EXPENSIVE DRUGS FOR RARE DISEASES:
An Anthropological Analysis of the Cultural, Political, and Economic Dimensions of Metabolic Disease

by

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Abstract

In the context of Canada’s publicly funded universal health care system, access to potentially life-saving and/or life lengthening orphan drugs costing anywhere from $100,000.00 to $850,000.00 per patient per year is a complicated matter. This study is an anthropological examination of the debates surrounding ‘expensive drugs for rare diseases’, a term that has come to represent the costly treatments developed for rare metabolic diseases like Mucopolysaccharidosis, Pompe Disease, Fabry Disease, and Phenylketonuria.

This study was conducted in British Columbia, Canada. It is based on several months of participant observation in hospital, industry, and patient advocacy contexts, as well as 14 semi-structured interviews conducted with the different stakeholders in the debate: patients and families, health care professionals, representatives of the provincial government’s Ministry of Health, pharmaceutical companies, and patient advocacy groups. This study looks at discussions of authority, responsibility, and rights to health care/health technology. It examines how complex systems of relationships shape these discussions in a particular time and place, and how the competing cultural models of publicly funded health care and profit-based pharmaceutical policy and industry operate in the context of extremely expensive drugs. The body of literature on orphan drugs in the social sciences/humanities is very underdeveloped, and there are no known comprehensive social scientific/ethnographic studies of the metaphors, constructs, and cultural context of debates surrounding orphan drugs/expensive drugs for rare diseases. This study attempts to fill some of these gaps by looking at the complexities of different stakeholder arguments and their structural and discursive context.

In attempting to reconcile and solve the problems of accessibility to EDRD, the different stakeholders directly implicated in the debate mobilize culturally shaped notions evidence, accountability, fairness, and responsibility. This study demonstrates that the problems, pitfalls, and provisional solutions articulated by the different people implicated in this debate throw in to relief the many contradictions between orphan drug policies, neglected diseases, drug regulation/assessment practices, and the relationship between pharmaceuticals and society. These frameworks and competing cultural models are creating tensions that may be irreconcilable with a publicly funded health care system.
Preface

The author conducted all of the research presented in this thesis. The UBC Children’s & Women’s Hospital Research Ethics Board approval number is H10-01512.
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This thesis is dedicated to my family, for teaching me what I know about relationships and responsibility.
Chapter 1: Introduction

This study concerns a set of pharmaceutical therapies, often called ‘orphan drugs’ that have been developed to treat what have come to be called rare diseases. Though not all of these drugs are very costly to develop and purchase, those that are form a category of drugs often called Expensive Drugs for Rare Diseases (EDRD). EDRD are costly and complex pharmaceutical treatments that treat diseases that are generally debilitating and terminal. These drugs are prohibitively expensive for most individuals or families to pay for out-of-pocket (between $100,000.00 - $850,000.00 per year), and obtaining extended health insurance for these types of conditions is difficult. The development and manufacturing of EDRD has been facilitated by the Orphan Drug Act of 1983, an American policy that provides incentives for pharmaceutical companies to pursue research and development on neglected disease treatments. This policy has led to the development of treatments for several debilitating and life-threatening rare metabolic conditions that were far too long ignored by pharmaceutical industry. However, one of the other end results of these policies is that publicly funded health care and drug plans such as the provincial systems in place in Canada are faced with the decision of whether to pay for these drugs or not. The importance of these drugs for patients and families vis-à-vis the potential cost of these therapies for health systems and society makes this issue ethically, politically, and emotionally charged.

This study focuses on the prescription of EDRD to children with rare inborn errors of metabolism like Mucopolysaccharidosis, Pompe Disease, Fabry Disease, and Gaucher Disease. These diseases are chronic, and the costs of EDRD are compounded over an individual’s lifetime, thus intensifying the issues at hand. If these drugs can lengthen children’s lives or improve quality of life, who should pay for the treatment? More importantly, who is willing to pay for the treatment? What roles do individual patients and their families, doctors, provincial
health insurance systems, federal regulatory bodies, and the pharmaceutical companies have in making these EDRD available to the children who need treatments for their life threatening diseases? In the Canadian context, the process of making these decisions over the past two decades has highlighted some of the contradictions between neglected diseases, drug regulation/assessment practices, and the relationship between pharmaceuticals and society.

The inborn errors of metabolism for which many of these expensive drugs have been created are the avenues through which much of the current knowledge of genetics, genomics, and epigenetics has been discovered (Childs 1999). If we look at the treatment history of these diseases as an indication of a possible future trajectory for other diseases where inborn chemical individualities may be a factor, as would be the case with personalized genetic medicine, high prices and accessibility issues may continue. For example, part of this study is an examination of sapropterin dihydrochloride, a new drug developed for PKU that is marketed under the name of Kuvan. Kuvan is a synthetic form of tetrahydrobiopterin that acts as a cofactor of phenylalanine hydroxylase, the enzyme that is deficient in PKU patients. The price of Kuvan is relatively low on the EDRD scale, at a price point per year of $24,000.00 for an infant to $180,000.00 for an adult dosage. However, given that PKU is one of the most common of the rare metabolic diseases, the cost to treat all responsive PKU patients will be very high in the aggregate. As will be explored in this study, the benefits of Kuvan are embraced by some and contested by others. Regardless of costs or disputes over whether the benefits offered by Kuvan are clinically significant or not, many PKU patients and patient advocacy groups naturally want access to this drug that has the potential to improve neurocognitive outcomes or quality of life—even if data proving that that will be the case has not yet been produced by the manufacturer. As more is learned about the genetic components of different conditions and how to target disease through different channels and pathways, it is likely that we will be seeing similar types of treatments and scenarios emerge in the future (Fleck 2010). Whether created for the rare metabolic genetic
diseases that are the central focus of this study, or expensive forms of treatment for cancer (Sinha 2008), pharmaceutical therapies set at extremely high prices but whose levels of benefit to a patient may be unpredictable or difficult to measure (Fischer and Cavazzana-Calvo 2008; Fleck 2010) create scenarios that demonstrate the complexity of the relationship between medical treatment and pharmaceutical policy.

Unlike many other wealthy industrialized countries, Canada has not formed a national rare disease strategy that sets standards of care for rare disease patients and addresses the unique challenges presented by rare diseases and the EDRD used to treat them. This stems in part from the Canadian constitutional division of federal and provincial responsibilities. Canadian provinces retain full control over their health care and prescription drug formularies, and each province makes different choices about how to fund these drugs in their budget. This has led to inconsistencies and inequalities of drug access between provinces. Decisions about whether or not to fund an individual rare disease patient are generally controversial, despite attempts to put evidence-based decision-making strategies in place. Consequently, the setting is ripe for political negotiations and a highly charged discussion of values and which types of diseases we are willing to treat and under what conditions we are willing to treat them.

Based on field research with participants involved in EDRD treatment in British Columbia, Canada, this study explores the perspectives of the multiple stakeholders in the discussions: patients, families, patient advocates, health care practitioners, pharmaceutical companies, and provincial government regulators. Combining semi-structured interview data with participant-observation in hospital, industry, and patient-based sites, this study is an ethnographic examination of the cultural dimensions of EDRD discourse.

In examining the ways that these new types of treatment and treatment options are forcing negotiations of values and responsibility in health care, I have looked at EDRD through the lens of three sub-questions:
• How do rare disease patients and patient advocacy groups frame their arguments for accessibility to EDRD? When confronted with these platforms, how are British Columbia’s provincial drug formulary managers justifying their cautious approach to funding EDRD?

• How are the EDRD pharmaceutical industry players balancing their dual role as creators of potentially lifesaving treatments and as market-based publicly traded entities?

• What pressures and expectations are put on health care professionals who treat patients with rare diseases, and as the interface between patient and health care system, how are they negotiating these pressures?

Through exploring these questions, we are given the opportunity to examine the interrelations among cultural values, policy, and power; to consider the competing cultural meanings of health care; and to see how people are managing political, financial, and social relationships in the context of emerging biomedical technologies.

**Chapter 2: Background**

**2.1 Rare disease policy frameworks**

To understand rare disease care and treatment in Canada requires an understanding of the ways in which EDRD is connected to pharmaceutical policies developed in other nations. This is because Canada’s lack of an orphan drug policy, small market for rare disease drugs, and proportionally small pharmaceutical industry leaves Canadian rare disease patients dependent on other affluent states to produce new pharmaceutical technologies. By extension, rare disease care in Canada is shaped by the policies and frameworks in place in other states to facilitate the creation of these drugs. The specific conditions examined in this study are genetic diseases of metabolism so rare that until relatively recently they were virtually neglected by the pharmaceutical industry due to the small patient population and by extension low profitability of pharmaceutical treatments. To offset the high unit cost of developing pharmaceutical therapies to
treat some of these conditions, many national governments like the United States and international consortiums like the European Union have established policies that offer incentives to persuade biotechnology companies to invest in creating pharmaceutical therapies for neglected diseases. The United States was the first to develop an orphan drug policy with the Orphan Drug Act of 1983, which offers a number of incentives and subsidies to pharmaceutical companies to develop rare/neglected disease products iv.

The vast majority of the drugs created in this model are set at extremely high price points. For example, Myozyme for Pompe’s Disease, manufactured by Genzyme, costs on average $500,000.00 per year per patient, with the cost depending on the size of the patient and the dosage required for effectiveness. Elaprase, an enzyme replacement therapy for Hunter Syndrome (Mucopolysaccharidosis (MPS) Type II) developed by Shire Human Genetic Therapies, costs around $300,000.00 per year for a small child. These are generally chronic lifelong treatments, meaning that the cost will need to be paid over the lifespan of the patient. These drugs are by no means cures for the disease they are treating, but they do reduce or eliminate some of the more debilitating symptoms. For example, Elaprase slows the accumulation of unmetabolized sugars in the joints and organs, which can lead to organ failure and brain damage, representing a potentially dramatic increase in the quality of life for these patients.

Enacted by the administration of American president Ronald Reagan, the Orphan Drug Act of 1983 was signed following a whirlwind of patient advocacy movements and media attention to unmet medical needs for rare genetic diseases and neglected tropical diseases. It is also part of a series of policies that came to be called ‘Reaganomics’: a monetarist economic policy model based on “a market-oriented political economy that freed the productive potential of individuals from the dead hand of government” (Morgan 2008: 101) by reducing corporate tax rates and regulatory bottlenecks. The Orphan Drug Act was originally intended to persuade large
pharmaceutical companies to devote part of their companies to rare disease care in promotion of the social good and solving political issues while still generating profit (Asbury 1985). What ended up occurring in many cases was that small biotechnology companies were developed whose only focus was rare diseases, and whose entire profit base depended on Orphan Drug provisions and high price points.

