Innovation, Myths and Equality: Constructing Drug Knowledge in Research and Advertising *

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Myths fascinate us because their surface simplicity invites exploration of more complex messages, promising universal truths. Myths are the representation of an 'active and communal process',[1] in which worlds have been built out of words.[2] They 'explain the unfamiliar in terms of the familiar'.[3] Myths, or signs as they are also known in semiotic theory, are a language that we use to state and understand content. It is a form that directs us to particular meanings.[4] What is denoted and appears to be the case in any representation rests in fact upon myths that reflect values in the viewer's community, drawing upon the values and limits of acceptability in the political culture, in a form that masks the means of production of these connotations, making them appear natural.[5] 'The myths which suffuse our lives are insidious precisely because they appear so natural. They call out for the detailed analysis which semiotics can deliver'.[6] Pharmaceutical advertisers use these processes in the construction of knowledge and value about their products, in a way that we will consider using semiotic theory, the theory of signs.

We argue in this paper that the advertisements created by pharmaceutical advertisers draw upon social stereotypes to promote their products to physicians. Advertisers create signs or myths that draw upon underlying social perceptions of groups and on attitudes among the medical profession to disease, cure, and the doctor-patient relationship. These stereotypes are based upon and visibly represent

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1 W Wesley Pue, 'In Pursuit of Better Myth: Lawyers' Histories and Histories of Lawyers' (1995) 33 *Alberta LR* 730 at 732.

2 Northrop Frye, 'The Rear-View Mirror: Notes Toward a Future' in N Frye, *Divisions on a Ground: Essays on Canadian Culture* (1982) at 183, quoted by Wesley Pue, ibid.

3 Jonnette Watson Hamilton, 'Metaphors of Lawyers' Professionalism' (1995) 33 *Alberta LR* 833 at 837.

4 Roland Barthes, *Mythologies* (1957; trans Annette Lavers, 1973).

5 Paul Cobley & Litza Jansz, *Introducing Semiotics* (1997) at 46.

6 Barthes, above n4.

the inferior status experienced by particular groups in society, as well as medical attitudes to patients and cures. Advertisers, who are well versed in these techniques, use the insights of semiotic theorists to create and power their ads.

New drug products are tested through the methodology of clinical trials. Through most of the last two decades, clinical trials in Canada and the United States were structured and analyzed in such a way that safety and efficacy data were available for only part of the population on which the drug would eventually be used.[7] Drug analyses were conducted primarily on men, but the drugs were prescribed to women without sufficient knowledge of the possible risks. Identification of the effects of these omissions from clinical trials and analyses has led to attempts to remedy this problem, and both omissions have been significant features of the past decade of writing on women's health issues.

Kuhn's work on the processes of scientific discovery shows how paradigms contain implicit assumptions that remain unquestioned, unexamined and unchallenged while the paradigm operates successfully on its own terms.[8] Paradigms determine the legitimacy of problems, removing problems that do not require solution. They prefigure solutions,[9] as they provide boundaries limiting the solutions. Our analysis of the drug research process demonstrates how this blinkering process has worked with respect to women. Law has contributed to this problem and has also been sought as a solution to it.

Drug advertising has replicated this paradigm of inequality and drawn upon it for commercial purposes. The under-representation of women and other sub-populations in some clinical trials and under-analysis of sub-population data where it existed have increased the risk of health problems for these groups. These problems are reified and amplified by the stereotypes used in drug advertising. Advertisements also have their own effects, creating an image of the doctor-patient relationship and the nature of cure that emphasises traditional models of practice and a heroic role for drug interactions.

The first section of this paper outlines the relationship between innovation and equality. Approaching pharmaceutical product innovation from an equality perspective makes apparent problems in the process of product development, problems with real health consequences. Innovation has had a disparate impact on women. During the last decade, attention has been focused on defects in research that have left particular groups of patients with inadequate information about the safety and efficacy of the products they use.

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7 Evlin L Kinney, Joanne Trautmann, Jay Alexander Gold, Elliot S Vessell and Robert Zelis, 'Underrepresentation of Women in New Drug Trials: Ramifications and Remedies' (1981) 95 *Annals of Internal Med* 495; United States, General Accounting Office, 'National Institutes of Health: Problems in Implementing Policy on Women in Study Populations' GAO/T–HRD–90–38 (18 June 1990); Vanessa Merton, 'The Exclusion of Pregnant, Pregnable, and Once-Pregnable People (a.k.a. Women) from Biomedical Research' (1993) 19 *Am J L & Med* 369; Rebecca Dresser, 'Wanted: Single, White Male for Medical Research' (1992) 22 *Hastings Centre Report* 24.

8 Thomas S Kuhn, *The Structure of Scientific Revolutions* (1962).

9 Michael Polanyi, *Personal Knowledge: Towards a Post-Critical Philosophy* (1958).

In the second section, we explore the efforts made in the United States and Canada to create research standards that are more responsive to all groups in society, changes whose effects are only beginning to be felt. These problems of injustice form the background within which the industry created advertising for drug products.

In the third section of the paper, we will use the theory of signs to analyse the process by which drug advertisements construct knowledge, and to define ways in which stereotypes are extended through the advertising process. Understanding the way advertisers engage viewers and call upon social perceptions can help us to guard against their capacity to create adverse health consequences. As we will demonstrate, advertising replicates the injustice observed in the creation of drugs and creates stereotypical perceptions that can undermine the doctor-patient relationship and may contribute to inappropriate prescribing. In both research and advertising, drug companies construct knowledge in ways that are detrimental to women.

1. Innovation and Equality

The Belmont Report in 1978 identified justice as a principle that should guide human subject research, along with respect for persons and beneficence.[10] Gradually, feminist scholars and policy-makers began to examine drug product innovation from an equality perspective, asking whether human subject research had been conducted in a non-discriminatory manner that achieved justice for women. An examination of the literature reveals an increasing awareness of the differential social effects of medical innovation. In the period prior to the 1990s, feminist scholars had been concerned that women's reproductive systems had been made the subject of much attention and research experimentation, as contraceptive products such as the early birth control pills, the Dalkon Shield, Depo-Provera and Norplant[11] were approved for distribution. Because these products were used exclusively by women, only women were subjected to the physical and psychological harms arising from the corporate failures and intentional acts that caused these reproductive products to be on the market without adequate testing, monitoring and information. As Lucinda Finley has expressed it:

> Medical science has long sought to control women's reproductive capacity and to surgically manipulate or technologically "improve on" women's bodies. Normal female attributes, such as small breasts or menopause, have been classified as disease conditions requiring treatment. It is women exclusively who have faced the risks of iatrogenic injuries and disease from drugs and devices designed to alter the natural processes or shape of their healthy bodies.[12]

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10 Institute of Medicine, *Women and Health Research, Ethical and Legal Issues of Including Women in Clinical Studies*, Vol 1 (1994) at 42.

11 Sylvia A Law, 'Tort Liability and the Availability of Contraceptive Drugs and Devices in the United States' (1997) 23 *NYU R of L & Social Change* 339.

Feminist jurisprudence has focused equality jurisprudence increasingly on the substantive outcomes of discriminatory conduct rather than simply on access to procedural justice and equality of opportunity. This concept of substantive justice is exemplified in the equality rights jurisprudence of the Supreme Court of Canada. Madam Justice Wilson, for the unanimous Court, described the purpose of the equality section of the Canadian Charter of Rights and Freedoms (section 15) as being 'to remedy or prevent discrimination against groups suffering social, political and legal disadvantage in our society'.[13] Groups that have been historically disadvantaged, 'discrete and insular minorit[ies]',[14] have suffered from prejudice, stereotyping and discrimination — the indicia of inequality. Inequality is a condition of disadvantage experienced by individual members of groups and it is experienced and amplified through discriminatory conduct.

This broad conception of substantive justice has been developed and theorised in academic health law literature informed by feminist analyses. Debra Debruin used Iris Marion Young's work on equality[15] as a conceptual framework for her work on including women in clinical trials, for the Institute of Medicine study, *Women and Health Research*:

> ... not all of the concerns of justice are matters of the distribution of benefits and burdens. Oppression qualifies as a concern of justice — indeed, justice requires that we eliminate oppression — but some important aspects of oppression are not purely matters of distribution.... In the second place, Young notes, the distributive paradigm considers only how social arrangements affect individuals as such. She argues that such an exclusive focus on individuals fails to capture important aspects of justice. After all, people are oppressed not as individuals, but as members of groups.[16]

Debruin made the argument that women suffer harms because of the practices that apply to inclusion in clinical trials, because of the failure to include women's health in the research agenda. The oppressed position occupied by women in society derives from these failures, reflecting the situation of women in relation to exclusionary norms.[17] The Committee on the Ethical and Legal Issues Relating to the Inclusion of Women in Clinical Studies based the Institute of Medicine Report on the principles of justice, noting that, 'Justice is not served when the nation's

12 Lucinda Finley, 'The Pharmaceutical Industry and Women's Reproductive Health: The Perils of Ignoring Risk and Blaming Women' in Elizabeth Szockyj & James G Fox (eds), *Corporate Victimization of Women* (1996) at 59–110; Patricia Peppin, 'Feminism, Law and the Pharmaceutical Industry' in Frank Pearce & Laureen Snider (eds), *Corporate Crime: Contemporary Debates* (1995) at 87–108.

13 *R v Turpin* [1989] 1 SCR 1296 at 1333.

14 Ibid. See also *Andrews v Law Society of British Columbia* [1989] 1 SCR 143; *Law v Canada (Minister of Employment and Immigration)* [1999] 1 SCR 497.

15 Iris Marion Young, *Justice and the Politics of Difference* (1990).

16 Debra A Debruin, 'Justice and the Inclusion of Women in Clinical Studies: A Conceptual Framework' in Institute of Medicine, *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies* Vol 2 (1994) at 131–132.

17 Id at 132–134.

research agenda ignores important questions regarding the health of one gender when one gender does not participate in clinical studies, and when one gender is treated with interventions that have not been adequately tested in that gender'.[18] The Committee recommended three general principles: that scientific advances benefit all and that the national research agenda ensure this; that preferential treatment in resource allocation may be needed to remedy past injustice and to avoid perpetuating it; and that enrolment in studies ensure generalizable results that apply to both women and men.

In Canada, the Strategic Research Network on Feminist Health Care Ethics made a submission to the Tri-Council Working Group on Guidelines for Research with Human Subjects about the nature of oppression:

> Drawing on the work of Iris Young, we understand oppression to be a state that effects (sic) groups and can be characterised as involving some or all of the following five conditions: exploitation, marginalisation, powerlessness, cultural imperialism, and violence.[19]

The Network went on to say that they made the further assumption that human subject research can significantly affect patterns of oppression, by focusing on health needs of the privileged rather than disadvantaged groups or by providing data of difference to support discriminatory treatment of groups, but that research may also play a significant role in achieving the dismantling of oppressive systems.[20]

If we look at the analysis of medical innovation over the past decade, we see that the debates about social effects have been informed by a concern for human dignity,[21] for equality and social justice, for the preservation of democracy,[22] and

18 Above n10 (vol 1) at 5.

19 Strategic Research Network on Feminist Health Care Ethics (Susan Sherwin, Principal Investigator), Submission to the Tri-Council Working Group on Guidelines for Research with Human Subjects (March 1995) at 1.

