at work in the construction of biomedical ideas or knowledge about the social world as truth, such that these biomedical social constructions come to be internalized and perceived by individuals as facts, or as a true representation of social reality. Biomedicalization theory, derived from the traditions of symbolic interactionism, SSK, and feminist epistemology, examines how the medical institution has come to effect social life through both ideologies-in-practice that operate as "regimes of truth," as expert knowledges, and as socio-cultural practices.

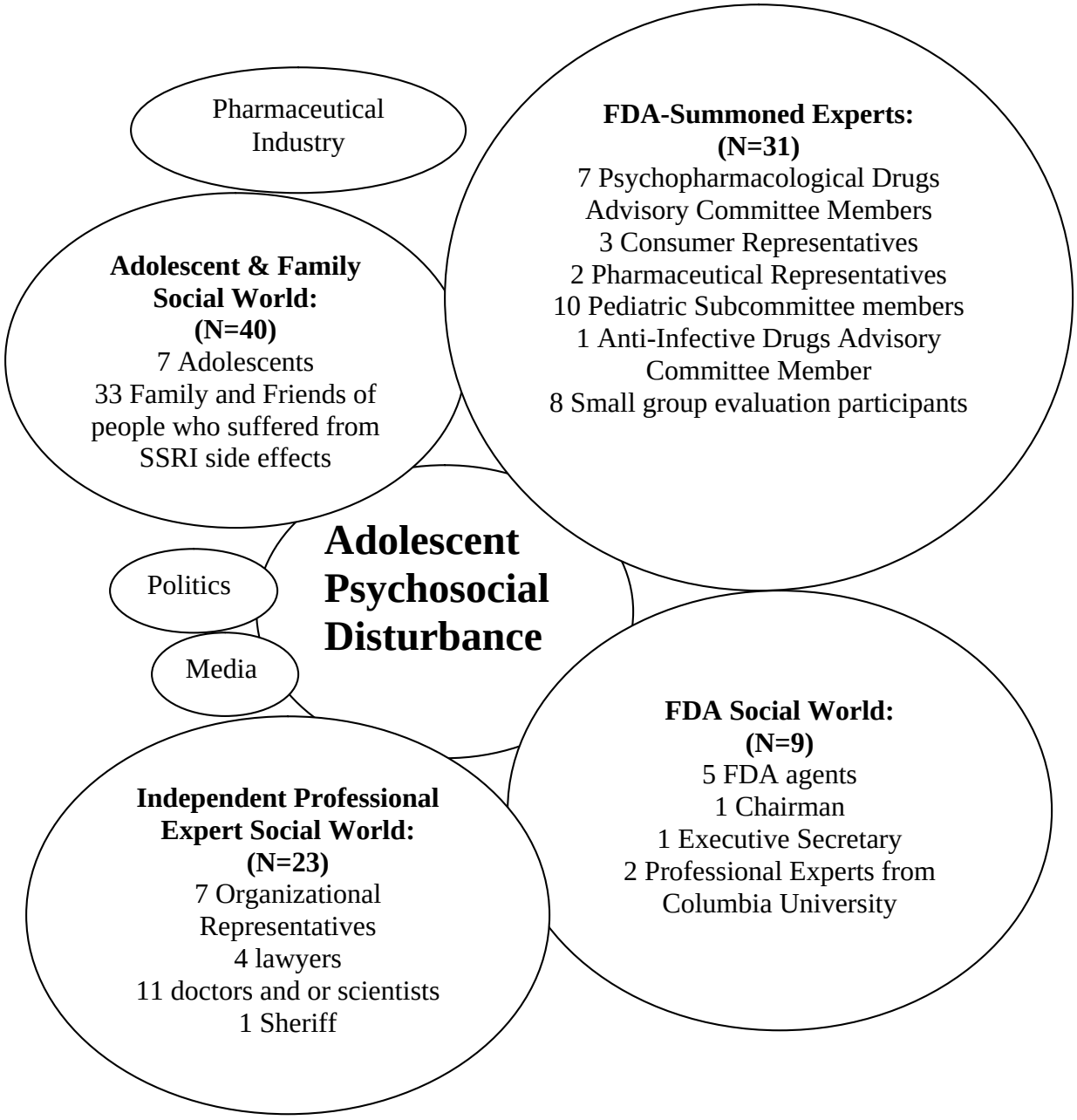
Following biomedicalization theorists, this analysis sought to understand the perspectives embedded in the definition of concerns and responses to the adolescent-antidepressant crisis as it unfolded. Biomedical regimes of truth have produced knowledge that defines social disturbance as disease or disorder, usually constructed as depression or anxiety. This type of truth or framework for constructing adolescent mental health focuses on explaining depression and treating it rather than understanding what is causing a manifestation of distress or disturbance to occur. Instead of asking why me, why now, biomedical constructions of disturbance leads patients to feel and think that the problem lies within their body, and therefore, the solution is the medication that can enter their body and restore or fix a biological malfunction. This prescription takes away from personal and social exploration and understanding; it effaces social

circumstances and the possibility of social or environmental changes from being involved in the definition of the situation at hand.