Early orphan drug research was conducted in the university setting and facilitated by funding from the National Institutes of Health (NIH) (Goozner 2005). The Bayh-Dole Act of 1980 is a United States legislation that permits entities like universities and non-profits intellectual property over research findings that result from federally funded research (Schact 2000). Universities are then free to sell their patents to corporations (Washington 2011), and this university-corporate exchange was the case with early key developments in orphan drug research (Goozner 2005). This legislation combined with the Orphan Drug Act helped the small biotechnology companies that would become large rare-disease pharmaceutical companies to gain full market control over the drugs that are now sold at the high price points being discussed here (Goozner 2005). The ethical viability of corporate control over research developed with government funding is one of the key issues in disputes over the cost of EDRD (for example McCabe et al 2005).

The high price points of the rare disease therapies developed following 1983’s Orphan Drug Act spurred the development of rare disease strategies in most developed countries over the past three decades. As of 2010, “2002 products have obtained orphan drug designation with 352 drugs obtaining FDA approval” (Wellman-Labadie and Zhou 2010: 216) and medical/pharmaceutical research on orphan diseases and orphan drugs is increasing. As the expiration dates of patents for many of the ‘blockbuster drugs’ created in the 1990s approach, larger pharmaceutical companies, or ‘big pharma’, like Eli Lilly and Pfizer, have started to show interest in rare disease products. Orphan drug designations and the ability to build solid business
plans around a market with chronic health needs helps to increase the attractiveness of the rare disease drug venture.\(^v\)

There is no federal rare disease drug policy or funding strategy in Canada. Now that these drugs have been developed as a result of the series of policies discussed above, Canadian rare disease patients are in the position of wanting access to treatment but live in a setting where there is no consistent strategy for ensuring sustainable access. In 2004, there was an attempt to create a Federal-Territorial-Provincial National Pharmaceutical Strategy, an action plan that would create a separate funding and reimbursement system for rare disease treatment. However, the federal government pulled out of key negotiations and the accord has been dormant for several years. This study explores the tensions that are generated by this lack of a structural framework in Canada and how this structural reality is situated in the global context of the development and marketing of EDRD.

2.2 Canadian Common Drug Review and the impact of evidence-based medicine

In Canada, the general regulatory framework of pharmaceutical therapies is an important factor controlling the debates surrounding reimbursement for EDRD. The Common Drug Review (CDR) is a service provided by the Canadian Agency for Drugs and Technology in Health (CADTH) a federally funded but independent non-profit agency that assesses new drugs and health technologies and provides “timely, evidence-based information” (www.cadth.ca, accessed 25 September 2011) to health care decision-makers, such as the managers of provincial drug formularies. The purpose of the CDR is to conduct pharmacoeconomic analyses of new drugs that have been approved by Health Canada. The pharmacoeconomic assessment measures, amongst other things, quality of life, cost per quality of life year, and the amount of evidence for effectiveness. Based on the results of the pharmacoeconomic analysis of a given drug, the CDR either recommends that provinces list the drug on their provincial formularies and subsidize or
reimburse patients who use the drug at a rate set by each province, or they declare that the drug is not cost-effective and do not recommend it for purchase.

While there are many expensive drugs for many types of diseases (including chemotherapies for cancer), all of the drugs that I am considering in this study were developed for rare metabolic diseases. Many of these drugs are listed on the formularies of other countries as these drugs were deemed safe and demonstrated some degree of effectiveness in clinical trials. However, with the exception of Myozyme for infantile-onset Pompe disease, the CDR has not recommended these drugs for purchase by the provinces and territories that look towards the CDR for these assessments. The CDR has consistently stated that while the drug may have very significant effects on individual patients, the costs of the drug are too high given the very limited ability of the manufacturers to provide evidence for effectiveness shown in statistically robust, double blind clinical trials of the drug.

As a result of the absence of a statistically significant sample of a large patient population, the available evidence for effectiveness of the EDRD is often deemed insufficient. Rare disease patient populations are very small, which leads to fundamental problems in developing treatments. The conventional epidemiological approach to designing trials and gathering data on the safety and effectiveness of drugs in the approval process is intended for treatments for which there are large numbers of patients, a sample of whom are recruited for clinical trials.

There are three phases that clinical trials must successfully pass through before the drug can be approved for purchase by the public: Phase I tests the drug’s safety and safe dosage levels in a small number of healthy volunteers (traditionally 20-80), Phase II tests the drug in a small number of individuals with the disease (traditionally 100-300) to determine if there is any effectiveness, and Phase III, tests the drug in a large sample (traditionally 1000-3000) of individuals with the disease to assess effectiveness at particular dosages. If a drug passes Phase
III, it is approved for marketing to the public and enters Phase IV, where post-market data is accumulated regarding a drug’s long-term effectiveness and safety (www.clinicaltrials.gov/ct2/info/understand). Rare disease patient populations simply do not have these numbers, especially for Phase III. Economic considerations are also a factor in study design, as a sizable trial sample could significantly reduce the size of the potential market population. Additionally, even if the sample size was larger, rare disease populations are very heterogeneous. The fact that many of these genetic metabolic conditions afflict individual patients via different chemical pathways and manifest in unique ways and in unpredictable patterns of progression is a significant methodological challenge.

Rare disease patient advocates argue that submitting rare disease drugs to the same pharmacoeconomic formula as more common drugs is unfair. At the federal level, the CDR is considering patient input in the evaluation of rare disease drugs, although the ways that these alternative ways of looking at effectiveness will be reflected in funding decisions is unclear at this point. Ultimately, it is the managers of the provincial drug formularies and not the CDR who are faced with the decision of whether to reject an application for EDRD treatment. Many provinces have elected to dismiss the CDR’s assessment of EDRD and reimburse EDRD for select patients whose doctors think they will benefit from the drug. The participants in this study working within provincial pharmaceutical regulation and insurance bodies acknowledge that it is not justifiable for rare disease drugs to go through the same pharmacoeconomic analysis as a drug for a disease like hypertension, because of the different sizes of patient populations and the levels and types of evidence they are able to achieve. However, provinces have a global budget for pharmaceuticals, and funding for these expensive drugs does not come out of a special budget. Reimbursing EDRD requires a reassessment of a province’s yearly drug budget and quite often taking other drugs for less debilitating but more common diseases out of the formulary to make up the costs.
Approaches to solving these problems differ among provinces. No matter what the route, this process is one that forces a re-evaluation of standard procedures because of the unique social and fiscal challenges presented by EDRD. Quebec elects to fund a drug any time it is prescribed. Ontario evaluates each drug in this category in an evaluation process separate from that of the CDR and then funds EDRD for patients who, based on their findings, have the best chance at optimal benefit from treatment. British Columbia has attempted to resolve the issues by setting up what is informally called the EDRD Committee. Similar to the strategy in Ontario, each time an expensive rare disease drug is prescribed, the case is evaluated by a multi-disciplinary team of experts including the patient’s doctor, other metabolic disease doctors, an ethicist, a health economist, and a pharmacist. The Committee understands the limits of the CDR’s drug evaluation formulas, and attempts to evaluate the drugs via a more ‘fair’ process, making important resource allocation decisions on a patient-by-patient basis. Nevertheless, all provinces face the problem described by the province of Ontario as described on their provincial ministry of health website, “One of the biggest challenges facing our public drug program is ensuring that Ontarians suffering from rare diseases can get access to the care they need” (Ontario Ministry of Health: 2011).

Chapter 3: Study design
Multiple interpretations of EDRD are generated simultaneously in hospitals, in advocacy groups, in industry, in society, and in government boardrooms. I have attempted to follow these expensive treatments across the different domains in which they operate to the extent that access would allow. A multi-sited approach (Marcus 1995) has helped illuminate the interconnectedness among the ways in which problems and personhood are framed across different domains and the wider structural realities that either subtly or blatantly shape the many interacting domains of medical care and social life.
3.1 Research sites and methods
My research focuses on the local context in British Columbia, and has involved participant-observation of clinical, industry, and patient advocacy activity, as well as interviews with patient families, health care professionals involved in the care of children prescribed EDRD, members of the provincial government boards that regulate and approve drugs for formularies, and representatives of the pharmaceutical companies that are developing these treatments. My primary research site was the Division of Biochemical Diseases (DBCD) at the British Columbia Children’s Hospital (BCCH), a major tertiary/quaternary care children’s hospital in Vancouver, Canada. BCCH is a tertiary/quaternary care facility that treats patients up to the age of 18. The DBCD is the only clinic in the province that specializes in the treatment of children with inherited metabolic diseases. Due to the nature of British Columbia’s diverse topography and demography, BCCH patients come from a range of geographical regions, cultural backgrounds, and socioeconomic positions. For many of the patients, an appointment at the BCCH means a day’s long car ride from the interior of the province through unstable mountainous weather, a ferry ride from one of the islands off the coast of the province, or a plane ride from a remote northern area.

I conducted participant-observation research within the DBCD at BCCH in the summer and fall of 2010, during which I observed how the doctors, nurses, dieticians, social workers, and administrative staff interpreted the diseases, the patients, and the controversial EDRD treatments. I observed and recorded the division’s approach to patient problems and EDRD access issues, and the ways in which the practitioners working within the division negotiated the diagnostic uncertainty and delicate psycho-social nature of metabolic disease treatment. I attended the majority of the division’s daily activities, including ward rounds, patient intake, psycho-social rounds, academic lectures, and educational sessions, for a period of six weeks. With the permission of the parents of the young patients and the practitioners treating them, I observed
several clinic appointments. I also reviewed the medical records of patients under the direction and supervision of the patients’ doctors. When appropriate, I was invited to attend meetings of different internal DBCD committees when they were discussing EDRD. These meetings included discussions of accessibility issues, meetings with pharmaceutical company representatives, and EDRD treatment plan design. Throughout my fieldwork, I paid particular attention to the Division’s involvement in a post-market Phase IV study gathering evidence of effectiveness for Kuvan, the new expensive drug developed to treat PKU patients.

I also observed the activities of the patient advocacy movement for access to EDRD. I conducted participant-observation at two patient advocacy events that were one day and three days in length respectively. These events served both as community-building and awareness sessions for patients and their families, but also served to inform the patient community regarding rare disease drugs or the processes attached to advocating for their accessibility. I was a participant-observer at a three-day conference hosted by a pharmaceutical company that manufactures rare disease products. My travel and accommodation expenses were paid for by the pharmaceutical companyvi. This conference was attended by business executives from the pharmaceutical company, doctors, scientists, and other health care workers, as well as a few patient advocates and patients. The papers presented at the conference were primarily medical and epidemiological studies. Many of the papers looked at how the researcher was attempting to add to the evidence-base of the company’s expensive products, such as setting up international patient registries or conducting small clinical studies.

In addition to participant-observation, I conducted 14 semi-structured interviews in the summer and fall of 2010. Interview participants were recruited through successive referrals and were conducted with a range of people with stakes in EDRD related discussions: regulators from the provincial Ministry of Health, health economists, ethicists, doctors, clinical fellows, nurses, dietitians, pharmaceutical company representatives, and parents of young rare disease patients.
Interviews varied in duration from 30 minutes to two hours. Thirteen of these interviews were recorded and transcribed; one interview was not recorded but extensive notes were taken. Data from the transcribed interviews was coded thematically. Coded data was joined with my discourse analysis of media and policy articles on EDRD and notes taken in the field. It is a combination of these sources that forms the data section of this study.