20 Ibid.

21 The Supreme Court of Canada jurisprudence of former Chief Justice Brian Dickson contains frequent reference to the significance of human dignity in a free and democratic society; Canada, Royal Commission on New Reproductive Technologies, *Final Report: Proceed With Care* (1993); Canada Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (1998): <http://www.sshrc.ca/english/programinfo/policies/ethics.htm>. See Dean Bell, 'Human Cloning and International Human Rights Law' (1999) 21 *Syd LR* 202 for a critique of essentialism in the concept of human dignity.

22 Maxwell Mehlman & Jeffrey Botkin, *Access to the Genome: The Challenge to Equality* (1998). They argue that genetic disparity will be increased by economic inequality and that this may have destabilising effects on democracy.

increasing concern about commodification,[23] geneticisation,[24] objectification,[25] and eugenics.[26] Each of these concerns has a relationship to the existence of oppression and injustice.

Inequality has been demonstrated in the way innovation has been conceptualised, in the oppressive effects of stereotyping and discrimination, in the distribution of benefits and risks of innovation, and in the way the imbalance of power has affected women's lives.[27] For example, Alta Charo, one author of the workshop and commissioned papers for the Institute of Medicine analysis of Ethical and Legal Issues of Including Women in Clinical Studies, concluded that,

> the exclusion of fertile women from the protocols burdens the fundamental liberty and right to life of fertile women, and functionally burdens the right to life of all women, who are thereby denied the benefits of research on women prior to marketing new drugs and interventions.[28]

Unequal access to benefits by women has been documented in many areas, including diagnosis (cardiovascular disease, HIV/AIDS), treatment (inadequate funding of breast cancer research), and testing (testing of oral contraceptives using dummy pills without consent in a way that also raised race and class issues).[29] Unequal distribution of risks between groups has been documented in the application of untested and unapproved products (thalidomide, DES,[30] and the

23 Christine Overall, *Ethics and Human Reproduction: A Feminist Analysis* (1987).

24 Abby Lippman, 'Worrying and Worrying About — the Geneticization of Reproduction and Health' in Gwynne Basen, Margrit Eichler & Abby Lippman (eds), *Misconceptions: The Social Construction of Choice and the New Reproductive and Genetic Technologies* (1993) vol 1 at 39–65. Geneticisation is the reductionist assumption that genes constitute human beings.

25 Margaret Atwood, *The Handmaid's Tale* (1985). Techniques of objectification facilitate treating women as vessels of reproduction or providers of reproductive materials, and undermine respect for women as humans.

26 Submissions by disability groups to the Canadian Parliamentary Committee on the never-enacted Bill C–47, An Act Respecting Human Reproductive Technologies and Commercial Transactions Relating to Human Reproduction (1996–1997); Studio D of the National Film Board of Canada, Canadian Broadcasting Corporation & Cinefort Inc (co-producers), Gwynne Basen (director), video 'Making Perfect Babies' in 'On the Eighth Day: Perfecting Mother Nature' Part 2 (1992).

27 See, for example, Diana Dutton, *Worse Than the Disease: Pitfalls of Medical Progress* (1988); Susan M Wolf (ed), *Feminism & Bioethics: Beyond Reproduction* (1996).

28 R Alta Charo, 'Brief Overview of Constitutional Issues Raised by the Exclusion of Women from Research Trials', in Institute of Medicine, above n16 at 90.

29 Karen L Baird, 'The New NIH and FDA Medical Research Policies: Targeting Gender, Promoting Justice' (1999) 24 *J Health Politics, Policy & L* 531 at 533.

30 DES (diethylstilbestrol) is a synthetic hormone that was marketed and prescribed between 1941 and 1971 to prevent miscarriage, although no clinical evidence existed of its efficacy for this purpose. When the children grew up, DES was found to have caused a rare form of vaginal cancer, infertility and pregnancy problems in DES daughters, and genital abnormalities in DES sons. It was the subject of significant litigation in the US. See for instance, Harriet Simand, 'The Iatrogenic Effects of DES' in *Misconceptions*, vol 2 above n24 at 82-85; the National Film Board (Canada) Studio D video, Bonnie Andrukaitis and Sidonie Kerr (directors) 'DES: An Uncertain Legacy' (1985).

Dalkon Shield, where risks were borne disproportionately by women and children), the application of untested therapy (*in vitro* fertilisation), and the prescribing of products tested only on other populations (drug testing affecting women, older people, non-white racial groups, children). Women use prescription drugs at a higher rate than men, and elderly people, who are disproportionately female, use more prescription drugs, and this means that elderly women are affected disproportionately by drugs.[31] The pharmaceutical industry has been ranked as one of the three industries most disposed to criminal activities[32] (along with the auto industry and oil industry), and as a result women run a higher risk of victimisation.[33]

Concern about the structuring of research extends beyond the unequal distribution of risks and benefits. The Strategic Research Network on Feminist Health Care Ethics in Canada identified, in addition to 'the exclusion of (some) women from clinical studies', four other concerns:

> the inappropriate use of women, ... the need for clear distinctions and norms governing therapy ... innovative practice and research, ... a research agenda sensitive to the actual needs of oppressed groups, ... and rethinking of the process of setting research agendas and conducting research.[34]

Writing through this period has also pointed to the ways in which society's views of women as unequal have been incorporated into conceptualisation of women's bodily processes, such as menstruation, menopause, and conception,[35] and the conceptualisation of certain diseases, such as osteoporosis. Human embodiment has been identified as a site for the generation of meaning and values.[36] Barbara Duden has written in *Disembodying Women* of how the capacity to visualise the unborn has transformed the experience of pregnancy into a public and accessible process and the foetus into a public idol, representing life.[37] Just as the first photo from space of the 'Blue Planet' removed us finally from the flat-earth view that had guided our daily lives, so visual imagery changes the

31 Jack E Fincham, 'An Overview of Adverse Drug Reactions' (1991) 31 *Am Pharmacy* 47 at 50; Robyn M Tamblyn, Peter J McLeod, Michael Abrahamowicz, Johanne Monette, David C Gayton, Laeora Berkson, W Dale Dauphinee, Roland M Grad, Allen R Huang, Lisa M Isaac, Brian S Schnarch and Linda S Snell, 'Questionable Prescribing for Elderly Patients in Quebec' (1994) 150 *Can Med Assoc J* 1801.

32 Laureen Snider, 'Directions for Social Change and Political Action' in Szockyj & Fox, above n12 at 247, citing Marshall B Clinard & Peter C Yeager with Ruth Blackburn Clinard, *Corporate Crime* (1980).

33 Snider, ibid.

34 Above n19 at 2–3.

35 Emily Martin, *The Woman in the Body: A Cultural Analysis of Reproduction* (1987); Elizabeth Grosz, *Volatile Bodies: Toward a Corporeal Feminism* (1994).

36 Paul A Komesaroff (ed), *Troubled Bodies: Critical Perspectives on Postmodernism, Medical Ethics, and the Body* (1995) at 15; Deborah Lupton, *Medicine as Culture: Illness, Disease and the Body in Western Societies* (1994).

37 Barbara Duden (trans Lee Hoinacki), *Disembodying Women: Perspectives on Pregnancy and the Unborn* (1993).

conceptualisation of this most intimate and invisible experience.[38] The recognition that images constrain meanings and reflect social stereotypes is a particularly important notion to keep in mind as we consider the construction of images in drug advertising.

2. *Innovation, Law and Equality*

A. Identification of Equality Problems in Drug Research

Medical innovation in Canada is governed by a variety of legal devices, including federal regulation of pharmaceutical products; tort law; professional regulation; intellectual property law; legislative control of institutional service providers; state funding of, and any limitations on access to, treatments; criminal law; international covenants concerning research on human subjects and bioethics; and funding council guidelines applying to research on human subjects.

Prescription drug and device innovation is affected by general laws governing experimentation in Canada[39] and by the particular laws applying to the drug and device development.[40] The federal *Food and Drugs Act*[41] is a criminal statute that applies to drugs and devices, food and biologics. Products liability law, in the area of tort law, is a matter of provincial jurisdiction as is professional regulation, while patent legislation is also a matter of federal jurisdiction. In this section, we shall examine the structure of law and guidelines affecting this area and consider the operation of the value of equality as a guiding principle for change.

The goals of safety and efficacy were established gradually through the twentieth century as standards for the evaluation of prescription drugs. It is hard to believe that the adulteration of medicines, with such products as plaster of Paris, cocaine and heroin, had only been brought under regulatory control with the first drug legislation in 1860 in Britain[42] and 1874 in Canada.[43] Patent medicines were also brought under control in 1908 in Canada, two years after the United States, in response to increasing public awareness, developed in part through campaigns in *The Ladies Home Journal* and *Colliers* magazines,[44] of the problems of unrestricted use of alcohol, narcotics and coal-tar derivatives, and of the excessive claims made for the products. It wasn't until later that food and drug legislation in the United States and Canada focused on the issue of demonstrable safety prior to

38 Ibid.

39 See David T Marshall, *The Law of Human Experimentation* (2000).

40 For an analysis of the history of Canadian regulation, see Lynne Kimiko Kamibayashi, 'Regulation of Biomedical Research with Human Subjects' LLM Thesis, Queen's University (1995).

41 *Food and Drugs Act*, RSC 1985 c F–27.

42 The first drug law was enacted in Britain only after a pharmacist's assistant, making up peppermint lozenges, mistakenly added arsenic instead of plaster of Paris and poisoned 200 people, killing 17 and causing horrible suffering. The standard initially adopted was purity of the product, which meant adherence to a pharmaceutical standard or manufacturer's description of what the product was claimed to be, in a form unadulterated by prohibited substances.

43 LI Pugsley, 'The Administration and Development of Federal Statutes on Foods and Drugs in Canada' (1967) *Med Services J* 387 at 392.

44 Id at 400.

marketing. The 1938 *Food, Drug and Cosmetic Act*[45] in the United States attempted to create better pre-marketing safety and tougher labelling requirements, following the use by the Massengill Company of diethylene glycol (anti-freeze) as a solvent in a sulfa preparation, poisoning more than 100 children.[46] Successive pharmaceutical disasters — thalidomide, DES, the Dalkon Shield, disproportionately affecting women — led to increased stringency in the regulatory regimes over drugs and devices in both countries.[47] The crisis of AIDS, in contrast, led to a loosening of regulatory control to achieve earlier release of experimental drugs.[48] Following on this successful consumer campaign to change drug research processes, the industry campaigned successfully to secure more expeditious approval processes in Canada and the United States and a longer patent protection period in Canada.

At the enforcement stage, the current system of drug regulation in Canada emphasises voluntary compliance by the industry, rather than using a more traditional criminal law enforcement model, even though the *Food and Drugs Act* is framed as criminal law. Cutbacks by the federal government through the 1990s significantly weakened the power of the regulator over the industry, as inspection staff were significantly reduced and the research laboratories in the Bureau of Drug Research closed, resulting in increasing government reliance on industry reports.[49] Laureen Snider has argued that there has been 'virtual abandonment of attempts to proscribe or sanction [corporate] crime'.[50] The disappearance of corporate crime enforcement means the symbolic effect of crime disappears and data about the events become unavailable; since no one is monitoring it, there is no one to report it to, and there are no data for people to see. Health Canada has conducted an internal reorganisation resulting in the Therapeutic Products Programme (TPP). It was developed as a response to industry criticisms of the lengthy approval process, the Krever Commission's identification of departmental failures in regulation of the blood supply,[51] public concerns about Health Protection Branch management, and global forces producing a centrifugal force in assessment and reporting.[52] In the United States, industry demands for faster approval processes have produced

45 *Food, Drug and Cosmetic Act* (1938) ch 675 Stat 1040. See Wallace F Janssen, 'America's First Food and Drug Laws' (1975) 30 *Food Drug Cosmetic LJ* 665.

