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**TABLE OF CONTENTS**

Chapter 1: Introduction 7

  Overview 7

  Specific Aims and Research Questions 10

  Conceptual Framework 12

  Research Design and Methods 28

  Human Subject Protection 43

  Description of Dissertation Chapters 44

  Study Timeline 46

  Significance, Innovation, and Expectations 47

  Study Limitations 51

Chapter 2: Background and Literature Review 54

  Introduction 54

  Data Collection Procedure 55

  History and Controversy in the Development of Newborn Screening Programs 56

  Recent Newborn Screening Debates 64

  Benefit for the Baby, the family, and Society from Screening 68

  Dealing with Uncertainty 70

  Informed Consent for Newborn Screening 72

  Newborn Screening Education 74

  The Adoption of New Medical Technologies in Israel 76
Israel’s National Insurance Law and the Health Basket

Committee 77

Genetic Screening in Israel 80

Newborn Screening in Israel 82

Chapter 3: Analysis of Newborn Screening Guideline Documents 85

Introduction 85

Data Collection Procedure 87

Data Analysis 88

Results 93

Discussion 96

Chapter 4: The Evolution of the Expanded Newborn Screening Program in Israel 109

Introduction 109

History of Newborn Screening in Israel 109

Pilot Testing and the Justification for Expansion 113

The Role of Advisory Committees in the Process of Expansion 115

Timing and Fundraising for Expansion 119

Structural Considerations: Centralization and Privatization of Newborn Screening in Israel 122

Criteria for Disease Selection 125

Determination, detection, and Reporting of “Screen Positive” Results 128

Parental Stress Following Receiving “Screen Positive” Results 134
Education and Public Awareness regarding Newborn Screening 135

The Inchoate Nature of Programmatic Policies and the various Interpretations of those Policies 142

Chapter 5: The Context of the Expanded Newborn Screening Program

In Israel 149

Introduction

Legal Basis of the Expanded Program 149

Economical Considerations in the Evolution of the Israeli Program 151

Disorganization, Informality, and Authoritative Biomedical Knowledge 154

The Political Context of the Expanded Israeli Program 157

The Social Context of the Routinization of Tandem Mass Spectrometry 159

Newborn Screening, Equity, and Sitgmatization 162

Benefit for the Baby, the family, and Society form Screening 163

Informed Consent for Screening and the Future Use of Bloodspots 167

American Influence on the Evolution of the Israeli Program 176

Chapter 6: Conclusion 188

Introduction 188

Challenges of the Israeli Program 189
Unique Characteristic of the Israeli Program: Significant

American Influence

Concluding Remarks

Appendix 1  List of Candidate Conditions in Expanded Panel, 2009

Appendix 2  In-Depth Interview Guide

Appendix 3  Participant Observation Guide

Appendix 4  List of Candidate Conditions in Expanded Panel, 2007

Appendix 5  List of Candidate Conditions in Expanded Panel, 2008

Appendix 6  Interview Coding Guide

Appendix 7  Tables (see next page for individual listing)

References
LIST OF TABLES (APPENDIX 7)

1. Documents, Authors, and Scope of Guidelines 225
2. Criteria for Disease Selection 227
3. Ethical, Legal, and Social Considerations 230
4. Program Organization and Daily Functioning 233
5. Program Assessment 236
6. Research 239
LIST OF FIGURES AND ILLUSTRATIONS

1. Conceptual Framework 9
2. Study Design and Methods 26
3. Interview Guide: Sample Questions 31
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The Expansion of Newborn Screening in Israel: Ethical and Social Dimensions

Abstract

by

SHLOMIT ZUCKERMAN

This dissertation is a bioethical study of the decision making involved in the recent expansion of newborn screening for genetic and metabolic disorders with the introduction of tandem mass spectrometry technology in Israel. It explores the ethical, social, and programmatic challenges posed by introducing new technology into a developing public health program. Newborn screening programs test infants in the first 24-48 hours of life to identify disorders while they are presymptomatic and preventive treatment is available. The number of tests performed and disorders screened for varies widely between programs, as do the methodologies used in testing. This study’s first aim is to locate the development of an expanded Israeli program in a broader social and international context by conducting a policy analysis of the evolution of newborn screening programs internationally. The study’s second goal is to analyze ethical, social, and policy issues in the formation and implementation of the expanded Israeli program based on in-depth interviews of program initiators and officials and practicing physicians in the field of newborn screening in Israel and internationally. Using social scientific theories regarding the social construction of medical knowledge, the concepts of medicalization and the technological imperative, this study examines the routinization of tandem mass spectrometry, and the influence of cultural quest for a “perfect baby” in Israeli society on the public perception of newborn screening and its expansion. I conclude that three issues have proved problematic in the development of the Israeli expanded newborn
screening program: the inchoate and contested nature of the policies that have emerged regarding basic programmatic aspects as practiced by different stakeholders; the insufficient evidence-base used to justify various programmatic aspects; the minimal involvement of the community in the process of decision making that shaped the program’s implementation. Finally, I demonstrate the significant influence of American newborn screening experience on various stages and aspects of the developing newborn screening program in Israel.
Chapter 1: Introduction

Overview

This study explores ethical and social dimensions of the expansion of newborn screening in Israel. Newborn screening is a term used to describe public health programs that test newborns for genetic and metabolic disorders in the first 24-48 hours of their life. Newborn screening programs allow for early detection of infants who have disorders that would cause irreversible clinical damage if not recognized at birth (Therrel, 2001). The objective of newborn screening is to identify disorders while they are presymptomatic and preventive treatment is available (Levy et al., 2000).

The physical process of newborn screening starts with lancing a baby’s heel and then soaking several circles on a filter paper card with drops of the baby’s blood. Newborn screening programs have diverse approaches to education of parents and regarding the type of consent (or lack of consent) process that is used prior to obtaining the blood specimen. The blood is then air-dried at room temperature and delivered by courier or mail to the testing laboratory. A major concern in newborn screening is the age of the infant at the time of specimen collection; blood is typically obtained at 24-48 hours after birth, although this represents a compromise as it is ideal for the detection of some conditions and suboptimal for others. The number of tests done on the blood specimen and, therefore, the number of disorders that are screened for, varies widely between newborn screening programs, as do the methodologies used in the testing. The results of newborn screening are communicated by the laboratory staff to the medical home that, in turn, deliver the results to parents of newborns detected as screen-positive and refer them for further evaluation. Follow-up evaluation of a screen-positive baby involves additional
testing and, sometimes, immediate clinical evaluation as well, depending on the condition that the baby’s screening test was positive for. For babies whose follow-up testing reveals that they definitely have the disorder that was screened for (i.e., true positives), further evaluation and care is typically provided by clinical specialists in medical genetics or endocrinology at academic or tertiary care centers.

The focus of this study is the development of the expanded newborn screening program in Israel; a program that was launched in May 2008. The conceptual framework consists of four components: 1) the social construction of medical knowledge as it relates to program parameters, among health care professionals and program officials involved in the expansion of the Israeli newborn screening program, 2) medicalization and biomedicalization, 3) the technological imperative and routinization of a new technology, namely tandem mass spectrometry, in the program, and 4) the influence of the quest for a “perfect baby” in the Israeli society on the public perception of newborn screening in general and its current expansion in particular.

Newborn screening has been practiced in the U.S. since the early 1960s and serves as a foundation for other types of genetic screening. There is significant variation in public health programs in the U.S. and internationally regarding the number and types of genetic conditions for which screening is conducted (Clayton, 1999; McCabe et al., 2002; Comeau et al., 2004; Therrel, 2007). In response to this variation, in 2005 the American College of Medical Genetics argued for a uniform screening panel consisting of 29 core conditions and 25 additional secondary conditions to be used in newborn screening programs in all U.S states (the American College of Medical Genetics Report, 2005). The methodology used by the working group that published the report sparked a heated
debate in the medical genetics community in the U.S. and internationally (see e.g., Natowicz, 2005; Botkin et. al, 2006). In Israel, mandatory newborn screening of 150,000 babies each year has been performed since the mid-1960s (Cohen et. al, 1966; Szeinberg et. al, 1970, Sack 1985). In May 2008, an expanded newborn screening program was established in Israel at Sheba Tel Hashomer Medical Center. The creation of the new center was made possible by a joint initiative of Israeli and American health care professionals (see chapter 4). Based upon prior experiences with newborn screening in the U.S., European nations, and Israel, the program directorship aims to improve existing testing using new technologies. The program is currently screening for a of conditions to consist of 11 more conditions in addition to Phenylketonuria (PKU) and Congenital Hypothyroidism, the two conditions that have been screened for in Israel since the 1970s. Screening for the expanded panel of conditions started in May, 2008. In its first stage, the expanded panel in Israel includes Amino Acid Disorders, Organic Acid Disorders, and Disorders of Fatty Acid Oxidation (for a final list of conditions see Appendix 1). Screening for the full panel of 29 core conditions recommended by the American College of Medical Genetics will be considered in the future. According to program officials, U.S. and European standards, procedures and performance metrics were taken into consideration by the Israeli expert team while developing the expanded panel of conditions. In particular, the newborn screening program in New York State has played an important role in the creation of the Israeli newborn screening program, as discussed in chapter 4.
**Specific Aims and Research Questions**

The overall goal of this study is to analyze the evolving ethical, social, and policy issues in the implementation of an expanded newborn screening program in Israel. The specific aims and associated research questions are as follows:

**Specific aim #1: To conduct a policy analysis of the evolution of newborn screening programs in the U.S. and internationally.** This component of the project reviews the development of newborn screening policies from its early days in the 1960s through the present. My specific research questions for this component of the study are:

1. What are the criteria for the selection of diseases for the newborn screening panels in different guideline documents?
2. What mechanisms are endorsed by different guidelines for balancing criteria in deciding what to include in screening panels?
3. What legal, ethical and social issues arise in the implementation and operation of newborn screening programs and how are they addressed in guidelines?
4. What are the procedures and practices supported by the guideline documents for the organization and functioning of the newborn screening program?
5. What are the guidelines’ positions regarding the use of newborn screening bloodspots for research?

**Specific aim #2: To analyze ethical, social and policy issues in the formation and implementation of an expanded newborn screening program in Israel.** In particular, this study addresses the following research questions:

1. What was the rationale for the decision to expand newborn screening in Israel in 2005? Who was involved in the decision making process that led to the current
expansion? How were the conditions that are included in the expanded screening panel selected and by whom?

2. How are the notions of the technological imperative and McKinlay’s model of routinization of innovative technology reflected in the introduction of tandem mass spectrometry?

3. What is the program’s policy regarding detection, determination, and reporting of “screen positive” results to the medical home and to parents of newborns?

4. How were program parameters’ socially constructed and how are the concepts of medicalization and biomedicalization reflected in interviewees’ views and attitudes towards the existing and desired policy?

5. How are the issues of education (of health care professionals and parents of newborns), public awareness and informed consent for screening regulated by the program? How did the quest for the “perfect baby” in Israel influence the public perception of newborn screening in general and its current expansion in particular in the eyes of the newborn screening program officials and other physicians involved in the process?

6. What is the impact of the U.S. and European experience of expansion of newborn screening on the design and functioning of the developing newborn screening program in Israel?

7. What are the unique characteristics of the Israeli newborn screening program and what challenges does it face?

The analysis of key documents and policies regarding the structure and function of newborn screening programs has a central role in this dissertation. This analysis places
the development of an expanded newborn screening program in Israel in a chronological and conceptual context through a review of the central issues confronting newborn screening programs since 1960s until the present time. These issues include controversy over what disorders to screen for and how to develop a decision making basis for such choices, what methodologies should be used, how newborn screening programs should be assessed, and to what extent newborn screening programs should relate to research endeavors in this area of medicine, among others. Each of these issues was/is relevant to the nascent expanded newborn screening program in Israel insofar as each issue needed to be considered as the program was conceptualized and being birthed. The successes of an expanded newborn screening program need to be considered, in part, on the basis of the history of the struggles of programs that preceded the expanded program in Israel. Failures and limitations of the expanded program in Israel need to be assessed, in part, on whether lessons learnt in the past were ignored. Knowledge of the policies of prior programs, then, is key to a full understanding of the development of the new newborn screening program in Israel.

**Conceptual Framework**

Figure 1 is a graphic illustration of the conceptual framework.
The conceptual framework for this dissertation has four components (Fig.1). 1) the social construction of medical knowledge, 2) the processes of medicalization, medicalization, and authoritative knowledge of biomedicine, 3) the technological imperative and the routinization of innovative technology, and 4) the influence of the quest of the “perfect baby” in the Israeli society on the public perception of newborn screening in general and its current expansion from the perspective of newborn screening program officials and other physicians involved in the process.
Social Construction of Medical Knowledge

The first component of the conceptual framework is the general theoretical orientation provided by the sociological scholarship that seeks to understand the “social construction of medical knowledge” (Brown, 1995, Nicolson et. al, 1987). This work proceeds from the premise that medical professionals’ ways of knowing are not limited to the scientific method, but also reflect the socialization of health care providers, their moral and ethical views, the institutional and professional procedures, and the social structure of society.

For much of the 20th century, positivist philosophers of science and medical professionals alike have conventionally assumed that biomedical facts are in “nature”, awaiting objective discovery and verification through the hypothetico-deductive Scientific Method (Churchland and Hooker, 1985; Robert Proctor, 1991). According to this “realist” view, well-founded scientific knowledge claims are taken to be universally “true,” and exist independent of the social and cultural domain. Therefore, for the clinician, abnormality and normality are distinguished from each other and represented as separate categories that are understood to transcend culture. As Wulf, Pedersen and Rosenberg note, this realist approach pervades contemporary medical thinking. As an example, the teacher who gives a lecture on bronchial asthma will describe the symptoms and signs of asthmatic patients, but he will also give an account of the underlying mechanisms. Those who wish to probe the experimental evidence will need to review large numbers of articles and the results of investigations may well be tables with numerous figures which have been subjected to statistical analysis. But these statistical truths are not an end in themselves. They are only a means to the establishment of a
coherent theory which we believe reflects the reality behind the observations” (Wulf, Pedersen, Rosenberg, 1986, P.37).

Social constructionists, on the other hand, view the production of medical knowledge and illness differently. For them, medical knowledge is inseparable from social knowledge. According to Bloor (1984), knowledge for the sociologist is whatever people take to be “knowledge”. Bloor suggests that the features of culture that usually do not count as science have a great impact on both the creation and evaluation of scientific theories and findings. In his words “…what we count as scientific knowledge is largely ‘theoretical’…. It is largely to their theories that scientists must repair when asked what they can tell us about the world” (Bloor, 1984; 16). However, theoretical knowledge does not originate from our experience but rather this is what gives meaning to experience. The other component of knowledge, apart from the physical world of experiences, is the social world. Therefore, the sociological perspective and social situations influence the understanding of the phenomena of health and ill-health, the determination of diagnosis, and the recommended treatment (Kass, 1981; Mishler, 1981; Atkinson at Lock, 1988; Shiloh, 2002).

Brown makes a distinction between the social construction of medical knowledge and the social construction of illness (Brown, 1995). The former refers to the ways of knowing that stem from the biomedical world, moral and ethical view the process of socialization of clinicians, the practices (both institutional and professional) utilized in the health care system, and the broader social structures of society. In particular, social factors such as professional advancement and patriarchal attitudes are the subject of this scholarship and the structural approach is most influential. The social construction of
illness takes an interactionist approach to the experience of illness at all levels (personal, dyadic, and group) rather than a structural view. The two constructions converge when people interpret their own and other illnesses using the dominant social elements of medical knowledge. For Nicolson, “Constructionist accounts of medical knowledge might provide clinicians and medical scientists with useful opportunities to be reflective about their own practice, serving as useful reminders of the limited, conjectural, and fallible nature of medical knowledge” (Nicolson et al. 1987:121). Other scholars have emphasized the relevance of the social constructionist perspective to studying the socio-cultural dimensions of medicine (Lupton, 2003). I argue that the major influence of the changing medical practices on the expanded newborn screening programs and the uncertainty surrounding newborn screening results (as discussed extensively in chapters 2, 3 and 4) reflect this form of social construction, in particular when it is coupled with the social processes of medicalization and biomedicalization, which will be discussed in the following section.

One set of social forces that influence health care decision making in the U.S. and internationally in general, and newborns screening programs in particular, is the prospect of commercialization. There was, for example, representation from Perkin-Elmer corporation, a for-profit concern that make mass spectrometry instrumentation and materials that can be used in expanded newborn screening, on the Advisory Committee on Heritable disorders and Genetic Diseases in Newborns and Children that recommended the expansion of newborn screening in the United States to include many disorders that can currently only be screened for by tandem mass spectrometry. Pediatrix Inc., a for-profit organization that conducts newborn screening independent of U.S. state
programs and which uses tandem mass spectrometry as one of its screening platforms, lobbied on behalf of expanded newborn screening. Genzyme Inc., another for-profit organization involved in both testing and treatment of many genetic disorders, has funded symposia and investigators on work directly related to further expansion of disorders that could be detected by newborn screening programs and for which that organization has proprietary treatments.

Such economic and political influences on newborn screening occur generally, and are not particular to newborn screening programs in the United States or in Israel. The minimal amount of newborn screening done throughout most developing nations is partly due to the substantial costs of the instrumentation needed in expanded newborn screening such as tandem mass spectrometers and the high costs of other aspects of newborn screening infrastructure. As discussed in chapter 4, even in a developed nation like Israel, the recent expansion of newborn screening only became possible through a major philanthropic gift that resulted in the purchase of the needed mass spectrometry instrumentations and the political environment between the United States and Israel that fosters such philanthropic endeavors.

**Medicalization and Biomedicalization**

Like medical knowledge, technological practices also are the socially constructed. In a recent study Vailly presents an ethnographic analysis of the biomedical definition of the normal and abnormal used in what she refers to as “the borderline forms of genetic disease in the context of newborn screening for Cystic Fibrosis (CF) in France” (Vailly, 2008, p. 2). Vailly poses the following research questions: first, how does the newborn screening process for CF contribute to the expansion of abnormality? Next, how does
this expansion alter professional practices? Vailly demonstrates how technical limitations of screening result in lowering detection and tolerance thresholds for CF. She then associates the lowering of those thresholds for disease with a wider social context that does not tolerate bodily impairment. In her study, Vailly relates the effects of adding CF screening to the newborn screening panel in France to the current expansion of the idea of medical abnormality.

The sociological discourse of medicalization (Zola, 1972) would consider this process a part of the “insidious and often undramatic phenomenon accomplished by medicalizing much of daily living, by making medicine and the labels ‘healthy’ and ‘ill’ relevant to an ever increasing part of human existence” (Zola, 1972; 487) or as “a process by which nonmedical problems become defined and treated as medical problems usually in terms of illness and disorders” (Conrad, 2007; 4 and see also Conrad, 1992). This application of the social constructionist approach is particularly relevant for this dissertation, because it illustrates the link between social constructionism as an approach to biomedical science and technology and “medicalization” as another sociological concept providing an important theoretical lens for my study.

The expansion of the practice of newborn screening affects the daily living of parents of approximately four million newborns in the U.S. and 140,000 newborns in Israel every year. In particular, labeling around 80 newborns in Israel every year as “abnormal” by detecting them as “screen positive” for one or more conditions included in the panel is a reflection of the link Vailly makes between medicalization and the social construction of knowledge.
A related social process focusing on the medicalization of techno-scientific developments is the process of biomedicalization, a process that is defined and analyzed by Clark and her group (Clark et. al, 2003). Clark et al, define the process of biomedicalization as a process in which “medicalization is intensifying, but in new and complex, usually technoscientifically enmeshed ways” (Clark, 2003; 161). The construct of biomedicalization is focused in clinical innovation. It presumes that sciences and social forms are co-produced within biomedicine. Clark proposes that the shift from medicalization to biomedicalization is historical rather than programmatic and has occurred since 1985. It is based on the transformation from modernity to late-modernity or post-modernity. According to Clarke, five major interactive processes define the concept of biomedicalization. Those processes are the politico-economic constitution of the social form they refer to as the Biomedical TechnoService complex Inc; the focus on health itself and the elaboration of risk and surveillance biomedicine; the growing techno-scientific nature of the biomedical practices and innovations; the transformation of medical knowledge production, information management, distribution and consumption, and the transformation of bodies to include new properties and the production of new individual and collective techno-scientific identities (Clark, 2003; 162). Social and cultural aspects of medicalization and biomedicalization in the context of genetics and genomics are discussed in recent social science literature (Lippman, 1991; Burri and Dumit, 2007). Scholars who revisited the concept of medicalization in the 21st century suggest that these days the power of doctors is constrained by aspects of law, bioethics, evidence-based medicine, and patients' demands (Metzl, 2007; Rose, 2007). In my work, I will draw upon the concepts of medicalization and biomedicalization and in particular,
on the aspect of the growing technoscientific nature of the biomedical practices and innovations in Clark’s model, for the analysis of the social implications of the routinization of the innovative tandem mass spectrometry technology in newborn screening. This leads us to the third component of the conceptual framework, the technological imperative and the routinization of new technology.

Routinization of a New Technology

The third contribution to the conceptual framework relies on recent medical anthropological analysis of the routinization of new medical technologies into ordinary clinical practice (McKinlay, 1982; Koenig et. al, 1988, Press et. al, 1997). Koenig argues that the experts engage the social surrounding of the technology and their social experience and rituals in their “reading” of it. Therefore, it is important to understand the involvement of those participants in the social process of routinization in order to improve decision-making. Koenig emphasizes the need for a thorough comprehension of the social and cultural roots of the technological imperative in medical practice. The technological imperative is the drive to use technology simply because it exists. For Koenig, understanding that the meaning of a new technology as at least in part, a social construction is crucial if one wishes to make fully informed decisions about the appropriate use of technology. The technological imperative was widely discussed in the literature in regard of childbirth technologies. Butter, for instance, describes the tendency to adopt medical technology prematurely and to routinize the use of technologies when there are varied physicians’ opinions and unproven medical benefit as “technological favoritism”. She analyzes this phenomenon in regard to three different childbirth technologies (Butter, 1993).
Sociologist McKinlay (1982) critically analyzes the typical career of a medical innovation that leads it to the point that it “gains privileged access to the House of Medicine” (McKinlay, 1982; 234) and becomes the standard of care. The career, according to McKinlay consists of seven distinct stages. He notes that not each and every innovation goes through all those stages but it has at least the beginning point and an ending (established procedure). For him, the beginning is the “promising reports” and the ending is the established procedure or erosion and discreditation. The usefulness of this model, is that it enables to break complex social behavior and political processes into manageable form. This model is particularly relevant to this work because it allows for the identification of the various levels of consideration of the activities of hospitals, physicians, and other interest groups.

The innovation studied in this paper is the utilization of tandem mass spectrometry for testing an expanded panel of newborn screening disorders. Although tandem mass spectrometry had been utilized by newborn screening since the 1990s (Ross, 2009) it is still new for many newborn screening programs, including the Israeli program. The first stage described by McKinlay is the “promising reports” about the innovation that are usually published in the media and later in professional journals. The latter, who tend to document only successful interventions (such as the use of tandem mass spectrometry for expanded newborn screening) are no more reliable than are the former. At this stage clinicians sometimes initiate pilot studies to learn about the effectiveness of the innovation. In McKinlay’s view those studies should be considered as uncontrolled observational reports. According to McKinlay, by publicizing the new technology the
pilot may seem to demonstrate as opposed to question the usefulness of the innovation. Soon enough the innovation appears valuable for the relevant sector of the public.