3.2 Theoretical framework
The study of EDRD offers an important perspective on many major questions about the social and cultural dimensions of health care, especially in a publicly funded health care system. Health care systems, events, and practices are often points of intersection between ideas about human bodies, constructions of meaning around human life, and economic realities. By looking at the questions raised by rare disease care, I am attempting not only to present a descriptive ethnography of an issue presenting itself in the Canadian healthcare system, but also to expose and unpack the wider understandings of relationships and cultural theories of morality and values, and how these are enacted in both daily life and medical encounters.

The literature on EDRD and orphan drugs is not well developed. There is a small selection of historical analyses (Asbury 1985; The Orphan Drug Oral History Project: Chemical Heritage Foundation), and a few short sociological and anthropological explorations (Boon and Moors 2008; Huyard 2009; Novas 2008), but there are no known comprehensive social scientific/ethnographic studies of the metaphors, constructs, and cultural context of debates surrounding orphan drugs/EDRD. This study attempts to fill some of these gaps by looking at the complexities of different stakeholder arguments and their structural and discursive context.

3.2.1 Responsibility: relationships and values
Access to EDRD in Canada raises important questions in the context of a well developed economic and health system that recognizes that responsibility for child health is both a private and a public good. Assuming responsibility for health and the health of children is a complex
issue, and varies by culture and nation. The anthropological study of kinship has long studied the dynamics between responsibilities, rights, and values in the everyday context of families. In families, relationships bind people together through what Meyer Fortes called “prescriptive altruism” (Fortes 1969): people do what they do in families because it is the moral thing to do. Fortes’ concept of “prescriptive altruism” and its binding (or unbinding) effect on relationships can be used to describe negotiations over health care system building and/or reform. For example, Strathern’s (2005) work on new reproductive technologies (NRTs) argues that the reluctance of the United Kingdom to accommodate infertility through NRTs is rooted in the way that these technologies upset previously well-worked out categories and relationships (i.e. the ‘cultural’ activity of embryo activity entering in to the ‘natural’ domain of childbirth). These types of narratives, which often have gendered, classed, and racial dimensions, then get socially reproduced through law and policy (Laslett and Brenner 1989; Picchio 1992; Luxton and Bezanson 2006; Bezanson and Carter 2006).

Consideration of the cultural values and categories surrounding EDRD cannot be removed from the wider sociological and cultural context in which decisions about them are made. As Csordas and Kleinman write, “therapeutic systems and the events they generate exist in historical and social context, as both products of that context and performances that construct it” (1996: 20). An example of this can be found in the analysis of the metaphors present in media coverage of the metaphors deployed in media coverage on orphan drug topics suggests that drugs are simultaneously portrayed as “gifts” and “important problems” and symbols of “equity”, “hope” and “market failure”. (Boon and Moors 2008: 1920). Many politically and socially important drugs have been developed under orphan drug designation, including the retroviral drug azidothymadine (AZT), the first major breakthrough in AIDS therapy in the late 1980’s. The cultural discourses of hope and progress that become attached to medical advancements are important driving factors of both cultural ideas of healing (del Vecchio-Good et al 1990) as well.
as capital investment and the generation of profit from drugs and technologies (Rose 2007; Rajan 2006).

Biomedical pharmacology products are also emblems of a wider financial system, connected to global scientific and financial networks/relationships and economic ideologies. For example, Rajan’s (2006) analysis of genetics research and colonial relationships highlights the interconnectedness between genetic research and global capitalist investment. The ability of biomedical innovation to conform to powerful value systems remains important in this process. One example is Novas’ (2008) analysis of the expensive rare disease drug Myozyme. Novas’ work explores how the story of a businessman whose two children had Pompe’s Disease and whose sheer will and capitalist prowess and connections led to the drug’s development corresponds to neoliberal ‘hero stories’ of determination and individualism, generating public support for a model of private pharmaceutical profit. Orphan drugs/EDRD are important examples of how the systems of meaning attached to pharmaceuticals become implicated in policy making and resource allocation decisions, reflected continually in the tenor of the different stakeholder arguments explored in this study.

Taking stock of these arguments, we can see the ways that discursive negotiations are shaped by whether emergent relationships are built into or denied space within the ethical theories that are scaffolded by cultural frameworks of values. However, we can also see that the boundaries of these frameworks are porous and permeable, subject to multiple and conflicting ideas of values. One ethical theory that has played a large role in structuring the Canadian health care system is utilitarianism (Postema 2006; Denier 2007; Flood and Choudhry 2002), the commitment to providing the greatest amount of good for the greatest amount of people. In this framework (which also includes justice theories and deontological principles), resource allocation decisions are made based on assessments of need (Shah and James 1994) and the belief in rational decision-making in a rational world (Jonsen 1986: 172). What are the limitations of
these ethical theories when the disease in question is rare? What principles are invoked in the debates when large portions of the resources are allocated to a small few? How do ‘claims’ of rights and arguments for the morally potent ‘rule of rescue’ (Jonsen 1986; Cookson et al 2007) come to complicate bureaucratically defined resource allocation processes (Mooney 1998)? In the context of British Columbia, it has been suggested that reform in complex chronic care needs to involve efforts towards public awareness about the systemic flaws in the system and solicit input from the wider society in what reform should look like (Miller et al 2004). At their core, these issues and debates point towards the recognition of the complexity of social, cultural, and political life renders the absolute adoption of one ethical theory, or even a set of different ethical theories in combination with one another, impossible. There will always be activity that cannot be structured or reconciled by a framework that attempts to crystallize a set of values developed in particular places and by people with particular positions and positionalities. While “the idea of society is a powerful image […] there is energy in its margins and unstructured areas” (Douglas 1970: 114).

3.2.2 Legitimacy and power relationships

One of the ways that contemporary forms of statehood have attempted to standardize the process of responsibility-taking and decision-making is through what Marilyn Strathern (2000) calls “audit culture”. Audit culture in Strathern’s definition describes process of attributing worth to something through the lens of a formula or a score relative to other things, ideas, or people. When health care is public rather than private it becomes subject to the ‘accounting systems’ used by government agencies to evaluate other politically acceptable and mandated services. In the context of publicly funded health care plans, governing bodies like the CDR and their employment of Evidence Based Medicine (EBM) as a resource allocation decision-making tool is an example of audit culture “characteristic of all state monitored public sector institutions
as public trust in authority declines and the perceived need for transparency and accountability arises” (Lambert 2006: 2640).

Appearing value-free and objective is an essential task of a state considered ‘legitimate’ in the Euroamerican context (Weber 1947). Weber reminds us that political power must not only be based on force: true legitimacy rests on the idea that, at least on the surface, the political authority is consistent with the moral views and needs of the general public. Strathern’s analysis suggests that objective routinization as expressed through accountability processes gives the appearance of an alignment of values, even if that congruity does not really exist. In real life contexts, values will never completely align, and it is in this space that political posturing and negotiations over power and meaning take place.

Though audit cultures are supposedly objective and routinized, rational categorization and classification cannot always adequately address those “grey zones” (Naylor 1995; Bowker and Star 2000) that are present in life and medicine. Rather, they seep into political and social life in the form of power dynamics between stakeholders and agents in different debates who exercise their relative power in ways that reveal discontinuities in cultural values between those operating from different perspectives on an issue. Resource allocation decisions are never purely bureaucratic and mechanistic operations. This is very much the case in EDRD access negotiations. Attempting to prove that one particular version of a debate is the more socially accepted one, as different EDRD stakeholders do, is a process analyzed by Bourdieu in his discussions of power and strategy. As he writes:

“The agent who “regularizes” his situation or puts himself in the right is simply beating the group at its own game; in abiding by the rules, falling into line with good form, he wins the group over to his side by ostentatiously honouring the values the group honours” (Bourdieu 1977: 22).

Gaining leverage in a political dispute depends upon the ability to play upon the values that hold currency in a given context. As will be explored throughout this study, different values are
mobilized by the different stakeholders in discussions surrounding EDRD, but each stakeholder does so in a way that attempts to appeal to sensibilities that will be supported by the wider society.

In the public arena, the politicization of a disease or condition by patients and advocates involves putting the onus of responsibility for treating a health problem on the state, but the process of building these policy relationships often involves a political negotiation over power and values. The responsibility that a government upholds in providing a service or treatment is embedded upon notions of citizenship, and what the citizen considers to be their right alongside what the government accepts that they owe to their citizens (Stevenson 2000). However, the history of the fight for civil rights for people with intellectual disabilities in the United States is instructive in looking at how the shift in value-laden public conceptions of intellectual disability over time showed how ideas of citizenship rights are not fixed and neutral. On the contrary, they are relational and dynamic, and granting rights to one group may be contested as infringing on the rights of a different group (Carey 2009: 28). In taking a deeper look at citizenship rights, we can see that both rights and citizenship are embedded in cultural values surrounding inclusion and exclusion: constructs that are made and remade in the context of relationships accepted in a given society (Lister 2007: 49). This means that what comes to be defined as a ‘right’ is something with historical and cultural roots that can be traced. One example is Petryna’s (2002) ethnography on the activism of “biological citizens” and the long and fraught value negotiations that eventually led to the Ukrainian state’s provision of biomedical care for Chernobyl-related disease. Another example is Rapp and Ginsburg’s (2001) study of disability rights and how the mobilization of kinship ties and affiliations in claiming rights their role in legal arenas has “problematized the presumption of American citizenship as the exclusive entitlement of a normative, able-bodied, nondependent, wage-earning individual” (552). Political-economy can become intertwined in the cultural creation of rights as well, as seen in Biehl and Eskerod’s
(200&) analysis of the process of universalizing AIDS therapy in Brazil. Biehl and Eskerod argue that this can be seen as an example of “pharmaceutical governance,” as the development of these AIDS treatment programs became, partly through the strategic work of health care access activists, one part of “the state’s attempt to position itself in the context of globalization” as modern and democratic and therefore worthy of foreign capital investment (2007:53). Similar types of processes are at play in Canada, and Canadian rare disease patients and patient advocacy groups are building social and/or financial capital-laden relationships (with industry, the media, and health care professionals) and becoming powerful agents in shaping both research directions and the EDRD policy-making process, both in Canada and elsewhere (Panofsky 2011; Ingelfinger and Drazen 2011).

Using these theoretical traditions and orientations as a guide for interpreting the data, this study looks at cultural notions of responsibility and values, and the ways that these become implicated in institutional, structural, and economic activity. Different stakeholders in the EDRD debate articulate their positions in deeply cultural ways, weighing their relative power and responsibility against the values that are current in a constantly negotiated ethical and moral field.