46 Chester N Mitchell, 'Deregulating Mandatory Medical Prescription' (1986) 12 *Am J L & Med* 207 at 208 n3.

47 Nancy MP King & Gail Henderson, 'Treatments of Last Resort: Informed Consent and the Diffusion of New Technology' (1991) 42 *Mercer LR* 1007.

48 Steven Epstein, *Impure Science: AIDS, Activism, and the Politics of Knowledge* (1996). Epstein argues that AIDS activism also led to significant changes in our understanding of the process by which knowledge was constructed and given credibility, based on power and trustworthiness.

49 Laura Eggerton, 'Federal Labs to be Shut Down. Ottawa Closing Facilities that did Independent Tests on Pharmaceuticals, Food Safety' *Toronto Globe and Mail* (11 July 1997) at A1.

50 Laureen Snider, 'Relocating Law: Making Corporate Crime Disappear' in Elizabeth Comack (ed) with Sedaf Arat-Koc, et al, *Locating Law: Race/Class/Gender Connections* (1999) at 197.

51 The Honourable Mr Justice Horace Krever, Chair, *Commission of Inquiry on the Blood System in Canada, Final Report* (1997).

52 G Bruce Doern, 'The Therapeutic Products Programme: From Traditional Science-Based Regulator to Science-Based Risk-Benefit Manager?' in G Bruce Doern & Ted Reed (eds), *Risky Business: Canada's Changing Science-Based Policy and Regulatory Regime* (2000) at 185–207.

significantly decreased approval times. More rapid review takes place, according to Robert Temple, FDA Director of the Office of Drug Evaluation, not only because of increased staffing, in part resulting from legislated industry fees, but also because of an internal change in FDA culture to the attitude that it is 'possible and necessary to be both timely and good'.[53] FDA has recently withdrawn approvals for drugs associated with serious health risks and death,[54] and the withdrawals have been linked to the faster reviews, in the Pulitzer Prize-winning series by the *Los Angeles Times*. Withdrawn drugs have been shown to have increased health risks to women.[55]

By the beginning of the 1990s, the groundwork had been laid for the changes in the direction of equality that took place in that decade. Particular problems in the drug industry in Canada and the United States had been identified through mass tort and individual litigation and research; the exclusionary limitations in clinical trials and research had been identified and further research on that topic had begun; and the women's health movement had begun to have a political impact. In 1985, the US Public Health Service Task Force on Women's Health Issues found that the quality of health information and health care available to women were compromised by the lack of emphasis on women's health in research.[56] Identification of the problem of women's exclusion led the National Institutes of Health (NIH) in 1986 to create a policy urging the inclusion of women in clinical research.[57] Vanessa Merton has noted that the policy sounded very promising but that it 'went unenforced and essentially disregarded for the first five years of its existence', as was documented in Congressional testimony and the GAO Report.[58] The Congressional Caucus for Women's Issues asked the General Accounting Office to investigate the implementation of this NIH Guideline for the inclusion of women. The failure to include women in sufficient numbers to carry out sub-sample analyses and the failure to carry out gender analyses were substantiated in the report of the United States General Accounting Office in 1990, which found that the sex analysis had been done for only 50 per cent of Phase 2 and 3 clinical trials for drugs approved in the period 1988–1991.[59] A subsequent US Food and

53 Robert Temple, 'Commentary on "The Architecture of Government Regulation of Medical Products"' (1996) 82 *Virginia LR* 1877 at 1882.

54 David Willman, 'How a New Policy Led to Seven Deadly Drugs' *Los Angeles Times* (20 December 2000) at A1.

55 United States, General Accounting Office, 'Drug Safety: Most Drugs Withdrawn in Recent Years Had Greater Health Risks for Women' GAO-01-286R (19 January 2001).

56 IOM, vol 1, above n10 at 43; Regina M Vidaver, Bonnie LaFleur, Cynthia Tong, Robynne Bradshaw, & Sherry A Marts, 'Women Subjects in NIH-Funded Clinical Research Literature: Lack of Progress in Both Representation and Analysis by Sex' (2000) 9 *J Women's Health & Gender-Based Medicine* 495.

57 National Institutes of Health (September 1, 2000), 'Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research', at 1.

58 Vanessa Merton, 'Impact of Current Federal Regulations on the Inclusion of Female Subjects in Clinical Studies' in IOM, vol 2, above n16 at 65–83.

59 Ruth B Merkatz, Robert Temple, Solomon Sobel, Karyn Feiden & David A Kessler, 'Women in Clinical Trials of New Drugs — A Change in Food and Drug Administration Policy' (1993) 329 *NEJM* 292; GAO, above n7 at xxi.

Drug Administration survey of 1991–92 new drug applications, after the 1988 guideline changes, found that about two-thirds of safety analyses and just over half of efficacy analyses broke the analysis down by gender.

As noted above, analysts had noted that women were regularly excluded from, under-represented in and/or under-analysed in clinical trials and research.[60] At the same time it was becoming apparent that the study of particular groups of women — elderly, women with disabilities, racial groups — and their male counterparts was inadequate. While not all studies fit this pattern of exclusion or under-representation, and the IOM Committee concluded, ironically, that data were not available to determine whether women participated to the same extent, it was most clear that research in the areas of cardiovascular research and AIDS suffered from this deficiency.[61] Where women were included in samples, sub-sample analyses of gender effects were insufficiently undertaken.[62] Non-inclusive research took place intentionally, sometimes in accordance with legal requirements that precluded pregnant women from participation and, as Vanessa Merton expressed it in the title to her detailed study, led to 'the exclusion of pregnant, pregnable, and once-pregnant people — a.k.a. women'.[63] Michelle Oberman pointed out that,

> One of the ironies of women's underrepresentation in clinical trials is that the federal regulations limiting women's participation as subjects in drug trials were promulgated not in the nineteenth or early twentieth centuries but as recently as 1977 ... Historically, women were popular subjects of medical research for precisely the same reasons that render them problematic subjects today. Specifically, women's reproductive capacity has always intrigued scientists.[64]

Such exclusionary research also took place inadvertently, through failure to advert, to undertake to conduct sub-sample analysis or to increase sample sizes to permit such analyses.

Johnston and Fee have noted that we need to remember that the problems are ones both of exclusion and of inclusion.[65] As Francoise Baylis, Jocelyn Downie and Susan Sherwin have noted, the concerns identified by many feminists are exclusion and under-representation, the risk of exploitation, and the setting of research priorities.[66] The systematic exclusion of women from trials took place, Sue Rosser demonstrated, on the basis of difference (men's bodies are the norm

60 Kinney; GAO; Merton; Dresser, all above n7; Institute of Medicine, above n16.

61 Institute of Medicine, above n10, vol 1.

62 United States, National Institutes of Health, *Monitoring Adherence to the NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research: Comprehensive Report* (1 September 2000).

63 Merton, above n7.

64 Michelle Oberman, 'Real and Perceived Legal Barriers to the Inclusion of Women in Clinical Trials' in Alice J Dan (ed), *Reframing Women's Health: Multidisciplinary Research and Practice* (1994) 266 at 267.

65 Tracy L Johnston & Elizabeth Fee, 'Women's Health Research: An Historical Perspective' in Florence P Haseltine & Beverly Greenberg Jacobson (eds), *Women's Health Research: A Medical and Policy Primer* (1997).

and women's bodies are too complicated having all those pesky hormones to mess up the research sample) and on the basis of sameness (women are the same as men and so we don't need them in the research sample).[67] Debra Debruin refers to this second factor as 'false universalism', noting that it has the two consequences of making women invisible and, to the extent that women are different from men, sub-standard and deviant.[68] Michelle Oberman described it as

> not simply garden-variety gender bias but a more complex reincarnation of the age-old phenomena of male normativity, complemented by the somewhat more modern obsession with potential legal liability ... two factors [that] have joined to perpetuate a system that not only neglects to develop safe and effective medical treatments for women but neglects to do so in the name of protecting women from harm.[69]

The protective approach to regulation[70] grew directly out of the massive harm created by thalidomide and subsequent mass harms. More recently, the protective approach has been challenged — ironically — by the claim to the benefits forming part of participation in clinical trials; these benefits include not only access to experimental technology, but also to the increased monitoring and attention provided in a clinical trial, and access to health care that is otherwise unavailable in a country like the United States that lacks universal health care.

B. United States Changes

Because changes made in the United States are so influential in Canada, it is worth examining the responses of the National Institutes of Health and the Food and Drug Administration before examining changes made to Canadian regulation of clinical trials and human subject research. Changes in the National Institutes of Health (NIH) guidelines were designed to promote greater inclusion of women and minorities in clinical trials and research. The NIH legislation[71] requires valid sub-sample analysis, allowing some exemptions, and mandates data collection. The

66 Francoise Baylis, Jocelyn Downie & Susan Sherwin, 'Reframing Research Involving Humans' in The Feminist Health Care Ethics Research Network (Susan Sherwin, Coordinator), *The Politics of Women's Health: Exploring Agency and Autonomy* (1998) 234–259.

67 Sue V Rosser, 'Re-visioning Clinical Research: Gender and the Ethics of Experimental Design' (1989) *Hypatia* 125.

68 Debruin, above n16 at 133.

69 Oberman, above n64 at 266.

70 For a useful outline of the development of protectionist and inclusionary policies, see Institute of Medicine, above n16 at 37–43. In 1974, the United States Department of Health, Education and Welfare put into place regulations for federally funded research, based on this protective approach to women and the Kefauver-Harris amendments to the 1938 legislation added efficacy to the safety standard in the drug approval process. The 1977 guideline for research 'virtually banned participation of women with childbearing potential from entry into the early phases of clinical trials', based more on gender stereotyping than on science: Johnson & Fee, above n65 at 34, citing Kinney, above n7.

71 The changes were incorporated into the 1993 NIH Revitalization Act and the 1994 guidelines in accordance with the Act and supported by the NIH Outreach Notebook: above n29 at 534–538.

NIH Office of Research on Women's Health (ORWH) held sessions with Institutional Review Boards, the local boards that assess clinical trials and other forms of research on human subjects, and created a database to analyse the results of the inclusive measures. It is important to note, however, that the 1994 NIH Guidelines were not applicable if gender differences were not indicated by current research or if the disease affected only one group.[72] Vanessa Merton has argued that the linking of the appropriateness standard to 'known incidence/prevalence' of a condition among women is problematic because of the 'enormous gaps in knowledge about the epidemiology of many conditions in women' because of the exclusion of women from research.[73] She advocated more research on women's health and gender comparisons, evaluation of all research to determine whether gender analyses can be conducted, pharmacokinetic screens of all new drugs in both genders and animal studies including females as well as males.[74]

Recent research suggests that women's participation in research and clinical trials is still insufficiently analysed and that it is not possible to say that the law and guidelines have succeeded in changing this problem. In 2000, a GAO study concluded that researchers receiving federal funding failed to analyze the effects of the drugs and treatments of women, as required under federal law.[75] The GAO Report indicated that inadequate sub-sample sizes continued to be a problem, although women were included. The Report also found that 'significant progress' had been made by NIH to implement its inclusion policy, including treating the participation of women and minorities as an issue of scientific merit.[76] The GAO recommended moving beyond inclusion to enrolment and analysis in order to learn whether differences exist between the genders, and recommended ensuring that studies be designed to allow for valid analysis unless they are exempt. GAO recommendations about sub-sample analysis and education led NIH to restate its requirement of design and conduct of Phase III clinical trials to enable sub-sample analysis.[77]

Regina Vidaver and co-authors found that in research published from 1993 to 1998 in four leading medical journals, very few researchers analysed the results by sex.[78] This was the case in spite of the inclusion of women in about 80 per cent of the studies. The 2000 GAO report, 'Women's Health', comments that analyses showing no difference between the sexes might not be published, even when carried out.[79] An editorial by Greenberger and Marts urged change in research design and analysis plans at the grant application stage, review of recruitment and

72 Carol Hansen Montgomery and Katherine Sherif, 'The Information Problem in Women's Health: A Piece of the Solution' (2000) 9 *J of Women's Health and Gender-Based Medicine* 529–35 at 529.