The power of these regimes of truth were not all-encompassing, there were several social actors at the hearing who defined the controversy using alternative logics. Although regimes of truth have the power to influence popular constructions and the practices of specific communities, knowledge/power relations themselves are multi-dimensional. This is not an example of the experts define and the lay public speak back with alternative knowledges. It is an example of the ways that knowledges are multiple, co-productive, and pliable to power.

The way you define the problem determines the type of answer that can be reached. If the problem of adolescent disturbance is defined as biologically based, or coming from a deficiency or imbalance of a chemical (problem located in the body or brain of an individual), then the solution can only be one which intervenes on the physiological level. If instead, the problem is defined as one that is much larger in scope, than a wider range or scope of solutions can be raised in addressing the issue at hand. In order to better understand a scientific problem or controversy such as this one, it is necessary to allow the voices of multiple social actors from various social locations who possess different types of experiences and knowledges to be heard. A public hearing is defined as a convention or gathering to "hear" something "officially", and thus, perhaps public hearings in the future could validate the perspectives and experiences of lay persons and independent experts by being more open to dialogue with these persons and their multi-faceted understandings of reality.

Appendix A: Social Worlds Mapping



Appendix B: Controversy Concerns by Social World

Adolescent & Family Social World Concerns

I. Side Effects

- A. Material Experiences of, changes of personhood (Including emotions, thoughts and behavioral changes).
- B. Lack of informed consent to parents and patients prescribed SSRI's.
- C. Medical community fails to recognize side effects as side effects.
- D. Call for FDA action (Warn about drugs, Ban drugs or increase prescribing practice restrictions, inform both parents and physicians about the risks of these drugs—get the word out).
- E. Poor Metabolization
- F. Withdrawal and Dependency Effects

II. Data Issues

- A. Data from pharmaceutical companies is biased
- B. Data from pharmaceutical companies is one-sided
- C. Challenge what counts as evidence

III. Policies and Practices

- A. Prescribing Practices
- B. Conflict of interest between pharmaceutical, regulatory and medical practices and politics
- C. Pharmaceutical companies miseducate physicians and consumers of risks of their medications

IV. Access to Information (Data and Knowledge)

- A. Lack of full disclosure of risks is a problem
- B. Need access to clinical trial data
- C. Physicians need to be fully informed
- D. Pharmaceutical companies misconstrue the ratio of risks and benefits in their advertisements

Independent Professional Experts Concerns

I. Side Effects

- A. No studies have been done explicitly designed to study side effects
- B. Lack of accurate information distributed on risks of side effects
- C. Medical community is not acknowledging seriousness of antidepressant side effect issues

II. Data Issues

- A. Current Clinical trials were not qualified to answer question of association between antidepressants and side effects issues
- B. Conflicts of Interest –contest that clinical trial data is the 'right' way to go about studying the issue

III. Policies and Practices

A. Prescribing Practices
B. Conflict of interest between pharmaceutical, regulatory and medical practices and politics
C. Pharmaceutical companies misinform physicians and consumers of risks of their medications

IV. Access to Information

A. Patients, parents and clinicians lack access to knowledge from clinical trials and accurate information about medication risks
B. Regulatory agencies must warn of risks when there is reasonable suspicion, not established causality
C. Regulatory agencies lack full access to data/knowledge

FDA Social World Concerns

I. Side Effects

A. How side effects were studies in clinical trials was important (how they were coded, defined, and analyzed).

II. Data Issues

A. What is currently known from 'data' about adolescents, depression and suicidality
B. Quality of clinical trial data
C. Reclassificaton of data
D. Re-analysis of data plan

III. Policies and Practices

A. Not concerned with reforming current practices or policies, were concerned with presenting how current regulatory and pharmaceutical practices of drug development fit into this controversy

IV. Access to Information

A. Pharmaceutical clinical trial data was not provided in a way to allow for regulatory science to make meaningful analyses of side effects
B. Missing information of science/data related to these issues

FDA-Summoned Professional Experts Concerns

I. Side Effects

A. Not enough information about side effects being distributed to physicians or parents or patients
B. Investigate side effects beyond suicidality
C. How to get stronger warning indications approved to inform public of risks of these medications

II. Data Issues

A. Limitations of clinical trial data is significant—context of clinical trials and everyday use in adolescents varies significantly
B. Have a lot of missing data on pharmacokinetics, dose range information, metabolism,
C. Classification categories and variables planned for re-analysis need revision
D. New studies need to be designed and implemented, need to study comorbidity issues and polypharmacological issues. Need to have studies that tell us more about benefit, not just harm of antidepressants.

III. Policies and Practices

A. Prescribing practices are inadequate—overmedication is concerning, dose levels commonly prescribed for youth are dangerous, physicians are not well informed of seriousness of risks, close monitoring of patients is not happening enough (medical practitioners are not taking side effects seriously).

IV. Access to Information

A. Lack of access to full disclosure of risks from pharmaceutical companies and FDA needs to change
B. Need stronger warnings of risks on antidepressant labels
C. Need access to all clinical trial data
D. Physicians need to be better informed, need to reach out to all professional organizations related to this controversy—so clinicians begin taking side effect risks more seriously.

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