Chapter 4: Data

4.1 Patients and politics: EDRD access stories

Stories of rare disease patients struggling for access to potentially lifesaving treatments remind us that there is a very human side to what can easily become an abstract economic or policy debate. Stories about seeking access to EDRD exemplify how a vast amount of social values are negotiated as the interests of different stakeholders and different interpretations of EDRD and health care meet and clash. These access stories are more than accounts, they are part of a historical record on how important questions were approached at a particular point in time, and show the tensions between the competing cultural models of the different stakeholders.
This section is composed of two stories that concern attempts to convince the state to provide access to pharmaceuticals. These two case studies act as an introduction to the important issues generated by the current status of EDRD and rare disease care.

The first is about Kelsey, a mother of a young child with a progressive-degenerative rare lysosomal storage disease in British Columbia, who is being treated with an expensive enzyme replacement therapy funded by the provincial government. Her experience of advocating for her son’s treatment showcases many of the issues that have become important components of EDRD access debates: questions of fairness and the worth of one human life over another, questions of political negotiation and moral legitimacy, and a lens into the ways that health care policy can become inscribed within a family’s narrative and sense of belonging within a culture of health inflected by ideas of a “biological citizenship” (Petryna 2002). This case study is accompanied by an exploration of the metaphors and values mobilized by the Canadian Organization for Rare Disorders (CORD) at their patient workshop held in April 2010.

The second case study focuses on the experiences of Rosie, a young Phenylketonuria (PKU) patient whose story is used in PKU patient advocacy literature, as well as two other PKU patients in the DBCD unit at BCCH. What unites these three patients is their relationship to the post-market Phase IV study of Kuvan, a new expensive drug being marketed for the treatment of PKU. The intellectual disability caused by PKU is avoidable through severely restricting protein in the diet; a therapy with a high burden of care and the social and emotional difficulties involved in not being able to partake in eating most foods. While Kuvan has been shown in clinical trials to be effective in regulating levels of Phenylalanine in the blood for PKU patients, it is difficult to determine at this point whether that regulation will be clinically significant. Data on whether treatment will translate into being able to loosen diet restrictions and improve neurocognitive outcomes has not yet been produced by the manufacturer. Kuvan, and the advocacy movement that has become attached to guaranteeing its accessibility is a case study
that brings to the fore the other set of questions attached to rare disease care: questions of low levels of evidence, relationships between patients and industry, and the way that these two interact and entangle in political processes. This case study is accompanied by an analysis of the ways that health care professionals working in the metabolic disease clinic at the BCCH are approaching the political issues that have become part of their clinical practice.

4.1.1 Reimbursement case study: a young child’s access to EDRD and questions of ‘fairness’

The provincial government is currently funding Kelsey’s son Erik’s enzyme replacement therapy, which costs around $300,000.00 per year. Erik has a lysosomal storage disease that left untreated can cause intellectual disability and eventually death. Diagnosed at the age of two, it was eight long progressive-degenerative disease months between his diagnosis and the day the first therapeutic enzymes entered his body. At time of diagnosis, the drug had passed through a phase III clinical trial, but it had not yet been approved by the FDA. Once it was, the CDR promptly declared that the drug did not demonstrate enough benefit to recommend to provincial formularies given the cost. Kelsey was prepared, however, to fight for the treatment for her son. She spoke with the drug company to see if they would provide compassionate treatment (the answer was no), she asked the hospital to fund his treatment (something which Children’s Hospitals are able to do on a very limited basis), and she arranged a meeting with the manager of the provincial drug formulary at the time, who promised to look in to options.

As she tells me this story on a sunny autumn Saturday on a coffee shop patio, these negotiations seem so far away. I watch her child play with several other children who have gathered on this patio outside a suburban mall, and it is striking to think of how his young, energetic body has been the site of an intensely emotional discourse of value and resource allotment negotiation. As she recounts her meeting with the provincial government representative:
Kelsey: So we had this appointment, and he said, you know there’s no federal plan for drugs for rare disease drugs and we need to come up with a federal plan before we can treat just your son because it’s not fair that all the other kids in the rest of Canada, we need to come up with a federal policy first, and I said, well you haven’t had a federal policy ever, you’ve been working on one for 15 to 20 years and I’m not going to wait another 15 to 20 years for you to come up with a plan while my child… while I watch my child die, so I said, you know, if you don’t do this for him I’m going to the media, and he said well let me talk to my boss, who was the deputy health minister, and he called the next day and said it was approved!

Presenting the issue through the lens of fairness and equality is one of the ways that many patients and patient advocacy groups draw attention to the perceived inadequacies of federal and provincial rare disease policies. The importance of one child’s access to therapy for a debilitating disease in the moment is mobilized as taking precedence over potential plans for creating rational decision-making structures and policies in the future.

Comparisons between rare disease care and cancer treatment in particular is a common theme in rare disease family narratives and patient advocacy platforms. As Kelsey articulates:

Kelsey: So, because it’s a rare disease, you know we had to deal with a diagnosis, and then we had to deal with the fact that it’s rare, and we don’t know if anybody thinks Erik’s life is really worth saving, you know, other families who go to Children’s [referring to the British Columbia Children’s Hospital], and cancer is the best example, they don’t have to deal with that, but the cancer probably costs the hospital and government a lot more money than rare disease drugs do.

Pointing out how the total yearly expenditure on EDRD is a ‘drop in the bucket’ compared to a drug budget’s annual bill for cancer treatment helps Kelsey and many other rare disease patients/family members highlight their sentiments of how rare disease care suffers from a lack of prioritization. Whether the health care system thinks that a child’s “life is really worth saving” becomes the question to a parent of a child with a rare disease, not whether reimbursing EDRD is fiscally and politically responsible. As Kelsey remarks:

Kelsey: it’s not Erik’s fault or my fault that it’s expensive, and I don’t know enough about the ins and outs of it all but I guess for me, why should he be denied treatment? He wouldn’t have been if he had had cancer, they would have been doing everything they could! And I wouldn’t have had to call the government and have this whole 4 month long conversation.
This feeling of being at the bottom of a hierarchy, where other types of treatments are funded more readily than expensive rare disease treatment, shapes Kelsey’s perceptions and pro-EDRD arguments in resonant and evocative ways. From the perspective of rare disease patients and families, it becomes less about the levels of evidence and the expense of treatment, but more about the value of one type of childhood disease over another, thus creating a hierarchy of worth of between different types of persons according to which type of disease they are unfortunate enough to have.

Operating in the backdrop of access stories like Kelsey’s and Erik’s is a rare disease patient advocacy movement, which (often through alliances with the pharmaceutical industry) sets the foundation required to lobby governments for access to treatment. This movement looks at rare diseases and the expensive drugs created to treat them as part of a category: even though many of these diseases are very different, their rarity places them in similar market- and medical scenarios. Their shared status as rare makes them subject to the same injustices and subsequent need for advocacy, and the partnership between people based on having or having a child with a rare genetic mutation allows for the accumulation of strength and power in numbers (Huyard 2009). Thus, whether speaking about Myozyme for Pompe’s Disease or Fabrazyme for Fabry’s Disease or any of the other EDRDs, advocates for drugs in this category are dealing with same set of issues and concerns with market problems and processes of decision-making.

As we see with Kelsey’s narrative, issues of fairness and pointing out the inequalities in levels of funding/research between diseases are made central in arguments for accessibility to EDRD. The following statement from the European Committee of Experts on Rare Diseases illustrates how discussions of fairness are poised by patient advocacy platforms as an argument for a right:

“That’s not fair!” seems to be the universal battle cry of childhood. Where does it come from, the innate desire for justice and fairness that children possess? At what point do we relinquish our ideals and accept that, life, indeed, is not very fair? How many of us have
been guilty of informing a child, “That’s too bad. Life isn’t fair!”? The theme of this year’s International Rare Disease Day, initiated by Eurodis in 2008, asks that we reach inside ourselves and retrieve that lost idealism of childhood – with its imperative that life be fair, that equality should prevail, and we should all be awarded equal – if not identical – portions of life’s pie. Specifically, today, 28 February, stakeholders are asked to contemplate, and if possible to take some small measure toward correcting, the gaps in healthcare that exist - not only between countries but between illnesses.” (Orphanews Europe Newsletter, 28 February 2011).

In the opening comments to a workshop on how to prepare patient input submissions to the CDR, Durhane Wong-Rieger, president of CORD, presented a newspaper article that documented a new drug that can be taken to block the development of lung cancer if you test positive for genetic risk of the disease. A number of Fabry’s Disease patients were present at the workshop. There are expensive enzyme replacement therapies developed to treat Fabry’s Disease, but those diagnosed with the disease at an early stage must wait until they are symptomatic before British Columbia’s drug formulary will consider reimbursing the drug for a patient. Thus, this lung cancer drug, created and indicated to suppress genetic risk, was presented skeptically: if a therapy for completely a-symptomatic people with mere genetic risk were to be reimbursed, it could be seen as an example of prioritization of lung cancer over rare diseases that are expensive to treat. As Wong-Rieger asserted to the group, “rules hurt some groups and help others… the technology is there, but there’s a hierarchy of what’s important”. By way of articulating the perception that cancer treatment is unfairly socially, medically, and politically prioritized, patient advocacy platforms can effectively cross-cut political rationalizations for not attending to rare disease care.

4.1.2 Kuvan case study: complications in the narrative of rights to access EDRD

The political and patient advocacy discussions surrounding Kuvan, a new enzyme activation treatment for PKU, are complicated because there remains an absence of data. Clinical trials demonstrated that 20-56% of PKU patients respond to treatment, and the response to treatment can only be gauged via a therapeutic trial of the treatment (Biomarin 2010), meaning that coordination of the study sample was undoubtedly costly and difficult. However, we are not
speaking here of an absence of statistically significant data for the new expensive drug, which has been acknowledged as difficult if not impossible to collect for rare disease products. We are speaking instead of an absence of good quality, transparent and well-researched data on the 20-56% of the responsive PKU patient population that the pharmaceutical company has been able to study.

The patients currently enrolled in the Phase IV post-market study of Kuvan are thus caught in a discussion that unites patient advocacy groups’ attempts to secure the best future for those with the disease, the potential physiological and sociological benefits offered by a treatment, and wider political and social questions generated by a profit-based pharmaceutical industry. By way of introducing some of the PKU patients at the BCCH, this section attempts to disentangle some of these problems and examine the ways that they interrelate.

Rosie is a young girl with PKU in British Columbia, and this is her story as it is represented in the literature disseminated by CanPKU, the Canadian Phenylketonuria (PKU) patient and patient advocacy group:

Rosie has been on Kuvan™ now for 18 months and has had no negative side effects. She has classical PKU and wasn’t expected to be a good responder, but it has doubled her protein tolerance. However, her parents have refused to introduce higher protein foods until Kuvan™ is covered by BC MSP [British Columbia Medical Services Plan]. Nicole [Rosie’s mother] and CanPKU are actively advocating for low protein food coverage and coverage of Kuvan™.

The daily food intake of a PKU patient like Rosie, can be as restricted as a half-cup of rice and a drinkable substance composed of amino acids that replace regular dietary nutrients. Even with strict diet therapy, simple developmental processes like teething or typical incidents like biting ones tongue can cause a spike in Phenylalanine levels in the system.