73 Vanessa Merton, above n58 at 73–74.

74 Id at 75.

75 Robert Pear, 'Research Neglects Women, Studies Find' *New York Times* (30 April 2000) at 14.

76 United States, General Accounting Office, 'Women's Health: NIH Has Increased its Efforts to Include Women in Research' GAO/HEHS–00–96 (2 May 2000).

77 Above n57.

78 Vidaver et al, above n56.

79 Above n76 at 8.

retention data during the grant and at grant renewal, and a requirement by journals that authors include reports of gender analysis or an explanation for its absence.[80] Another study showed that fewer than 15 per cent of published research did gender analysis.[81] They concluded that this results in doctors failing to recognise dangerous drug combinations, giving as an example the disproportionate number of women who had life-threatening heart rhythm abnormalities as a result of taking Seldane, the antihistamine, in combination with either erythromycin or the antifungal agent, ketoconazole. Stephen Fried reported in his book, *Bitter Pills*, that Seldane was bringing in $700 million in sales annually and was just about to go over-the-counter when the FDA was alerted to the interaction data, which had been reported to the FDA only as drug overdoses, for which the individuals themselves would have been considered responsible. Doctors had made reports of 30–40 deaths from these interactions.[82]

The US Food and Drug Administration issued new guidelines in 1993, lifting the ban on inclusion of women of child-bearing potential, stating that the clinical sample should represent the population that would receive the drug, for comparison purposes, and indicating that they expected a full range of patients in all phases of trials and analysis of gender differences on efficacy and adverse effects.[83] Karen Baird has argued that although these are only guidelines and women of childbearing potential were not required to be included, making these weaker than the NIH changes,[84] the FDA didn't have as far to go in creating representative samples; they were reacting against the considerable pressure to deregulate, and they have, in fact, carried out educational activities and used persuasion with the industry, working to define the presentation of gender data in new drug applications, sponsoring educational sessions, and creating a gender analysis working group within the agency.[85] A 1997 legislative change has required the Secretary, in consultation with the NIH Director and industry representatives, 'to review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials'.[86]

In 1998 a Final Rule on Investigational New Drug Applications and New Drug Applications issued by the FDA clearly defined for companies the requirement to tabulate analyses of safety and effectiveness for important subgroups (gender, age

80 Phyllis Greenberger & Sherry A Marts, 'Editorial: Women in NIH-Funded Research Studies: There's Good News, and There's Bad News' (2000) 9 *J Women's Health & Gender-Based Medicine* 463.

81 Carol Hansen Montgomery & Katherine Sherif, 'The Information Problem in Women's Health: A Piece of the Solution' (2000) 9 *J Women's Health & Gender-Based Med* 529.

82 Stephen Fried, *Bitter Pills: Inside the Hazardous World of Legal Drugs* (1998) at 97–101.

83 United States, Food and Drug Administration (1992) 'Guideline for the Study and Evaluation of Gender Differences in Clinical Evaluation of Drugs'; above n29 at 539.

84 Baird, id at 539–540.

85 Id at 562.

86 United States, *Food and Drug Administration Modernization Act* (FDAMA) of 1997, s115 Clinical Investigations (b) Women and Minorities, amending s505(b)(1) 21 USC 355 (b)(1); FDAMA Women and Minorities Working Group Report (1998): <http://www.fda.gov/cder/guidance/women.pdf> at 1.

and racial subgroups) for new drug applications (applications for approval to market) and required that enrolments in clinical trials be tabulated by important subgroups (age, gender and race) for investigational new drug annual reports, to enable early identification of any enrolment deficiencies that could lead to problems in the NDA submission.[87] This rule is intended to deal with the critical problem of analysis of sub-population data. As the FDA noted in its comment,

> Despite repeated agency encouragement in both regulations and guidance, FDA and GAO have found that the analysis of effectiveness and safety data in relevant population subgroups, including age, gender, and racial subgroups, is not being carried out consistently. This rule makes the need for these subgroup analyses completely clear.[88]

Under the clinical hold rule created as a Final Rule on June 1, 2000, FDA is empowered to put a clinical hold on certain investigational new drug applications if men or women of reproductive potential who have the disease or condition and were otherwise eligible have been 'categorically excluded' solely on the basis of the perceived risk or fetotoxic potential.[89]

The picture of inclusion and exclusion from clinical research is multi-faceted. The proportion of women in clinical trials has sometimes been found to be similar to their representation in the patient population for the disease, as the FDA noted.[90] As we analyse later, however, diagnosis of disease is affected by perception of the typical patient for that disease, and women with the disease may be under-diagnosed. Vivian Pinn has said,

> Rather than think of diseases as specifically male or female, we've come to a realisation that the same disease may have different manifestations that are gender specific and that these manifestations may provide important clues in the effort to improve disease diagnosis, treatment, and prevention ... For instance, we know that women are more vulnerable to auto-immune diseases than men, but we don't know why.[91]

Given this, a comparison of the research sample with the patient population may simply replicate the problem. It is essential to design and conduct studies with sub-samples large enough to carry out these sub-sample analyses, so that scientific discoveries benefiting both genders can result[92] and any differential effects of the

87 Food and Drug Administration, Final Rule on Investigational New Drug Applications and New Drug Applications Federal Register, 11 February 1998; effective 10 August 1998.

88 Id at 3.

89 United States, FDA, Final Rule, 'Investigational New Drug-Applications; Amendment to Clinical Hold Regulations for Products Intended for Life-Threatening Diseases and Conditions', Fed. Reg. June 1, 2000, 65 at 106.

90 Above n87 at 2.

91 Vivian Pinn, NIH Associate Director for Research on Women's Health, Interview, 'Women's Health at NIH: Catalyst for Change' (Fall 1997): <http://www.nih.gov/news/nf/womenshealth/1.html>.

92 Ibid.

drug can be identified. The FDA rule is a further step in the direction of remedying these problems.

C. Canadian Changes

Changes in Canada have been much less extensive. They have taken the form of guidelines for funded research, in the Tri-Council Policy Statement (TCPS), 'Ethical Conduct for Research Involving Humans'.[93] The three federally funded granting councils in Canada adopted the TCPS after an extensive period of development and consultation. The TCPS is being implemented by universities for federally funded research and, at the discretion of the universities and other institutions, for other forms of research on human subjects. The content of the guidelines moves the governance of research into a more complex analysis of the effects and nature of such research by setting out a set of values to guide decision-making and by pointing out the combination of values changed by the context. The Research Ethics Boards are considered the 'cornerstones' of the policy, and the National Council on Ethics in Human Research has carried out an analysis of how to increase their effectiveness and improve support for them.[94] These Canadian changes have taken the form of a policy statement, and so their primary force comes through funding availability and institutional application to broader forms of human subject research.[95]

Paragraph 5.2 of the TCPS provides that: 'Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity.' Paragraph 5.1 provides that, where research is of a generic nature, and not specific to a group, researchers shall not exclude prospective or actual subjects on the basis of attributes, including sex, race and age, 'unless there is a valid reason for doing so'. Focused research on a particular individual or group is permissible (Par 5.1 (b)). This comparatively weak statement focuses on non-exclusion rather than required inclusion, provides a potentially broad and vague exception, and does not require analysis of sub-samples.

In April 1997, Health Canada issued a guideline for inclusion of women in clinical trials, applying to all drug trials.[96] The general principle of the guideline is the important one that, 'Drugs should be studied prior to approval in subjects representing the full range of patients likely to receive the drug once it is marketed.' Recognising the potential differences in dose-response, maximum size of effect or risk of an adverse effect, the guideline states its intent as encouragement of the inclusion of women, especially women of child-bearing potential at the earliest stages of drug development, to ensure that gender differences are identified and taken into account in the Phase III trials and to

93 Tri-Council Policy Statement, above n21.

94 National Council on Ethics in Human Research, 'Governance of the Ethical Process for Research Investigating Human Subjects': <www.sshrc.ca/english/programinfo/policies/governance_ethical.html> (posted 25 May 2001). The new structure of the Canadian Institutes of Health Research which is modelled on NIH, forms part of the TCPS governance structure.

95 The website for CIHR is <www.cihr.ca>.

96 Health Canada, Therapeutic Products Directorate Guidelines, 'Inclusion of Women in Clinical Trials' (17 April 1997).

generate data to inform physicians and patients about gender-related qualities of a new drug. Since it is only a guideline, it lacks the force and reach of a regulation. This guideline is put into effect by clinical reviewers of New Drug Submissions who check data affected by the guideline to identify any gender differences that would require dosage variations.

We know that the exclusion of women from some drug trials and limited sub-sample analysis has led to a situation where drugs used during pregnancy have been untested on pregnant women.[97] The guideline simply states that enrolment of pregnant or lactating women must be individualised and assessed on a risk-benefit basis taking into consideration the nature and severity of the disease, the availability and results of preclinical animal data, the availability and risks associated with alternative therapy, the stage of pregnancy and the potential for harm to the foetus or infant. It further specifies methods to minimise foetal exposure. Leaving issues of risk and benefit to be decided on an individual basis has clear advantages, although Research Ethics Boards need to have explicit guidelines to assist in their decision-making process. The guideline further states that pharmacokinetic studies for both genders should be carried out and that, for women, they should consider the effects of the menstrual cycle, supplementary estrogen and oral contraceptives in relation to the drug's nature. Gender influences should be assessed in individual studies and in the overall integrated analysis of efficacy and safety, the guideline states.

These inclusion principles are also to be followed within the context of the International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use/Therapeutic Products Programme guideline, 'Timing of Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals'.[98] The TPP guideline on inclusion of women in clinical trials contains useful starting points for the development of stronger measures to support the inclusion of women in clinical research and to require analyses for sub-populations. Creating a regulation with fully developed design and conduct criteria should be given high priority by Health Canada.

The Tri-Council Policy Statement is being implemented by the research ethics boards (REBs) in local institutions such as universities and hospitals across the country. Canada has also adopted the TPP Guidelines/ICH Harmonised Tripartite Guideline, 'Good Clinical Practice: Consolidated Guideline', and this guideline includes responsibilities of institutional review boards and ethics committees.[99] Research Ethics Boards, like their United States counterparts, the Institutional Review Boards, are responsible for assessing protocols for research on human

97 Ruth B Merkatz, 'Inclusion of Women in Clinical Trials: A Historical Overview of Scientific, Ethical, and Legal Issues' (1998) 27 *J Obstetric, Gynecologic, and Neonatal Nursing* 78, citing Edward Connor et al, 'Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment' (1994) 331 *NEJM* 1173.

98 Canada, Therapeutic Products Directorate Guidelines/ICH Harmonised Tripartite Guideline, 'Timing of Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals' (18 June 1998).

99 Canada, TPP Guidelines/ICH Harmonised Tripartite Guideline, 'Good Clinical Practice: Consolidated Guideline' (adopted September 1997).

subjects for conformity to the ethical principles and legal standards in effect in the jurisdiction. REBs should also be engaged in assessing the implementation of the federal guideline on inclusion of women in clinical trials.