The second stage is characterized by support of influential and powerful interest groups and institutions that commit resources for the utilization of the technology. This second stage is described as “the stage of professional and organization adoption”. Next, a general approval or acceptance of the innovation emerges among the public. The acceptance relies on the general perception that the innovation is a good thing and should become available. The enthusiasm of consumers at this stage of acceptance depends on that of the professionals but it also strengthens it. Following the adoption by professionals and acceptance of the public, the endorsement or support of the innovation comes from the state. The next step, which is defined by McKinlay as “the point of no return,” takes place once the state initiates the implementation of a social policy to support the innovative technology. After a period of time the innovation achieves the privileged status of a “standard procedure”. The last three stages (randomized controlled trial, professional denunciation, and the stage of erosion and discreditation of the technology, that brings the career to its end, are not relevant to this analysis and therefore will not be discussed). Press and Browner (1997) use McKinlay’s model to explore the routinization of the maternal alpha fetoprotein prenatal screening test in one Californian Health Maintenance Organization.

My analysis of the policy guidelines (chapter 3) and the expansion of newborn screening in Israel (chapters 4 and 5) address the process by which tandem mass spectrometry is currently routinized to become the accepted screening practice. I argue that there are many similarities between the process of routinization of maternal alpha
fetoprotein for prenatal screening as it was described by Press and Browner and the routinization of tandem mass spectrometry for newborn screening. First, the target universe of patients consists of all pregnant women in the former case and all newborns in the latter. The fact that so many individuals are tested by the same procedure expedited it becoming a standard of care in prenatal screening. The same process is currently taking place in newborn screening, as tandem mass spectrometry is rapidly becoming the standard of care. Secondly, screening, as opposed to testing, also implies that following the detection of positive result the findings should be diagnostically confirmed. Third, in between detection and clinical confirmation, the patient (or her parents in the case of newborn screening) may experience anxiety and distress. Fourth, in both fields, there are many areas of uncertainty of screening results and finally, in the international arena, in both cases the adoption of the test seems to be rapid and widespread.

Given those similarities I intend to use McKinlay’s and Press’s works to investigate the routinization of tandem mass spectrometry in the expanded newborn screening program in Israel. Significantly, despite the fact that in Israel, as the literature suggests and my data demonstrates, prenatal screening enjoys long lasting and uncritical acceptance by the public (Lewando-Hundt, 2001; Remmenick, 2006), newborn screening is hardly acknowledged. The explanation to this gap in knowledge is the subject of the next section.

The Quest for a “Perfect Baby” in Israel

The last body of theoretical work my conceptual framework draws upon is the socio-cultural literature focused on reproduction and the quest for a “perfect baby” in Israel. In “the quest for a “perfect baby”: why do Israeli women seek prenatal testing?”
Remmenick (2006) explores the social forces behind the rapid expansion of elective prenatal screening for genetic conditions in Israel, as they emerge from Jewish Israeli women’s perspectives. She argues that medicalization of reproduction and women’s bodies play a major role in Israel, maybe more so than it does in the U.S. due to the universal health care system and the traditional respect for medical science and doctors among the Jewish community. Just as prenatal follow-up was routinized a few decades ago, genetic screening is now rapidly becoming a part of the normative conduct of mothers-to-be who aim to secure the future of their babies.

Remmenick suggests that the basis for the mass acceptance of prenatal diagnosis in Israel is the inherent deep intolerance of physical and mental disability in the Israeli Jewish culture and the fear of having to raise a sick or deformed child alone, unsupported by the larger society. In order to minimize the risk of having a disabled child, women are willing to go through as many prenatal tests as they are offered. Jewish parents, in particular those of Ashkenazi origin, are characterized by a higher level of genetic awareness, or genetic anxiety, compared to other ethnic groups. This ethnic trait is explained by the many generations of endogamy in European Jewish communities (Zlotogora et. al, 2000). The new genetics and related prenatal tests promise to ease this anxiety. Remmenick reports that women she interviewed were anxious while awaiting prenatal testing results and later on while trying to interpret them. In particular, those who received borderline or positive results felt confused in light of the uncertainty they were facing. The uncertain results opened a “Pandora’s Box” of questions about loyalty in the family, the need to share genetic information with family members and above all, about whether or not to continue the pregnancy.
Browner and her colleagues associated the importance of technology in prenatal care to the authoritative knowledge of biomedicine in this area (Browner et. al, 1996). The authors investigated why women defer to biomedical authority in the domains of prenatal care. For Browner, the dominance of clinical technologies in this field is integral to the hegemonic efforts of biomedicine in those domains. With the increasing utilization of clinical technology the deference of women to biomedical authority should be anticipated, and this, in turn, is strengthening the consensus that biomedicine holds authoritative knowledge in prenatal care. Remmenick’s conclusions supports this position. She found that, despite the negative psychosocial affects of prenatal testing experienced by pregnant women, only a minority of the respondents expressed resistance to the medical control of pregnancy or refused testing. Remenick argues that as medicine has gained control over the experience of pregnancy in Israel, adding more procedures to the existing ones is perceived by the women as taking one more step towards achieving the ultimate goal of having a “perfect baby.” The uncritical acceptance of prenatal diagnosis is not influenced by the poor understanding of the medical genetics and elective tests taken by pregnant women. The genetic anxiety among Ashkenazi women only contributes to this trend.

Mostly relevant to the present study is the provider’s perspective on prenatal diagnosis. In similarity to Browner’s analysis, according to which with the growing utilization of clinical technology the deference of women to biomedical authority increases, and this, in turn, is strengthening authoritative knowledge of biomedicine in prenatal care, Remmenick has found that providers of prenatal genetic services in Israel were the major force behind the routinization of prenatal genetic diagnosis. Physicians
and nurses referred women to all available tests in order to avoid malpractice suits. Given the rarity of the conditions tested for by prenatal screening and the findings of her study, the author suggests that the public health benefit of prenatal diagnosis is debatable. Remenick concludes that the current expansion of prenatal testing should be reevaluated by health professionals involved in the practice, including ob/gyns, medical geneticists and counselors, and health policy makers, and by pregnant women as well.

In light of Remmenick and Browner’s work, I suggest that the rationale for newborn screening coincides with that of prenatal screening in three aspects at least; 1) the goal of the parents to secure the future of their babies, 2) the fear of having to raise a sick or deformed child alone, not supported by the community, and 3) the potential of genetic screening to ease the genetic anxiety of parents, those of Jewish ethnicity in particular. Of course, the fact that the baby is already alive and the alternative of abortion does not exist in the case of newborn screening as opposed to prenatal screening could weaken the rationale of newborn screening in the eyes of parents, health professionals, and the general public. However, as will be discussed in chapter 3 there are at least four strong arguments in favor of performing newborn screening: 1) the direct benefit to the baby from screening if an effective treatment exists, 2) benefit to the baby and family from early detection and avoiding of the diagnostic odyssey in the case of untreatable conditions, 3) the benefit to the family from screening and in particular the provision of information for future family planning and 4) the benefit to society stemming from avoiding the social and economical burden of mentally retarded individual on society.

In similarity to prenatal screening, and as a result of the process of medicalization of genetic screening in Israel, I would anticipate that adding more procedures to the existing
newborn screening panel be perceived by the women as taking one more step towards
achieving the ultimate goal of having a “perfect baby” who leads healthy and full life
despite the poor understanding of the medical genetics basis of the practice. This
question, however, is beyond the scope of this study as my main focus in this study were
the views and attitudes of newborn screening program officials and other involved
physicians.

I argue, in this regard, that just like providers of prenatal genetic services were the
major force behind the uncritical public acceptance of prenatal screening, providers of
newborn screening are the driving force behind the public ignorance in regard of
newborn screening. Only if and when gynecologists, pediatricians, and public health
agents are well informed and educated about newborn screening practices in general and
the current expansion in particular and, in turn, start educating the public about the
process of newborn screening and its major significance to the well being of their baby,
will the indifferent approach of the public regarding the procedure and its possible
outcomes turn into an active support in the process of expansion of the newborn
screening panel, despite the uncertainty that surrounds many of the conditions in the
expanded panel. In chapter 4, the views of newborn screening program officials and other
involved physicians in Israel and internationally regarding those issues are discussed and
analyzed.

Summary

In sum, my work on newborn screening draws on four theoretical components from
the social scientific study of biomedicine: the social construction of medical knowledge,
the concepts of medicalization, biomedicalization, and authoritative knowledge of
biomedicine, the technological imperative and the routinization of new medical technologies, and the quest for a “perfect baby” in the Israeli society. Using these constructs, I address the following set of questions:

1. How are the social forms and medical information co-produced in the ongoing expansion of newborn screening programs in general and in Israel in particular?

2. How do social values, ethical beliefs and medical knowledge interplay and shape the attitudes and opinions of newborn screening program officials, laboratory personnel, and practicing physicians as they confront the required modification of procedures and practices of screening and in light of the possibilities and challenges posed by the routinization of the new technology?

**Research Design and Methods**

**Introduction**

This study describes the historical development of the expansion of newborn screening programs in Israel. The primary focus is on the formation and implementation of an expanded newborn screening panel of genetic and metabolic conditions in Israel. In particular, it looks at the introduction and routinization of advanced technologies (tandem mass spectrometry) for the new program. This study also includes a policy analysis for the evolution of newborn screening programs internationally.

Two qualitative methodological approaches were used in data collection. First, a comprehensive policy analysis of national and international newborn screening guidelines accompanied by a literature review was implemented to investigate the goals, developments, and challenges in the field of newborn screening in national and international settings from its early days in the 1960s through the present. This analysis
included a systematic literature review of scholarly articles and a comprehensive analysis of public policies discussing state, provincial, national and regional practices regarding newborn screening in the past four decades.

The main empirical component of this study consists of 20 in-depth interviews. Three groups of health care professionals were interviewed: a) public officials who are/were substantially involved in the creation and implementation of the newborn screening program; b) clinicians who will play a role in the communication of screen positive results and the follow up of newborns detected through screening in the expanded program; and c) American and European officials whose newborn screening programs influenced the creation and implementation of the Israeli program. Interviewees from the first group included officials from the Israeli newborn screening program and from the Ministry of Health. Interviewees from the second group included physicians who serve as the medical home for screened newborns. Finally, interviewees from the third group included American consultants and advisors for the developing program, and European public officials of newborn screening programs which influenced the Israeli program.

To further explore the process of actual routinization of newborn screening, and ethical issues raised by the use of advanced technologies, two participant observation sessions at the Israeli newborn screening laboratory were conducted. The observations provided contextual background information to augment findings from the in-depth interviews. Mixed methodology is particularly important in a study that investigates the development of a public health service. The triangulation achieved by using various methodologies yields a more precise picture of the interaction between different aspects of an emerging public health program.
Throughout data analysis, questions about how laboratory staff integrate the use of tandem mass spectrometry to their routine work, why they set the advanced device to allow for detection of certain conditions but not of others, and how they determine and report “screen positive” results for conditions of unknown or uncertain clinical significance are explored. In addition, ethical, social, and policy concerns raised by the current expansion are discussed in light of the international process of expansion of newborn screening currently taking place. The impact of the international experiences of newborn screening, in particular American and European influences on the formation and implementation of the program, is investigated and analyzed. In a broader perspective, this comprehensive analysis of the evolution of an expanded screening program provides a unique opportunity to advance our understanding of the growing establishment of clinical and genome-based knowledge resources and the ways in which those resources are translated to inform public policy.

*Figure 2* is an illustration of the study design and methods in accordance with the two specific aims:

*Figure 2: Illustration of Study Design and Methods*
Specific aim 1: Conduct policy analysis of the evolution of newborn screening in the U.S. and Internationally

Specific aim 2: Analyze ethical, legal, social, cultural and policy issues in the formation and implementation of an expanded newborn screening program in Israel

International policy analysis

Literature Review & background analysis

Public officials, physicians & consultants’ interviews

Ethnographic observation at newborn screening laboratory

Data was collected from several sources: 1) comprehensive literature review to investigate the foundations, developments, and challenges in the field of newborn screening in the national and international setting since its early days in the 1960s and until the present; 2) in-depth interviews with public officials and clinicians in Israel and internationally concerning the process of formation and implementation of expanded newborn screening programs in general and the Israeli newborn screening program in particular; 3) comprehensive policy analysis of national and international newborn screening guidelines; and 4) participant observation at several newborn screening laboratories.

Two data collection techniques were employed. The first was a comprehensive analysis of public policies discussing practices and procedures of newborn screening programs from the 1960s until the present. The policy guideline documents were selected based on their focus on policy-making issues in regard of the formation and
implementation of newborn screening programs. The data was collected and analyzed with Marvin Natowicz MD, PhD. The questions addressed by the policy analysis focused on the decision making process and the criteria for selection of diseases to screening panels; ethical and legal considerations of expansion of newborn screening; issues related to program organization and functioning, and research-related issues.

The second method consisted of in-depth interviews with public officials and clinicians who are or will be substantially involved in the creation, implementation, and follow-up of newborns detected by screening. Interviewees included the Israeli newborn screening program officials, public officials in the Israel Ministry of Health (MOH) and physicians who will play a role in delivery of results obtained from the expanded panel, U.S. consultants and advisors for the program, and European newborn screening program officials whose programs served as a model for the Israeli program. Finally, brief periods of ethnographic observations at the laboratory conducting the newborn screening program were conducted in order to learn more about the routinization of the tandem mass spectrometry device. Data in this study is described and organized using an editing approach and emersion-crystalization approach. A description of the methods used for data analysis for each one of the study components -- policy analysis and in-depth interviews -- is included in this chapter. A discussion of human subject protections conclude this chapter.

The specific aims and research questions of the study are described below:

Specific aim #1: Conduct policy analysis of the evolution of newborn screening programs in the U.S. and Internationally.
Specific aim #2: Analyze ethical, legal, social, cultural, and policy issues in the formation and implementation of an expanded newborn screening program in Israel.

The specific research questions to be answered by each method are discussed at the beginning of each section, followed by a description of the data collection procedure and sampling strategies when applicable.

In-depth Interviews

The questions addressed by interviews included background information about the interviewees and their connection to the expanded newborn screening program in Israel. In addition, they were questioned about their knowledge and views regarding the following issues: a) current testing; b) the decision making process that led to the expansion of the program; c) utilization and routinization of new technologies (in particular tandem mass spectrometry) for newborn screening; d) mechanisms for determination and reporting of positive results; e) ethical, social, and cultural concerns regarding the expansion; and f) influence of the American and/or European experience on the process of expansion. The questions were adjusted to the particular interviewees based on their involvement and/or role in the development and operation of the expanded program.

Sample Description

I conducted semi-structured in-depth interviews with public officials and clinicians, who were involved, are currently involved or will be involved in the process of expansion of newborn screening in Israel. Twenty interviews were conducted. Fourteen of the respondents reside and work in Israel, four are clinicians from the U.S., and two interviewees are public officials in Europeans newborn screening programs. In Israel, the
Interviewees included people in key positions at the newborn screening program and the Division of Community Genetics at the Israel Ministry of Health and Tel Hashomer Medical Center, people at the management level of the Ministry of Health, members of the Israeli Newborn Screening Advisory Committee, specialist physicians who were involved in the creation or implementation of the expanded newborn screening program, and other specialists who will play a role in the management of “screen positive” results and its dissemination to parents of newborns. International interviewees included Americans who either played a role in the initiation of the program, or served as consultants or advisors for the new program, or were involved in newborn screening in Israel prior to the process of expansion, and European officials at newborn screening programs which, based on the data gathered from key informants in Israel, served as a model for the developing Israeli newborn screening program. Two of the interviewees were females and 19 were males. Four interviewees were scientists (one of them Israelis, one American and two Europeans) and 17 were medical doctors. Of the fourteen Israeli interviewees three were located in peripheral hospitals and 11 at the center of the country.

To ensure appropriateness of sampling strategy, I used a snow ball sampling technique up to the point of theoretical saturation. I started by interviewing a small group of people affiliated with Israel’s Ministry of Health and newborn screening who have been actively involved in the initiation and implementation of the expanded newborn screening program in Israel. I used those respondents to identify other respondents who were involved in the formation or implementation of the program, or who may be responsible to the management of “screen positive” results and its dissemination to parents of detected newborns. Those interviewees were asked to identify more qualified
respondents. I stopped interviewing when I felt that new interviewees do not contribute substantially to the breadth or richness of my data. I reached the point of theoretical saturation of categories and interpretations after interviews. Achieving saturation at this point is supported by the literature ((Denzin and Lincoln 1998, Crabtree and Miller, 1999).

**Data Collection Procedure**

Several key informants were contacted in Israel and the U.S. The key informants are people in official positions in the Israeli and the U.S. newborn screening programs with whom I have established strong professional and social relationships throughout my previous work in the field. With all key informants I have had many informal discussions. In addition, I have performed at least one formal interview with each one. The interview guides were developed in English (*Appendix2*). For the Israeli interviewees, the final version of the interview guide was translated into Hebrew using a process of back translation. The interview guides for the American and European interviewees were left in English. Some of the questions addressed by a typical interview guide are described in

*Figure 3:*

*Figure 3: Sample Questions of an Interview Guide*

1. Which conditions/disorders will be included in the expanded panel on the first phase?
2. How were the conditions/disorders to be included in the panel chosen?
3. By whom were the conditions/disorders included in the panel chosen?
4. Do you agree with this process of expansion? Would you have done this differently?
5. What is your opinion regarding identifying and reporting secondary conditions?
6. What is the benefit to the baby, the family and society from newborn screening?
7. What is the impact of the American experience on the formation and implementation of the expanded panel?
8. What, in your opinion, are the challenges the expanded program is facing?
9. What, in your opinion, are the unique characteristics of the expanded newborn screening program in Israel?
10. Do you think the initiation and implementation of an expanded panel in Israel at this point is warranted?
the interviewee’s background, specialty, and/or the role he/she played or will play in the expanded newborn screening program.

Participant Observation

As a second method I used participant observation in the laboratory of the newborn screening program at Tel Hashomer Medical Center. At the laboratory I have observed how the expanded newborn screening program actually works “on the ground.” Throughout the observation I was particularly interested in addressing three questions: a) how do the newborn screening program’s officials and laboratory staff utilize advanced technologies (namely Victor, tandem mass spectrometry, and Autodelphia) for the purpose of screening for various conditions; b) the mechanism for setting cutoff levels for the conditions included in the expanded panel; c) how the newborn screening program’s officials and laboratory staff detect, determine and report to the medical home and to parents of newborns “screen positive” results. In this part of my work I was particularly interested in the steps undertaken once a positive result for either a primary or secondary condition (i.e., a condition that was not tested for deliberately) is detected by the tandem mass spectrometry. A primary condition is defined as a condition purposefully screened for by the program, whereas a secondary condition is defined as a condition with unknown or uncertain clinical significance.

Data Collection Procedure

Data collection for this section was based on a participant observation guide (Appendix3). Consent for the observation was obtained from the director of the newborn screening program at Tel Hashomer Medical Center in writing in May 2007. Before the initiation of the observation at the laboratory the director introduced me to the staff. I
have briefly explained my aims to the staff. While presenting the project to the staff, I made an effort to avoid disclosing information that might influence their actions and routines while the observation took place. I protected the privacy of the staff members by keeping my field notes anonymous. I have participated and observed the laboratory twice in September 2007. At this time, the upgrading of screening for PKU and Congenital Hypothyroidism had already taken place. However, the actual expanded panel, had not yet been implemented. Each time I spent between two to three hours at the lab. Questions addressed through participant observation are outlined below:

1. Who operates the tandem mass spectrometry machine? Is it always the same person or are there different technicians operating the machine?

2. If several people operate the tandem mass spectrometry machine, how do their techniques/customs differ?

3. How comfortable with the use of tandem mass spectrometry do the various operators of the machine seem?

4. Does the staff seem knowledgeable about tandem mass spectrometry? Are they familiar with its capabilities and limitations?

5. Where and what kind of tandem mass spectrometry training did the laboratory technicians receive?

6. What happens when a peak is detected for a certain condition?

7. How is a “screen positive” result for a primary and secondary condition determined?

8. How are peaks for conditions with uncertain/unknown clinical significance handled?
9. Who is reported about a screen positive for uncertain result or a result with unknown clinical significance? What kind of information does he/she receive?

10. How is the reporting of screen positive results for the various conditions being done?

Data Management

Each interview and each journal describing participant observation at the newborn screening laboratory were assigned a code number and the date and location of the observation, respectively, to ensure tracking and confidentiality. A separate list included the code numbers and full names of all interviewees. This list was kept in a locked file. The digitally recorded files were then transferred to a folder on my personal computer. This file was accessible only to me. The non-digital tapes were also kept in a locked file. Code numbers of the interviewees were used in the transcriptions for purposes of confidentiality. In the observation journals no identifiable information was used. The data was backed up daily and the password was protected. Data will be destroyed one year after the completion of the study.

Data Analysis

Data analysis for this project is exclusively qualitative. Data was analyzed in a circular manner, using the interpretive cycle. Data was described and organized using an editing approach. According to this approach, the creation of coding schemes starts after entering the data and before the end of all texts. In addition, emersion-crystalization approach which consists of coding at the end of the texts was used (Crabtree and Miller, 1998).

Analysis of In-depth Interviews
Interviews were recorded on high-quality digital tape recorders. Digital files were downloaded from the tape recorder to a notebook computer. The access to those files required my personal password. Interviews were transcribed from the tapes in the language they were performed (English or Hebrew). Interview data was entered into the computer using Atlas/ti, a software program for the coding and analysis of textual ethnographic and interview data.

In-depth interviews were coded and analyzed using the method of Grounded Theory with increased attention to the voice of the respondents, to achieve rigorous comprehension of their experiences. Interview transcripts were read several times and key phrases were underlined. Open coding was performed by reading through the interviews and identifying important and repeating themes. A code list was created using Atlas-ti. The interview coding guide is attached as Appendix6.

Coding categories emerged from the text and were linked into theories of the social construct of medical knowledge, routinization of new technologies, evidence based medicine, research paradigm for the introduction of technological advance, and finally, the unique social and cultural context in Israel and the influence of American and European experience on the creation and implementation of the Israeli newborn screening program. Code notes and theory notes were recorded to describe relationships among themes. Verbatim quotes from informants were used to exemplify the concepts and theories (Denzin and Lincoln, 2003).