Because of the high burden of care in PKU treatment, it is a disease where it is easy for children to ‘fall through the cracks’. The systemic gaps in a child’s life become amplified when that child has a disease that requires a constant and consistent restricted diet, especially in cases
where a child’s family is not equipped to deal with the problem and its implications. As an introduction to the complexity and variability of the lifeworlds of PKU patients, below are portions of my fieldnotes on two of the DBCD’s PKU patients:

Jenny is on the Kuvan trial, thin, and full of energy. Her mother is concerned about how much she is sweating recently, and wonders if it could be the Kuvan. Jenny’s mom has been told to report any strange side effects, and she tells the doctor in broken English (they moved to British Columbia from Taiwan just a few years ago) that she seems a bit young, 7 years old, to be sweating so much. The doctor and study coordinator are not sure, but writes the information down on the study sheet. It will be reported to Biomarin. Her mom says that Jenny is otherwise doing really well. Her levels are stable. They were recently able to increase her portion of rice for the day, and Jenny seems to really like being able to have a bit more rice at dinnertime.

Jenny’s story shows the optimistic side of treatment on Kuvan. Annie, on the other hand, is not on the Kuvan study, but her story shows the potential positive effect that Kuvan could have on patients in families with less ability to cope with the treatment regimen:

Annie’s story is presenting in DBCD’s psycho-social rounds. Annie’s parents are very busy, and the dietitian and the nurse attending the psycho-social rounds nod their heads when discussing how they have a clear sense that the parents find the diet to be an immense burden of care. Her Phenylalanine levels have stayed more or less within treatment range, but it is clear that Annie does not follow the diet perfectly. As the dietitian says, “she’s at risk, what can you do?.” Annie’s doctors has tried to get her parents to sign her on to the Kuvan trial, but they have refused because they don’t have the time. They would have to keep detailed records and monitor her Phe levels daily, in addition to having to come in to the clinic for an appointment more often. The social worker and the dietitian discuss trying to motivate the parents by telling them that Kuvan could help to loosen the diet, but they know that that’s not the right thing to do. Each case of PKU responds to Kuvan differently, and while Kuvan may end up doing that for some patients, there’s no evidence that Annie would be able to incorporate more foods into her diet without damaging her neuro-cognitive abilities.

Given the high burden of care and difficulties associated with the PKU diet, a drug that can help regulate Phenylalanine levels and improve neuro-cognitive outcomes could be beneficial for a disease where patients cut across all socioeconomic and family situations. However, Kuvan is very highly priced, and metabolic doctors who have seen these processes play out over the past decade are fairly certain that it will be difficult to have the drug listed on provincial drug formularies. The CDR did not recommend Kuvan for reimbursement in their January 2011
assessment of Kuvan (Common Drug Review 2011). It is currently being reassessed by the CDR based on some new data provided by the manufacturer.

Despite the potential possibilities offered by Kuvan, there are important questions of evidence that are symptomatic of issues from within the pharmaceutical industry itself. Kuvan’s major selling point is that it will have a positive effect on the quality of life of children with PKU. However, the extent to which it will is still to be determined. Biomarin’s Kuvan website (www.kuvan.com, Accessed 29 July 2011) is very careful to state a legal disclaimer that Kuvan is indicated to be used in conjunction with diet, and that the long term neuro-cognitive data of the drug has not yet been collected and assessed. Despite these disclaimers, many families still seem to associate Kuvan with a potential loosening of diet restrictions, and patient group input submitted to the CDR for use in their evaluation of cost-effectiveness focused very strongly on the potential of Kuvan to improve quality of life for PKU patients by liberalizing the PKU diet for responders (Common Drug Review 2011). Returning to Rosie’s story and the way it is portrayed, her response to Kuvan is evocative but it is not necessarily typical. For most children on Kuvan, if they are able to increase their diet intake at all it may be very minimal.

There is also ample skepticism among metabolic health care professionals regarding the fact that Kuvan is being aggressively marketed through both conventional advertising and patient advocacy groups despite the fact that Biomarin has not yet produced data that the drug would actually improve neuro-cognitive outcomes. We know that there are some ‘invisible’ benefits of Kuvan for PKU patients in that they stabilize Phenylalanine levels—but it is the doctors and other health care workers who then have to give patients more realistic assessments of how the drug will actually tangibly change their lives. Despite these factors, Kuvan is the subject of an intense patient advocacy platform, and CanPKU is already asking patients in their database to write letters to their provincial health ministers telling them how important it is for the provincial government to reimburse the expensive treatment for PKU patients. A portion of my
conversation with a health care professional who works closely with PKU patients is transcribed below:

Diana: Well, the parents are hearing about the drug and then are coming back to us, asking us about the drug and I have some issues with that.

MM: Because they’re not given accurate information or?

Diana: Well, people tend to hear what they want to hear, and if you have a good working relationship you can hear what the patient is saying and make it very clear. You know, this for most people is not a significant change in the diet, what it’s marketed for is to have more stable levels, so yeah it’s a tough call.

[…]

Diana: It’s a very difficult position to be saying, like I was driving in to work today and they were talking about alternative treatment for MS [Multiple Sclerosis] and if you’ve got $100 to spend, how are you going to spend it? And a lot of spending and health care dollars goes for you know things like cholesterol control and all that kind of stuff that you know, who… it’s not an easy decision and I can see it from the patients I work with, who have bouncy levels, if the Kuvan makes it better and these kids do have better neurocognitive outcomes, great, but the data isn’t there yet, you know? When they went about marketing this they should have looked at that, and then kind of five years in to it they’re just starting to collect neuro-cog data.

MM: Right, which would have been better to have…

Diana: Yes, which would have been better to have up front, before all of this was here. If it turns out that it does improve neurocognitive outcome, then there’s going to be no question that we should be funding it, but to just have another couple of slices of bread in your diet? If you get stable levels, if you get better outcome, no question but we’re just, we don’t have the data yet for that.

Bolstered by the ethical principles set out by the World Medical Association’s Declaration of Helsinki vii, patients who have been enrolled in a clinical trial for EDRD in Canada have historically launched strong cases to their provincial drug formulary for access to the treatment once the trial was completed. In other cases, rare disease pharmaceutical companies have paid for compassionate treatment for trial patients for a period of time following the completion of the trial. However, in most of these cases, the company stopped providing treatment once the drug was not listed on provincial formularies, putting pressure on the provincial formularies to make exceptions. For example, many PKU patients using Kuvan are currently part of the Kuvan
Access Program (KAP), a program run by Biomarin to provide treatment to patients while provincial funding decisions remain pending until Biomarin is able to produce more data. Biomarin is under no obligation to continue funding the treatment if provincial governments determine that they will not list the drug on their formulary. In these types of cases, the patient and their family then look towards their doctor to help them convince their provincial drug insurance plan for continued access to the drug.

4.1.3 Health care professionals and the field

At the center of the patient-accessibility nexus are the health care professionals who work in the metabolic field and experience these tensions firsthand. At the same time as being advocates for their patients, they are also often aware of the problematic networks of relationships that form the context of EDRD. The following comment by a health care professional raises an important issue clouding EDRD access debates:

Heather: From my sense of why it gets magnified with the rare diseases is because of what all the investigators say, that we’ll never have the data in the way you want it and so that’s it, and pharmaceutical companies say that all the time, they often don’t provide the data that they do have. I can't remember which drug they were looking at, but they’ve been sitting on the results of this trial for a couple of years, the trial is done but they haven’t released it even to the investigators that were involved! So you know something’s wrong (laughs) because they would be out there like that if it was good and that sort of thing. I see far less of a reluctance to fund something that works and that’s how it’s been, how the evidence has been accumulated versus the stuff that’s just really iffy.

Heather’s comments are indicative of an issue, not of inadequate governmental recognition of the evidence for effectiveness of EDRD, but of an issue of transparency and accountability with respect to industry, and the speculation that industry strategically deploys arguments about the low level of evidence achievable in rare disease research. As one metabolic disease doctor noted in our interview:

Bianca: It’s so important to distinguish between evidence of no effect and no evidence of effect… I think that because there is less evidence based medicine within rare diseases, I really think it’s a flaw in reasoning, because look, we’re making our life too easy by saying there’s no evidence or it’s too difficult to do that. We should try to generate evidence, and evidence starts with one case.
The DBCD at BCCH is particularly focused and devoted to filling in the gaps in evidence for rare disease treatments, as they see firsthand how low quality research affects the ability of rare disease patients to access treatments. This is one way that health care professionals are navigating the tensions created in the current EDRD framework.

Given that patient advocacy platforms on this topic are armed with evocative stories, have a sizable impact on health care policy in Canada, and are fairly silent as to the expense of the treatment, the articulations of a “right to access” Kuvan will raise complicated questions about the more intricate layers of the data quality and evidence-base of EDRD. Another health care professional brought up the delicate issue of industry financial support of both patient advocacy groups:

Natalie: Yeah, I think that it's going to be interesting, you know the drug companies and the kind of pressures that they exert on things. The relationships that families and drug companies end up having would be a very interesting thing to look at, because, these are desperate families, and they start to ally themselves with people who are going to come up with the answers, and the drug companies are very happy to embrace that. Whether that's good or bad, I don't know, I mean there's some really positive things that come out of that, I think there's probably some negatives as well, and it would be interesting to look at that alliance, because it for sure happens, every single parent group is allied with a drug company, you just look, cause they have the money to be able to support them for one thing, like medical conferences and that kind of stuff, well they do the same stuff with families, potential families, and it's quite competitive now so they're actually starting to offer extras, like come with us and we'll pay for you to have your infusion at home or come with us and we'll do stuff for you.

The interaction between patient advocacy groups and industry stakeholders also raises several questions about the hopes that a patient group invests in a treatment versus the reality of the treatment’s potential to benefit a patient. Kuvan is an example of how these issues operate in clinical practice and social life, but they are much the same across most diseases treatable with EDRD. One metabolic disease doctor I spoke with who is very critical of many of the rare disease pharmaceutical companies laments the high industry involvement in the rare disease patient advocacy movement. She now refuses to attend conferences put on by pharmaceutical
companies—they provide funding for patients and advocates to attend, and she feels that her presence, and the presence of other doctors validates the drugs and the problems that have become attached to them.