The debate that led up to the TCPS and the considerably expanded understanding of ethical questions contained in it are likely to have a useful influence on the overall quality of decision-making at the local level, where numerous decision-makers had already developed significant expertise. The responsible agencies need to ensure that standards are applied consistently by the Research Ethics Boards across the country and need to provide education and continuing support.[100] REBs are usually under-funded and generally lack the capacity to monitor adherence to the standards during the clinical trial. Continuing review becomes increasingly important as it forms part of the Good Clinical Practice Guideline adopted in 1997.[101] REBs operate in universities, where there is powerful motivation to support researchers in obtaining and maintaining funding. This potential conflict of interest was noted, but discounted in the TCPS.[102] Research Ethics Boards themselves are subject to liability where a court determines that the board has failed to fulfil its responsibilities with respect to the protocol. In *Weiss v Solomon*,[103] a hospital ethics board shared responsibility for the death of a patient in a research study after it failed to require that the protocol exclude this patient on the basis of his existing health problem, to emphasise the risks on the comment form and to be adequately prepared for such an adverse reaction.

D. Further Problems

The pharmaceutical industry's concern for litigation resulting from injury through clinical trials on fertile women needs to be taken into account in any guidelines, if manufacturers are to include fertile women in clinical trials.[104] A further point developed by Ellen Flannery and Sanford Greenberg is of some assistance in this respect: 'Inclusion of women in clinical studies is unlikely to significantly increase the risk of liability for harm to subjects participating in the clinical trials, while exclusion of women could lead to liability for injuries to women after the product is marketed.'[105] Similarly, Ellen Wright Clayton noted in her study of paediatric effects of clinical trials that,

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100 Harold Edgar & David Rothman, 'The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation' (1995) 73 *Milbank Q* 489.

101 Above n99 at s3.1.4.

102 The conflict of interest problem is receiving intense examination at this point. See, for example, the symposium on human subject research and the role of institutional review boards in Jesse A Goldner (ed), (Winter 2000) 28 *J L, Med & Ethics*; Trudo Lemmens & Benjamin Freedman, 'Ethics Review for Sale?: Conflict of Interest and Commercial Research Review Boards' (2000) 78 *Milbank Q* 547.

103 *Weiss v Solomon* (1989) 48 CCLT 280 (CS Que).

104 Oberman, above n64 at 274–275.

105 Ellen Flannery & Sanford N Greenberg, 'Liability Exposure for Exclusion and Inclusion of Women as Subjects in Clinical Studies' in Institute of Medicine, above n16 vol 2 at 97.

> From the perspective of investigators and particularly of the manufacturers whose interventions are being tested, the risk of incurring liability during the early stages of drug investigation is actually quite small whereas the potential for substantial liability is much greater once a fetotoxic drug enters widespread use.[106]

Post-marketing surveillance is not carried out in a systematic way under the Canadian system and this serious deficiency has been repeatedly drawn to the attention of the federal government.[107] An effective post-marketing surveillance system would be able to pick up adverse effects that were not apparent in the Phase III clinical trials, either because of sample size or sample composition. If adverse effects are not being reported effectively and accurately, then data for sub-populations are unavailable. Reporting of adverse effects is mandatory for the pharmaceutical industry but reporting by other groups, including doctors and hospitals, is done only on a voluntary basis. This hit-and-miss system leads to insufficient information about adverse effects being available for physicians, regulators and patients who are trying to participate in making informed decisions.[108] Identification of adverse effects is particularly important for vulnerable populations and for groups inadequately assessed at the clinical trial stage.

Current regulation in Canada, as in the United States, permits unapproved, or off-label, uses of drugs approved for other purposes. For example, the hazardous diet drug combination 'fen-phen' was an off-label long-term combination of a drug, fenfluramine, approved for short-term use, in combination with a second appetite suppressant, phentermine.[109] The approval of thalidomide by the FDA in 1998, in spite of negative reviews by the three scientific reviewers, has created the possibility of off-label uses beyond its approved use for leprosy treatment.[110] The *Los Angeles Times* has reported that it has already been marketed for other uses, cancer and AIDS, and that thalidomide has been reported as a suspected cause in 16 deaths in the two years since approval, although these were among very sick patients. Off-label use creates a further problem for the tracking of gender-based consequences. Further, such a practice creates a disincentive to drug research.[111] From the company's perspective, there are advantages in ensuring that physicians

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106 Ellen Wright Clayton, 'Liability Exposure When Offspring Are Injured Because of Their Parents' Participation in Clinical Trials' in Institute of Medicine, id at 103.

107 Denis Gagnon, et al, 'Gagnon Report', *Working in Partnerships: Drug Review for the Future: Review of the Canadian Drug Approval System* (1992) at 113; see discussion in Patricia Peppin, 'Drug/Vaccine Risks: Patient Decision-Making and Harm Reduction in the Pharmaceutical Company Duty to Warn Action' (1991) 70 *Can Bar R* 473 at 494; Krista Foss, 'Loosening the Cap on Drug Approvals: the Slow Pace of Canada's System for Ensuring the Safety of New Drugs is Under Fire from Patients, Academics and Manufacturers' *Toronto Globe and Mail* (30 May 2000) at R7.

108 Linda T Kohn, Janet M Corrigan & Molla S Donaldson (eds), *To Err is Human: Building A Safer Health System* (2000).

109 GAO, 'Drug Safety: Most Drugs Withdrawn in Recent Years Had Greater Health Risks for Women' GAO–01–286R (19 January 2001) at 5.

110 David Willman, 'A Long-Feared Drug Gets the Green Light' *Los Angeles Times* (20 December 2000) at A27.

111 Fried, quoting Raymond Woosley, above n82 at 101.

become aware of the new use for the product, without advertising it formally. The law of negligence applies to off-label prescription and doctors need to be wary of prescribing for uses that might not meet the standard of care.

Even some drugs that have gone through recent approval processes have the potential to create serious and in some cases life-threatening adverse effects unobserved during the three phases of clinical trials. The GAO found that 51 per cent of the 198 drugs approved between 1976 and 1985 caused serious adverse effects, basing their conclusion on changes in labels and withdrawals from the market.[112] Until recently, drugs were infrequently removed from the market. For example, Omniflox, a so-called 'me-too' antibiotic that added no therapeutic benefit for consumers, was withdrawn from the market by Abbott Laboratories in 1992, only the ninth drug to be withdrawn in 'modern FDA history'. It had been on the market for 16 weeks, during which the adverse effects included renal failure, hemolytic anaemia (blood cell destruction), anaphylactic shock, severe hypoglycaemia, and some cases of multiple organ failure resulting in death.[113]

A 2001 GAO study found that health risks to women were greater among the drugs withdrawn from the US market over the past three years.[114] Four of the ten withdrawn drugs posed greater health risks for women, even though they were widely prescribed for both genders, while another four posed greater health risks for women that might reflect the higher level of usage among women. A Pulitzer Prize winning series in the *Los Angeles Times* demonstrates how Congressional and Presidential demands for faster approval times for new drugs has led to speeded-up processes of approvals, FDA approval decisions that disregarded internal warnings in some cases, and ultimately the withdrawal of seven drugs after reports of serious adverse effects, including deaths.[115] They reported that these seven drugs were reported as the leading or primary suspects as causes of death in 1002 adverse event reports filed with the FDA. While the drugs may not have been the actual cause in each case, it is also true that adverse event reports significantly underestimate incidence. Six of the seven withdrawn drugs were prescribed for conditions that were not life-threatening — heartburn, appetite suppression and pain relief.

One important feature of tort litigation is its provision of a forum for the examination of corporate and government activities. The forensic potential of tort litigation should not be underestimated, as it provides information to guide policy-makers who can craft legislation to prevent similar occurrences and motivates regulators to take stronger action. Its indirect ability to identify publicly the wrongs needing remedy is one of tort law's important contributions to the law of innovation in the 20th Century and mass tort litigation was a significant force in changing the nature of drug regulation.

112 Lucinda Finley, 'Female Trouble: The Implications of Tort Reform for Women' (1997) 64 *Tenn LR* 847 at 869.

113 Above n82 at 170–171.

114 Above n109.

115 Above n54.

Many of the drug and vaccine innovations in the past century have produced immense health and social benefits, and it is in this context that mass harms created by the products appear so shocking. To avoid this consequence, any health regulatory system needs to have the means to ensure safe and efficacious products, tested on the populations on which they are being used, tested for the purpose for which they are being prescribed, and assessed through surveillance after marketing. In this section we have discussed how the knowledge constructed about women's health through the drug development process was identified as a significant problem. As political pressure mounted, government agencies and research councils sought better analyses of the problem and solutions to it. At the same time, advertisers were creating portrayals that drew upon and reinforced social and medical stereotypes. In the next section we analyse this myth-making process and its detrimental effects.

3. *Constructing Images in Drug Advertising*

Advertisers construct knowledge about their products and the value to be attributed to them. This is done in a context in which the value attached to their product is always positive. Advertising in professional journals is a primary means of communicating with prescribing professionals. Marketing of prescription drugs is subject to certain limitations, incorporated into federal legislation and regulations in Canada. Apart from these requirements prohibiting direct-to-consumer advertising, prohibiting claims of cure for particular treatments, and accepting delegation of *Broadcasting Act* authority to preclear advertisements, limits are not imposed on the drug's conceptualisation in advertising.[116] We argue that drug advertising needs to be transformed to incorporate greater respect for disadvantaged populations and that readers of drug advertisements — prescribing physicians in particular — need to be educated about the means by which messages are transmitted so that they can guard against the construction of hidden motivators. Advertising draws on aspects in the political culture, including stereotypical representations of particular groups to power the advertisement. These ideological characterisations have the potential to create distortions in the diagnosis and treatment of disease, and to reinforce biases in perceptions of women and other under-analysed groups.

Semiotic theory provides concepts to analyse the construction of advertising messages and to uncover the hidden values. The theory of signs is drawn from the theories of Barthes, Lévi-Strauss, Saussure,[117] and modern analysts Williamson and Goldman[118] who have examined myths and theorised about the construction of knowledge and value. The essential concepts in the theory of signs are:

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116 Food and Drugs Act and Regulations, above n41. For an overview of US drug regulation at the beginning of the 1990s see David Kessler, 'The Federal Regulation of Prescription Drug Advertising and Promotion' (1990) 264 *JAMA* 2409.

117 For example, Roland Barthes, *The Semiotic Challenge* (trans Richard Howard, 1988); Claude Lévi-Strauss, *Structural Anthropology* 1 (trans Claire Jacobson & Brooke Grundfest Schoepf, 1977); Ferdinand de Saussure, *Course in General Linguistics* (trans Wade Baskin, 1974).

118 Judith Williamson, *Decoding Advertisements: Ideology and Meaning in Advertising* (1978); Robert Goldman, *Reading Ads Socially* (1992).

- The sign, which is the material object plus its meaning
- Signification, which is the process of attributing meaning to an object.[119]

Judith Williamson has demonstrated how the drug advertisement process works through a Chanel No. 5™ advertisement, made up of a close-up of Catherine Deneuve with a bottle of Chanel No. 5™ superimposed in the bottom right-hand corner. The advertisement is designed to engage the viewer in generating the meaning of Catherine Deneuve, the sign, and then transferring this meaning to the product. As a result, the perfume is seen as something chic, elegant and sensual. In the final step, we transfer the meanings to ourselves: we will be beautiful if we use the product.