The following is a sample of the major thematic codes that were developed for the in-depth interviews:

1. Decision/policy making issues
Against centralization of program
Ambiguity panel of conditions
Ambiguity reporting of results
Ambiguity of schedule
Mechanism for determination of conditions in panel
Pilot is unnecessary
Pilot testing was unethical
Pilot: reasons to stop
Reporting of results
The decision making process towards implementation
The role and consistency of the advisory committee

2. Criteria for screening

Criteria for screening: early and effective treatment, severity
Criteria for screening: specificity and sensitivity
Direct benefit to the baby
Benefit for society from screening
Benefit for the family from screening
Importance of quick and smooth diagnosis
No screening for non prevalent diseases
Prevalence is important to epidemiologists
Changes in criteria for screening: from treatment to counseling
Changes in criteria for screening: from prevalence to severity and psychological stress
3. **Ethical and Social Issues**

Informed consent - currently no requirement

Informed consent - need for informed consent

Informed consent - opting out

Informed consent - when should it be obtained?

Ministry of Health should make the decisions regarding informed consent and storage

Newborn screening improves equity

Public interest more important than the individual

Purpose of screening, diagnosis and treatment

Parental anxiety

Stigmatization of detected newborn

4. **The Context: Legal, Cultural, economical, and political issues**

Cultural aspects: awareness in prenatal vs. no interest in postnatal

Cultural aspects: setting up the booth and then deciding what to sell

Different panels to different populations

Legal aspect: the National Health Insurance Law, 1995

Need for collaboration and the politics of newborn screening

Need for consultants for the screening directorship

Need for expansion

Rarity of conditions leads to lack of budget for testing

Economical aspect, use of money for other purposes

No metabolic specialty in Israel
Comparison of newborn screening to vaccination

Temporality of program

5. **Education**

Education for professionals

International experience

Parental education is necessary

Parental education obtained gradually

6. **International Influence**

American influence

We should follow international experience

Working following international experience

7. **Uniqueness and Challenges of program**

Advantages of program

Avoid over treatment

Challenges of program: need for resources

Challenges: dealing with uncertainty by international experience

Disorganization of program

Feeling I am not included

Program challenges, unique characteristics

Resentment of interviewee

The challenge of adapting the screening to the state and data

The challenge of maximal treatment and minimal parental stress

The new system is healthier
Uncertainty of newborn screening results
Gaps between the center and periphery
Tailored to different regions/communities

For the entire coding guide developed for the in-depth interview analysis see Appendix6.

Analysis of Participant Observation

Field notes from participant observation at the newborn screening laboratory were taken (in Hebrew) and transcribed into computer files. The transcriptions were coded using Atlas/ti, software program for the coding and analysis of textual ethnographic and interview data. Data was coded and analyzed using the method of Grounded Theory as described above for in-depth interviews

Human Subject Protection

Written and oral informed consent was obtained from all interviewees. Prior to data collection, consent was obtained from the head of the program for the participant observation. All interviewees and observation participants’ were provided with a description of the study goals prior to data collection. All interviewees serve as public officials in Israel, U.S. or Europe. An application for human subject research was submitted to the Case IRB and an exemption was granted in June 2007. No risk of harm was associated with the in-depth interview or participant observation. Respondents’ privacy was respected by choosing an appropriate location for the interviews. Confidentiality of the data was protected by using number codes instead of full names of respondents in all files. All data, records, and audio-tapes were stored in a locked cabinet.
Description of Dissertation Chapters

This section briefly outlines the chapters that follow. Chapter Two presents the background for the dissertation project and includes a systemic review of the literature pertaining to the major developments of newborn screening and its impact on the current expansion of newborn screening panels. It describes the history of newborn screening programs in the U.S. and internationally and analyzes issues encountered in the evolution of newborn screening programs. Some of those issues are the criteria for inclusion of conditions in screening panels, informed consent for screening, and ethical issues related to detection and reporting of primary and secondary “screen positive” results to the medical home and to parents of newborns.

The 2005 report of the American College of Medical Genetics (ACMG) is a milestone in the development of expansion of newborn screening programs in the U.S. and internationally. The ACMG working group used a panel of experts and a survey to determine the criteria that should be used for selection of conditions to the screening panel and proposed a unique system of weighing the relative merits of different criteria. The authors concluded the report with a recommendation for 29 core conditions and 25 secondary conditions that should be included in the panel. The report and its impact on the expansion of newborn screening programs, both national and international, are analyzed in the background section. Next, the role emerging industries and advanced medical technologies play in the process of expansion of newborn screening are reviewed. The following section analyzes the impact of two stakeholders -- parents of sick children identified by newborn screening and advocacy groups -- in the expansion of newborn screening and the recent public conversation regarding a broadened notion of
benefit regarding newborn screening. A discussion of possible future developments in newborn screening concludes the background chapter.

Chapter Three reports the results from the policy analysis of newborn screening guidelines from their inception in the 1960’s through the present. Analysis of 24 documents was performed. The results summarize the name, authors and scope of the documents(table 1); criteria for disease selection (table 2); ethical, legal, and social considerations (table 3); program organization and daily functioning (table 4); program assessment (table 5), and research-related issues(table 6). All tables are in Appendix7. Guidelines are analyzed, compared, and discussed.

Chapter Four considers the evolution of expanded newborn screening program in Israel. This chapter includes an analysis of two brief periods of ethnographic observation at the newborn screening laboratory, as well as 19 interviews of program officials, non-program officials and international interviewees who were involved in some way in the evolution of the program.

Chapter Five examines the larger context within which the program is embedded and in particular the ethical, legal and social issues surrounding the expansion of newborn screening programs in Israel. This chapter discusses the ethical, legal, and social issues in the evolution of the expanded newborn screening program in Israel. Issues include the legal basis for the expansion; economical considerations; cultural, social and political context; technology and policy; the purpose of screening; informed consent, and the Euro-American influence on the expanded Israeli newborn screening program.

Chapter Six concludes the discussion by summarizing the unique challenges the expanded newborn screening program in Israel is facing. Concerns and issues associated
with the unclear policy regarding various programmatic aspects, the lack of evidence base for basic programmatic aspects and the invisible role of the community in the decision making process are discussed. This chapter also discusses the American influence on the program.

**Study Timeline**

**Months 1-3 (April-June 2007):** Study instruments were developed, pretested, and finalized. Interview guides and observation guide were created in English, translated to Hebrew, and back retranslated to English by an objective reviewer. In the first three months of the project lists of possible interviewees in Israel were obtained from the key informants. An application for human subject research was submitted to the Case Institutional Review Board.

**Months 4-7 (July-Oct 2007):** Participants’ enrollment and data collection in Israel continued. In-depth interviews and participant observation at the newborn screening lab in Israel were conducted.

**Months 7-9 (Oct-Dec 2007):** Participant enrollment and data collection in the U.S. was conducted. Writing of the dissertation manuscript started. Arrangements for professional transcriptions of audiotapes in Hebrew and English were made.

**Months 10-12 (Jan-March 2008):** Actual transcription was started. Coding guides for interviews and observation guiding questions were developed. Coding was conducted using **Atlas-ti** for qualitative analysis. Policy analysis and secondary analysis of laboratory practices survey started. Data collection (in Israel, Europe and U.S.) was completed at month 12. Actual coding of the transcribed interviews started at month 12. First draft of the first chapter was sent to the dissertation committee in February 2008.
Months 13-15 (April-June 2008): Analysis of in-depth interviews and participant observation started. Manuscript writing continued. Preliminary study results were presented at the ELSI meeting in Cleveland in April 2008. Following a meeting with the chair and co-chair of the dissertation committee in April 2008 the first chapter was revised and edited. The second draft of first chapter was sent to the dissertation committee in May 2008.

Months 16-19 (September 2008- January 2009): Data analysis and writing of manuscript continued in parallel. Data Analysis was completed in January 2009. Chapters were sent to the committee upon completion for review and comments. Partial results of policy analysis which were presented by Dr. Natowicz at the ELSI meeting in May 2008 were transcribed and published at the Health Matrix Journal.

Months 19-27 (January –June 2009): Dissertation manuscript was completed. Full manuscript will be submitted to the committee for review and comments at the end of this period. Defense is scheduled for June 2009. Following the defense, the manuscript will be revised and submitted to the School of Graduate Studies AT Case by late January.

Significance, Innovation, and Expectations of Study

The proposed study is significant because it sheds light on the social processes of the construction of medical knowledge and the routinization of a new technology within a society that is highly medicalized and technologically oriented. As will be discussed on chapter 2, in the Israeli society, genetic screening for reproductive purposes is widely accepted. At the same time, financial resources and genetic education of the public and health professionals, which both play a major role in newborn screening, are substantially limited. More specifically, the formation and implementation of an expanded newborn
screening program in Israel is important for several reasons. First, the study sheds light on challenges faced by many other newborn screening programs, including the decision making process regarding the selection of conditions to include in screening panels, the utilization of advanced technologies that require trained staff that are not always available, and the determination of screening cutoff values to fit the needs of diverse populations. Secondly, it opens a window to examine the opportunities and challenges arising throughout the integration of genetics services into a public health system -- integration which is becoming increasingly common as innovative technologies for genetic and metabolic testing and screening emerge and are being routinized into public health programs. Put differently, the newborn screening program in Israel can serve as a model system to study larger issues related to the emerging discipline of public health genomics. As such, it can inform improved policy making in these areas.

The study is particularly innovative in that it explores a developing process of formation and implementation of a new genetic screening program, while it is being integrated into the public health system. In other words, this study is novel in that it explores and analyzes the social, political, and cultural forces affecting the expanded newborn screening program in Israel, while the dynamic process of formation and implementation is actually taking place and modifications could be made. The main segment of the work empirically examines the process of a development of an expanded program in Israel. To support the analysis and interpretation of data, the study offers a comprehensive policy analysis of international newborn screening guidelines. The findings of this study yield new knowledge which contributes to the improvement of
policy in the Israeli newborn screening program as well as in other genetic screening settings.

In addition, the study examines the unique context of a newborn screening program under the auspice of a universal health care system. In this context, looking at mechanisms for the routinization of a new technology, the detection and reporting of positive results, and communication of those results to the medical home may significantly differ from analogous procedures performed in state newborn screening programs in the U.S. As the largest application of genetic testing being provided under the auspice of public health services, newborn screening programs could serve as a powerful model for the study of general questions in the cross roads of genetics, medicine, and public health. Throughout the evolution of newborn screening programs in the U.S. and internationally, experts in the field have emphasized how difficult it is to stop a mandatory screening program that is already up and running (Fost, 1992). Consequently, Fost argue that tests for certain conditions should not be introduced rapidly, before a well - designed study has been performed that clearly defines benefits and risks to the children. Since the publication of the American College of Medical Genetics report in 2005 and the implementation of its recommendations in many states in the U.S., geneticists and ethicists advocate proceeding to expanded panels with caution and only within a research paradigm (Botkin et. al, 2006). Following Botkin’s research paradigm and Fost’s concerns, in this study I intend to address the need for evidence-based policy making, rather than to advocate stopping the mandatory screening program in Israel that is already up and running.
Before I began my research, I anticipated that the form the expanded newborn screening program in Israel would take would be highly influenced by the American and European experience for several reasons. First, drawing on successful pre-existing models is presumably more cost effective and less time consuming than starting a screening program “from scratch.” As one of my key informants, who plays a major role in the establishment of the new program in Israel (interviewee #3) noted: “We are trying to take the best of all worlds and incorporate it into our program” (May 2007).

Secondly, U.S. public health officials and clinicians drove the initiation of the Israeli program to a great extent. Throughout the interviews with American public officials, they expressed their commitment to assist the new program in its early phase and in the future. In terms of program organization and functioning (including issues such as decision-making regarding the inclusion of conditions in the panel, the determination of cutoff values for screen positive results and reporting policies, etc.) data analysis showed that the design of the newborn screening program in Israel relies on U.S., UK, Swiss, and German models (interview with a program official, June 2007).

At the same time, I anticipated that the contemporary political, social, and economic reality in Israel, along with cultural and structural differences between the Israeli and Euro-American societies, would result in a different application of pre-existing models and the creation of new models for newborn screening. In particular, I believed that the existence of a universal health care system in Israel (including regional clinics providing nationally covered routine prenatal and postnatal care for all citizens) would result in the adoption of practices and procedures in the Israeli expanded program that are not similar
either to the U.S. model or to European ones. As will be discussed later, the findings of this study confirmed some of my expectations, but not all.

**Study Limitations**

This study is focused on the process of formation and implementation of a genetic screening program as part of the public health service in Israel. Since a major part of the research is based on an assessment of the policy-making process its findings may reflect on the professional performance of public health officials. Therefore, the concern of subject response bias due to the threatening nature of the questions is of importance. In addition, socially desirable expectations may evolve around issues related to decision making conducted by public health officials, and mechanisms used by laboratory staff for determination and reporting of screening results, in particular in regard to uncertain results or results of unknown clinical significance.

Testing effect poses another source of bias. That is, the reactions of respondents may change as a result of being interviewed, surveyed or observed. This concern is particularly important in this study, given that the expanded newborn screening program in Israel is still in its early phase, and also due to the uncertain nature of some of the screening results. Under these circumstances, public officials’ responses may not be fixed. Therefore, there is a special need for sensitivity when interviewing public officials and other specialist physicians about the development of professional routines and management of conflicts following the introduction of tandem mass spectrometry and other advanced technologies. To avoid subject response bias and testing effect, professional literature and key informants’ knowledge were used in order to learn more about the natural history of the genetic and metabolic conditions screened for in the
expanded panel, the routinization of advanced technologies and health policy-making, and strategies to approach public officials and other health care professionals regarding aspects of their profession without intimidating them. An effort was made to remain neutral with respondents about those topics.

Finally, the rarity of conditions detected by newborn screening and the fact that the expanded panel was not yet fully working at the time of data collection and analysis makes it difficult to observe the determination and reporting of positive and uncertain results at the newborn screening laboratory. The annual live births of babies in Israel is 139,535 (2002, Statistical Abstract of Israel, Central Bureau of Statistics). The approximate number of true positives for classic PKU is 12 per year (or 1 per month). In the past, the percentage of false positive PKU was around 5%. Since the recent change in technology (from the use of the qualitative Guthrie card method into a quantitative Victor kit) the positive rate is predicted to be 100 times lower. The approximate number of positive results for Congenital Hypothyroidism is 75-80 (consisting of 3% of all newborns). Considering the rarity of conditions combined with the fact that the expanded program did not actually start operating throughout data collection and analysis, many questions regarding the short- and long-term impact of the expanded newborn screening program remain to be answered.

As the expanded newborn screening panel becomes routinized, however, more opportunities for a retrospective study will evolve. In the near future, increased knowledge regarding the diseases screened for in newborn screening, along with the accumulation of experience concerning the utilization of new technologies, will hopefully yield more certain results and valuable data. When this happens, the issues discussed in
this study should be revisited and re-evaluated. Those issues include the criteria for inclusion of conditions in screening panels; the mechanisms for determination, detection, and reporting of “screen positive” results for primary and secondary conditions and conditions of uncertain or unknown clinical significance to the medical home; issues of informed consent for screening, privacy and confidentiality and other ethical and legal issues, and finally, research-related issues. The findings of this study can then serve as a baseline for a longitudinal large scale study looking at the integration of new genetic services into existing public health systems. The next chapter describes the methods used for data collection and interpretation, and other aspects of study design.
Chapter 2: Background and Literature Review

Introduction

Studying the dynamics of newborn screening in Israel requires two important sets of background knowledge: a familiarity with the history of newborn screening programs in the U.S. and a familiarity with several features of Israel’s health care culture. The former is important because it provided, at least in part, the model Israeli policy-makers looked to as they developed their own program. The latter is important because factors particular to the delivery of health care in Israel were key considerations in that development. This chapter reviews both of these starting points. It starts with a historical overview of the development of state-run newborn screening programs in the U.S. to identify and treat infants with PKU since their introduction in the early 1960s, through the present process of global expansion of newborn screening programs. Then, it examines the evidence base required for inclusion of conditions in the screening panel and the role emerging technologies play in the process of expansion. The next section analyzes the ethical, legal, and social issues around the expansion of newborn screening. I conclude this chapter by presenting the current situation in Israel regarding the use of advanced technologies for medical practice, the health care reform that took place in the last decade, and the socio-cultural aspects of genetic screening and in particular, prenatal diagnosis. I argue that the practice of prenatal diagnosis in Israel is similar in many ways to the socio-cultural perspective of newborn screening. However, unlike newborn screening, prenatal screening is characterized by a long-lasting acceptance and popularity in Israel, and therefore serves as a particularly valuable point of comparison.
The critical review and analysis of background literature in this chapter rely to a large extent on the conceptual framework discussed in chapter 1, and in particular on the social construction of medical knowledge, models of medicalization and biomedicalization, and the technological imperative in routinization of new technologies. In addition, I consider newborn screening in light of the overarching quest for a “perfect baby” in the Israeli society.

The questions addressed by the literature review are: What were the circumstances that led to the first introduction of newborn screening in Massachusetts in the early 1960s and to its expansion to other regions, states and countries throughout the years? How did newborn screening programs across the board change since they were first introduced? What are the factors influencing the development of newborn screening programs in different times? What are the social and ethical implications of the adoption and routinization of tandem mass spectrometry by newborn screening programs?

Data Collection Procedure

Throughout the years 2003-2008 I have collected numerous articles discussing the history of newborn screening in general and ethical, legal, and social issues in the expansion of newborn screening in particular. For the search, PubMed Central data base was reviewed using the following key words: newborn screening, neonatal screening, genetic screening, prenatal screening, expansion, policy, decision making, social, ethical, and Israel. Articles on newborn screening evolution and expansion were also accessed by searching the databases www.humgen.umontreal.ca, www.nice.org.uk, www.nsc.nhs.uk and www.consensus.nih.gov, www.ahrq.gov, and www1.umn.edu/humanrts/. Relevant citations from articles found through those databases were identified and discussed too.
The social science databases ISI Web of Knowledge and JSTOR was reviewed using the key words: innovative, medical technology/ies, medical knowledge, diffusion, routinization, technological imperative, social construction, medicalization, and Israel. In addition, several book chapters discussing the evolution of newborn screening from its very early days until the present were used. In particular, the focus was on literature discussing ethical, legal, and social issues in the evolution of newborn screening programs. Literature revealing other relevant aspects in the development of newborn screening such as social and ethical issues in the introduction and routinization of new technologies for genetic testing and screening was included in the review. Literature discussing the social context of newborn screening in Israel was reviewed as well. Finally, professional literature concerning the diseases currently screened for by newborn screening panels and/or conditions that are being evaluated for possible inclusion in screening panels was also used and referenced.

History and Controversy in the Development of Newborn Screening Programs

The use of newborn screening as a population-based public health service was first demonstrated in Massachusetts in 1962 in statewide screening for phenylketonuria (PKU) (Guthrie, 1963; Guthrie, 1992). PKU was discovered in 1934 by the Norwegian Dr. Asbjörn Fölling. It is a metabolic disease resulting from a defect in the enzyme phenylalanine hydroxylase. The malfunctioning enzyme creates a failure to convert the amino acid phenylalanine to the amino acid tyrosine, thus elevating serum phenylalanine up to toxic levels that cause severe mental retardation. It is considered an inborn error of metabolism manifesting an ‘unsimple’ phenotype in patients (Scrivcr. 2001). Maternal PKU is a teratogenic syndrome affecting the fetal brain, fetal growth, and cardiac
development (Levy, 2003). The incidence of PKU is 1 in 10–20,000 births. A special “mind–saving” diet was developed in the 1950s (Centerwall et. al, 2000). Newborn screening for PKU by a bacterial inhibition assay was first introduced by Robert Guthrie, who is acknowledged as the father of newborn screening, (Pass, 2000). The rationale for screening of PKU was clear. With dietary treatment starting in early infancy babies affected with PKU grow up to be normally functioning adults, rather than having severe retardation (Alexander, 2003). Recent literature (Pass, 2000) suggests that Guthrie’s decision to focus his efforts on PKU turned out to be a fortuitous rather than calculated. The high incidence of PKU, along with the fact that its major (classic) form is detected easily by an inexpensive, reliable, and an easy-to-perform test that Guthrie was already familiar with from his past cancer work enabled him to establish newborn screening.

Today, the incidence of 1:16,000 births, results in approximately 250 children with PKU each year in the United States alone. Nevertheless, in the newborn screening community there is a claim that the history of PKU screening is not an unqualified success story (Gross et. al 2001; Lindee, 2005, Steiner, 2005). Rather, those scholars argue, its negative impact is twofold. First, it exemplifies decision making based on evidence that is insufficient to prove that the benefit from screening outweighs harm. Next, it does not address how the medical knowledge obtained by screening will be used to improve health. As Diane Paul notes in her “double-edged sword” published in “Nature” on 2000: “PKU has become an exemplar for the promise of genetic medicine....but the history of PKU also provokes skepticism about simple scientific fixes. ‘Solving’ the initial problem created the new one of maternal PKU. Moreover, for men and women, coping with PKU has turned out to be a lifelong effort, requiring substantial

The second phase of the development of newborn screening programs started in the mid-1970s and continued through the early 1990s (McCabe, 2002). As pointed out earlier, throughout this phase, the screening panel in most states was extended to include not only PKU but a number of other genetic and metabolic disorders. The second disorder added to the screening panel following PKU is Congenital Hypothyroidism. This condition is now being screened for by the vast majority of newborn screening programs around the world (Daussalt, 2008). Congenital Hypothyroidism causes mental retardation in infants due to a congenital malfunctioning or absent thyroid gland or a genetic metabolic block in thyroid hormone production. The thyroid hormone of the mother allows the fetus to develop normally in utero, but deficient levels of thyroid hormone after birth result in slowed growth, especially of the brain. By the time the condition is detected at 3–6 months of age, the damage to the brain is irreversible in most cases. In the mid-1970s the Canadian Harvey Guyda demonstrated that congenital hypothyroidism could be detected by mass screening and if started by two weeks of age, treatment could prevent mental retardation (Dussault et al., 1975). As of today, in Quebec, Canada it is estimated that one million newborns are tested yearly and 2800 detected. The anecdotal history of screening for congenital hypothyroidism since then has led the American Office of Technology Assessment to conclude that screening for congenital hypothyroidism is one of the few programs in preventive medicine that has an impact on public health with a positive cost to benefit ratio (Daussalt, 2008). In Israel, screening for Congenital Hypothyroidism began in the 1970’s (Sack, 1985; Sack, 1998) when Israel
became the second nation to begin a screening program for this condition (Anikster, 2006). In the four decades that passed since their introduction, state newborn screening programs for PKU and Congenital Hypothyroidism have prevented intellectual disability in thousands of children (Alexander, 1998). The process of expansion of newborn screening during this second period occurred differently for each program. While some programs used expert advisory committees to consider the addition of more disorders based on scientific criteria, other programs experienced a political process led by government officials and influential citizens (McCabe et al., 2002).

In the early 1980’s the introduction of tandem mass spectrometry dramatically changed newborn screening. The innovative device made it possible to perform genetic screening for many conditions on a single blood specimen relatively quickly and at a reasonable cost. In 1990 a group of laboratory medicine specialists proposed to use this technology in newborn screening. By the mid-1990’s it was possible to screen for amino acid, organic acid, and fatty acid disorders, all with the same procedure (Arn, 2007).