4.1.3.1 Section summary

By way of presenting two case studies and some of the issues attached to them, this section has explored the simultaneously poignant and problematic features of patient advocacy and patient access stories for EDRD. So far we have seen that patients and patient advocates force a renegotiation of the inconsistencies in health care policy and a re-examination of the values upon which decision-making processes are based. On the one hand, Kelsey and Erik’s case study demonstrates that bureaucratic decision-making is not always mechanical, and that the grey zones in health care access negotiations can and perhaps should be acknowledged, even when a federal policy structure on rare disease care is lacking. On the other hand, the patient and clinician experiences in the Kuvan case study show how discussions of evidence in medicine stretch beyond the scientific and in to profoundly social, cultural and political terrain. While it can be (and is) successfully argued that using traditional cost-effectiveness models to assess rare disease drugs is unfair, a closer look at the EDRD industry and arguments about evidence show that there are other dynamics in the rare disease/orphan drug pharmaceutical industry that complicate the issue. This does not mean that the drug is ineffective and does not have the potential to save lives—in many cases they do, and that is why provincial drug insurance decision makers are attempting to devise solutions to these problems. However, what it does mean is that larger social and political issues about transparency and interest-laden relationships are becoming a central part of rare disease care. As the front-line mediators between EDRD stakeholders, health care professionals are pioneering the reconciliation of important social, ethical, and political questions in the clinical context.
4.2 Balance of powers: provincial drug insurance systems and industry

The subject of the high price point of EDRD is rarely touched upon by patient advocacy groups. Instead, it is the provincial drug insurance plan managers who attempt to problematize the cost while the rare disease pharmaceutical industry frames answers to these questions in carefully crafted declarations of responsibility and values. Drawing on interviews with representatives of the provincial drug insurance plan and evaluation apparatus in British Columbia as well as promotional literature generated by rare disease pharmaceutical companies and interviews and participant-observation with industry representatives, this section looks at how relationships that are often flattened in EDRD discourse are in fact multi-dimensional and connected to wider social and systemic issues. While both of these sets of stakeholders are saying different things, they are both partaking in the same discursive activity: attempting to define the relationship between emerging biomedical technologies and society.

4.2.1 Provincial drug insurance formularies

Given the type and tenor of the EDRD access debates, how are the provincial drug insurance regulators interpreting the situation? Interviews with members of the EDRD Committee as well as representatives of the British Columbia Ministry of Health revealed that working within these systemic relationships involves an uncomfortable balancing between two competing narratives: that of providing universal health care coverage and providing drugs developed in a system designed for the maximization of profit.

Chief among the effects of the absence of a comprehensive orphan drug policy in Canada is the pressure that is placed on provincial drug insurance systems to deal with problems of the political economy of drug development that are beyond their mandate. Drug development is in many ways a negotiation between government regulators and industry, and drugs developed under the American Orphan Drug Act are placed in this negotiation with the FDA, the American regulatory agency. The American health care system ethos is based upon a privatized model,
which is very different from the publicly funded model in place in Canada. Consequently, the questions that require answers in the Canadian system, mainly regarding the high price point of these drugs, remain open. The Canadian federal government’s virtual silence on these negotiations has placed all responsibility for dealing with these issues squarely on the shoulders of those who manage provincial health care formularies. It is this structural context that sets the stage for so many of the problems described in the two case studies above. Representatives of the EDRD committee and of the provincial insurance program appreciate the complexity of the moral and social issues they face.

Drew has a background in health care and now plays a role in the provincial government’s decision-making apparatus. Below are his thoughts on what he calls ‘the nature of the beast’:

Drew: I think part of it is just because of the underserviced population, it just kind of swings the balance of those social, ethical, moral obligations of providing some treatment to somebody who otherwise has no options, and trying to figure out OK well if we’re going to swing that balance, can we maybe put a monetary value on what the length of that swing is, right. And people have often said, well, should we? Be putting a monetary value on that? And people get really kind of antsy sometimes about trying to monetize health care, and think about almost to the point of well, this is all they have, it doesn’t matter what it costs, and then trying to convince them well, unfortunately it does, it does, unfortunately it does, because it’s a finite pot of money, right, and trying to make people understand the opportunity cost, realizing there’s no budget for the treatment of rare diseases in the province.

His comment represents the struggle that provincial drug insurance plans face: claims for a right to health care by people who become embroiled in political and philosophical disputes by virtue of the fact that their disease is rare and the treatment implicated in systemic market problems.

These tensions have resulted in a system where at the provincial drug insurance level in British Columbia resource allocation decisions are made on the back of an individual on a case-by-case basis. The health care professionals who work in the metabolic disease field in British Columbia and who sit on the EDRD Committee are enlisted to design starting and stopping guidelines, setting increasingly strict criteria about when an individual’s particular manifestation
of disease suggests that there may be benefit, and how much benefit needs to be seen in order to continue receiving the therapy. For example, if a child will have brain damage or be on a ventilator despite treatment, then they will be less likely to be approved for EDRD access than someone who will have less severe symptoms of disease progression. If a child has been previously approved for treatment but then starts showing a decline in these areas, they will likely be taken off treatment. Evaluating benefit then becomes political and social as well as medical. These are profoundly important ethical issues, and as Fleck writes, “If there were a thick, bright line separating minimal and maximal responders, we could allocate treatments fairly. But the reality is a ragged edge, and ragged edges mean rough justice” (Fleck 2010: 17).

On this topic, Drew states:

Drew: A lot of these drugs won’t improve survivability, they won’t make an impact on mortality per say, but they might be life extending, depending on what stage you are in your disease process they might improve quality of life for a certain period of time and then what do you mean by quality of life how do you measure that, you know so it gets, really it can get quite intricate.

These deliberations illuminate the social and contextual nature of ‘benefit’. As Heather, one of the health care professionals introduced earlier ponders:

Heather: so you know from a philosophical point of view sometimes it really begs questions around what counts as evidence? Because within traditional scientific milieus you know we’ve got what’s called a hierarchy of evidence, OK, and that’s a social construction, you know it’s a social construction of how we look at data, and you can take a look at that and say, you’ve made value based decisions along here, here, here— it’s not just pure ‘this is a better means of doing this and that’. But when you come with rare diseases you are really faced with a very, very difficult problem of when there is no evidence or the evidence is so small and the drug is so very expensive and you’re just not knowing what benefit it’s going to produce, how do you monitor benefit? And how do you evaluate benefit? We’ve got all these different kinds of scientific scales or medical scales at times and if you showed your scales to the normal lay person I don’t think they would support this. You know, for example a two minute walking test, so you improved twenty seconds on a two minute walking test, or something of that nature, how many times you blink your eye, so you can say you’ve achieved vast improvement from a strictly medical point of view depending on your criteria but I step back or I try to step back and I say well from a social point of view, would that be considered to be relevant criteria?
The methodological difficulties inherent in the evaluation of drug benefit are already complex questions in pharmacology, but when the treatments are so expensive they become politically charged as well.

While critical of the access restrictions and the starting and stopping guidelines, patient advocacy organizations in Canada for the most part have been have relatively silent about the effect these high price points have on EDRD accessibility. One patient advocate explained that the reluctance to contest the pricing issue in Canada is partly due to a fear that pharmaceutical companies will elect to just forego the market in Canada (which amounts to a relatively small amount of patients), rather than deal with negotiating lower price points with the Canadian government that would set a precedent elsewhere. “It is a non-starter for us”, this particular patient advocate made clear. In this dynamic, the main target of patient advocacy platforms remains government policy and policy makers.

Provincial drug insurance programs are sometimes demonized in rare disease drug accessibility discourse, as though they are composed of bureaucrats who disregard rare disease patients with an ideological sleight of hand. Speaking with the provincial drug insurance program stakeholders revealed a different reality, one which fully recognizes the plight of rare disease patients but at the same time touches upon a rarely approached or problematized layer of the EDRD debate: the high price point. As one interviewee, Jonathan, stated:

Jonathan: The way I'm seeing it, at least from the government payer side, especially if we are being asked to fund it, is when we're faced with this big ticket, and we're the payer, we're seen as the bad guys, when I think it actually should start from the manufacturers who sets those prices right, why do they need to charge that much? Well they go in to the argument that because it's rare and we invest all these dollars in to it, we have a right to charge this much to recover our research costs right, and so I go, OK, well I see some of that but at what point is the profitability justified?

Provincial insurance representatives see pharmaceutical companies as sometimes pursuing economic advantage in a new ‘untapped’ market pipeline. As patents for ‘blockbuster’ drugs run
out, Orphan Drug designations become increasingly appealing, meaning that EDRD will continue to be created. As Jonathan expressed in our interview:

Jonathan: Yeah so in the end we are accountable to how every dollar whether it's small or big, it has to be justified right, but I think the other thing we're finding is that a lot of the new drugs that are saying that they are for rare diseases, they're in fact not so rare anymore, so we're seeing it as a potential growth area, and I think some companies are taking advantage of the fact that governments historically have just said, yeah sure, sure, because they're usually making decisions on one case saying yeah it's rare it won't happen again but then what we're seeing is there's more and more and more of these right, so it will be a growth area. Is it small overall? Yes but it is disproportionate when you look at how much you're actually funding on a per patient basis.

Accountability here becomes a safeguard against pressures to blindly accept high price points for drugs set by an industry that is unapologetic about the prices that they charge.

Taking a cautious approach to rare disease drugs in many ways becomes an act of resistance. In Drew’s comments that follow, we see the way that two important aspects of state legitimacy—accountability and evidence—are used as tools in leveraging their position as the one who ultimately pays the ticket to resist unregulated rare disease product pricing and the lack of transparency that sometimes accompanies it. Provided below is his explanation of why it is important to assess what society is ‘willing to pay’ for rare disease drugs:

Drew: Sitting at the decision making table, you know, there’s questions around, say we’re paying $100,000 a year for a patient or we’re paying $875,000 a year for a patient, does society, does the general public think we should be paying that and if they do, let’s just say it’s a million, what if it was two million, what if it was four million? We don’t know what the answer to that is, I’m not sure that $875,000 isn’t above what we should be paying, but we really have no idea. […] This is all anecdotal right, so we need some more empiric evidence to at least give us a frame to get an idea of what frame we should be working in right, because right now without that evidence, when we come back to the cost of the drugs there is no evidentiary base to force the manufacturers to look at the appropriate price point, right now if there’s no evidence and we are continuing to fund these drugs at a million dollars a year then that looks like that is society’s willingness to pay… I would suspect if we had a fatal disease and a lifesaving treatment that people would be willing to pay a million dollars for that, but I don’t have any evidence for that, that’s only my expectation right. So the development of some of this evidence may influence what the cost of some of these products might be, I don’t know that’s just, because again, I don’t know it might cost them $10,000 to make that $875,000 a year drug, again I have absolutely no idea.
Yet another complicating factor of EDRD is that companies with products that have orphan drug designations receive tax breaks and patent protection in the US, amongst other incentives, and these incentives represent less money in the public purse and more in private pockets. It is true that subsidies to the private sector result in a treatment option for rare disease patients, but what does that treatment mean in a wider sense if patients aren’t able to access the drug in a sustainable way? What if the current system enables pharmaceutical companies to produce highly priced drugs with low benefit, or creates a lack of incentive for innovation? What if publicly funded health care systems cannot sustain these high price points in the long term? These questions are not unique to Canada. Norway (Desser et al 2010), the United Kingdom (NICE 2004), and multidisciplinary research roundtables (Drummond et al 2007) are also looking towards assessing how willing citizens are to pay for these drugs. As Christopher McCabe et al. (2005: 1017) write of the United Kingdom context:

“The justification for special status for orphan drugs is often couched in terms of the costs of developing a drug for a rare disease relative to the small market and consequently the high costs of treatment for each patient. The real costs faced by the pharmaceutical industry are open to argument, but the fundamental question is whether society should subsidise the private sector to invent in the development of technologies when the cost to society exceeds the value it places on the health gain produced. If the answer is no, then the costs of production cannot justify any special treatment.”