Advertisements are designed to draw the reader into the process of identification and attribution — identification of meanings derived from one myth system and attribution of those meanings to the product.[120] Advertisements engage the viewer through a process of calling the reader forward into the advertisement, to participate, produce meaning, give value, and identify. This process is an active one, involving identification and transfer of meanings, even though the process may occur without the reader's awareness and even though the initial object or person and the product being sold may be dissimilar.[121] Robert Goldman has provided this description of the process: 'Advertising is a system for producing a currency of signs ... a dialogue which is the site for interpretive exchanges.'[122]

The viewer creates the meaning in the ad, on the basis of what the viewer already knows. The source of the significance in our own belief systems is called the referent system in semiotic theory.[123] The qualities signified by the person or object, beauty in the Chanel No.5™ case, have their source in the referent system. The referent system is a system of meaning operating within that cultural context,[124] which provides the meaning that will be attributed to the sign and transferred to the product. This prior knowledge of the viewer is drawn out by the advertiser based on the ideological assumptions that the advertiser anticipates will be successful for that group of viewers. The meaning that the viewer constructs for the object is combined with the object to create the sign. Barthes talks about myths as combinations of the sign, signified and referent system. 'Myth has a double function: it points out and it notifies, it makes us understand something and it imposes it on us.'[125] That meaning is then carried over, in an unconscious way, to

119 Judith Williamson has described the elements in this way: 'A sign is quite simply a thing — whether object, word or picture, which has a particular meaning to a person or group of people. It is neither the thing nor the meaning alone, but the two together. The sign consists of the Signifier, the material object, and the Signified, which is its meaning. These are only divided for analytical purposes: in practice a sign is always thing-plus-meaning': id at 17.

120 Goldman, above n118 at 143.

121 Williamson, above n118 at 30.

122 Goldman, above n118 at 174. The ad process is 'powered' by a desire for meaning and self-actualisation on the part of the viewer, and this makes the transition across the space between the viewer and the object: Williamson, above n118 at 60, 66.

123 Id at 26.

124 John Berger, *Ways of Seeing* (1972).

the object to be marketed — the perfume, the blue jeans, the soft drink or the drug.[126]

Consumer advertising has become more sophisticated since viewers became conscious and 'knowing' about their own participation in the process. Advertisers have made use of this awareness by incorporating playful self-referential elements into consumer advertisements, and by creating advertisements specifically for the aware viewer to deconstruct.[127] Medical advertising has not reached this stage and the techniques used in drug advertising can still be understood using the basic tools of semiotic analysis. As the audience for drug advertising changes with a new media-literate and more diverse generation of medical students and practitioners, however, drug advertisers may find themselves caught between two very different kinds of viewers.[128]

The advertiser appropriates the system of meaning from a segment of society for the purpose of targeting that group.[129] Medical advertising is constructed to draw upon two referent systems: first, the assumptions doctors will make about their practices, their professional self-images, patients, doctor-patient relationships, and the nature and expression of diseases, and second, the social attitudes to groups in the society to which the drug is targeted. Advertisements also call upon views about the doctor-patient relationship that include heroic and interventionist roles for doctors and passive and compliant roles for patients. Because of the values depicted in the advertisements, discriminatory portrayals are reinforced, and practices encouraged that are ultimately harmful to health. The process by which advertising values are created takes place unconsciously, with the active participation of the viewer and yet is designed by the advertiser to make the connotation appear natural. Williamson has said that,

> Images, ideas or feelings, then, become attached to certain products, by being transformed from signs out of other systems (things or people with 'images') to the products, rather than originating in them. This intermediary object or person is bypassed in our perception .... So a product and an image/emotion become linked in our minds, while the process of this linking is unconscious.[130]

Later, she notes that, 'The obvious ideological function of this is to make the subject feel knowing but deprive him of knowledge.'[131]

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125 Roland Barthes, 'Myth Today' (1957) in Lucy Burke, Tony Crowley & Alan Girvin (eds), *The Routledge Language and Cultural Theory Reader* (2000) at 411.

126 Goldman, above n118.

127 Robert Goldman & Stephen Papson, *Sign Wars: The Cluttered Landscape of Advertising* (1996).

128 Medical students at some medical schools, including Queen's University and Albany Medical College have received education in the evaluation of the claims made in drug advertising: Solomon Garb, 'Teaching Medical Students to Evaluate Drug Advertising' (1960) 35 *J Med Educ* 729. See also Jacqueline N Glasgow, 'Teaching Visual Literacy for the 21st Century' (1994) 37 *J of Reading* 494. A good starting point would be Michael S Wilkes, Bruce H Doblin & Martin F Shapiro, 'Pharmaceutical Advertisements in Leading Medical Journals: Experts' Assessments' (1992) 116 *Annals of Internal Med* 912.

129 Goldman & Papson, above n127 at 9.

130 Williamson, above n118 at 30.

131 Id at 116.

The advertisements we have selected to demonstrate this process appeared in the *Canadian Journal of Psychiatry*, the *Canadian Medical Association Journal* and the *American Journal of Psychiatry* over the period between 1996 and 2001. They show some common approaches to the depiction of mental illness, patients, doctors and cures. They also illustrate stereotypical representations found in drug advertising generally. We have chosen mental illness as a disease prototype as there is a significant literature that indicates that women are over-represented in the advertisements for drugs to treat such illnesses as depression, schizophrenia, anxiety disorder, obsessive-compulsive disorder and panic disorder. These advertisements provide illustrations of our theoretical perspective on innovation, equality and myths.

Astra Zeneca Pharmaceuticals offers a triptic of ads for its drug Seroquel,™ a drug used for the treatment of schizophrenia.[132] The first ad is of a young woman, the second of a young man and the third of an older man. Each ad has the same structure: a half-face photo on the right side of the ad showing pale faces on an even paler background, with text in a font that appears hand written. The messages in the text indicate key differences among the three people. The first ad depicts the young woman looking sad, with her eyes wide open and staring into space with a dazed look that is stereotypically associated with individuals with mental illness. In large print beside the picture are the words, Will I gain weight?, graphically presented, as in all the ads of this triptic, to give the impression that she has written the words by hand. There is great personal appeal in this ad, with the questioning face and the handwritten question designed to draw in the doctor. The drug company provides the doctor with the answer to the young woman's question in scientific terminology just under the question. The answer, however, says two different things depending on how far you read. In larger print the reader is told that the drug was rarely associated with weight gain in patients, while in very small print it states that in phase III trials, the mean weight gain at one year was 5.6 kg.

A young woman, experiencing the serious illness of schizophrenia, primarily concerned with weight gain, perpetuates the stereotype that girls and women have excessive concerns about their weight. The overall message of the ad, if viewed quickly, is that she doesn't have to worry — that is, if you don't think that a mean weight gain of 5.6 kg. is significant. The stereotypes continue in the remaining two ads of the series. The second ad in the same journal depicts a young man. He appears to be in his twenties, and he too looks sad and unwell. His question is, Will it affect my sex life? In the third ad, a sad older man is asking, Will I be able to sit through a movie? Under the name of the drug in each ad is the phrase, 'As good to the body as it is to the mind.' The stereotypes are obvious and concerning.

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132 The Seroquel™ ads were published in *Canadian Journal of Psychiatry* 46(1) (2001). The Zoloft™ 'pentimento' ad may be seen in a number of versions. One of these was published in the *Canadian Journal of Psychiatry* 45(1) (2000). The Paxil™ man imprisoned in stone ad was also published in several versions, one of which was printed in *Canadian Journal of Psychiatry* 46(5) (2001), while the Paxil™ labyrinth ad appeared in *Canadian Journal of Psychiatry* 44(4) (1999). These ads have also been published elsewhere.

The next ad to be considered is for the drug Paxil,™ which is intended to treat depression, generalized social anxiety disorder, panic disorder and obsessive-compulsive disorder. The photograph in this ad is intended to represent the labyrinth of King Minos on the island of Crete. The image is very detailed, consisting of stone columns and multiple stairwells. The labyrinth is dark and has as ominous feeling about it even though it is lit by torches on the walls. There are no people in this ad, but we are drawn to a thread that winds from the bottom of the labyrinth, up through the stairs and out an open door to the sunlight. This ad depicts mental illness as a labyrinth. The mythological elements of the sign are clearly presented. Theseus has left the thread to follow back out of the labyrinth, the text tells us. While unseen, the Minotaur's threatening presence is read into the ad. We begin in the middle of the labyrinth but are led out of it by the visual thread.

The depiction of the labyrinth owes something to MC Escher, as we wonder whether it is his perspective-altering continuously joined stairs that we are viewing. The threatening Minotaur of more serious illness adds a dimension of emotion to the ad, while the thread provides relief from the immediate experience of the illness. The ad's text explains that 60-90 per cent of depressed patients experience anxiety connected with depression, that Paxil treats both, and that the drug is the thread that leads back to the world they lost. The sign for the patient, Theseus, is someone lost and threatened. In the Greek myth, Theseus sought out the Minotaur to kill it so that he could rescue the Athenian victims about to be offered to the Minotaur. Theseus acted with the assistance of Ariadne, who provided the magic thread that unrolled in front of him. The magic power of the thread in the myth is left unspoken in the ad. The sign for the patient Theseus is portrayed not as the hero he was in the myth but instead as a victim who can be rescued.

In further ads in this Paxil™ series, we find that the patient has become a woman. Layered over the labyrinth is the following text, 'She trembled every time she met someone. Felt embarrassed by her shaky voice and sweaty palms. She avoided people. Abused alcohol. And eventually fell into the depression so common with generalized social anxiety disorder.' In this case the ad strategy includes starting a text with a complete sentence and gradually reducing the words to sentence fragments to catch the attention of the reader and to make the meaning have more impact. The reader can almost feel the trajectory of the fall to depression. An important feature of the campaign to sell this drug is the patient compliance program. The pharmaceutical company, SmithKline Beecham has developed 'The Aurora Program' designed to help patients on Paxil™ see compliance in a new light. Aurora, the goddess of the dawn, can lead to 'the dawn of a new day in patient compliance'. No doubt she is in the light at the end of the thread leading out of the labyrinth. The patronizing language in the ads for the compliance program suggests that the patients, mostly women, do not do what they are told and when experiencing side effects, often decide to discontinue the drug. Given that Paxil™ has over 1.9 billion dollars in sales, and ranks 9th in prescriptions in the US market,[133] it is in the interests of the pharmaceutical company to maintain patients on this drug.

Another ad for Paxil™ uses rescue imagery, a common motif in pharmaceutical advertising. This ad shows a statue of a man carved out of a cliff. The image is located on the left side of the ad while the text is on the right side. In script at the top of the ad is written 'The imprisoned patient'. That text helps the physician reader to understand the intent of the sign in case it isn't obvious. The sign includes the patient who is the man carved in stone and the need for rescue from the stone face of mental illness. Although we don't see the doctor in this ad, we sense the doctor's presence because the text reads, 'You can use a different medication for each condition (depression, anxiety, panic disorder, obsessive compulsive disorder) or you can use one'. When the doctor is portrayed as a rescuer, the ad draws upon heroic and interventionist models of medicine that have had particular salience for doctors in traditional medicine. The heroic imagery appeals to beneficent and altruistic motives. It is also a macho form of medicine — aggressive, doctor-centered, and reductionist.[134]

Interventionist medicine requires active physicians, who must do things and be seen to be active. Both interventionist and heroic forms of medicine have legitimacy in a culture that places a high value on activity.[135] We see in the imprisonment ad the idea that a patient with this illness is unable to act. The active intervention of the drug releases a whole person. Technology saves the day! Significantly, the medicine itself supplants the doctor in this version of the heroic model and it is the drug that is the knight in shining armour. In one version of this imprisoned patient ad, we find on the page overleaf a free man who has used Paxil™ to carve his way out. In contrast to the imprisoned patient ad, this patient throws off the stone, the weight of the disease, and carries on with his life.