Some of the conditions screened for in expanded newborn screening panels (for example, Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) can only be detected by advanced multiplex technologies, mainly tandem mass spectrometry. Other conditions, such as Phenylketonuria (PKU), can be detected either by tandem mass spectrometry or by the traditional Guthrie test. In the past few years, most states and countries have chosen to use the advanced technology rather than the traditional Guthrie test for PKU if they can afford to do so. Levy (1998) argues that tandem mass spectrometry is the most important development in newborn screening since the addition of screening for congenital hypothyroidism in the mid-1970s, because it expands significantly the
disorders screened for by newborn screening and most importantly, because it reduces the rate of false positive results, which are both costly and elevate the anxiety level among parents of screened individuals. The growing utilization of tandem mass spectrometry among newborn screening program directors is attributed to its ability to identify and significantly decrease the number of false positive results that occur by screening with other technologies, despite the increased number of disorders that are detected by tandem mass spectrometry and in a shorter period of time (Chace et. al, 1998; Abdenur, 1998; Levy, 2000, Banta-Wright, 2004; Lacey et. al, 2004; Feuchtbaum and Lorey et. al, 2006).

With the introduction of tandem mass spectrometry morbidity and mortality of affected babies have substantially decreased (Wilcken, 2007). Given the capabilities of tandem mass spectrometry to detect multiple disorders it is not surprising that hand in hand with its introduction to newborn screening programs, the panel of conditions in the vast majority of U.S. states has expanded significantly. In the decade between 1995 and 2005 one state mandated 5 disorders, another state decreased the number of conditions screened for on its panel, and two states neither added nor decreased disorders on their panel. On average, however, states added 19 conditions to their screening panels (Tarini et. al, 2006). In the clinical genetics community many anticipate that in the near future, the number of genetic and metabolic conditions detectable through advanced technologies will increase further and support this development (Howell, 2006; Green et. al, 2007). In order to keep control over the process of expansion, recent measures for evaluation of programs have already been applied to ensure program improvement in the U.S. (Therell, 2006).
The routinization of this technology, however, raises issues of cost-effectiveness (Cipriano et. al, 2007). In specific, the cost of screening and diagnosis, the development of appropriate analyte cut-offs, high costs of equipment and supplies, and accepted protocols and guidelines for diagnostic work up have been up by newborn screening program coordinators as the most challenging issues (Feuchtbaum et. al, 2006). As a consequence, not all U.S. states have integrated tandem mass spectrometry into their newborn screening program. Ethical issues have also been raised by the inclusion in the panel of disorders so rare that their natural history is unknown or clinical outcomes are uncertain (Watson, 2006; Green et. al, 2006). In addition, the technological imperative, or in other words, the urge to offer a technology routinely just because it is available (Grody, 2007), is a major dilemma presented by the introduction of tandem mass spectrometry. Burke suggests that the first step in the analysis of the ethical, legal, and social issues of new genetic tests should be the consideration of what is known about two characteristics of the test: its clinical validity and the effectiveness of the interventions for people detected as positive for the disease (Burke et. al, 2006). The key role that the purchase of the tandem mass spectrometry device played in the decision to expand the newborn screening panel in the Israeli program and its ethical and societal implications are discussed at the end of this chapter and in chapter 4.

One particularly important feature of the debate over expansion of newborn screening using tandem mass spectrometry is the decision regarding which conditions should be included in the screening panel. The Newborn Screening Task Force report (2000), along with other reports, a (Pass et. al, 2006) recommended that pilot studies should be conducted to demonstrate the safety, effectiveness, validity and clinical utility
of tests for additional conditions and new testing modalities. The pilot testing that was conducted using Israeli blood samples in 2005 will be discussed in chapter 4. Some scholars suggest less categorical decision tools other than the classical criterion of proven medical treatment to reduce morbidity and mortality (Poliott, 2006, Bailey, 2004). In the past decade, the different approaches regarding the criteria for selection of conditions to the screening panel and the activity of advocacy groups lobbying for the expansion of the screening panel have led different states and countries to select different conditions for the newborn screening panel (Green et. al, 2004; Pollitt, 2007, American Academy of Pediatrics, newborn screening task force, 2000; U. S. General Accounting Office, 2003) This variability has led to growing disparities across different state newborn screening programs for disorders being screened for by tandem mass spectrometry, and confusion regarding whether or not asymptomatic newborns detected by tandem mass spectrometry, would actually become symptomatic if screening had not been conducted (Garg et. al, 2006, Wilcken et. al, 2003, Alexander et. al, 2006).

In addition to the diversity of screening panels, programs developed different algorithms and cut-off levels for testing of conditions in the screening panel. The algorithms used for the disorders included in the panel were based on specific mutations and gestational age at birth (Lott, 2004). Those methodologies have been useful but not free of shortcomings. For example, in one program using multiple CFTR mutation testing for detection of cystic fibrosis, sensitivity was improved, but the number of false positives increased, resulting in increased referrals and carrier identification (Comeau et al., 2004, Lott et. al, 2004). The determination of cut-off levels for screened conditions is significant as it allows for certain levels of analytes to be considered screen positive in
one state and screen negative in another. The difference in cut-off levels among programs is, therefore, a variation on the debate over inclusion of conditions in the screening panel.

In regard to the institutional home of newborn screening, or more specifically the provision of newborn screening as a public health service, scholars in the field of medical genetics are divided into two camps. The first camp considers newborn screening one of the most successful public health measures introduced in recent times (Green et. al, 2006, Marsden, 2006). This group of researchers favors the current structure according to which newborn screening programs are provided under the umbrella of public health services, as they believe it ensures safety and effectiveness of screening (Levy et. al, 2000; Howse et. al, 2006; Holtzman, 2006) or as Pass notes “It takes a system to help a child” (Pass, 2000:390). In practice, newborn screening for at least one to two conditions is performed through state public health programs in the U.S. (Newborn Screening Task Force Report, 2000).

The second group is concerned about the lack of clear distinction between research and a public health service; they advocate resolving it before establishing an expanded panel of conditions (Dhondt, 2007). For example, Botkin argues that the state-level organization of newborn screening services is “an accident of history but should not be a barrier to evidence base analyses of the benefits and risks of these complex programs” (Botkin, 2005:870). Botkin advocates for evaluation of newborn screening applications prior to their implementation as a public health measure, using a structured sequence of research protocols (Botkin, 2006). Others in this camp discuss the need for more research to build evidence-based recommendations regarding the best approach to educate and counsel parents about the newborn screening process (Tluczek, 2005; Hoff, 2005;
Kenner, 2005; American Academy of Pediatrics Committee on Bioethics, 2001; Sewell, 2004). Similarly, the argument goes, programs should offer screening on a voluntary basis after the newborn period for conditions that do not meet the Wilson and Jungner criteria (Ross, 2006). Yet others in the newborn screening community call for making newborn screening programs a joint responsibility of federal agencies and state government (Cunningham, 2002; Moyer et. al, 2008; Simopoulos, 2009).

The history of PKU screening demonstrates how public health services became the natural home of newborn screening programs and as such contributes to the debate over the institutional home of current expanded newborn screening programs. In the case of PKU, over 170 possible mutations were identified through newborn screening, leading to the discovery that each defect in the phenylalanine pathway leads to a different clinical and biochemical phenotype (Brosco, 2006). Consequently, the implementation of mass screening was necessary in order to learn about the complex metabolism of Phenylalanine (Brosco, 2008). This scenario is likely to repeat itself in the case of most candidate conditions for expanded newborn screening.

**Recent Newborn Screening Debates**

In response to the diversity of newborn screening panels within the U.S. and internationally, the American College of Medical Genetics (ACMG) published a report in September 2005 in which it recommends a standardized uniform screening panel of 29 core conditions. In addition, the report recommends inclusion in the screening panel of 23 additional secondary target conditions detectable by tandem mass spectrometry (American College of Medical Genetics Report, 2005). The report distinguishes between three groups of conditions: 1) the core panel; 2) secondary targets, or conditions that are
part of the differential diagnosis of a core panel condition); and 3) conditions not appropriate for newborn screening (either because no newborn screening test is available or because there is poor performance with regard to multiple other evaluation criteria).

The American College of Medical Genetics suggested the following: mandate screening for all (29) core panel conditions defined by the report; mandate reporting of all (25) secondary target conditions defined in the report and reporting of any abnormal results that may be associated with clinically significant conditions, including the definitive identification of carrier status; maximize the use of multiplex technologies; and consider that the range of benefits realized by newborn screening includes treatments that go beyond an infant’s mortality and morbidity (American College of Medical Genetics report, executive summary). Shortly after the publication of the American College of Medical Genetics report, a nomenclature system was proposed to remove ambiguity and increase national uniformity in naming and counting disorders (Sweetman et. al, 2006).

The ACMG report sparked a heated debate in the medical genetics community in the U.S. and internationally. Opponents questioned the credibility and validity of its empirical basis and methodology, since the natural history and epidemiology of many of the primary and secondary conditions it recommends including in the panel are not well understood. In regard to metabolic disorders in particular, there is considerable heterogeneity of clinical presentations. This makes the prognosis of the various mutations more complicated and raises concerns about the effectiveness, desired design, and ethical conduct of expanded panels that are already operating in U.S. programs (Holtzman, 2003, Natowicz, 2005, Botkin et. al, 2006). (For a comprehensive analysis and discussion of the
criteria for inclusion of conditions in the screening panel following the American College of Medical Genetics report and other policy guidelines see Chapter 4).

The requirement for a strong evidence base to support various aspects of the newborn screening program has been discussed extensively in the newborn screening literature, and more so following the publication of the American College of Medical Genetics report (Waisbren, 2006). In a leading article Botkin et al. (Botkin et al. 2006) recommend that research protocols should be regional or national in scope in order to ensure uniformity, standardization of research protocols, and efficient long term follow up. Botkin 2006), Natowicz (2005) and Grosse (2006) emphasize the importance of a strong evidence base to justify the disorders selected for screening. Among the questions Botkin and his group recommend to use in newborn screening research are the following:

1. How should technology be evaluated from a public health and community perspective and how should this evaluation affect the expansion or contraction of conditions in the panel?

2. What is the responsibility of the program to disclose results for conditions that do not meet the established criteria for screening?

3. What is the responsibility of the program to disclose results of uncertain clinical significance?

4. What are the roles of the medical home and newborn screening program in managing the disclosure of results for secondary conditions and conditions of unknown clinical significance to parents of newborns?

In addition, other commentators argue the evidence base should encompass the effectiveness of screening (Moyer, 2008). In addition, fair distribution of costs and
benefits of screening of the program and uniformity in the access to follow-up and treatment are imperative (Hoff, 2007). Others focus on issues of consent for screening. Abbing (2004) argues that if benefit for the baby is essential, the program should respect human rights by ensuring that newborn screening is mandatory. However, if the benefit for the newborn is uncertain, the program should require informed consent. Similarly, newborn screening programs must clarify issues of consent for use of bloodspots for future research, whether related to newborn screening or not (Atkins et. al, 2005; Grosse, 2007; Baily et. al, 2008). Others claim that new screening programs should only be introduced on a national basis, in order to allow review of evidence against explicit criteria and ensure that benefits outweigh harms (Elliman et. al, 2002).

Tarini et. al (2008) argue that pilot testing of new conditions should be eligible for a waiver of consent under current federal regulations. Ross (2008) argues that if screening panels are expanded to include screening for diseases such as Duchene Muscular Dystrophy that do not meet the Wilson and Jungner criteria, such screening should be voluntary (Ross, 2006). Other scholars advocate a separate screening system in regard to carrier screening for diseases such as diabetes, since the level of knowledge regarding its pathogenesis, harms and benefits, and costs is insufficient to allow appropriate facilitation of it within the existing newborn screening infrastructure (Kerruish et. al, 2005). Similarly, Bailey and his group argue that the question of expansion of screening for untreatable conditions and disclosure of carrier status (such as for Fragile X) necessitates studying the informed consent process (Bailey et al. 2008). Finally, ethicists and experts in the field alike argue that even successful state-run newborn screening programs should be expanded with caution (Natowicz et. al, 1991, Clayton, 1999, Pass,
In this dissertation work, the evidence base required by international policy documents in order to justify inclusion of conditions in newborn screening panels and other programmatic aspects are analyzed in chapter 3. The evidence base that led to the decision to expand the Israeli newborn screening program and the required evidence to justify selection of certain conditions to the screening panel, as well as other aspects of the program are investigated in chapter 4. The benefit from screening to the baby, family, and society is of major importance and relevance to the discussion regarding expansion of newborn screening programs and it is closely tied to the issue of consent for screening. The next sections discuss those issues.

**Benefit to the Baby, Family, and Society from Screening**

Some critics argue that the early history of newborn screening for PKU in the early 1960s resulted in widespread harm for healthy children who were falsely identified as affected (Fost, 1992; Botkin et al, 2006). Comprehensive literature search and oral-history interviews, however, showed no evidence for harm ensuing from medical treatment provided to children with false positive newborn screening test results for various conditions including PKU, Congenital Hypothyroidism and other conditions, (Brosco et. al, 2006) although data revealed that experts in PKU confronted many problems in the first decade of newborn screening programs (Brosco, 2008). Whichever position one takes in this controversy, in those early days of screening the focus of benefit was clearly the screened newborn.

Following the publication of the American College of Medical Genetics report in 2005, a major topic on the public radar of newborn screening has been the changing perspectives on the benefit of newborn screening to include not only medical treatment
that results in improved physical health of the baby, but also perceived benefits for the family and society, such as genetic counseling and testing of other family members and prenatal diagnosis (Bailey et al., 2006). The vast majority of proponents of further expansion of newborn screening justify it if there is evidence for reduction of mortality and morbidity or other benefit to the child from screening (Marsden et al., 2006; Vockley, 2007; Lin et al., 2008; Rinaldo et al., 2008). Others call for a conservative approach to intervention to avoid unnecessary treatment or ‘medicalization’ of individuals with no significant disease (Wilcken, 2008). Ross argues that pediatric genetic testing and screening forces us to look into the psychosocial, clinical and reproductive implications of genetic information for the child and the family, the environmental effect on genotype-phenotype correlations, and finally the meaning of genetic susceptibility (Ross, 2008). Pass argues that “when newborn screening programs attempt to expand their activities beyond the immediate care of the newborn and mother, oftentimes the program becomes muddled and ineffective” (Pass, 2000:396).

In a controversial article, Alexander and Van Dyck question the tenet of effective treatment to the child as the only justification for screening. In their view, this approach was appropriate in the early years of newborn screening, but now is the time for “changing the dogma.” The authors criticize the old dogma for failing to take into account other benefits of early diagnosis and for enforcing continued ignorance and unavailability of treatment, because preventive interventions cannot be applied after symptoms appear (Alexander et al., 2006). Yet others go even further to justify the inclusion of conditions in the panel even if there is no direct benefit for the baby from
screening, by arguing that there is sufficient benefit for the family in simply making an early diagnosis and thereby avoiding a lengthy diagnostic odyssey (Howell, 2006).

Finally, harms to the baby and family from screening are commonly associated with the advanced technology used by public health services for genetic screening. In particular, the tandem mass spectrometry device allows the detection of metabolic variation, including potentially asymptomatic conditions (such as MCADD), thus raising a controversy regarding its inclusion in the panel (Stadler, 2006). Incidental findings could create unwarranted anxiety in parents and health care professionals (Khoury, 2003). Other possible harms associated with newborn screening include parental emotional stress while waiting for the IRT repeat test results for CF (Moran et. al, 2007) or following the reception of false positive results (Gurian et. al, 2006, Hewlett et. al, 2006). In chapters 3 and 5, I analyze both international policy guidelines and the perspectives expressed by officials involved in the expanded Israeli newborn screening program in regard to the existing and warranted benefits from screening and their concerns about possible harms.

**Dealing with Uncertainty**

As noted earlier, as a result of the rarity of conditions screened for by newborn screening, the natural history and epidemiology of some of the conditions selected for expanded panels, including intervention or treatment alternatives, is uncertain or in some cases even unknown (Natowicz, 2005; Brosco, 2008). The limited understanding of the natural history of many of the conditions leaves a gap in knowledge regarding the benefits and harms of screening for the baby, the family and society at large. In addition,
uncertainty surrounds the practices for determination of cutoff values and reporting of screen positive results for the various detectable conditions, as discussed in chapter 4.

The importance of genetic counseling in reducing uncertainty of genetic testing has been demonstrated in other genetic testing programs (Baty et. al, 2006). Like newborn screening, prenatal testing can also result in uncertain and troubling screening results. Two ethical traditions inform the practice of prenatal diagnosis: the therapeutic imperative of clinical medicine, which would limit the diagnosed conditions based on the welfare of the fetus, and that of genetic counseling, which emphasizes the use of counseling to enhance parental autonomy in reproductive and therapeutic decision making (Juengst, 1998). Juengst has suggested practitioners involved in prenatal diagnosis cope with the inherent uncertainty of screening results by improving the fit between these two approaches. Theoretically, the same rationale could be used as a mechanism for handling the uncertainty of newborn screening results. In reality, however, and despite the genuine intentions of health care professionals, newborn screening education and counseling services are far from satisfying parents’ needs. As a response parents rely on the physician to provide them with guidance. For example, physicians’ approach influenced parents’ emotional distress while waiting to get the results of their newborn’s sweat test, a test used to confirm a diagnosis of cystic fibrosis (Tluczek et. al, 2005).

The authors of the American College of Medical Genetics report suggest that the gap in knowledge regarding under-investigated conditions should be further explored, in order to reach an evidence-based model for an expanded newborn screening panel. Lack of clarity surrounds other aspects of NBS programs. Even if an agreement about clear
criteria for inclusion of conditions in the expanded panel exists, the system within which
the criteria are used is not as clear (Watson, 2006). Collecting and disseminating data
about the clinical and psychosocial impact of screening from different newborn screening
programs may assist to improve future policy decisions (Wilfond, 2005). Whichever is
the best protocol for detection of a given disease, the efforts to determine when genetic
tests are reliable enough to be used for routine clinical use could not be undermined
(Clayton, 2003).

On a more positive note, Whitmarsh suggested that while parents see the biological
and genetic aspects of certain genetic syndromes as stable and permanent, they in fact
embrace and value the uncertainty about the condition by focusing on the individuality of
their own child and her special characteristics, as well as the variation between siblings
diagnosed with the conditions (Whitmarsh et. al, 2007). The uncertainty, it seems, allows
parents to keep hoping that their children might do better than might otherwise be
expected. In chapter 5, respondents’ views and attitudes regarding three issues
surrounding the uncertainty of screening results are discussed: a.) determination,
detection, and reporting of newborn screening results, b.) the official policy of the Israeli
program regarding those procedures, and c.) the challenges stemming from the inherent
complexity in handling uncertain results.

Informed Consent for Newborn Screening

Addressing the imperative issue of informed consent for screening becomes critical
with the expansion of the panel to include more conditions, including “untreatable”
conditions for which the benefit from screening is uncertain, as well as cases in which
there is a risk for inadvertent disclosure of carrier status. In those instances, parental
informed decisions are a central issue (Baily et. al, 2008; Bailey et. al, 2008). It has been argued that although parental refusal for newborn screening may be morally unjustified, the right to legal noninterference may be stronger (Newson, 2006). Tarini et. al, (2008) suggest that waiving informed consent for population-based newborn screening research is justified when there is a clinically well-defined test and an effective therapy, as waiving informed consent facilitates the development of flexible strategies for informing and educating parents about newborn screening research. These strategies are commensurate with the goals of population-based newborn screening.

However, Diane Paul argues that the mistake of waiving consent for PKU testing should not be repeated with other conditions (Paul, 1999). Consent for expanded newborn screening was a hotly debated issue in the past decade. In 2001, the American Academy of Pediatrics recommended that states evaluate an informed consent process for the newborn screening tests to foster parental education and promote informed response to test results. The American Academy of Pediatrics stated that there is no need for a signed consent form for tests with established value, but required parents be provided with basic information on the purpose of screening and emphasized the importance of a timely response to abnormal results (the American Academy of Pediatrics, 2003). In 2002, an empirical study revealed that in most U.S. programs (thirty-eight out of fifty-one) parents were notified but not asked to give consent for collection of the sample for mandatory testing. Ten states neither notify parents nor ask for consent, and only three states require parental signed consent. In two states parental refusal is not permitted but in twenty-seven out of fifty-seven states refusal based on religious reasons is permitted. Verbal refusal for religious reasons is permitted in five states and for any
reason in one state. In fifteen states parents must sign a waiver refusing screening (Mandl et. al, 2002).

A recent legal suit portrays the problematic issue of parental refusal for newborn screening based on religious convictions. In 2007, in the state of Nebraska, the Ayanas refused to test their son for newborn screening disorders. The Anayas claimed that the relevant newborn screening statutes Neb. Rev. Stat. §§ 71-519 to 71-524 (Supp. 2007), violate the free exercise of religion provisions found at article I, § 4, of the Nebraska Constitution and that the separate juvenile court of Douglas County erred in ordering that their son, Joel Anaya, be tested following those statutes and remain in the custody of the State of Nebraska while awaiting the results of the testing. The appeal court concluded that the screening statutes were constitutional, and that due to insufficient proof, the separate juvenile court did not have jurisdiction under Neb. Rev. Stat. § 43-247(3)(a) (Cum. Supp. 2006) and its orders were a nullity. However, because the appeal court concluded that the instant appeal is moot it dismissed the present appeal.

In contrast to all other ethical issues, the required level of parental consent for screening emerged as a major topic of concern in interviews conducted with newborn screening program officials in this study as discussed in chapter 5. At the same time, in the international arena, not all policy guidelines emphasized either the need to obtain parental consent or the appropriate form it should take (see chapter 3).

**Newborn Screening Education**

Among the very few topics of agreement in newborn screening policy is the need for newborn screening education for parents and health care professionals. What do parents know about the conditions included in the panel and the process of newborn screening?
When is the optimal period of time for provision of newborn screening education to parents and health care providers? In 2003, the Committee on Genetics of the American College of Gynecologist and Obstetricians recommended the provision of counseling about newborn screening by obstetricians (Committee on Genetics of the American College of Gynecologist and Obstetricians, 2003). The endorsement was welcomed by many ethicists, in particular in regard to the expanded screening panel. At the same time the limited practicality of the recommendation, given obstetricians’ other responsibilities, was acknowledged (Clayton, 2005). Empirical data regarding parents’ attitudes towards the best time to be informed about newborn screening and its expansion provided support for the American College of Gynecologist and Obstetricians’ recommendation (Parsons et. al, 2006). Data revealed that parents would prefer to be informed about newborn screening during pregnancy and would like to have an opt-out option, when screening for the specific disorder is performed for the purpose of prevention of irreversible harm (Detmar et. al, 2007). User-friendly materials are needed for the provision of effective education (Almond et. al, 2006).