Through looking at these types of arguments, we can see that these negotiations are fundamentally about rearticulating the relationship between public and private interests.

4.2.2 Industry

At the opening reception of the conference put on by a rare disease product pharmaceutical company that I attended, I exchanged business cards with one of the company’s business managers. When he glanced down at my card, where “Expensive Drugs for Rare Diseases” was clearly printed in blue ink, he looked up at me and laughed. “You mean effective drugs for rare diseases, right?” he said, playful but serious. One of my first research events, this was my introduction to the touchy subject of the price point of these pharmaceutical therapies. As a
statement, it brought together two of the overarching challenges of EDRD and attempted to resolve them: their high cost and the disputed levels of evidence for their effectiveness. If effective at saving lives of people with rare diseases, the statement suggests, the price should not be a matter for concern: the pharmaceutical company has met their responsibility to develop and manufacture a sorely-needed treatment and the rest is up to society. My research on the rare disease pharmaceutical industry and the discourse that surrounds it reveals that carefully crafted discussions around ideas of ‘responsibility’ and a patient-centered value system are central to the process of rationalizing the high price point of EDRD.

Pharmaceutical companies that manufacture EDRD maintain that it is the high cost of bringing new drug products to market and the small patient populations they serve that cause the costs of EDRD to be so high, and understandably, they need to recover their research costs. Many maintain that the public money they receive or the academic knowledge that they capitalize upon is not sufficient to lower the costs (for example Tambuyzer 2010). As one representative from a pharmaceutical company that specializes in rare disease drugs explained in our interview:

MM: How do you deal with situations when people ask you why the drug is so expensive in the first place?

Naila: I think you need to explain to them the economics of these drugs, and because it is much different than the economics of other commonly prescribed pharmaceuticals, you just don’t have a large patient base on which to recuperate your developmental costs, your research costs, your manufacturing costs, so prices are reflective of what it costs to discover these drugs, test these drugs, manufacture these drugs, and the costs have to be recuperated. Otherwise there’s no incentive for companies to produce them, so you recuperate the costs by pricing them accordingly, and I mean, I think people most of the time they understand now because there are a number of drugs out there that are considered orphan drugs, and people are beginning to understand the economics of it.

In this framework, high price points are portrayed as a necessary evil of sorts. The need for a financial incentive for rare disease drug creation is an important theme that arose in my interview with Kelsey:
Kelsey: Well my understanding is I mean it costs a lot of money to put these drugs through trial and getting them approved and all of the research involved and because there’s not a lot of patients you’ve got to charge a lot, the company wouldn’t do the research if they’re not going to get money on the other end.

The profit-based bottom line of the pharmaceutical industry is seen as sufficient rationale for high prices, especially given that new rare disease drugs will depend on revenue from other drugs.

Many rare disease pharmaceutical companies invest substantial resources and finances in what is commonly referred to by industry as the ‘community’. For example, one of Genzyme’s promotional pieces, a short booklet illustrated with pictures of rare disease patients from around the world includes the following statement:

Another important means of contributing to the community is through the long-term partnerships Genzyme forms to advance research and quality of care. We regularly make available research, support patient registries to better understand disease progression and patient outcomes, and sponsor academic research into major areas of study such as kidney disease, cancer and cardiovascular disease. We also provide support services for patients with rare genetic diseases and partner with other organizations (patient advocates, medical centers and healthcare authorities) to provide a range of other services, from genetic counseling to home treatment.

Following on that:

Everything we do at Genzyme is guided by our responsibility to patients and our desire to make a major positive impact on human life worldwide. This is who we are, as a company and as individuals.

Highlighting the positive impact of these drugs is invoked in attempts to reconcile the obvious accessibility issues stemming from such a high price point. Most EDRD pharmaceutical companies also stipulate that they provide ‘compassionate treatment’ to those who cannot pay for it or get access through an insurance plan or a publicly funded health care system. For example, under the heading “Our Commitment to Corporate Social Responsibility”:

At Genzyme, we believe our first responsibility is to develop safe and innovative products, and to ensure that as many patients as possible have timely access to them, regardless of location or ability to pay.
Under what conditions and to which patients do rare disease pharmaceutical companies provide compassionate treatment? Not all requests made to pharmaceutical companies for compassionate treatment are granted, and Kelsey’s request to the pharmaceutical company that manufactures the therapy for Erik’s particular disease was rejected. As Kelsey reflects on this event:

Kelsey: “I mean, they didn’t give him treatment, compassionate treatment, however when I talked to the head guy in Canada, it’s not, they shouldn’t be paying for it, it’s not their responsibility and you know I agree with them.”

While rare disease pharmaceutical companies take a difficult and medically and socially valuable path in negotiating the scientific and regulatory complications involved in meeting unmet medical needs, a pharmaceutical company’s first responsibility is to their shareholders. While at least in Genzyme’s case, patients follow closely behind stock market value as a top priority, the high prices points are presented as an unchangeable given.

Articulating values and contributing to a community are part of a wider business culture of creating a corporate ‘culture’ that emphasizes corporate social responsibility. Practicing corporate social responsibility can be both a competitive advantage (Esteban 2008) and a way to resolve ambiguities about the interface between public and private interests (Smith 2008). This is especially salient in cases where drugs developed in a profit-based model are marketed in a socialized health care system. The encounter of these two different narratives results in an unsteady framework where tensions are generated, resulting in the emotionally charged and loaded arguments that we see with EDRD. It is my impression that representatives of pharmaceutical companies are well aware of and extremely sensitive to the ambiguities generated in this context, but as is so often the case when dealing with multilayered and entrenched social problems, see few ways around it. As the conversation between Naila and I reflects:
Naila: Whether or not it’s ethically appropriate to do this is up for argument.

MM: You mean pricing them like that?

Naila: I mean, I think it originated in the US where companies do have deeper pockets, the government did create this orphan drug policy where they said OK, we do want companies to make these drugs, we know that they can make these drugs, we want them to do it so we’re going to incent them to do it, we’re going to give them attractive incentives to do it, thus began the orphan drug movement, then it spread around the world, and well, you can’t just sell these orphan drugs and let orphan drugs go to the rich country, so I mean patients in poor countries, what the companies then have to do in order to have a clear conscience and sleep at night is to say OK, well then we’re going to have these compassionate programs available, our company president has said no patient should go without this drug, regardless of their financial ability to pay or the government’s willingness or ability to pay

MM: Right so then they will provide the drug for them?

Naila: Yeah, yeah, so that’s what happens but when people do complain in Canada about how you know these drugs you know we didn’t really come up with this in Canada it was sort of an offshoot of the states and a lot of these companies are based in the states.

Publicly funded health care plans struggle in a profit-oriented health technology and pharmaceutical industry. We see here how in a global market, narratives run up against each other and result in social and political questions of accessibility that are symptomatic of the tensions generated by this uneasy framework.

In September of 2010, Antonio Tajani, the Vice President of the European Union’s commission responsible for industry and entrepreneurship released the following statement:

“I attach great importance to corporate social responsibility. In the field of pharmaceuticals it is all the more important for the activities to be in line with the general interest. However, these companies have to operate in a commercial market. I think that it is time to launch a specific consultation at European level in this sector so that commercial imperatives can be combined with the needs of society.” (Tajani 2010; emphasis mine)

In December of 2010, the National Institute of Health (NIH) in the United States voted in favour of a National Center for Advancing Translational Sciences, dedicated to the advancement of translational medicine and therapeutics. The Center would facilitate the development and collaboration of a network between the pharmaceutical industry, biotechnology research, and academia. As Garrett Fitzgerald, director of the new center, writes: “paradoxically, as we have
witnessed a successful revolution in drug discovery, a crisis has emerged in drug development” (Fitzgerald 2010: 869). Thus, the “NIH funded researchers can explore the earlier stages in the drug-development pipeline to ‘de-risk’ projects that would otherwise lie untouched” (Francis Collins quoted in Wadman 2010: 877). How much imperatives like this one are actually working towards a solution to the root problems of the primacy of profit over the development of accessible health technology requires further research.

**Chapter 5: Discussion**

In one of the only historical accounts of the Orphan Drug Act, Caroline Asbury (1985) details the dilemma of an orphan drug for Parkinsonism that had been set at what Asbury called in 1985 the “astronomically high price” (1985: 198) of $300 per month per patient. On this matter, Asbury posed the following question: “should orphan drugs be developed regardless of cost? If not, who will decide where to draw the line? In either case, who will pay?” (Asbury 1985: 198).

In an era where a drug can cost upwards of $35,000 per month, Asbury’s question is even more relevant today. While this study has not had the time or the space to dwell on the macro-economic context of the expensive rare disease drugs created under Orphan Drug designation, it is impossible to deny that due to the larger systemic context in which these drugs are created, rare disease patients and rare disease care are in a difficult position. In the Canadian context, this position plays out on the ground through relationships: between health care system and patient, between patient and health care professional, and fundamentally and perhaps most importantly, between pharmaceuticals and society.

Different stakeholder groups in any type of debate often work hard to portray their perspective on the debate as the most pivotal, but this can often cause a clouding of the bigger picture. The goal of this study has not been to solve the problem, but to take a critical look at the conversation among stakeholders. What has emerged is that by looking at the debate from a position of understanding and empathy about the constraints that people are facing, we can see
that the problem does not reside necessarily within any one of the stakeholder groups, but within the tension-generating framework that they are working within.

5.1 **Health care systems and patients: negotiating value-laden frameworks**

Through case studies like Kelsey and Erik’s, this study has explored how rare disease patients and patient advocates demand fairness in levels of access to pharmaceutical therapies between diseases. In my research, claims for access to EDRD by groups of middle- to upper-class rare disease patients and patient advocates were often powerfully articulated by invoking ideas about fairness and the responsibility of the state to support the worth of human life. They speak out in a context where it is possible to ‘speak truth to power’ in some ways, and challenge the decision-making strategies of institutional bodies, casting doubt on bureaucratized processes of resource allocation by rearticulating them as matters of social justice. Fairness here is not articulated as fairness between diseases in the number of dollars allocated to them, but fairness between diseases in the levels of access to treatment, making it possible to claim a right to treatment and enhanced quality of life regardless of cost.

These claims to fairness in rare disease care run up against some of the ethical theories upon which the Canadian health care system is built, notably utilitarianism and the attempt to provide the greatest amount of good for the greatest amount of people. The notions of audit and accountability that underlay the CDR explored in this study are designed to maintain and bolster that ethical framework. Claims for access to EDRD, however, are cases where the amount of beneficiaries is small and the cost large. The value systems that institutional decision-making frameworks are based upon expose cracks and inconsistencies when they are critically questioned by non-normative communities.