We might expect to find physicians portrayed in ads but in fact doctors are largely missing from contemporary advertising. Patients, in contrast, are shown in a high proportion of ads. For example, the drug's effect may be illustrated in an obvious way such as before-and-after shots of the same patient, a popular format in psychotropic drug advertising. Neill[136] and Lupton[137] have found that doctors are portrayed relatively infrequently in current ads, and that the incidence has declined. For instance, earlier ads commonly showed doctors, in white coats and stethoscopes, interacting with patients. The disappearance of doctors might have several explanations. Deborah Lupton observed that the doctor's role had been

133 'Prescription Audit', quoted by Andrew Sullivan, 'Pro Pharma' *New York Times Magazine* (29 October 2000) at 21.

134 It is also worth noting that the idea of a woman rescuer is a virtual oxymoron. The rescue imagery of childhood stories is replete with male princes and needy maidens, and it is against this norm that *The Paper-Bag Princess* plays with such fine irony. Robert Munsch, *The Paper Bag Princess*. Toronto: Annick Press, 1982, illustrations by Michael Martchenko.

135 Social preference attaches to youth, physical activity, and individual assertion — all qualities shown in the well-known Coca-Cola ads run during the winter Olympics — shown by the polar bears and the Olympians — and Coke? Activity's antithesis is the forced inactivity of disease. Infirmity, disability and weakness are connected and disparaged. Equation of a disease with the person leads to construction of the disabled or sick person as undesirable.

136 John R Neill, 'A Social History of Drug Advertisements' (1989) 28 *Soc Sci Med* 333–338.

137 Deborah Lupton, 'The Construction of Patienthood in Medical Advertising' (1993) 23 *International J of Health Sciences* 805–819.

transformed to that of only a mediator between patient and drug[138] and this notion of a change in the active agent seems correct. Neill's study showed the power of cure being attributed to the drugs rather than, as previously, to the doctors, as we have seen in the rescue ad. The drug itself has assumed the central role of healer. If this interpretation is correct, drug advertising should be seen as deeply subversive by the medical profession.

Semiotic theory suggests a further explanation for absent doctors. Doctors are present in the ads as the viewers, the essential creators of meaning in the ad process. The doctor is 'hailed' into the ad to participate in creating and attributing meaning, becoming 'the transformational space'.[139] This is where we find the doctor then — not portrayed within the ad but acting within the ad process. Because this process of linkage between sign and product occurs largely without consciousness, doctors are unaware of their own roles. This too can be seen as a subversive process.

The final ad for discussion shows a painting of a woman suffering from depression. The woman has a quality of Renaissance beauty and mystery. She has long dark hair, parted in the centre, pulled back from her face with soft tendrils falling in front of her ears. Her eyelids are heavy as she stares downward in sadness. She is wearing a demure scooped neck dress made with cloth of a diaphanous quality. The painting is dark except for the portion over her face that looks as if it has had the surface layer removed, like pentimento, to allow the reappearance of the painting underneath. The text at the top of the ad says, 'When panic disorder, OCD or depression darken a patient's profile — Choose Zoloft First.' The word Zoloft is written in thick font to make it stand out. Depression is depicted as a dirty covering on the surface of the painting. Mental illness exists only on the surface and may be wiped clean by using the drug. Underneath the surface is the original painting. Depression covers up the real person, who is there to be restored. This 'pentimento ad' implies that mental disease exists only on the surface and that the drug can remove that surface layer to reveal the real person underneath. The gauzy clothing replicates the idea of the surface and removing it to see the original self. It is perhaps meant to be seductive although the woman's persona is more suggestive of a Renaissance beauty. We would like to believe this simple myth about drug efficacy, and willingly acquiesce in its hopeful message.

A paternalistic and hierarchical model of decision-making envisages the doctor in control, responsible for treatment and decision-making. Beneficence on the part of the doctor is to be reciprocated by deference and reliance by the patient.[140] This type of relationship, which typified medical practice historically, was reflective of

138 Id at 897, 816.

139 Williamson, above n118 at 43–45.

140 The structural disparity based on knowledge was heightened when accompanied by professional scepticism about the reliability and validity of patients' information about their own bodies and by mistrust of their abilities to understand and act responsibly on the basis of medical information. A paternalistic model of medicine is based on a hierarchy of power between the health professional and the patient. Trust — by the patient of the doctor — has been a key factor in the paternalistic model of health care.

the patriarchal culture in which it developed. Cultural norms about gender, race and class have formed a prism through which a male-dominated, white upper-middle class profession viewed patients. The 'pentimento ad' illustrates a patient who is so far from a participatory model that she is static. She is the ideal woman of the Renaissance past. She is incapable of efficacious behaviour. And when she is restored, she will be on an easel.

The context within which an individual's illness is precipitated is not often evident in the advertisements. Instead advertisements more typically show women being returned to their social roles as providers of family support. If she is given the drug, then she can go back to the family where she's needed.[141] Gendered stereotypes of grandmotherly women baking cookies and women who need to be cured so that they can resume their roles as caregivers are in sharp contrast to sportsmen grandfathers, playing at hunting and gathering in the woods.[142]

Drug advertising plays a role in depicting the causes of disease as well as their cure. Kleinman and Cohen have found in their research that advertisements for psychotropic drugs individualise responsibility by portraying 'normality and the ability to adapt to the mainstream as attributes of individuals'.[143] Kleinman and Cohen characterise this process as decontextualisation, a process in which social factors contributing to health and recovery are ignored and the individual is held totally responsible. Accountability is located in the individual, who becomes responsible to friends, family and workplace for the illness and for finding a cure.[144]

Advertisements that individualise diseases over-simplify both the disease process and the process of cure. If diseases occur within the individual, the cure may be established within these same boundaries. This conceptualisation makes disease appear more amenable to cure, and particularly to an individualised cure. This simplification assists the selling of drugs as we have seen in the 'pentimento ad' where the product is depicted as capable of gently acting to restore what is underneath the surface. Goldman and Montagne have made a similar observation in their analysis of antidepressant medication, noting that depression is represented as a universal human condition apart from any particular social context but always amenable to the solution presented by the drug.[145]

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141 Elizabeth Ettore & Elianne Riska, *Gendered Moods: Psychotropics and Society* (1995).

142 Scandinavian journals showed some differences in this respect. Riska and Hägglund's content analysis of psychotropic drug advertising in Finland, Sweden and Denmark showed an increasing number of men represented, although women still predominated in Sweden and Denmark. Finnish journals emphasised women in professional roles, a finding that they interpreted as fitting the stereotypes of the professional woman under stress and of professionals as needing to be in control: Elianne Riska & Ulrica Hägglund, 'Advertising for Psychotropic Drugs in the Nordic Countries: Metaphors, Gender and Life Situations' (1991) 32 *Soc Sci Med* 465 at 470.

143 Daniel Lee Kleinman & Lawrence Jack Cohen, 'The Decontextualization of Mental Illness: The Portrayal of Work in Psychiatric Drug Advertisements' (1991) 32 *Soc Sci Med* 867 at 867.

144 Murray Edelman, 'Law and Psychiatry as Political Symbolism' (1980) 3 *Int'l J L & Psych* 235.

145 Robert Goldman & Michael Montagne, 'Marketing "Mind Mechanics": Decoding Antidepressant Drug Advertisements' (1986) 22 *Soc Sci Med* 1047.

Decontextualisation ignores important aspects of life and health, including inequalities that people experience in their own lives. The patients simply need to take the drugs in order to return to their social roles — without any acknowledgement that these roles contribute to the condition — along with 'poverty, sexism, social inequality, employment status, domestic violence, eating disorders and sexual, physical and substance abuse'.[146] Nikelly also argues that disclosing these social determinants of psychiatric health is contrary to the drug companies' economic interests, and those of the journals from whom they purchase advertising space. Similarly, stereotyping and attribution of roles based on group characteristics such as aboriginal status or age affect the ability to lead lives of dignity and fulfilment. Such factors are being recognised as important determinants of health by health researchers and policy-makers but they are not part of the decontextualised approach to disease depicted in drug advertising.

The semiotic method of analysis points to the referent system as the source of meaning upon which the advertiser calls. We argue that drug advertising draws on social stereotypes as one referent system. Drug advertising draws on social stereotypes in several ways.

First, advertisements use commonly accepted characterisations to signify qualities to be associated with the product. The community values constituting the reference system activate myths or signs. For example, activity has a gendered aspect, as men are stereotypically perceived as active in this culture, while women are seen as passive or, if active, as dangerous.[147] This may be one reason why the male body has appeared more often in advertising. When shown engaged in activities such as sports,[148] the signification of activity by the male body is transferred to the drug, which is endowed with the active quality.[149] Because of the cultural association of passivity with the female body, this transfer of meanings can't be accomplished for the female body without dissonance.[150] In the advertisements presented in this paper, we find the man, although carved in stone, potentially having the strength to free himself, not just with the strength of Paxil™, but also with the strength we see in his 'abs', while the woman in the 'pentimeno ad' is the serene Mona Lisa.

146 Arthur G Nikelly, 'Drug Advertisements and the Medicalization of Unipolar Depression in Women' (1995) 16 *Health Care for Women International* 229.

147 Emily Martin, 'The Egg and the Sperm: How Science Has Constructed a Romance Based on Stereotypical Male-Female Bias' (1991) 16 *Signs* 485.

148 Nature and science are two powerful and authoritative referent systems operating in advertising: Williamson, above n118. In its benign and pastoral expression, nature is used as a feature with which viewers will identify positively. There is, however, an implicit opposition between drug intervention, which is constructed and inherently non-natural, and the natural processes of the body, which must include disease. Drug intervention is not natural, and the sick body, which is natural, is not benign. The attempt to construct drug therapy as equivalent to the natural is achieved through semiotic methods in which the transfer of meaning is meant to occur unnoticed.

149 For example, one advertisement shows a man looking through a frame showing him riding the horse. An advertisement for oral contraceptives, a selectively active drug, makes use of a tranquil scene of walking, next to a waterfall, showing a selectively active woman next to a temporarily inactive man.

Second, stereotyping is used to determine what will be shown and what will be omitted from advertisements. For example, physical disabilities are rarely depicted, and when they are, the portrayal relates to prosthetic devices and other forms of treatment rather than as an incidental feature of a person. The literature on drug advertising has often focused on issues of representation. Much of the early literature used quantitative methodology, examining the representation of groups, and particularly women's as opposed to men's representation. This literature, developed through 20 years of examination of European, North American and Australian journals, found men outnumbering women represented in drug advertising in a ratio of 2:1.[151] The exception to this gender rule, in addition to the obstetrical/gynaecological area, is found in psychiatric advertisements. Women's incidence ratio for psychiatric illness is 2:1 in relation to men.[152] Psychiatric disability in women is displayed in psychotropic drug advertisements in a manner disproportionate to this relatively higher rate of diagnosis in the population.[153] One early study, by Mant and Darroch, analysed gender portrayals in 500 drug advertisements for mood-altering drugs in two Australian medical journals, the *Medical Journal of Australia* and *Australian Family Physician*, from 1969 to 1975, concluding that women were over-represented, a pattern that they thought reflected and might reinforce prescribing

150 An early example is found in the use of notions of modern womanhood and empowerment by the industry to create the stereotype that women are solely responsible for birth control. Andrea Tone shows how the pharmaceutical industry in the 1930s marketed birth control they knew to be completely ineffective, and even dangerous in certain cases, and did so as 'feminine hygiene' products, in order to get around the prohibition on contraception. This was a convenient marketing device since the ostensible purpose was well-recognised but the marketing as something else prevented regulation of its false claims. What was most insidious, Tone has argued, was the marketing of birth control as a separate sphere under the control of women, through stereotyping women and creating sole responsibility for family planning: Andrea Tone, 'Contraceptive Consumers: Gender and the Political Economy of Birth Control in the 1930s' (1996) 29 *J Soc Hist* 485.