Researchers in the field agree upon the importance of the provision of clinical genetic services to parents of newborns identified by newborn screening, in order to avoid the negative effects, and in particular parental anxiety, associated with screen positive results (Politt, 2004; Sawyer, 2004; Weisbren, 2004; Kaye et. al, 2007; Bailey et. al, 2008). The other group that should receive newborn screening education is health care professionals. Here, too, ethicists are in agreement that practicing physicians should understand the benefits and limitation of expanded newborn screening, and have clinical knowledge regarding the conditions screened for as well as communication skills.
(Kenner et. al, 2005, Thompson et. al, 2005, Longo, 2006). Researchers disagree about pediatricians’ comprehension of the process of newborn screening. While some argue that pediatricians are not ready to handle expanded newborn screening (Gennaccaro et. al, 2005), others claim that pediatricians recognize its benefits, believe that they play an essential role in delivery of results, and emphasize the importance of communication of results from the newborn screening lab to the medical home in a timely manner (Desposito et. al, 2001). Chapter 4 provides international perspective on the requirements regarding the education of parents and health professionals; chapter 5 discusses the views of interview respondents regarding education of parents of newborns screened for by the Israeli program.

The Adoption of New Medical Technologies in Israel

The main focus of this study is the ethical and social dimensions of the development of the Israeli newborn screening program. Therefore, the background analysis would not be complete without a review of the literature relevant to the socio-cultural context of newborn screening in Israel. The literature discussed in the following section is centered on two major issues: attitudes of stakeholders towards the introduction of innovative medical technologies and the culture of genetic screening in Israel.

In regard to attitudes towards the introduction of medical technology in Israel, empirical studies Greenberg et. al (2003, 2005) have discussed the need for the development of criteria for assessment and adoption of new technology by hospital decision-makers in Israel. Although the newborn screening program in Israel is a national one, it is centralized and located physically in one hospital which also owns the tandem mass spectrometry device (Tel Hashomer Sheba Medical Center). Therefore, the data
presented by Greenberg is of particular relevance. In Israeli hospitals, the study shows, the most frequent listed consideration in favor of adopting a new technology was increasing the cost effectiveness compared with another technology, increased efficacy, and potential for reduction of complication rates. The general public influence on the decision making process was negligent. In terms of the initiative to introduce and support the use of a new device, the medical director is the most important player while in some hospitals ad hoc committees are responsible for the decision making process. The committees consist of medical directors, senior physicians, administrative and financial directors and representatives from other disciplines. In regard to the sources of information used for the decision making process, the three main sources were recommendations of local experts in the specific medical field, participation in scientific conference and meetings, and leading professional journals. Finally, the main barriers to making optimal adoption decisions were the lack of timely information regarding safety, cost effectiveness, and clinical efficacy. Data analysis of the present study strengthens those findings, as discussed in chapter 4. For example, one of the main themes emerging from the interview analysis was the dissatisfaction of interviewees with the decision making - process regarding the introduction of the tandem mass spectrometry device and the implementation of the expanded panel of conditions.

Israel’s National Insurance Law and the Health Basket Committee

Israel’s National Health Insurance Law, which came into effect in 1995, is a major health care reform. The law made health insurance compulsory for all Israeli residents by means of one of four existing sick funds of their choice, with the ability to switch funds once a year (Horev et. al, 2004). Under the National Insurance Law, the Israeli
government is committed to providing a health care basket of medical services to all residents. The basket is comprehensive in that it covers both preventive care and almost all acute care. Sick funds may charge extra premiums only for supplemental insurance that does not cover services included in the basic basket. Determining the contents of the health basket is a central yet problematic aspect of this reform. The Law states that services and technologies can be removed from the basket only by approval of parliament; new services may be added following a recommendation of the minister of health, the law entitles the Ministry of Health to set up a professional advisory committee in order to recommend how the basket should be updated every year (Chinitz et. al, 1998). The authors describe the situation in Israel following this significant health care reform. Because of considerable funding deficits no new services were added to the basket. However, requests to restrict the services provoked opposition that led to the allocation of funds by the government to include more medications in the basket. In addition, the sick funds could demand copayment and limit access to those drugs. The authors suggest that both explicit and implicit approaches to rationing and priority setting were used to support each other. Based on data analysis, I will argue that a similar mechanism of priority setting was used by the newborn screening program directorship to justify the expansion of the panel (see chapter 4).

Eight years later, Seidman (2006) focused on a different aspect of the decision-making process of the committee. He argues that the consistent under-funding of the committee leads to the adoption of a policy that favors the purchase of expensive new drugs for the treatment of a small number of severely ill patients, rather than the improvement of public health of a larger population. The author describes the
committee’s evolution, and the political, medical and ethical pressures influencing its work. In regard to the former, Seidman points out that “the entire budget allocated for the annual expansion of the basket only equals the price of two military tanks, not much at all” (Seidman, 2006: 11). This comment reflects the Israeli set of national priorities, which was also discussed by interviewees in this study (see chapter 5). The author emphasizes the need to establish a clear national health policy in Israel. He then demonstrates the dominant political nature of the basket by noting that during the 2006 general elections the Israeli State Attorney General instructed the committee to postpone its final decisions for two weeks so they would come after the Election Day.

The dynamics of the health basket committee is relevant to the development of the newborn screening program in Israel on two levels. First, the decisions of the health basket committee directly affect the budget allocated to the newborn screening program, an issue that was widely discussed by interviewees (see chapter 4). Secondly, the occurrences and dynamics of the committee reflect the internal and external forces that influence health service policy-making in Israel and as such are particularly relevant to this study, as discussed in chapters 4 and 5.

The health basket raises the issue of equity; an issue which poses a challenge for the Israeli health care system. Several aspects of equity deserve attention. First is the equity between different ethnicities. The geographical distribution of the population also adds to the ethnic separations between Jews and Arabs. The reason for this distance between the two ethnic groups is twofold. First, a disproportionate number of Arab-Israelis live in the southern and northern districts as opposed to the center of the country (Israel Central Bureau of Statistics 1990-1995). The large communities of Arab-Israeli who live in the
periphery are less educated about the health resources available for them. Secondly, even for the educated individuals among those groups, the access to health resources is relatively limited because of institutional and political reasons that are beyond the scope of this paper. As a result, the Jewish population consumes one third more of health care resources. In addition, infant mortality is higher and life span is shorter in the Arab sector. Although these gaps are beginning to decrease, Gross (2002) suggests that allocation of funding resources of screening for newly discovered, rare, and expensive-to-treat genetic diseases, should be postponed until health care becomes equitable. The second factor relevant to a discussion of equity is the geographic distribution of health care resources between the center and the periphery. This distribution in Israel does not represent appropriately the incidence of illness and mortality. (For our purposes, the center of Israel is defined as the areas in and around Tel Aviv and Jerusalem. All the rest of the country is considered the periphery.) While literature on this issue is limited, the social and ethical implications of inequitable distribution between the center and the periphery in regard to newborn screening services are discussed and analyzed in chapter 4.

**Genetic Screening in Israel**

In addition to its context in Israel’s health policy making, the Israeli newborn screening program is set against the backdrop of other population genetic screening efforts, such as prenatal screening and adult carrier screening. Prenatal genetic screening, in particular, has been increasing significantly since the mid-1990s. Some of the genetic diseases that are extremely rare in most other countries are relatively common in certain communities in Israel. For some of those conditions, the clinical expression is highly
variable and sometimes mild and therefore the justification for screening of those
diseases is questionable. The national screening program for Tay Sachs exemplifies the
complexity of decision making regarding inclusion of conditions in the prenatal screening
panel (Zlotogora and Leventhal, 2000). For Zlotogora and Leventhal, two fundamental
questions that should be addressed before the inclusion of a disease in a national carrier
screening are the relative incidence of the disorder in the population and the goal of
screening. In regard to the first question, a striking sociodemographic process is currently
taking place in Israel: the genetic make-up at the population level is changing so that the
carrier frequency for diseases that were limited to one community has started to decrease,
while the size of the population at risk is increasing because of mixed marriage (between
Jews from Sephardic and Ashkenazi origin). This process leads to new carrier
frequencies of genetic diseases. Also, the possibility of an error in very rare diseases may
be higher than the chance for carrier identification. Therefore, for disorders that are
frequent in small communities, or for those that are present in larger communities but not
in a high frequency, the mixing of the populations may result in frequencies that do not
justify screening.

The second imperative question is the goal of screening. Zlotogora and Leventhal
compare newborn screening and prenatal screening from that perspective. They argue
that in contrast to newborn screening in which the goal is clear: to detect severe
phenotypes rather than identifying carriers of all possible mutations, and to allow for
preventive treatment. In contrast, the purpose of prenatal (as opposed to premarital)
screening for Tay Sachs Disease in Israel is termination of the pregnancy if an affected
fetus is detected. Since the only way to achieve this goal is the interruption of pregnancy,
screening should be offered only for tests allowing for detection of severe genetic disorders, and an agreement should be achieved in the target population that the disease is severe enough that abortion is anticipated. This framework set up by Zlotogora and Leventhal for the purpose of decision-making regarding inclusion of conditions in the prenatal screening panel indicates that prevalence of the candidate conditions and the purpose of screening would be considered the top criteria by newborn screening policymakers and involved physicians. However, as chapters 3 and 4 show, the high priority of those criteria is not explicitly stated by many newborn screening guidelines nor are they articulated by all interviewees.

A good example of a controversial existing prenatal screening program in Israel is the screening for Gaucher Disease. The controversy stems from the wide variation of the different mutations of the disease. The common Type 1 variant is asymptomatic in many cases and even when it is symptomatic, an effective treatment for it exists. Moreover, empirical data shows that most couples choose not to terminate a pregnancy of a fetus affected with the disease (Zuckerman et.al, 2007). The question therefore arises, what is the purpose of screening for Gaucher Disease? Carrier screening in Israel for conditions such as BRCA1 and BRCA2, for which the treatment options are not clear, is another debatable issue (Sagi, 1998). Providers and consumers of prenatal testing services hold different perceptions and opinions regarding the appropriate extent of testing for fetal abnormalities (Mishori Dery et. al, 2007).

**Newborn Screening in Israel**

The literature on the history of newborn screening in Israel is quite limited. Newborn screening for Phenylketonuria was initiated in Israel in the mid 1960s (Cohen et. al, 1966;
Szeinberg et. al, 1970) soon after it first started in the U.S. screening for Congenital Hypothyroidism started in 1978 and proved to be efficient in terms of early detection and treatment (Sack et. al, 1985). Chapter 5 describes and analyzes the development of the expanded newborn screening program in Israel. The data used for this historical analysis was obtained mostly form interviewees. Scant documentation of the efforts that led to the initiation and implementation of the program has been available. Two regulations of the Ministry of Health were available (Israel Ministry of Health Regulation 52/2003 and 17/2009). Both documents were directed towards directors of general hospitals; the earlier one also referred to directors of neonatal units. The earlier document referred only to screening of PKU and Congenital Hypothyroidism while the recent one discussed the expanded panel of 11 conditions (for a final list of the conditions see Appendix1).

Significantly, the 2003 document does not mention parental consent for screening, while in the 2009 document informed consent for screening is one of the main topics. In particular, refusal of testing following a home birth is regulated in the 2009 document. The 2009 regulation sets up a detailed procedure for informing a woman who decides to have a home birth about the significance of screening, the harm to the newborn if it is not performed, her responsibility of conducting it at the right time and the alternative physical locations for performing the screening—which include every neonatal unit of a hospital, maternal and child health clinic, or screening performed by the physician or midwife at home. The physician or midwife are responsible for the follow-up and must ensure that the tests were conducted at the right time. They must also document the provision of information to the parents, in particular if the parents refused to permit screening. The time window for the testing in case of a home birth is determined by the
document to be 48-72 hours following the birth. Possibly, the emphases on parental consent for home birth and regulation of the possibility of refusal are the result of the lesson learnt from the Ayana Case discussed above. The evolution of those guidelines, as well as the ethical and social issues behind it is discussed in more details in chapters 4 and 5.
Chapter 3: Analysis of Newborn Screening Guideline Documents

Introduction

One important facet of the complex undertaking of the implementation and routinization of a public health program such as the expanded newborn screening program in Israel is the adherence, in theory and in practice, to the relevant policy guidelines regulating its operation. From this perspective, the development of the Israeli newborn screening program can be best understood by situating its function in the context of the history of other similar programs. Since newborn screening was initiated for clinical purposes in the 1960s, the overall design and implementation of programs internationally has varied substantially, and has continued to change over time even within countries with newborn screening programs. The guidelines reflect these changes, as they address program design, what diseases should be included in screening panels, and how the information gained by screening should be used. The ways in which these issues are conceptualized and addressed is dependent on context, as each country varies in demographic composition, system of healthcare delivery, and cultural and political context. The unique demographic composition of the Israeli society, along with the political and cultural context the Israeli program is embedded in and its influence on the Israeli newborn screening program development are discussed in chapter 4. In order to better understand the context of the history of newborn screening programs, a comprehensive analysis of international newborn screening program guidelines is beneficial. The following chapter presents the findings of newborn screening guideline documents’ analysis and provides a critical evaluation of the major documents of newborn screening policy since the inception of newborn screening programs. This
analysis serves as a steppingstone for the analysis of the nascent expanded newborn screening program in Israel.

Since the early days of newborn screening in the 1960s, an assortment of national, international and professional groups have published guidelines regarding the formation and operation of newborn screening programs. The policy analysis presented here addresses the following issues: (1) What are the criteria for selection of diseases for the newborn screening panel discussed by different documents? (2) What are the mechanisms suggested by different policy guidelines for evaluating and balancing these criteria? (3) What legal, ethical, and social issues are addressed by newborn screening policy guidelines? (4) How do the documents discuss issues concerning the organization and daily functioning of the program? (5) How, if at all, is the issue of assessment of newborn screening programs discussed? (6) How, if at all, do the documents discuss issues relating to various research applications of the newborn screening specimens or data derived from the newborn screening program? The data regarding these issues is organized and analyzed in six tables described below. The newborn screening guideline documents were selected for analysis based on their focus on policy making regarding newborn screening programs. The data was collected and analyzed with Marvin Natowicz MD, PhD. A manuscript for publication using the analyzed data is underway.

The questions addressed by policy analysis focused on the four following topics: a) criteria for selection of diseases to be included in screening panels, b) ethical and legal considerations regarding the creation, implementation and operation of newborn screening programs; c) various aspects of program organization and functioning; and d) research related issues.
The general research questions explored throughout the policy analysis were: 1. What have been the published criteria for newborn screening programs in particular states, countries, or regions? 2. How are the different criteria balanced against each other in screening decisions in newborn screening programs? 3. How are legal and ethical issues being addressed by newborn screening programs? 4. What are the views of the various documents in respect research-related issues?

In particular, the topics addressed by policy analysis were: a) the requirements set by various newborn screening programs regarding evidence for benefit to the child, family and society from screening; b) severity of disease if untreated and existence of effective treatment; c) training for health care professionals and education for parents about newborn screening; d) issues of privacy, confidentiality, provision of information to health care professionals and parents; e) parental consent for screening and for use of residual bloodspots for research, equity in provision of newborn screening services; and e) periodic evaluation of effectiveness of screening program.

**Data Collection Procedure**

More than 40 national and international guideline documents discussing newborn screening were collected. Twenty-four documents were selected based on two major categories: a) documents dealing specifically with provision of newborn screening services; and b) documents dealing with provision of genetic testing services that include a specific section on newborn screening. Documents included international, national, and regional guidelines. Most guidelines were published by organizations (i.e., American Academy of Pediatrics, American College of Medical Genetics). Other guidelines were published by groups of individuals (i.e., specialist physicians, policy makers and
consumer representatives) offering guidelines for the formation and operation of a newborn screening program. Chronologically, guidelines collected were published from the 1960’s through the present. Geographically, documents encompass newborn screening programs in the U.S., Europe, Asia, Australia and New Zealand. Public policies on state, provincial, national and regional practices regarding newborn screening were obtained by searching the PubMed Central data base annually in 2005-2007 using the key words: newborn screening, neonatal screening, and policy or policies. Public policies on newborn screening were also accessed by searching the databases www.humgen.umontreal.ca, www.nice.org.uk, www.nsc.nhs.uk and www.consensus.nih.gov, www.ahrq.gov, and www1.umn.edu/humanrts/. Articles and documents that provided an overview of the policies or guidelines used by newborn screening programs or that made recommendations regarding these issues were considered for further review.

Data analysis

Guideline documents regulating newborn screening were classified into five tables. The tables are sub-divided into 38 columns. For each guideline document, each column was checked as either “+”, “implied” or left blank if the criterion was not discussed by the authors. The following is a description of the tables’ major columns according to which documents were classified.

1. List and scope of analyzed documents

This table includes list of all documents analyzed and the scope of each one. The two possible categories for classification were either specifically newborn screening or genetic testing in general with a section on newborn screening.
2. **Criteria for disease selection**

This table looks into the criteria for disease selection discussed by the documents. Major categories in this table are direct benefit to the child from screening; benefit to the family and society from screening; birth prevalence known; natural history understood; existence of accepted or effective treatment; and acceptability of program or test to the public.

3. **Ethical, legal, and social considerations**

This table investigates the ethical, legal, and social considerations the various documents find essential. Major categories for classification are consent to participate in newborn screening discussed; privacy and confidentiality discussed; research benefits are equitably distributed; alternative uses of resource considered.

4. **Program organization and daily functioning**

The topic of this table is which aspects organization and daily functioning the documents discuss. Major categories in this table are provision of information to health care professionals and parents, description of quality assurance and quality control; description of staff training, and consultation regarding results.

5. **Program assessment**

In this table documents were classified mainly, by its consideration of various aspects of cost of tests and program, evaluation of affects of screening; and evidence for reduction of morbidity and mortality.

6. **Research related issues**
This table describes the consideration by documents of the need for research regarding effectiveness, diagnostic issues and natural history, improvement of health services, and parental consent for use of blood spots for future research.

Based on the primary categories for classification, dominant themes and trends were identified and described.

**Description of criteria for analysis**

*Table 1 (Appendix7)* is a list of the documents used in this analysis. Twenty-four documents, published between 1965-2007, met our criteria for inclusion in this analysis. The documents either describe an existing newborn screening program or discuss the key elements of newborn screening programs in general. Many of the documents discuss screening principles and implementation of programs in particular states (e.g., Massachusetts), countries (Australia, Finland, Japan, Netherlands, United States) or regions (United Kingdom, Europe); the other documents are not linked to a specific locale and discuss the issues in a more general way.

Each document describes specific criteria for inclusion or exclusion of disorders in a newborn screening program (*Table 2 see Appendix7*), although the documents vary regarding what specific criteria are deemed most important. One of the major topics examined and presented in Table 2 relates to the notion of benefit. What are the benefits or significance of testing to the screened individual, and to the family and society? In terms of the clinical aspects of the candidate conditions for a newborn screening panel, does a document consider knowledge of the birth prevalence of a disorder and its natural history when untreated as essential criteria for its inclusion in a screening program? Treatment is yet another major clinical factor contributing to the decision-making
regarding selection of conditions to the panel. Therefore, the analysis addresses whether
the document discusses the existence of an accepted/effective treatment for a disorder as
a requirement for its inclusion in a newborn screening program and if it considers
whether or not there is a presymptomatic phase of a disease. Similarly, do the documents
consider the significance of screening followed by diagnosis and treatment as clinically
superior to treatment after symptom presentation in the absence of screening? Finally, in
this section I have investigated how, if at all, each document balances the importance of
each of the above criteria.

*Table 3 (Appendix7)* addresses ethical, legal, and social considerations in newborn
screening programs. Here I explore whether and how the documents discuss issues of
acceptability of testing to parents, physicians and/or the general public, as well as the
issue of parental consent to participate in the newborn screening program. How do they
discuss the protection of privacy or maintenance of confidentiality? Do the documents
address issues of equitable distribution of the resources and benefits of newborn
screening? Finally, do the documents require consumer involvement/ participation of the
general public in newborn screening policy-making?

*Table 4 (Appendix7)* discusses the organization and daily functioning of newborn
screening programs. In this part, the description of the purpose and scope of the screening
program was analyzed; other categories I sought were the description of the roles of the
newborn screening personnel and the description of the quality control/quality assurance
required for the program. As discussed in chapter 2, education is another crucial
parameter in the successful operation of newborn screening programs. Therefore, the
analysis includes a discussion of provision of information about screening to parents prior
to screening, description of staff training and of genetic counseling services regarding screening results, and finally, whether a document discusses the availability of adequate facilities for diagnosis and treatment as part of the analysis of the organization and daily functioning of the program.

An important step in the implementation of a screening program is its assessment. *Table 5 (Appendix 7)* discusses the criteria used for program assessment. Here I wished to know whether or not the documents discuss various cost components as part of the required evaluation of the screening program. Those included cost of organization and running of the program; cost of follow-up and diagnosis for each case of a screen positive result; confirmation of screen positive results; cost of test, and the cost of case finding. In addition, I looked for the description of the following categories in guideline documents as indicators for the assessment of the screening program: the process of continuous evaluation of the screening program; the process of revisiting the criteria for screening; training and continuous education of program professionals, and finally, evidence for reduction of mortality and morbidity of disease due to newborn screening.

The relationship of research to newborn screening programs is yet another important issue to settle when a program, is implemented. Therefore, the last component of the analysis is focused on research aspects. *Table 6 (Appendix 7)* describes research-related issues that may have been addressed in the documents. The issues that were considered include: discussion of the need for research regarding effectiveness of screening; consideration of the need for research regarding the diagnosis and natural history of a disease; discussion of the need for research regarding improvement of health services,
and, finally, consideration of the need for parental consent to use bloodspots for future research.

Results

The first criterion discussed by all documents was that the inclusion of a disorder in a newborn screening panel should be contingent on the likelihood of significant clinical benefit occurring for the baby as a result of the screening test. Significant benefit to the family or society as a result of the screening test was explicitly or implicitly discussed by 13 out of 24 (54%) and 17 out of 24 (70%) of the documents respectively. Over half of the documents (58%) stipulated that the birth prevalence of a condition must be known to be included in a newborn screening panel, while half of the documents (12 out of 24) stipulated that the natural history of a condition must be known if the condition is to be included. As expected, all documents specified that there must be an accepted or effective treatment in order for a condition to be included in a newborn screening panel; thus, they were uniformly against predictive testing of children for adult onset conditions and carrier status where no childhood interventions would change the course of the diagnosed condition. The existence of a latent or asymptomatic phase of the disorder and a clinical advantage of detecting the disorder through newborn screening as compared to detection at a later time in life, such as when a child might present with symptoms, were stipulated as preconditions for inclusion in screening programs in 8 out of 24 (25%) and 17 out of 24 (71%) documents, respectively.

All of the documents discussed various ethical, legal, and social considerations of the screening program, such as consent or confidentiality (see Table 3 Appendix79). Approximately two–thirds, or 16 out of 24 of the documents specified that the specific
test or program had to be acceptable for the parents, physicians, or the general public. Three-fourths (18 out of 24) of the documents discussed parental consent in newborn screening. The need for the protection of the privacy of screened individuals or and/or the confidentiality of the medical information of individuals screened was noted by 12 out of 24 (50%) of the documents. The issue of equity in distribution of newborn screening benefits was considered by 19 out of 24 (79%) documents and 3 out of 24 (12%) noted that the issue of resources used in newborn screening compete with other public health programs should be discussed. Significantly, consumer involvement or public participation in newborn screening policy-making was required or implied for by 10 out of 24 (41%) of the documents.