Rare disease patient advocacy and EDRD access claims create new conceptualizations of disease, expose the hierarchies between types of diseases and disease treatments (i.e. between levels of access between cancer and rare genetic disease), and force negotiations of the meaning
of health care in Canada. As Marilyn Strathern contends, it is these types of accessibility negotiations that “throw certain forms of sociality into relief” (Strathern 2005: viii). Rare disease patient advocacy and negotiations of access to EDRD are attempting to replace outmoded ways of approaching citizenship issues, which are at their core issues of values. In the patient advocacy context, EDRD accessibility is cast within a larger debate where it is possible to create a relatively stable idea of right and wrong: values of the equality of worth of all human lives.

Straightforward as these claims for equality and fairness seem, it is the wider sets of relationships that are less clear-cut, and the political and financial context of EDRD clouds the ability of these arguments to move forward. EDRD accessibility claims are complicated by deeper issues that stretch beyond the policy context in Canada, connecting the local with the global through legislation generated in the United States that has had repercussions worldwide. Ideas of fairness are articulated by patient and family stakeholders, but the substance of that idea of fairness is not embedded in to the policy frameworks that facilitate EDRD, as we see with the Orphan Drug Act. This leads to dead-ends in negotiations and will continue to do so unless the legislative framework around orphan drugs shifts gears from a corporate profit-orientation to a drug-accessibility orientation.

5.2 Patient and health care professional: social questions implicated in medical care

The unique and unsteady position of EDRD within medicine and health care systems generate many ethical ambiguities. Each of the health care professionals working in the field of rare disease care who participated in this study, and especially those who sit on the EDRD Committee, acutely experience the tensions generated by these ambiguities.

In some ways, the pharmacists, physicians, and ethicists who sit on the EDRD Committee are similar to the women that Rayna Rapp called “moral pioneers”: the pregnant women who were first offered the use of new technologies like amniocentesis and prenatal genetic screening and confronted with what to do with the results (Rapp 1998: 68). In designing
stopping and starting guidelines for EDRD treatment, those on the EDRD Committee are asked to make decisions about who is worthy of treatment and who is not, much like the pregnant women Rapp studied were faced with the decision of whether their unborn child was worthy of life or not. When making a resource allocation decision on a case-by-case basis, making assumptions about what constitutes benefit and what quality of life means are part of the discursive process. New biomedical technologies, especially those like EDRD that have important social, political, and ethical questions attached to them, thus become the channel through which interpretations of the body and personhood are shaped.

The day-to-day aspects of medical care in the field of rare genetic diseases are also rife with difficulties. As we saw with the case studies of PKU and the Kuvan trial, those working in rare disease care teams are placed at an awkward intersection between serving as advocates for their patients while also being aware of some of the problematic elements of the rare disease pharmaceutical industry. Additionally, as the interface between patient and health care system, health care professionals are put in a difficult spot. On the one hand, if they actively voice their concerns or are skeptical about the rare disease drugs, they are contributing to rationales of the federal government to not act to put a rare disease drug strategy in place, and not work towards an EDRD reimbursement fund for rare disease patients. On the other hand, if they do not voice their concerns, they enable the rare disease pharmaceutical company to emerge from these debates unquestioned.

We see here how clinical care and shifting canons of scientific evidence become entangled with social and political issues, and how part of learning to work within a system involves learning how to navigate these types of tensions. As health care professionals move forward with improving rare disease treatments and rare disease care, the highly politicized context and unstable networks of relationships of EDRD reminds us that understanding and remaining aware of the social and the political and how it presents itself in rare disease care will
be necessary as well. Emily Martin writes: “Like a rhizome, culture is discontinuous, some links are invisible and disappear from time to time below the surface of what we can know into dreams, memory, or the account books of multinational corporations” (1998: 40). Making these tensions apparent and visible and politicizing them will be integral in helping a new era of rare disease care to emerge.

5.3 Pharmaceuticals and society: the social reproduction of a political and ethical problem

When looking at the dynamics of EDRD accessibility debates, it becomes clear that reimbursing EDRD is not only about defining the relationship between provincial drug insurance formulary and rare disease patient, the relationship between patient and health care professional, or the relationship of an individual patient to his or her society. These relationships are poised within a wider and very economically and politically powerful relationship: EDRD access negotiations are also about negotiating the relationship between society and the wider economic and power structures in which the pharmaceutical industry is situated.

The ethnographic approach of this study points insistently to the ways that the lack of a structural framework around rare disease care in Canada allows for the perpetuation of the clash of the incongruent narratives that come to a head in EDRD accessibility debates: a private profit-based health care industry versus a publicly funded socialized approach to health care and drug treatment. The members of the different EDRD stakeholder groups who participated in this study each revealed a delicate and difficult position. Patients and patient advocates mobilize ideas of fairness and human rights, simultaneously engaging in deliberations of “the politics of life itself” (Rose 2007). Health care professionals attempt to carve out an appropriate role for themselves that balances both advocacy and critical awareness, but as they pioneer the development of methods to deal with emergent technologies in clinical care, they are confronted with important ethical questions that need to be addressed. Provincial drug insurance formulary administrators
balance dealing with potent human rights claims while simultaneously facing a growing fiscal and ethical challenge. The rare disease pharmaceutical industry attempts to resolve these ambiguities through substantial investment in showing how much they care for patients and the development of strong patient communities. The reality is that each of these stakeholders are sensitive to the issues, but they are struggling to work within a pre-existing and problematic framework when what is needed is a change in the tenor and type of conversation.

Reconciling the tension between the cultural values underpinning publicly funded health care and the profit-based pharmaceutical industry will require a sensitive rearticulation of the relationship between the two. As it stands currently, representatives of the provincial drug insurance formularies state that while they are attempting to strategize in creating solutions, they are in a weak position to do so given the structure of the relationship between provincial and federal levels of health care and the power imbalance between pharmaceutical companies and a society that wants the treatments they produce and sell on the market. Whatever happens has to happen nationally (in the form of a federal rare disease strategy), and preferably globally (in the form of a reshaping of the pharmaceutical industry and the control it holds over lifesaving technologies). Otherwise, those attempting to do the best for rare disease patients in publicly funded health care systems will see the continuation of these irreconcilable narratives clanking against each other.

Chapter 6: Conclusion
This ethnographic study has been an opportunity to explore how cultural, political, financial, and social relationships are being managed in the context of a set of extremely expensive rare disease treatments in the context of British Columbia, Canada. These relationships are fundamentally entangled with ideas of rights to health care, Canadian health care politics, and the rootedness and dependence of health and drug technologies in industry profit.
When speaking of frameworks that generate tensions and expose unresolved social questions, we can take the different stakeholders involved in EDRD debates in British Columbia as an example. We have seen how patients and patient advocates are locked within a framework where the interests of rare disease patients are not secure, and thus mobilize ideas of fairness and equality in trying to convince public opinion and delegitimize the current cautious approach to EDRD reimbursement that is being used in Canada. In doing so, there are many alliances made with rare disease pharmaceutical companies, whose positions of power are tentative and dependent upon the social and cultural acceptance of their activities and mandates. These industry stakeholders are embedded within a profit-based industry that puts pressure on both rare disease drug research design and public relations and sales departments to ensure that the cultural climate surrounding reimbursement of these drugs is in their favour. Provincial health care formularies are under pressure to balance budgets while meeting the health needs and rights claims of rare disease patients, mobilizing cultural notions of accountability and democratic processes of decision-making in order to justify their response to the pressures they face. At the center of these debates are the health care professionals who at once treat rare disease patients, interact with pharmaceutical companies, and participate in drug funding decision making processes at the provincial level. In trying to mediate these conflicting relationships, their roles stretch beyond the therapeutic and into the discursive.

These competing cultural viewpoints and models are reflective of a unique political, social, and historical context, and a stable future for both rare disease treatment and publicly funded health care systems will require that these tensions be negotiated. The debates surrounding EDRD can in many ways be seen as debates surrounding an extreme: extremely high prices for extremely debilitating diseases. However, within this extreme, we see how key social and ethical issues that are present in many other examples of medical care and social and political life in general are consolidated in the example of EDRD. Questions of corporate
regulation, questions of whose responsibility it is to ensure accessibility to the resources (be it drug treatment, housing, employment) needed to fulfill emerging concepts of positive rights and human rights, and questions of the congruence between public ideas of fairness and the legislative policy context: these are all issues that shine through in an ethnographic examination of EDRD as it plays out in the local context. It is no coincidence that these are also some of the more profound subjects currently being deliberated in the contemporary world.

Further research on the internal dynamics of the rare-disease pharmaceutical industry and attempts to resolve ambiguities about the interface between public and private interests through practicing and performing corporate social responsibility would be extremely helpful in developing anthropological insight into the cultural dynamics of this area. A study on the interconnections between pharmaceutical development, pharmaceutical policy, and the economic theories and relationships that are espoused by and exert control over governments will also help to unravel some of the discourse that shapes drug accessibility debates in this period of human history.
Endnotes

i I call them Expensive Drugs for Rare Diseases (EDRD) here as not all orphan drugs are expensive.

ii The category of ‘rare diseases’ is itself a socially constructed category and particular cultural formation. The sociologist Caroline Huyard (2009) has examined the process by which patients with infrequently occurring diseases and patient groups in the United States constructed the term in order to draw political attention towards the social justice issues surrounding rarity in a profit-based health care system, and fostered collaboration between patient groups, industry, and government as the term suited the contrasted needs of the different groups it was related to” (Huyard 2008: 466). I use the term freely here with the awareness that it is itself historically and culturally rooted.

iii Obtaining extended health care coverage to pay for EDRD is generally not possible. Many insurance companies operating in countries with publicly funded health care plans will only cover drugs that are listed on government’s drug formularies, or as in countries like the United States, do not provide coverage for pre-existing conditions.

iv As detailed by Asbury (1985: 165), these incentives include:
   - A seven year period of market exclusivity
   - Tax credits of 50 percent in any taxable year of the costs of human clinical trials for orphan indications. The remaining 50 percent of such costs are deductible, resulting in a total reduction in tax liability of 73 percent of the costs of such trials.
   - The Department of Health and Human Services is authorized to make grants and enter into contracts for orphan-drug clinical trials (these authorizations were $4 million each for FY 1983, FY 1984, and FY 1985).

v This is also because the pharmaceutical industry is changing: as patents run out, the pharmaceutical industry is losing ground. Thus, many players in the pharmaceutical industry are starting to look towards types of products that will be more ‘sustainable’ over time, which essentially means drugs that will be protected by market exclusivity and patients who will need a treatment over the course of their lives (see Financial Times: 27 March 2011, “Euro pharma: sweetening a bitter pill”)

vi This particular pharmaceutical conference provided full funding for all attendees, which included doctors, nurses, researchers, PhD students (in pharmacology/sciences), patient advocates, and corporate managers. A sales representative for the company arranged for an invitation for me as a researcher and as such my expenses were paid.

vii Principle 33 of the World Medical Association’s Declaration of Helsinki states: “At the conclusion of the study, patients entered in to the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits”.
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