151 Deborah Lupton, above n137.

152 Wanda Leppard, Shirley Matile Ogletree & Emily Wallen, 'Gender Stereotyping in Medical Advertising: Much Ado About Something' (1993) 29(11–12) *Sex-Roles: A Journal of Research* 829.

153 Finy Josephine Hansen & Dawn Osborne, 'Portrayal of Women and Elderly Patients in Psychotropic Drug Advertisements' (1995) 16 *Women & Therapy* 129. Hansen and Osborne found this disproportion in psychotropic drug advertisements of the 1960s and 1970s continuing into the 1980s, and also found that the rate in the psychiatric journal remained at 80% while in the primary care journal women made up 100% of the patients. They found that elderly people were more often shown in the journal addressed to family physicians. Jelley and Owen's study of the *British Journal of Psychiatry* showed that while women were portrayed in numbers that reflected incidence rates, the portrayals drew on stereotypes about men's roles at work and women's roles at home or with children: Matthew Jelley & John Owen, 'Letter: Portrayal of women in advertisements' (1991) 159 *British J of Psychiatry* 586. In the most extensive study, King found that women appeared in 81% of the advertisements for psychoactive drugs in the *American Journal of Psychiatry* between 1959 and 1975, and that the portrayals of women indicated helplessness and anxiety while the portrayals of men indicated physical illness or work-related stress. Ellie King, 'Sex Bias in Psychoactive Drug Advertisements' (1980) 43 *Psychiatry* 129.

patterns for these drugs.[154] Mant and Darroch found that the advertisements overall were 'highly stereotyped as to sexual and social roles, notwithstanding the professional and clinical context in which they appeared'.[155] Beginning their article with studies that showed women were stereotyped in drug advertising as in commercial advertisements, as 'temptress, wife, mother and sex object', they observed that people come to doctors with needs and, in order to meet the needs, doctors must be able to move beyond stereotypical perceptions, and '[a]nything which reinforces the doctor's understandable tendency to accept a stereotyped view of patients interferes with the capacity to perform these functions.'[156]

One study, by Hansen and Osborne, that examined representation by race in addition to other factors, found that too few advertisements depicted members of racial groups other than white to include race as a study variable.[157] Racially mixed advertisements were beginning to appear in the mid-1990s, using a framing technique with portrayals of people from a variety of racial groups, age groups, and both men and women or a diverse group of people (for example, the 'broad spectrum' anti-depressant drug Effexor™).

Third, advertisers draw on perceptions of the typical patient for a particular disease, such as middle-aged to older white males with cardiovascular disease. Diseases, once recognised — another process subject to incorporation of social values, as discussed above — are organised into categories, which have certain physical attributes associated with them. Doctors are taught to diagnose disease through a process of comparing physical conditions with the disease category characteristics, through pattern recognition. Barbara Bates, the author of the leading text on diagnosis, has described how she based her system on Roger Tory Peterson's *Field Guide to the Birds*.[158] The paradigm for a particular disease will have classic attributes, not all of which would be present in an atypical presentation. When one part of the diagnostic category has been based on research that has examined only one part of the population and has been silent on other parts, or when the category has been associated with stereotypes in society, then the category itself contains fundamental flaws.

Stimson indicated that companies try to create 'diagnostic images' by associating age and lifestyles with a condition and its cure.[159] These images are intended to provide a shortcut to the drug for the practitioner in the diagnostic setting. In this way advertising creates a prescribing image in the minds of doctors and one that is intended to act as a diagnostic tool. Stimson's conclusion was this:

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154 Andrea Mant & Dorothy Broom Darroch, 'Media Images and Medical Images' (1975) 9 *Soc Sci & Med* 613.

155 Id at 617.

156 Id at 613.

157 Hansen & Osborne, above n153 at 134–135. Deborah Lupton, in her study of a weekly Australian medical journal, found that non-Anglo-Celtic ethnic groups were not depicted as doctors or patients: above n137 at 81.

158 Barbara Bates, 'Lessons from Writing a Textbook' Hannah Lecture in the History of Medicine (1992) Queen's University Archives; Roger Tory Peterson, *A Field Guide to the Birds* (1934).

159 Gerry V Stimson, 'The Message of Psychotropic Drug Ads' (1975) 25 *J of Communication* 153.

'To the extent that doctors accept the images in the advertisements, they have lost control over their diagnoses.'[160] The diagnostic profile suggested by Stimson adds another layer to the medical symptoms that combine to provide a profile for diagnosis, and provides linkages that may be partial or otherwise flawed. The fact that such linkages are made without being perceived by the viewer means that the control of medical expertise that might otherwise operate will not do so.

In our opinion, the diagnostic image can be extended to include these associations of disease with a particular group when it is prevalent in many groups, in this way both creating and perpetuating stereotypical associations. The omission of groups from advertisements, and their under-representation may have an effect on health professionals, creating and reinforcing the image that certain diseases occur only or predominantly in certain groups. If this association is made, then diagnostic hints may be missed and prescribing practices affected. These include the possibility of overlooking the condition in one group, the risk of pursuing it more zealously in the other group, and missing the disease when it manifests differently in various social groups. While our study is unable to reach a definitive conclusion on the process by which prescribing patterns are affected, we believe that the stereotypes and exclusions replicated in drug advertisements have a significant effect on physician attitudes. By combining the insights of semiotic analysts with those of drug advertisement researchers and feminist analysts, we have shown how the process of creating meaning works, through reinforcement of the inequalities present in the broader area of drug research.

Inequalities are not limited to portrayals in drug advertisements for psychological illnesses such as depression. For example, the over-representation of men in cardiovascular drug advertising replicates and reinforces the association of heart disease with men. Cardiac disease is the leading cause of death in women.[161] Yet it continues to be under-diagnosed and untreated, not only in women but also in specific ethno-cultural groups.[162] Inequality is also evident in the way women are portrayed in advertisements promoting hormone replacement therapy. The images depict women suffering from the symptoms of an estrogen deficiency disease and risking a life crippled by osteoporosis, heart disease and Alzheimer's unless treated with hormones. This representation creates the impression for obstetrician/gynaecologists that all women need hormones. There is no room to see menopause as a normal physiologic process that does not require treatment. As long as the diagnostic profile replays stereotypes generated in the culture, the doctor-patient relationship and women's health care will suffer.

160 Id at 160.

161 Whynne Caves, 'Women and Heart Disease: Same Disease, Different Issues' (1998) 9(2) *Can J Cardiovascular Nursing* 29.

162 Ruth SoRelle, 'Studying Populations and Heart Disease Risk' (1999) 99 *Circulation* 598.

4. *Conclusion*

Pharmaceutical advertising expenditure in Canada has been estimated at close to a billion dollars for 1995,[163] while the US drug advertising budget has been described as approximating the budget for the NIH.[164] Pharmaceutical product retail sales for 1999 totalled $111.3 billion, an amount two and a half times greater than the 1991 figure of $42.7 billion.[165] An expenditure of this magnitude is unimaginable without strong evidence of its effectiveness.[166] Research indicates prescribing practices are affected by exposure to advertising.[167] Controls on advertising, to the extent that they exist, fail to address the advertising content with which we are concerned.[168]

These types of stereotyping show us how existing paradigms of social worth can be used by the drug industry to create other perceptions of their products, with the intention of promoting sales. The pharmaceutical company anticipates the values that will be attributed by physicians, basing its expectations on social values and on the political culture of medicine. As the medical profession changes, with younger, more representative and media-wise practitioners, advertisers must find it harder to create resonance with stereotypical, paternalistic and heroic imagery. This may explain why we have begun to see a change to more representative forms of patient imagery, with multiple patients depicted in the advertisement or in the frame around it.

Doctors and patients need to be aware of the processes used by the advertisers to create these perceptions and to insulate themselves from them. These advertisements are profoundly undermining of a healthy and participatory relationship between patient and doctor, individualising responsibility for disease, reinforcing social stereotypes about women's roles, reifying drug intervention and creating diagnostic images of the particular patients for diseases. The under-

163 Joel Lexchin, 'Enforcement of Codes Governing Pharmaceutical Promotion: What Happens When Companies Breach Advertising Guidelines?' (1997) 156 *Can Med Assoc J* 351.

164 Martin F Shapiro, 'Regulating Pharmaceutical Advertising: What Will Work' (1997) 156 *Can Med Assoc J* 359; Jean G Desjardins, 'Editorial: The PMAC Code of Marketing Practices: Time for Improvement?' (1997) 156 *Can Med Assoc J* 363.

165 Above n133 at 21.

166 Jerry Avorn, Milton Chen, & Robert Hartley, 'Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians' (1982) 73 *Am J Med* 4; above n141; Sidney Wolfe, 'Letter: Drug Advertisements That Go Straight to the Hippocampus' (7 September 1996) 348 *Lancet* 632; Joel Lexchin, 'Doctors and Detailers: Therapeutic Education or Pharmaceutical Promotion?' (1989) 19 *Int'l J Health Services* 663.

167 One survey of physicians' attitudes to drug advertising showed that the group most favourable to advertising and most influenced by it were the younger, less experienced and urban doctors. The authors suggest that older doctors are more ad-resistant, but the more obvious explanation is that younger doctors are less discriminating about the information coming from sources with strong economic incentives to persuade, and that the younger doctors are more vulnerable: Susan M Petroshius, Philip A Titus & Kathryn J Hatch, 'Physician Attitudes Toward Pharmaceutical Drug Advertising' (1995) 35 *J of Advertising Research* 41.

168 The industry itself has adopted guidelines for content: above n163. The industry participates in the pre-clearance of ads conducted by the external Pharmaceutical Advertising Advisory Board, which has the industry organizations as board members. See www.paab.ca..

representation of particular patients in the advertisements and their social stereotyping should be vigorously resisted by viewers. By educating health professionals, legal academics and the public about the process of drug advertisement creation and by revealing the stereotypes used to power the advertisements, we intend to strip the advertisements of some of their power and to increase the power of patients and doctors to insulate themselves from the destructive messages as a way of achieving a participatory and well-informed dialogue. The myth-creating process for drug innovation should itself respond to the fundamental value of equality.

Drug companies construct knowledge of their products through the design and conduct of clinical trials and through their promotional activities. Through the past decade increasing attention was drawn to inequalities in representation and analysis in the clinical research process. Regulators and funding councils in Canada and the United States responded to varying degrees, by removing limitations on participation, by encouraging representation of women and, in some cases, by promoting sub-group analysis. The same inequalities have been demonstrated in the construction of drug advertising — stereotyping by gender, targeting for particular drugs and exclusion from others, and creation of health stereotypes of typical patients for diseases. Drug advertising further promotes views of the doctor-patient relationship that impede effective decision-making and subverts the roles of doctors and patients in the healing process. In each case the purpose is generation of industry profits. The power and legitimacy conferred by myths in the construction of drug knowledge needs to be challenged through an understanding of the myth-making processes in research and advertising.