Most of the documents included discussion on one or more aspects of the organization and daily functioning of newborn screening programs (Table 4 Appendix7). The need for a description of the purpose or scope of the screening program was considered by 19 out of 24 (79%) documents; the need for a description of personnel roles was discussed by 5 out of 24 (21%) of the documents, and 15 out of 24 (62%) included discussion regarding quality assurance/quality control of the newborn screening program. The provision of information to parents and health care professionals was discussed by 19 out of 24 (79%) and 17 out of 24 (71%) documents, respectively. Staff training and genetic counseling services were discussed by 11 out of 24 (46%) and 18 out of 24 (75%) of the documents, respectively. The availability of facilities for diagnosis and treatment was specified by 19 out of 24 (79%) of the document as an important requirement of newborn screening programs.
With respect to long term management and assessment of the newborn screening program (*Table 5 Appendix7*), 8 out of 24 (33%) documents discussed the cost of organizing and running the testing program and the cost of follow-up and diagnosis as an important consideration. Confirmation of positive newborn screening results was discussed by 16 out of 24 (66%) documents. The cost of screening tests in general was specified as an important consideration by 18 out of 24 (75%) documents and 4 out of 24 (17%) documents discussed that the cost of case finding is assessed. The need for continuous evaluation of the screening program was discussed by 17 out of 24 (71%) documents and 5 out of 24 (21%) discussed a need to revisit earlier criteria regarding the inclusion of disorders in a screening panel. Training and continuous education was considered by 13 out of 24 (54%) of the documents as an essential component of a screening program and 6 out of 24 (25%) of the documents discussed the need to show evidence for reduction of morbidity and mortality of particular disorder due to the screening initiative.

Many, but not all, documents discussed research issues pertaining to newborn screening (*Table 6 Appendix7*). The need for research regarding effectiveness of the newborn screening program was discussed by 13 out of 24 (54%) of the documents. Research regarding diagnostic issues and the natural histories of the conditions screened for was considered by 14 out of 24 (58%) of the documents and 10 out of 24 (42%) of the documents specified the need for research regarding improvement of health services for individuals with health conditions identified through the newborn screening program. Finally, 11 out of 24 (46%) discussed the requirement for parental consent for use of bloodspots for future research.
Discussion

Wilson and Jungner (World Health Organization, 1968) set forth principles for early disease detection that have been extremely influential in the development of numerous medical screening programs, including the newborn screening programs around the world. They propose ten criteria that must be met in order for a condition to be included in a screening program and in order for a program to function effectively. First, the condition must be an important health problem. Next, there must be both an accepted treatment for patients with recognized disease and facilities for diagnosis and treatment. The diseases for which screening is performed must have a “recognizable latent or early symptomatic stage.” They also argue that there must be a “suitable test or examination” that is “acceptable to the population.” In order to be included in a screening program, the “natural history of the condition, including development from latent to declared disease” must be “adequately understood.” Furthermore, “there should be an agreed policy on whom to treat as patients.” Wilson and Jungner also consider how the expense of screening programs fit with other public health goals, noting “The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.” Their final principle is that “case finding should be a continuous process and not a ‘once and for all’ project.” Most, but not all, of these criteria are incorporated in the documents on newborn screening programs.

As discussed in chapter 2, the present study frames the discussion around several concepts: the social construction of medical knowledge, the social processes of
medicalization and biomedicalization, McKinlay’s (1982) model of routinization of new technology, authoritative biomedical knowledge and the quest for a “perfect baby” in the Israeli society. I argue that the discussion of the purpose of newborn screening in the various guidelines exemplifies McKinlay’s first stage in the career of the technology; the stage of the “promising report”. At this stage, support for the routinization of the innovative technology comes from the media and medical journals. In addition, as will be discussed in the conclusion, the social and ethical aspects considered by newborn screening guidelines can also be viewed as a part of the social policy created by the authors of the documents in order to justify the adoption of this device.

A number of important issues emerge from the analysis of these key documents on newborn screening policies and practice. The first relates to the issue of how to weigh the numerous criteria for the purpose of determining which diseases merit inclusion in a screening panel. In terms of how to balance the criteria for inclusion of disorder in a newborn screening program (Table 2 Appendix7) the guidelines used in the documents fall in two distinct categories. All but one of the documents (96%) had a direct or implied use of the criteria in an absolute or ‘all-or-none’ sense. These documents seemed uncompromising regarding the criteria that needed to be met for any condition to be included in a newborn screening program; in the absence of meeting all of the criteria, a condition would not be included in the program. In contrast, one group, the American College of Medical Genetics (ACMG), offered a different approach in the use of such criteria. The ACMG model weighed the relative merits of different criteria, rather than insisting upon an absolute requirement for any one criterion or group of criteria. This is an entirely novel way to evaluate whether or not a disease merits screening. Their
approach included an overall score for each disorder that was under consideration for inclusion in a newborn screening program that was, in turn, based on the sum of the scores for all of the possible criteria. In this scheme, whether or not a specific criterion is fulfilled by a disorder would not necessarily result in its inclusion or exclusion into a newborn screening program. For example, while most documents of the first category include an uncompromising requirement that the diagnosis of a particular condition in the newborn period must result in a significant clinical benefit to the baby, that criterion was not a sine qua non for inclusion in the ACMG guidelines. Instead, the decision making framework of the latter group allowed for inclusion of conditions without known benefit for the newborn child if enough justification could be established based on fulfillment of other criteria.

The next significant issue to emerge from an analysis of the guidelines relates to the issue of benefit and the way the concept of benefit is broadening in regard to newborn screening programs. As noted earlier, benefit for the screened individual from screening was required or implied for by all of the documents. However, the language used by different documents to define this fundamental requirement varied between different chronological times and in different geographical settings. Several earlier documents used for this analysis do not use the term “benefit” at all while setting forth criteria (Committee on Fetus and Newborn, 1965; World Health Organization, 1996, Tomoeda et. al, 1998). Other earlier guideline documents implied the requirement for direct benefit to the baby from screening by stating “the testing batteries of certain regions include disorders that are potentially life threatening on the neonatal period” (Congress of U.S., 1988; 347) or “efficient screening should produce the desired effect on infant morbidity
and mortality” (the Council of Regional Network for genetic Services, 1992). In documents written later, however, the trend to explicitly specify the benefit for the baby as a requirement for screening becomes more apparent. (Committee on Assessing Genetic Risks, 1994;6; Committee on Bioethics, 2001; HGSA, 2004).

In terms of the importance of this criterion, some of the documents are uncompromising about the direct health benefit for the baby required as a condition for justification of screening (Council of Europe, 1994, International Society of Newborn Screening, Neonatal Screening Netherlands, 2005), while others refer to the seriousness of the disorder (Committee on Fetus and Newborn, 1965) or how severe a condition must be to justify neonatal screening (World Health Organization, 1996). Still others require as a precondition for screening that the condition must be an important health problem (Illona Auti Ramo, 2005), emphasize the significant morbidity and mortality with which the disorder is associated (Health Technology Assessment, 1997) or specify that without early detection and subsequent medical care, the disorder could be life-threatening (Congress of the U.S., Office of Technology Assessment, 1988;Committee on Genetics 1992; UK Newborn Screening Programme Centre, 2005).

In addition, in recent documents the scope of benefit is extended to include the family as well as the newborn. Most of the documents that discussed benefit for the family did so explicitly. However, the recent guidelines of four influential groups in the United States and Europe implied rather than explicitly stated the expansion of the notion of benefit to include the family as well as the newborn (Newborn Screening Task Force report, 2000, New York Task Force, 2000; UK National Screening Committee, 2005, International Society for Neonatal Screening). Other documents explicitly referred to
benefits for the family and society from screening (Council of Europe, 1994; European Society of Human Genetics, 2003, Health Council of the Netherlands, 2005). The trend in recent newborn screening programs to broaden the notion of benefit to include families rather than just the infant, as well as its societal and ethical implications are discussed in chapter 2.

As for benefit for society from screening, most documents discussed it explicitly except for three documents in which it was implicitly stated (Congress of U.S., 1988; UK National screening Committee, 2005, International Society of Newborn Screening). For instance, the recent American College of Medical Genetics Report (2005) does not require that a disease be associated with a clinical benefit to the baby in order to be included in a newborn screening program. By virtue of the scoring system used in that document, here too, the notion of benefit from newborn screening is broadened to include other members of the family and/or society, and not just the baby who is screened. Nevertheless, a concept of benefit that allows for no direct benefit to the baby is presently controversial and it is unclear if it will become more generally adopted (Baily et. al, 2008).

A third theme that emerges from analysis of the documents is the variable and, usually, minimal requirement of an evidence base for the various aspects of newborn screening programs. Although the earliest document in the field, that authored by the Committee on Fetus and Newborn in 1965 (Committee on Fetus and Newborn, 1965) indicated the need for an adequate evidence base regarding the criteria used in the selection of disorders for a newborn screening program, since then, most of the other documents contain language that implies the importance of having an evidence base with
respect to one or several issues. An example of an implied need for an evidence base is the criterion that screening for a disorder must result in significant benefit to the baby. Nonetheless, with one exception - the American College of Medical Genetics guidelines for newborn screening - all other documents do not define how evidence should be gathered or evaluated.

In my view, all three themes described up to this point -- the mechanism chosen by health professionals for selection of conditions to the screening panel, the scope of the notion of benefit in newborn screening, and the required evidence base for certain programmatic aspects -- are best interpreted in light of the concepts of the social construction of medical knowledge, medicalization, and biomedicalization. I argue that those policy aspects are shaped by the attitudes and beliefs the scientists and policy-makers hold regarding the purpose and goals of screening. This is what Bloor refers to in his “Strong Programme” as “the causality of (social and other) forces that cooperate in bringing about belief (Bloor, 1984; 7) or the fundamental premise of biomedicalization set forth by Clark and her group according to which “…increasingly important sciences and technologies and new social forms are co-produced within biomedicine..” (Clark, 2003; 163).

For example, if the mechanism used for selection of conditions to the panel is an absolute one, and the program directorship believes that the availability of an effective treatment for the baby from screening is a necessary requirement for inclusion of a disorder in the panel, then there is no room to even consider the inclusion in the panel of conditions that do not meet this criterion. Consequently, the relevant body of knowledge being utilized by the program is reduced to clinical information about disorders that are
treatable. If, on the contrary, the decision makers use the relative mechanism of selection of disorders to the screening panel, and in their view an evidence base for the direct benefit for the baby from screening is not fundamental, then the picture is different. In this case, the relevant clinical knowledge obtained by newborn screening that is utilized by health professional is much broader. In addition to conditions for which an effective treatment exists, it might also include disorders for which early detection might be beneficial for the family, even though they are not treatable. In the case of such disorders, newborn screening information that avoids the ”diagnostic odyssey” or allows for a more fully informed reproductive decision making in the future on the part of the parents could satisfy the criterion of benefit.

Fourth, this policy analysis reveals the modest attention devoted to the ‘non-philosophical’ dimensions of the newborn screening programs in these key documents. Thus, issues that are relevant to the day-to-day functioning of screening programs are variably addressed in the documents (Table 4 Appendix7). These include the provision of information to parents and health care professionals before screening; description of staff training; description of genetic counseling following transmission of screening results, and availability of facilities for diagnosis and treatment. Only one - fifth of the documents, for example, discussed the roles of program personnel, less then half of the documents considered staff training, and only half of the documents specified the purpose or scope of the screening program. Only 79% of the documents discussed the provision of information to parents and only 71% of the documents discussed the provision of information to health care professionals, yet both are imperative to the daily functioning of newborn screening programs.
While discussion of these issues might be viewed as secondary to the ‘larger’ philosophic issues concerning what types of disorders to include in a screening program and to be subject matter of a ‘standard operating procedure’ type of document, there are central ‘philosophical’ issues embedded in the consideration of the ‘day-to-day’ issues of running a newborn screening program. For example, at one level the discussion of quality assurance/quality control issues concerns the day-to-day function of a newborn screening program, yet there are different conceptual approaches to the quality assurance/quality control of a newborn screening program. As discussed in chapter 4, the Israeli program is using both American and European measures for quality control. Despite its importance, only 15/24(62%) of the documents specified the need to discuss quality assurance/quality control of the program.

This modest attention to the non-philosophical dimensions of newborn screening is yet another example of how social forces and ethical views influence the understanding of the technoscientific standards and procedures. While for certain policy-makers, various programmatic issues including the purpose or scope of the screening program; provision of information to parents and health care professionals before screening; description of personnel roles and staff training; description of genetic counseling following transmission of screening results, and availability of facilities for diagnosis and treatment seem important enough that it should be settled prior to the operation of the program, at least half of the investigated documents do not discuss those issues. Yet handling these issues during the development of the screening program and prior to its actual operation is crucial to its success and effectiveness. The history of PKU screening provides examples of the consequences of the premature implementation of programs, before the
fundamentals of the program were fully settled (Brosco, 2008). Chapter 5 reveals the
deep concern expressed by the Israeli newborn screening community regarding the fact
that those issues have not been settled ahead of time by the program directorship.

Fifth, data analysis reveals the minimal consideration of issues related to the varied
research dimensions of newborn screening programs in the documents (Table 6
Appendix7). Approximately half of the documents discussed either the need for research
regarding effectiveness of the program (54%) or the requirement for research regarding
issues of diagnosis and natural history of the diseases (58%), and less then half of the
documents (46%) considered parental consent for future use of bloodspots for research as
an issue that should be settled by the program. Less than half (42%) of the documents
discussed the need for research regarding improvement of health services. It should be
noted, however, that some types of research that are now feasible with dried bloodspots
from newborn screening programs were not feasible when many of the documents were
written; thus one can not be entirely critical of the ability of the authors of those
documents to fail to foresee such applications. Nonetheless, other forms of research
involving newborn screening programs could and should have been recognized and the
related issues acknowledged. I believe that the minimal attention paid by fully half of the
documents to research - related issues is another reflection of the process of
biomedicalization that has taken place in the past 25 years (see chapter 1). Because the
focus of this social process is clinical innovation it is particularly relevant to the
expansion of newborn screening programs that are based on advanced technologies. In
this process, the clinical dimension has expanded while other non-clinical dimensions,
and in particular the research aspect of the program has receded in perceived significance.
A sixth conclusion is that the authors of only a minority of the documents recognized the need for a public health program to revisit earlier criteria for inclusion of disorders in the panel and, more generally, to periodically and regularly revisit all other aspects of the program (Table 5 Appendix7). For example, only 21% of the documents discussed the importance of revisiting the criteria for inclusion of a disorder in a newborn screening program. Such reassessments are an important means to reveal weaknesses of programs and areas for possible improvement. This is particularly important in the context of newborn screening programs where advances in scientific and medical knowledge can impact on the ability to diagnose and provide effective treatment for conditions that might be included or excluded from screening programs.

A seventh observation relates to the role of the community in approving the screening test. The Wilson and Jungner criterion that the “test should be acceptable to the population” is a central concept of population-based screening programs. Yet only 66% of the documents discuss this criterion, possibly because of its vagueness. What does “acceptable” mean and how should it be measured? Should the population have a say in the determination of the test and, if so, how? A key lesson from the history of genetic screening is that despite its vagueness, the condition of ‘acceptability to the population’ has proven to be essential to the effectiveness of genetic screening and testing programs. The heterozygote screening programs for Tay-Sachs disease provide a good example of a screening program that succeeded due to the inclusion and support of Jewish communities in North America and elsewhere (Natowicz et. al, 1991). The importance of community involvement and support is reiterated by the example of screening for beta-thalassemia in Cyprus (Cowan, 2009). In contrast, the early history of screening for sickle
cell anemia in the U.S. was much less successful and fraught with controversy, partly because of limited involvement of the ‘target’ community and incomplete community support (Rutkow et. al, 1974)

Finally, it is instructive to evaluate the documents from the perspectives of what they have to say concerning who should be making newborn screening policies and the process by which such policies should be made. This is a topic of major importance in newborn screening for at least three reasons. First, most developed countries have mandatory screening of newborns and, consequently, policy decisions regarding newborn screening programs affect millions of citizens. Moreover, in comparison to other genetic testing and public health programs in the case of newborn screening the target community is particularly vulnerable. Finally, the general public pays for the cost of newborn screening programs through tax revenues and other forms of payment. Yet less than half (41%) of the documents either discussed or implied that involvement of members of the general public is essential with respect to the policy-making that governs all aspects of newborn screening programs.

I argue that the relatively slight consideration devoted to both the requirement to revisit earlier aspects of the program and the role of the community in approving the screening test and in policy-making can be understood in relation to Mckinlay’s model of the routinization of a new technology. The third stage portrayed in Mckinlay’s model of the process of routinization of new technology, following the stage of the promising report and the adoption by professionals and organization is the stage of public acceptance and state endorsement. At this stage, social policy to support the routinization of the innovative technology could be implemented. This stage is furthered by the
enthusiasm of the consumers, which in Mckinlay’s view depends in turn on that of the professionals. I suggest that revisiting earlier aspects of the program and the involvement of consumers and the general public in newborn screening policy-making and in particular, in approval of the screening test, are all reflections of this stage of the creation of social policy to support the routinization of the innovative technology. In my view, public participation is essential for an appropriate development of a newborn screening program. Consequently, the relatively low participation rate of the consumers in creation of policy guidelines indicated by this analysis should be addressed in order to successfully complete the process of routinization of the tandem mass spectrometry and other testing technologies in newborn screening. Only then, if to use Mckinlay’s metaphor, the advanced technology could reach the final stage of its career.

To summarize, this chapter has analyzed newborn screening guideline documents from the early days of newborns screening in the 1960s through 2005. The documents were classified according to various programmatic aspects. Seven important themes emerged from the analysis: first, only one document, although a recent and mostly influential one (the American College of Medical Genetics Report), used a method of weighing the relative merits of different criteria for inclusion of a condition in the panel rather than an absolute requirement for any one criterion or group of criteria. This framework allowed for inclusion of conditions without known benefit for the newborn child if enough justification could be established based on fulfillment of other criteria.

Second, there has been a recent broadening of the notion of benefit in newborn screening programs to include not only direct benefit for the newborn but also the utility to the family and society from screening and early detection. The third point is the
minimal requirement of an evidence base for the various aspects of newborn screening programs in most policy documents. I argue that those findings demonstrate how the social situation and sociological perspectives held by decision-makers influence their perception of the desired practice of newborn screening.

Fourth, policy analysis reveals the modest attention devoted by policy documents to the ‘non-philosophical’ dimensions of the newborn screening programs, including predetermination of the purpose of screening, provision of information to parents and health care professionals, and discussion of personnel role and staff training. This is yet another example of how social forces and ethical views influence the understanding of the required technoscientific standards and procedures. Other issues that were minimally acknowledged by documents are the varied research dimensions of newborn screening programs, the need to periodically and regularly revisit all other aspects of the program, and the role of the community in participating in the decision making and in particular, in approving the screening test. I argue that the involvement of the consumers in newborn screening policy-making the need to periodically revisit the criteria for inclusion in screening programs, and to pay attention to the research dimension are all crucial for the complete routinization of technology following Mckinlay’s model, as all contribute to the implementation of a successful and effective screening program with high standards of ethics. From this global perspective on the nut and bolts of newborn screening policy-making, I move in the next chapter to focus on the evolution of one particular expanded newborn screening program in Israel.
Chapter 4: The Evolution of the Expanded Newborn Screening Program in Israel

Introduction

This chapter discusses the evolution of the newborn screening program in Israel. It opens with an overview of the history of newborn screening in Israel, focusing on the circumstances that led to the decision to expand the panel of conditions by the introduction of the tandem mass spectrometry device. Next, it examines the social and ethical dimensions of the decision making process that surrounded the implementation of the program. The concept of the social construction of medical knowledge (Zola, 1972; Conrad, 1992) was applied on the determination of program parameters and procedures. The routinization of the tandem mass spectrometry device was analyzed through the lenses of the technological imperative (Koenig, 1988), the concept of biomedicalization (Clark, 2003) and McKinlay’s (1982) model of routinzation of an innovative technology. Finally, this chapter draws on Remmenick’s (2006) concept of the quest for the perfect child in Israeli society, to analyze the lack of public awareness and education regarding newborn screening in general and the process of expansion in particular.

History of Newborn Screening in Israel

In Israel, there is an annual rate of 150,000 live births (Statistical Abstract of Israel, 2008). Of those, about 10 will be identified as new PKU patients and 65 as new congenital hypothyroidism patients (Interviewee #2). The occurrence of the different errors of metabolism in Israel has never been studied, mainly because of its low incidence. For example, Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD), the rare hereditary disease that is the main motivation for the introduction of
tandem mass spectrometry to newborn screening programs in many countries, has never been diagnosed in Israel. Newborn screening for PKU in Israel began in 1964, only a few years after it started in the U.S. (Cohen et. al, 1966). At first, it was performed at Sheba Tel Hashomer Medical Center Institute of Pathological Chemistry. In fact, the broad experience gained by Sheba Tel Hashomer Medical Center on the topic led to the hosting of the second International Conference on PKU in Tel Aviv in 1969. The infrastructure that was developed by the center for PKU enabled the establishment of screening for Congenital Hypothyroidism in 1978 (Sack et. al, 1985), making Israel one of the first countries in the world conducting newborn screening for Congenital Hypothyroidism at the national level (Interviewee #3). Ten years later, the program signed an agreement with an American private funder for donation of diagnostic kits for Congenital Hypothyroidism screening. The agreement continued for 30 years, until recently.

The first time the possibility of expanding newborn screening in Israel was considered was in 2003. Two public officials in the Ministry of Health were involved in the decision-making process and concluded that it was not the right time to expand screening. The basis for the decision had to do with the justification for using the tandem mass spectrometry device. As noted, historically, the primary reason for using tandem mass spectrometry has been to screen for MCADD, which is undetectable by more traditional screening methods. Once the tandem mass spectrometry is utilized, screening for many more conditions becomes much simpler and faster. In Israel, until that point in time, there was not even one case of diagnosed MCADD. Similarly, in the New York State database and in the Pediatrix (a private firm conducting newborn screening for several U.S. states) databases there was no evidence for a case of an Ashkenazi MCADD
patient. Given the fact that there was no indication regarding the prevalence of disorders screened for by tandem mass spectrometry, the National Advisory Committee did not think expanding the panel to include those conditions and using the device for this purpose was justified.

The second effort to establish an expanded panel of conditions took place five years later. The first step towards the creation of an expanded program was taken by two American interviewees. Both testified that they have strong connections to Israel. (interviewees #18, 17). In 2005, during a time of heated debates regarding expansion of newborn screening in the U.S., the two got acquainted with the Israeli newborn screening program. They wondered why the program, which was one of the early adopters of PKU screening in the 1960s and Congenital Hypothyroidism in the 1970s, was still screening for only the same two conditions forty years later. Following a conversation with an Israeli colleague at a professional meeting interviewee #17, who was committed to the message of the March of Dimes Organization at the U.S. decided to look into the newborn screening situation in Israel. He made contacts with his counterpart at the Ministry of Health in Israel, who was happy to share the empirical data he had collected regarding the numbers of individuals affected with metabolic mutations all over the country. From this data he learned that there was in his words “a great need” to make earlier diagnosis of metabolic diseases in Israel. The great need was indicated by the presence of significant prevalence of genetic mutations in the Israeli population and the high consanguinity of the Arab and Haredi (Ultra-Orthodox) sectors. He then contacted a friend (Interviewee #18), an expert in genetics, and “…just on a whim” the two of them decided to study the topic more thoroughly.
In an electronic search they conducted the two American interviewees found out about a major manufacturer of Newborn Screening kits, PerkinElmer. They contacted the manufacturer and were invited to visit its labs. In this visit they learned how newborn screening programs are set up and run. Following this visit they have decided to move forward with the initiative of expansion. The next step was reaching out to possible financial donors. Through networking and connections, they contacted Friends of Sheba in Los Angeles who made the connection with Sheba Tel Hashomer Medical Center in Israel. They contacted a public official in Israel (Interviewee #4), and discussed the possibility of the expansion of the existing screening panel with him. Interviewee #4 reported that he had been transformed from a listener to “a catalyst” in the process of expansion. A second public official (Interviewee #1) visited the New York State newborn screening program in order to learn more about it before the decision to move forward with the initiative was reached.

Up to this point of the story, the development of the initiative to expand the program fits well with McKinlay’s first stage in the career of the innovation, the stage of the “enthusiastic report” or “promising performance” of the technology (McKinlay, 1982:236). Indeed, McKinlay focuses on promising reports published mainly in the media, associated with “respected scientists” that usually do not meet any methodological criteria, but he also notes that another source of promising reports may be coming from the manufacturers of the technology and/or from enthusiastic researchers, which is the case here. Importantly, for McKinlay, both kind of reports are no more reliable than media stories and are useless as a basis for social policy.
According to interviewee #18, the people at the Ministry of Health have chosen to develop the program using a philanthropy-based model, following her suggestion. It is noteworthy that the philanthropy-based model makes more sense in the context of the original initiative of the Americans. According to a program official (interviewee #3), the idea was to establish a world center of genetics, which would integrate newborn screening, Jewish Genetics, and biobanking. Among the collaborators with the proposed centers were Yeshiva University and Albert Einstein College of Medicine in the U.S. Sheba Tel Hashomer Medical Center was asked to be in charge of the newborn screening part. Eventually, the greater initiative did not work out and the newborn screening part was all that remained. It was unclear from the interview with Interviewee #3 why the larger initiative fell apart. My interpretation of the motivations of the financial donors and how it fits with the conceptual framework is laid out later in this chapter.

**Pilot Testing and the Justification for Expansion**

Following those developments, in 2005 a pilot testing for a panel of genetic and metabolic disorders was performed at the New York State newborn screening laboratory. Throughout data collection, respondents discussed this topic either very briefly or off-the-record. The information I gathered about the testing is described in the following section. The pilot study was initiated by people involved in newborn screening at Sheba Tel Hashomer Medical Center, a fact that will become significant as the newborn screening program materializes. 45,000 Guthrie cards of Israeli newborns, excluding filter papers positive for PKU or Congenital Hypothyroidism, were sent to New York State Newborn Screening Program for the purpose of an analysis by the tandem mass spectrometry technology. The sample consisted of Israeli and Palestinian bloodspots. The latter came
from Palestinian newborns born in Israeli hospitals. The bloodspots were screened for over 20 inborn errors of metabolism. In the study, the first presymptomatic Medium Chain Acyl-CoA Dehydrogenase Deficiency baby was identified and diagnosed. A Maple syrup urine disease case was also found and proved positive at the DNA level. In addition, samples with elevated levels of other analytes were identified.

Following the detection of the Maple syrup urine disease case, an Israeli interviewee (interviewee #2) recalls, the program directorship stopped looking for more cases as the total number of screen positive results was more important than specific cases. The goal, as explained by an Israeli interviewee (interviewee #3), was to show that detection rates in Israel are comparable with other parts of the world, thereby establishing the need for an expanded newborn screening program in Israel. According to this interviewee, the study shows that the overall positive frequency for the disorders tested in the initial screen is 1 in every 2500 newborns. This study was among the factors underlying the Ministry of Health decision to expand the program (interviewees # 2 and # 3). The study was performed anonymously and positive results were not disclosed to patients, a fact that was criticized by one interviewee as an unethical move (interviewee #8). The findings convinced the people in charge at the Ministry of Health and Sheba Tel Hashomer Medical Center that expanded screening is justified and served as a persuasive argument to start fundraising for expansion (interviewee #18).

According to McKinlay, the pilot study is considered a part of the first stage of the enthusiastic report. In his eyes, a pilot study is at times a trap that may be the major factor leading to the lack of randomized control trials in the evaluation of new therapies. However, in the case of newborn screening, where pilot studies are not feasible due to the
rarity of conditions (see chapter 2) the conduct of a pilot study to justify the establishment of a newborn screening program may be necessary (Pass et. al, 2006) . Nevertheless, the pilot study should provide good evidence base to justify screening. The circumstance surrounding the conduct of the Israeli pilot testing as well as the evidence base it provided are questionable. No clear criteria for what the desired results that would justify expansion were articulated by the program directorship other than a certain overall positive frequency (1; 2500) for the disorders tested in the initial screening. The actual detection of one presymptomatic Medium Chain Acyl-CoA Dehydrogenase Deficiency baby and one Maple syrup urine disease case, it seems, did the work as the total number of screen positive results was more important than specific cases. The next step in the development of the program was the establishment of a second advisory committee on behalf of the Ministry of Health to reconsider the idea of expansion.

The Role of Advisory Committees in the Process of Expansion

Several committees were involved in the development of the expanded newborn screening program in Israel: the National Newborn Screening Advisory Committee, which consists of members from the Ministry of Health and Sheba Tel Hashomer Medical Center; the higher advisory committee for issues of genetics, and an external advisory board. The higher advisory committee for issues of genetics (the Helsinki Committee) consists of geneticists, lawyers, ob-gyns, epidemiologists, and public representatives. In addition, it includes a legal counselor on behalf of the Helsinki Committee. The committee is responsible for the approval of any test or examination that involves the collection or use of DNA samples. In addition, it provides consultation to governmental agencies regarding ethical and legal dilemmas related to the appropriate
use of genetic information by governmental agencies. The person in charge of the newborn screening program at the Ministry of Health asked the committee to discuss the possibility of expansion of the program and submit its conclusions to the Ministry of Health. However, the committee responded that the pilot testing that was performed is not considered research and therefore did not fall within the scope of the committee’s responsibility (interviewee #1).

Consequently, The National NBS advisory committee was reconvened in 2005 following the pilot testing at the New York State newborn screening labs. This time the committee consisted of pediatricians, geneticists, endocrinologists, a nutritionist, and metabolic experts. The committee discussed several topics prior to making the decision regarding expansion of the screening panel. They discussed what conditions should be included in the expanded screening panel, what technology was appropriate to use, and what funding sources were available. The committee concluded that as long as funding was available, expansion of the program was warranted (interviewee #3). Based on the results of the pilot testing at the New York State newborn screening lab, the advisory committee set up several conditions for the approval of the establishment of the program: first, newborn screening data files that had been manually operated until then had to be computerized, current assays had to be upgraded, and the screening panel had to be expanded to include 13 more conditions in addition to the existing panel of two conditions, Congenital Hypothyroidism and PKU. The committee recommended that in the future, the option of expanding screening for the full American College of Medical Genetics panel of 29 core conditions should be considered.
So how did the committee reach the conclusion that screening should be expanded to include 13 more conditions? An Israeli interviewee who took part in this process was extremely critical of the committee’s functioning (interviewee #13). He described the decision making process as an opportunistic one in the sense that it was hardly based on philosophical or scientific reasoning. The decision to expand, he explained, was not planned in advance. Its philosophical and/or scientific basis was severely lacking. To a very high extent the decision-making process was driven by economical considerations and, in his words, other “extremely random” considerations. Throughout the discussion of whether expansion of the screening panel should be adopted in Israel or not, no written documents were presented to committee members as the evidence base that could justify expansion. The decision to recommend expansion was based on estimated values of the expected prevalence of candidate conditions in other countries. Then, an extrapolation was made to evaluate the expected prevalence among Israeli newborns. The extrapolation was performed orally using gross calculations. The interviewee noted that there could have been up to 10 times error in the calculations. He indicated that this might be an efficient decision making model, yet he criticized its evidence base.

In terms of the routine work of the committee, this interviewee recalled that the committee had convened only three times since the day it was established. The last meeting took place in 2005 (interviewee #13). Others noted that some meetings were conducted by phone, yet many meetings were described by interviewees as spontaneous “hallway discussions”. Interviewees noted that committee meetings were not necessarily scheduled in advance. Sometimes they took the form of “hallway conversations” and in other cases decisions were made by phone conversations. Interviewee #13 described the
decision making process: “...we were like friends having coffee together and talking about expansion...but isn’t that how you divide the world in Yalta?” Another Israeli interviewee (interviewee #2) described the point in time at which the decision to establish an expanded panel of conditions was made, as the time the people in charge at the Ministry of Health were caught up by the idea of expansion and thought it was interesting. From that moment on, the funding issue was considered a non-issue.

Similarly, an Israeli interviewee, from the geographic periphery of Israel (interviewee #11) was skeptical about the decision making process in regard to implementation. He noted that he was never notified about the process even though he is a metabolic expert who identifies newborns detected with metabolic diseases in his geographic area. He speculated that the decision to expand screening was made by two officials at the Ministry of Health, a pediatric endocrinologist and a geneticist, neither of whom he noted, are laboratory people. Finally, an Israeli interviewee (interviewee #3) explained that some of the discussion in regard of the requirements for informed consent for screening and facilitation of follow-up of newborns detected by screening took place between several members of the appointed committee at ad hoc committees or over the phone. The term “ad hoc committees” was mentioned more than once throughout the interviews in reference to the form the decision-making process regarding implementation took. I think that this dynamics of policy making, as described by interviewees, consisting of hallway conversation and ad hoc committees, on having coffee together and by the way talking about expansion, and most importantly relying on a questionable evidence base fits McKinlay’s (1982) critical vision of how medical innovations become a part of established medical practice without appropriate evaluation.
We can think of the presentation of the estimated values of prevalence of the candidate conditions in other countries, the extrapolation of those numbers, and the other “extremely random” considerations interviewee #13 refers to as the second stage in the career of the innovation; its adoption by powerful institutional structures. McKinlay discusses the motivations for this adoption. He brings up the peer pressure which is very dominant among physicians as a main reason, but also notes the wish to improve care, to be seen up-to-date or helpful as other motivations. I think that all of the above motivations are expressed by interviewees.

**Timing and Fundraising for Expansion**

One of the major research questions of this study was, why now? What are interviewees’ views regarding the need for expansion of the newborn screening panel in Israel at this point in time? The vast majority of interviewees responded to the question without hesitating: expansion is needed, and the sooner the better. Interviews showed that the reasons for expansion are threefold: a. the global process of expansion of newborn screening currently taking place across the board has increased the public awareness of the issue, b. technology which has developed enough to provide for a good assay and c. a monetary donation granted to the Ministry of Health for the purpose of expansion and purchase of the tandem mass technology.

Among interviewees, the pressing need to expand the newborn screening program as soon as possible was expressed in different ways. For instance, one Israeli interviewee who took part in the decision making process about whether or not to expand, supported expansion at the earliest time possible, even if it meant skipping the research regarding the prevalence of diseases in Israel, given the existing knowledge of high prevalence of
detectable conditions in Israel (interview #9). Another Israeli interviewee, who is involved in the current newborn screening program, justified the need for expansion at this time in that it promotes continuity, which he argued never existed in the Israeli system (interviewee #7). An Israeli interviewee defined the expansion process as a big achievement of the Israeli health care system (interviewee #6).

In terms of the local driving force behind the development of the expansion in Israel, the “bottom-up” model was mentioned by several interviewees (Interviewee #2 and #3). According to them, the metabolists and geneticists from Sheba Tel Hashomer Medical Center, rather than the Ministry of Health or physicians’ organizations and associations, were the ones who pushed for the creation of the expanded program. Moreover, it was not until the recommendation of the advisory committee to expand that the Ministry of Health joined the effort to implement the program. Why in their views did the Ministry of Health not initiate the program before? An Israeli interviewee (interviewee #2) pointed to the poor public awareness of newborn screening in Israel, in contrast to the long-standing acceptance of prenatal screening that is reflected in the attitude of the Ministry of Health towards newborn screening. This topic is discussed and analyzed in chapter 5. The same respondent thought that it was the result of the inherent lack of initiative on the part of Ministry of Health, while a third interviewee (interviewee #14) indicated that the people who were involved in the initiation of the program strongly influenced the Ministry of Health’s decision. Another interviewee thought that the fact the Ministry of Health did not push for expansion was mainly a result of lack of financial resources (interviewee #3). Interestingly, one Israeli interviewee (interviewee #6) viewed it differently; in his eyes the initiation of the program actually followed the top-down rather
than bottom-up model. It started at the Ministry of Health, was followed by a discussion among relevant health professionals, and ended up at the policy-making level of the Ministry of Health.

McKinlay (1982) brings up the bottom-up approach that leads to the routinization of a new technology as part of the second stage; the adoption of the innovation by medical organizations. He suggests that the motivations behind the administration willingness to adopt the technology following an intense pressure from the medical staff may be the potential of the innovation to enhance the reputation of the hospital in the community or the adoption may be affected by the relationship of the hospital with other interests. Data did not provide evidence for either claim.

In my view, the fact that officials in different levels of involvement in the program viewed the driving force behind the expansion process differently reflects the impact of the social knowledge of these officials on the decision making process. As different stakeholders have different social, ethical and political standpoints, their interpretation of the situation will be based on those standpoints. In the particular case, while respondents who are not affiliated with the governmental agency (Ministry of Health) perceive the flow of events as if the decision making was driven by practicing physicians working in the field of newborn screening, others, affiliated with the public health agency, consider the governmental agency the key player in the initiation of the program. While these contradicting views of the social dynamics that lead to the outcome of expansion do not involve clinical or scientific knowledge per-se, it does demonstrate Bloor’s (1984) view that theoretical knowledge does not originate form out experience but rather it gives meaning to experience. In the present case, different respondents hold different social
perspectives on the same experience of initiation of the expanded program. Based on
their own perspective, interviewees interpreted the same social situation, the dynamics of
creation of the program, either as a bottom-up or top-down approach.

**Structural Considerations: Centralization and Privatization of Screening**

Historically, screening for PKU and Congenital Hypothyroidism was centered at
Sheba Tel Hashomer Medical Center. PKU screening was based at the Pathological
Chemistry lab and Congenital Hypothyroidism screening was conducted at the
Endocrinology lab. Until recently, a single physician at Sheba Tel Hashomer Medical
Center was seeing all PKU patients and another one was in charge of all Congenital
Hypothyroidism patients. This history, coupled with the fact that the American
physicians who initiated the expansion were connected to Friends of Sheba in Los
Angeles, who raised the funds, ultimately influenced the eventual location of the
expanded program at Sheba Tel Hashomer Medical Center. However, with the upgrading
of current screening and the expansion of the program, a structural transformation took
place. The national newborn screening program is now an independent unit of the
Ministry of Health, located at Sheba Tel Hashomer Medical Center. Despite this
transformation, it appears that Sheba Tel Hashomer Medical Center still has more of an
influence in the expanded program. This can be attributed to its historical ownership of
the program, its geographical location, and ultimately, to the fact that the tandem mass
spectrometry device used for the expanded universal screening is owned by Sheba Tel
Hashomer Medical Center.

As an Israeli interviewee (interviewee #2) explained, however, once the expanded
panel starts operating and screen positive results start pouring in, even though screening
for all newborns will still be conducted at Sheba Tel Hashomer Medical Center, the responsibility for confirmatory diagnosis, hospitalizing, treatment, and follow-up of detected newborns will go to the relevant sick fund in the newborn’s area of residence.

Background on the Israeli Health system is included in chapter 2. In short, the Israeli Health system consists of four major sick funds (Clalit, Maccabi, Meuchedet, and Leumit). In 1995, the National Health Insurance Law came into effect. This statute directed that membership in one of the existing Health Maintenance Organizations is compulsory for all Israeli citizens. The law determined a uniform package of benefits for all citizens. This package (the Hebrew translation of “health basket”) includes a list of medical services and treatments that each of the Health Maintenance Organizations is required to fund for its members. In addition, certain services are under the direct administration of the State, most of them, including newborn screening, by means of the Ministry of Health.

Newborn screening services will operate in the following way: Ministry of Health will set up the criteria, and in order to be eligible to treat sick babies, the sick fund will have to prove that it can perform the above procedures at one or more of its facilities. In addition, the sick fund must have a metabolic expert and an endocrinologist on call. To make sure the baby is located and followed-up, positive results will be delivered to Tipat Chalav, the local Maternal and Child Health clinics of Ministry of Health at the baby’s area of residence, in addition to being delivered to the referring hospital (interviewee #2).

When asked for their opinion regarding the centralization of the program at Sheba Tel Hashomer Medical Center, most interviewees, including program officials and non-program officials, Israeli and international interviewees, were in favor of keeping the
expanded screening lab centralized at Sheba Tel Hashomer Medical Center. Their argument was threefold. In a nation the size of New Jersey, one centralized lab enables better follow-up of detected newborns. One centralized lab is also more economical, with better quality control and best management. Finally, they argued that a centralized lab, combined with ad-hoc committees, allows avoiding problems that other international newborn screening programs have encountered. However, one American interviewee (interviewee #17) argued that keeping the screening centralized at Sheba Tel Hashomer Medical Center could pose a problem, because while the lab officially operates as an independent unit of the Ministry of Health, it is also located at Sheba Tel Hashomer Medical Center. Given the rivalry between hospitals in Israel, this duality might complicate the situation. A European interviewee (interviewee #21) indicated that in Germany, where parents may choose one of numerous newborn screening labs regardless of the region they live in, this introduces huge competitiveness and channels some of the resources to lowering newborn screening costs but does not necessarily lead to a better quality of screening. Among the interviewees there was only one who opposed the centralization of the screening lab at Sheba Tel Hashomer Medical Center (interviewee #13). In his view, decentralization will encourage competition between labs that, in turn, would improve the service provided, economically as well as in terms of quality.

Another issue that emerged from the interviews was the strong objection to the concept of privatization of the newborn screening service. The issue came up in the interviews of four Israelis (interviewees #1, #2, #3 and #4). Those interviews revealed that the original plan for expansion was to establish a private firm and run the national newborn screening through it. This idea was discarded at an early stage, and the Ministry
of Health took the responsibility for the program. Interviewees -- Israeli and international, program officials and non-officials alike -- who were opposed to the privatization of newborn screening, argued that screening is a public health service par excellence and as such it ought to be state run. They claimed that the public health system is better fit to deliver screen positive results and be in charge of follow-up and treatment than a commercial entity whose main interest is the financial profit rather than the quality of service. In addition, sending out the bloodspots to a commercial firm would have a negative effect on the continuity of the program, if the delivery of positive results to the medical home would still be the responsibility of the program.

Criteria for Disease Selection

As discussed extensively in the previous chapter, one of the main issues that ought to be discussed as part of the decision-making process regarding the implementation of a newborn screening program is the criteria for selection of conditions to be included in the screening panel. Following the policy analysis of international guidelines, one of the first questions interviewees were asked to address concerned the appropriate criteria for inclusion of conditions in newborn screening panels. As expected, most interviewees articulated the classical Wilson and Younger criteria: severity of disease (important health problem); high prevalence; good assay; sensitive, specific, and reliable test; test acceptable for the population; effective treatment; confirmatory diagnosis; early detection is beneficial. Only one Israeli interviewee (interviewee #13) implied that treatability should not be a necessary criterion for screening. For him, the psychological support that parents receive following the detection of their baby could serve to justify screening, on humanistic grounds if not economically. In his words, by early detection of an untreatedable
disease “we can make an unbearable catastrophe to a bearable one.” All the others either noted explicitly or implied that existence of an effective treatment for the disease is a major, if not the most important, criterion for screening. This consensual view regarding the essentiality of the criterion of effective treatment resembles the findings of the policy analysis (see chapter 3).

Other criteria mentioned by interviewees as important criteria to be considered throughout the establishment of a newborn screening program were the performance of pilot studies and having knowledge about the disease, both in the local setting and internationally; cost of test; equitable distribution of resources, and availability of facilities for treatment and follow-up, including staff training, genetic counseling. Almost all Israeli interviewees (interviewees #2,3,4,5,7,8,9) also noted that a low percentage of false positives was an important criterion affecting the selection of conditions to screening panels, as it helps to avoid psychological stress for the parents. The reason for it, as discussed in chapter 2, a high percentage of false positives may result in delayed delivery of results and lack of public trust towards screening. Both criteria could be viewed as part of the classical Wilson and Jungner criteria of whether or not a test is acceptable for the population. An Israeli interviewee (interviewee #2) emphasized that according to Ministry of Health regulation the medical home (i.e., hospital of the sick fund insuring the detected newborn) would have to report back the results of confirmatory diagnosis, so that data regarding false positives and false negatives could be collected, evaluated, and used for publications.

Knowledge about prevalence was mentioned by most interviewees as an important factor in the decision making process towards inclusion of conditions in the screening
panel. However, when asked about its significance, interviewees emphasized that studying prevalence is not the goal of newborn screening but rather a high prevalence is a justification to screening (interviewees #1, 2, 4, 9, 13, 14). In addition, a couple of interviewees (interviewee #9, 17) noted that in Israel, because of consanguinity in the Arab and Orthodox Jews communities, there is relatively high prevalence of metabolic disease. An Israeli interviewee (interviewee #2) noted that the Israeli screening panel will only include conditions which are being screened for around the world and for which there are clinical patients in Israel. Another Israeli interviewee (interviewee #1) explained that at first the program directorship planned to receive data regarding prevalence through the pilot study; however the legal consideration of this research makes it hard to conduct. Therefore, the idea was neglected. Other Israeli interviewees, who participated in the decision-making process (interviewee #4) and another one, who participated in the early phase of the decision-making regarding expansion (interviewee #9), claimed that local and international data regarding prevalence of conditions screened for by newborn screening provides a sufficient evidence base to justify screening in Israel. Yet another Israeli interviewee (interviewee #13) criticized the decision-making process regarding inclusion of conditions in the panel, in which he took an active part, as it was conducted using non-mathematical extrapolations of international prevalence.

We can learn more about the process of decision making regarding what conditions to include in the screening panel, from the response an Israeli interviewee who was involved in the decision making process towards expansion (interviewee #2) and explained why the following conditions were not added to the panel although they were seriously considered: G6PD, Cystic Fibrosis, Sickle Cell Anemia, and Galactosemia.
The decision not to include any of those conditions, he recalls, was the following: In Israel, G6PD is conducted for patients of certain ethnicity; Sickle Cell Anemia is performed only in cases where there is known family history, and Cystic Fibrosis is screened for prenatally. Galactosemia is very rare, easily detected (clinically) and the treatment is relatively easy. In addition, he noted, since the funding source for the expanded program is not the government but rather a donation, the plan was not to waste money on unnecessary conditions, and to focus on one technology only. The device selected for that purpose was tandem mass spectrometry, a machine that leaves no room for uncertainty. As we will find out in the next section, this last point is debatable. To summarize the issue of prevalence, interviewees considered high prevalence a justification of screening rather than its purpose. In theory, program directorship considered the estimated prevalence of the candidate conditions in other countries a good enough justification for expansion in Israel. In practice, one presymptomatic Medium Chain Acyl-CoA Dehydrogenase Deficiency case and one Maple Syrup Urine Disease case was sufficient evidence to move along with the process of expansion.

**Determination, Detection, and Reporting of “Screen Positive” Results**

For the following discussion, a definition of the term cut-off level is in place. *Cut-off level* is defined as the value under which an individual is determined to be “screen negative” and above which is determined to be “screen positive.” Cut-off levels depend on the newborn’s age and birth weight. Consequently, premature babies are measured using a different cut-off than full-term babies for certain conditions. As a result of the upgrading of methods, analytes, and assays used for the detection of diseases in expanding programs, the values used as the cut-off levels for different conditions are
sometimes transformed. In addition, using kits of different manufacturers may contribute
to a different definition of thresholds for conditions in the screening panel. Lab
technicians, while utilizing the tandem mass spectrometry device, have one of three
options in regard of policy for detection of analytes. a) set the device to detect abnormal
values (peaks) of certain analytes only; b) set the machine to detect every abnormal value
and disclose all the information available to parents and the medical home; or c) set the
machine to detect all information available but keep it at the lab files and report it back to
the medical home or parents only in case of emergency.

Three questions the study aimed to address regarding the policy for determination,
detection, and reporting of results in the Israeli expanded program were: a) who
determines the cut off levels for a “screen positive” result and what is the evidence base
for it?; b) who makes the decision regarding the detection of abnormal results for
conditions not included in screening panel (i.e., incidental findings) and what is the
evidence base for it?; and c) who makes the decision regarding reporting of “screen
positive” results for conditions not included in screening panel, and what evidence base
supports that decision? The complementary normative questions were: d) how should
“screen positive” results be determined; e) what levels of analytes should the program set
up the machine to detect; and f) what kind of results should the lab report to the medical
home. The next section addresses the policies of the Israeli newborn screening program
regarding those questions.

Generally speaking, data analysis showed the inchoate nature of the policies and the
varying interpretations of those policies regarding basic Programmatic aspects as
practiced by different stakeholders in the newborn screening program. The following
section will analyze this theme regarding the Israeli policy regarding the determination, detection and reporting of results.

The varying opinions surrounding other issues in the Israeli newborn screening program, such as the mechanism for selection of conditions to the panel, and the length of the pilot phase of newly added conditions, also characterized this essential question of the policy regarding reporting of results. Data shows that less than half of the interviewees were more supportive of the position to find out as much as possible and report it to the parents or the medical home (interviewees #2, 5, 6, 13, 16). One Israeli interviewee (interviewee #2) was skeptical about the ability to ignore a high peak indicating an extremely abnormal value of a disease not included in the panel. For him, this could indicate a quality control issue that should not be missed. However, while justifying this model, some called for caution regarding opening a “Pandora’s box” by disclosing all available information (interviewee #10). In particular they were concerned about reporting abnormal values of analytes that indicate conditions for which the clinical significance is uncertain or unknown.

Most interesting in this regard were the views of European interviewees (interviewees #20, 21) who explained that in their programs, guidelines were established to prevent program officials from disclosing results for conditions that are not included in the panel. However, they admitted that if a newborn screens positive for a conditions that is not in the panel, they find an unofficial way to get the information regarding the abnormal values back to the medical home of the baby. They justify not following the guidelines with the rationalization that the baby is no longer a newborn screening patient but rather a metabolic patient and admit that perhaps this distinction makes it easier for
them to break the rule. One interviewee (interviewee #21) justified not following the guidelines by saying: “...It would be very hard for me to sleep somewhere to know that I know about a sick child with Citrullinemia and I don’t know if they know about it at the ward there and you just say, “Okay, whatever.. Next child.” I mean even if I know that, I probably cannot save the child or there’s no treatment at that point of time, but still getting the diagnosis may be helpful, even in terms of prenatal planning later, or just having a diagnosis for the parents...”

The fact that the same analytes used for identification of disorders that are included in the panel are also used for the detection of other conditions, makes setting up the cut-off levels a complicated issue. As the following example shows, for many conditions in the panel the determination of the appropriate cut-off level can be a delicate decision. Such is the case for Tyrosinemia. In this disorder, the metabolic defect doesn’t cause an elevation of the Tyrosine directly. Rather, the disorder causes a liver defect that eventually leads to an elevation of the Tyrosine level. This process takes place gradually over time. Thus, at the age of 48 hours, the baby will not have a high enough level of Tyrosine to be detected by a high cut-off level. At the same time, premature babies also present high levels of Tyrosine. If the cut-off level is set up too high, in order to avoid a high percentage of false positives because of premature babies, the screening mechanism will miss those Tyrosinemia cases that do not yet manifest the high level of Tyrosine, but will manifest it soon.

Given the complexity of the decision about cut-off levels, I would expect interviewees to realize the important social and ethical implications of the decision regarding cut-off levels. However, a surprising theme that emerged from the interviews
was the message coming from non-program officials interviewees, at times implied (interviewee #3) and at others explicit, (interviewee #11,14) that setting up certain cut-off levels and deciding which conditions should be detectable is no more than a “technical, chemical, professional issue.” Not only were interviewees unfamiliar with the values used as cut-off levels for the various conditions, they didn’t seem to be bothered by their lack of knowledge. Furthermore, they seemed surprised to hear the question. If at all, the only thing they were concerned about was the validity and reliability of the test. When I emphasized the question of who should make the decisions regarding the cut-off values of conditions in the screening panel, the answer I most frequently received was that it should be based on international experience. In practice, it looks like the cut-off levels are the business of the newborn screening lab director and his only.

I suggest that the concept of medicalization is particularly relevant to the discussion of those policy issues. I agree with Vailly (2008) who argues that lowering thresholds for disease on the newborn screening panel reflects a social message that does not tolerate disability, or in other words, it expands the idea of medical abnormality and as such contributes to the process of medicalization of increasing parts of the human existence (Zola, 1972). In practice, the expansion of the panel in Israel will define 80 more newborns every year as abnormal, at least up to the point of diagnosis. I associate the simplified view of respondents, seeing the determination of cut-off levels as a technical issue with their highly medicalized attitude.

In a brief observation I conducted at the newborn screening laboratories in September 2007, before the expansion took place, the technicians pointed out the gradual shift in the assay for Congenital Hypothyroidism throughout the years. According to the
technicians, the assays, cut-off levels, and equipment used at the lab have changed several times. In general, they say, the cut-off levels have gone up. Throughout my conversations with the technicians, I felt that they, too, prefer not to get involved in complicated policy-making issues including the determination of cut-off levels and procedures for reporting of screen positive results. Instead, they leave those decisions to the discretion of the laboratory director. I suggest that the interpretation of respondents regarding the task of setting cut-off levels for newborn screening tests being a technical detail that carries no moral or ethical consequences reflects their attitudes towards the institutional and professional procedures as being a given that they have no influence over. In addition, it reflects their perception of their passive role in adhering to policy rather than creating it. The lab technicians deferred from getting involved in the determination of cut-off levels despite their clear advantage in doing so, considering their extensive experience. I argue that this position circles back to the concept of authoritative medical knowledge described by Browner (1996). For Browner and her group, the dominance of clinical technologies is a part of the hegemonic efforts of biomedicine in these domains. With the increasing utilization of medical technology, as in the case of adoption of the tandem mass spectrometry, Browner anticipates that women will defer to the biomedical authority. Georges (1996) discussed similar issues in an international setting. I suggest that lab technicians defer from getting involved in this policy matter and prefer to let the lab director do the job for similar reasons. The explanation for the deference of technicians from taking part in the determination of cut-off values may be associated with the patriarchal structure of the clinical and technical staff of newborn screening program in Israel. This issue is, however, beyond the scope of the present
study. Following the determination of results, its communication to parents is the next step. Here, too, problems arise, as the next section reveals.

**Parental Stress Following Receiving “Screen Positive” Results**

A major psychosocial implication of expanded newborn screening discussed in the literature is parental anxiety following detection of positive newborn screening results that turn out to be false in confirmatory testing (Weisbren, 2004; Hewlett, 2007). Interviewees followed this trend and the vast majority, when asked about harms resulting from expanded screening, discussed parental stress following the detection of newborn screening positive results (interviewees #2,4,7,8,9,10,11,13,18). However, interviewees also brought up the stress surrounding the detection of results with unknown or uncertain clinical significance, such as detection of asymptomatic cases of MCADD (interviewee #3) or mild variants of Organic Aciduria (interviewee #2). While in the international literature there is an ongoing debate regarding the appropriate policy of reporting results with unclear or unknown clinical significance (see chapter 2), data analysis showed that in Israel the practice leans more towards not reporting it. One interviewee (interviewee #10) recommended disclosing this kind of information only if there is a strict criterion that justifies it. Otherwise, he thought, the information should be kept within the program. Similarly, an Israeli interviewee (interviewees #4) was in favor of keeping this kind of information from families who may suffer unnecessary anxiety because of it. He expressed the view that disclosing results with unclear or unknown clinical significance would elicit tremendous anxiety within the family who would see the results as catastrophic. A third interviewee voiced his concern that if parents didn’t even know their baby was screened for certain conditions, the disclosure of screen positive results could
cause massive parental anxiety (interviewee #13). He therefore called for revisiting the whole consent process for the screening (the issue of consent will be discussed in the next chapter). To summarize this point, the vast majority of interviewees acknowledge the high levels of parental anxiety associated with the detection of screen positive results, either true or false ones, however, no clear guidelines regarding how this anxiety should be relieved exists or is being discussed at present. I suggest that the concept of social construction of biomedical knowledge offers an explanation to those findings. For the physicians, the social aspects of the newborn screening process become inferior to the scientific or medical issues. Therefore, they do not pay attention to the essential part of communication of results. This results in harmful psychosocial effect on the detected newborn’s family. The importance of public awareness and education about newborn screening in alleviating this stress is discussed next.

Education and Public Awareness regarding Newborn Screening

Program officials and non-program officials, Israelis and international interviewees, all agreed on the need for better education of both parents of newborns and clinicians regarding the process of newborn screening.

Education for parents

Interviewees voiced their deep concerns regarding the lack of parental education. There was consensus between interviewees regarding the right timing of parental education—during the prenatal period. Interestingly, a couple of program officials declared that at the early stages of the expansion process, the policy of the program directorship was to avoid providing information about the process. As a program official noted “I thought we would start with public education but we could not afford it because
it would create panic...so at first women will not receive information during the pregnancy but closer to delivery and in the next few months we will do it at the prenatal period.”

Interviewees tried to reason the lack of public discussion regarding newborn screening. In contrast to prenatal screening, which has been in the center of the Israeli public conversation for several decades, newborn screening has never been a topic of public interest (see chapter 2). In addition, unlike the situation in the U.S., in Israel the activity of advocacy groups, including groups of parents of sick newborns, gets little attention. Program officials find the lack of public interest in newborn screening surprising because it is in contrast to the high public interest in Israeli society of medical issues in general, and the intense public interest, not to say pressure, in decision making regarding prenatal screening in particular. The lack of interest among Israelis in newborn screening contrasts markedly with the strong interest in these issues among geneticists and families affected by genetic diseases in the U.S. A public official recalled that when he first started his job at the Ministry of Health he set up a meeting to discuss the newborn screening panel, which at the time included two conditions only. He wanted to prepare for potential public criticism of the minimal newborn screening panel in Israel. Apparently, there was no need for such a meeting. Since he began his new position at Ministry of Health nobody has ever approached him to complain about the minimal newborn screening panel. Only one Israeli interviewee (interviewee #2) puts the “blame” for the lack of public interest in newborn screening on a reason other than the lack of education.
Program officials are fully aware of the fact that the public’s lack of awareness regarding the current process of expansion of newborn screening assists them in quick implementation of the expanded program, by saving the program’s directorship the need to deal with possible public objections to the expansion. They realize that once the public is informed about the expansion, program officials will need to become more responsive to public opinion. Before they start notifying and educating the public about the expansion they are trying to get as much done in terms of the implementation of the program.

One interviewee, critical of the lack of public engagement in the process of expansion, discussed a future possible scenario in which parents will find out about the partial expansion of the panel and will accuse the newborn screening program for not including one or more of the 29 American College of Medical Genetics core conditions in its panel. In their favor, two remarks are noteworthy. First, program officials are self-reflective and forthcoming about their role in the public’s lack of education. They are well aware that there is a price to their policy of under-publicizing the process of expansion and they explicitly voice their concerns that in the current situation the rights of the sick children are not protected. To remedy this, in the near future a website aimed to inform parents of screened newborns about negative newborn screening results will start operating.

**Education for Professionals**

Again, there is a consensus among interviewees that education for professionals about the various aspects of the newborn screening process is critical. Education should include information about the diseases screened for, testing methods, natural history of
the disorders and treatment alternatives. In addition, professionals -- in particular ob-
gyns, pediatricians and family physicians -- should understand the meaning of basic
terms such as cut-off levels and false positive results. Interviewees agree that the level of
knowledge of the newborn screening process among professionals is extremely low. As
one Israeli interviewee who was involved in the decision making process (interviewee
#13) said “…they know that the program exists, every once in a while they see a baby
with a low T4 (the alanyte that indicates that the baby is affected in Congential
Hypothyroidisn-S.Z.) and panic. They call the parents to bring the baby for a second
testing, get the low T4 again and send it to the endocrinologist to deal with it…they ought
to understand the mechanism, the disease, they are the ones who will need to handle
parents, they will be the first line of questions and should know to address them…if those
things become part of the system widely we’ll need to have an educational program to
pediatricians, family physicians, all physicians who see kids.” Another respondent
(interviewee #9) claimed that it would be hard to put the entire burden on nurses and
physicians at Tipat Chalav (the Maternal and Child Health Clinics) who are unfamiliar
with the process. One Israeli interviewee (interviewee #6) argued it is therefore the
responsibility of the Ministry of Health to put together a campaign and involve all the
participating sectors in it, including hospitals, Tipat Chalav clinics, and health
professionals, as the families will arrive there with babies who are still completely
healthy, and the nurses and physicians will need to handle uncertainty and avoid the
provision of misinformation. An international interviewee (interviewee #16) noted that
education should start in medical school and continue as ongoing or continuing education
and education for practitioners who are not performing well, as well as at regular meetings.

The lack of public awareness regarding the practice of newborn screening in general, and of the expansion of the panel of disorders screened for in particular is situated in sharp contrast to the happenings in the international setting. There, public awareness of both parents and health care professionals are leading concerns when it comes to genetic screening in general and newborn screening in particular. The lack of public awareness regarding the expansion of newborn screening also contrasts sharply to the extremely high public awareness regarding prenatal testing within Israel, where an expanded panel of prenatal screening tests, with specific recommendations for use determined by the parents’ ethnicity, a panel that is continuously growing, is available to all citizens and covered by the national health insurance. While there is a longstanding acceptance of prenatal screening, very limited attention is paid by the public and health care professionals to the process and outcomes of newborn screening. In addition, one respondent (interviewee #2) brought up the active role advocacy groups in Israel play in influencing the selection of disorders to prenatal screening panels. For example, in Israel, parents of children affected with two disorders screened for prenatally, cystic fibrosis and Familial Disautonomia, are considered active in advocacy work while parents of newborns detected with other conditions are far less active. In contrast, in the U.S. parent of detected newborns are as engaged in these issues as parents of babies detected prenatally (see chapter 2).

In order to explore the reasons for this gap in public understanding between newborn screening and prenatal screening, I looked at the changing circumstances in
Israel in both fields in the past two decades. Since the 1990’s prenatal genetic testing in
Israel has increased substantially. Among the key motivations driving the choice of
pregnant women to have prenatal testing is the fear of having a sick or disabled child, and
the lack of a supportive environment in which to raise such a child (Sher et. al, 2003;
Remennick, 2006). The situation is different, however, for newborn screening, which
occurs after the baby is born.

Expansion of the panel of conditions adds another level of complexity, since more
affected newborns are detected. Recent qualitative research on newborn screening for
cystic fibrosis shows that early detection of a disease, as opposed to diagnosis after
symptoms appear, affects parents’ feeling of competence to care for their newborn and
their sense of who the child is. Rather than “falling in love with the new baby,” the
disease becomes the center of attention (Grob, 2008). Those psychosocial affects of early
detection of metabolic conditions by newborn screening that are described by Grob are a
partial explanation of the gap between parents’ indifference regarding the process of
newborn screening as opposed to the high levels of interest they express about prenatal
screening. I have anticipated, before I started my interviews, that the main reason for this
indifference is simply the lack of education regarding newborn screening. My
expectations proved right.

Indeed, when asked about the varying levels of public awareness and education
regarding newborn screening and prenatal screening, most interviewees agreed that a
considerable gap between the two exists. Very few of them, however, provided an
explanation for it. An Israeli interviewee (interviewee #2) claims that until the baby is
born the fear from the unknown is very intense. Therefore, prospective parents will do
everything in their power to check out the health of the fetus. However, once the baby is
born and they see it has ten toes and ten fingers, and looks “normal” the level of anxiety
goes down drastically, and it is difficult to get the mother interested in future disorders
that may or may not affect her baby. As feelings of love and competence to care for the
child develop, screening for diseases before symptoms appear seems far less compelling.
This argument corresponds with Grob’s findings and I find it very persuasive.

As I have argued in the introduction chapter, the data presented here shows that the
Israeli quest for the “perfect baby”, which is strongly demonstrated by the acceptance of
prenatal screening, is not reflected by the situation regarding newborn screening for one
major reason, lack of knowledge about the program. Just as providers of prenatal genetic
services drive the uncritical public acceptance of prenatal screening, newborn screening
program directorship lead the public ignorance about newborn screening and its current
expansion. By deliberately hushing the process of expansion while awaiting the right
timing and keeping it away from both parents of newborns, health professionals and the
general public they contribute to its neglect by all parties. Only when the program
directorship starts publicizing the program and educate health professionals who in turn
will educate parents about the process and its significance to the well being of their baby,
will the indifferent approach of parents change into an active support in the process of
expansion of the panel, despite the uncertainty inherent to many disorders included in it.

Coupled with the minimal levels of education provided to health professionals and
parents in Israel, as described by respondents in this study, the increasing utilization of
technology leads to almost complete deference of parents of newborns to the biomedical
authority in this field. Following the parallel analysis of Remmenick in prenatal care, I
anticipate that adding more conditions to the newborn screening panel will change this state of deference. Consequently, newborn screening will be perceived by both health professionals and parents as taking one more step towards achieving the ultimate goal of having a perfect child, if education is provided to the public and health professionals in the field.

**Inchoate Nature of Policies and Varying Interpretations of those Policies**

The most dominant theme that came out of data analysis was the inchoate nature of the policies and the varying interpretations of those policies regarding basic programmatic aspects as practiced by different stakeholders. Those included the final panel of conditions; the mechanism for determination of cut-off levels; the policy regarding the detection of conditions not included in the screening panel and the reporting of those incidental findings; mechanisms for diagnosis and follow-up; program timeline; policy regarding storage and future use of residual bloodspots, and as will be discussed in chapter 5 also the form the American consultation for the program would take. Other specific concerns raised by respondents during the interviews emphasized the program’s inchoate policy. The lack of clarity surrounded the following issues: who the chair of the advisory committee was; who sat at the table when the final decisions regarding expansion of the panel were decided; which institution would cover repeat testing and confirmatory diagnosis of screen positive individuals, and at which medical facility (i.e., the metabolic unit of the hospital, emergency room) those procedures should be performed. Non-program officials, program officials, people at the management of Ministry of Health, members of the advisory committee and people who were involved in
the decision-making process at various stages, have all been unclear about basic programmatic issues.

Before we examine this theme in more detail, it is important to make a distinction between three elements of policy that together highlight its dynamic nature: the official policy regarding various programmatic issues; the diverse and varied ways those policies are interpreted in practice by program officials and other stakeholders, and the way that even official policy is never “finished” in the context of technological change. Given the newness of the Israeli program and the introduction of tandem mass spectrometry, all three elements are highly relevant. For instance, the Israeli policy regarding the determination, detection and reporting of results seems inchoate. This problem could be fixed with time and following the operation of the new system. However, inconclusiveness regarding the appropriate form that informed consent should take is the result of the different interpretations of the policy regarding those issues by different players in the Israeli newborn screening field. As such, it may not get resolved with time without deliberate effort on the part of those involved. Rather, it necessitates a deliberate decision-making process. Following is a discussion of the various programmatic aspects demonstrating this theme.

To begin with, the issue of **the selected panel of conditions** remained unclear all throughout data collection and up to few months before the program started operating. Almost all interviewees, including program officials, seemed uncertain about the conditions selected for the panel. Even those interviewees who were familiar with the selected panel of conditions emphasized that the list of conditions selected for the panel is a temporary one (interviewees #1, 2,3). If at the beginning of data collection (May 2007)
the proposed panel included 13 conditions (see Appendix 4) one year later the number was reduced to 10 conditions (see Appendix 5); close to submission of the manuscript (May 2009), one year into actual operation of the expanded program, the panel included 11 conditions (see Appendix 1).

The other subject of inchoate policy on the side of the program directorship was the mechanism for selection of conditions to be included in the screening panel. In earlier interviews (performed around mid 2007), several program officials and committee members indicated that the plan was to conduct a pilot study of screening for the selected conditions for a six months period. At the end of this time, a decision would be made whether or not screening for those conditions was economically justified. Interviewees were skeptical about the ability to stop testing for a condition once it was already on the panel. At some point in the midst of data collection, the length of the planned pilot period reported by interviewees changed. In later interviews (2008), Israeli interviewees (interviewees #1,2) reported that the plan is to add conditions gradually in order to keep the system running throughout the expansion process and avoid human errors. At first, common conditions for which there are sufficient knowledge and effective treatment will be screened for. Two years later, once the system is up and running, and after it gains the trust of health care professionals and parents and the increased workload is successfully controlled, more conditions may be included in the panel. This way, an Israeli interviewee (interviewee #3) explained, the program will not face the obstacle of having to stop screening for conditions that were added to the panel all at once, without sufficient evidence to justify its inclusion in the panel. This is, in his words, “the middle ground between the American way of adding tens of conditions and then considering the
panel’s appropriateness, and the European way of keeping a minimal panel of conditions” until there is enough evidence to justify expansion. Finally, in complementary conversations with program officials, after the program started operating in February 2009, Israeli interviewees (interviewees #1, 2, 3) revealed that other than the 10 disorders in the panel, known to occur with higher incidence in the Israeli population, other disorders are now run as pilot in order to learn more about their frequencies.

A third area of different interpretations of the official policy, which is inchoate in itself, was the mechanism for detection and reporting of results for conditions not included in the panel. Once again, the vast majority of interviewees (including program officials, interviewees at the management of Ministry of Health, and physicians involved in the decision making process at various stages) were all unsure about whether or not the newborn screening program has in fact a formal policy regarding those issues, as well as what the appropriate policy is. An Israeli interviewee who participated at the earlier phases of the decision making process (interviewee #9) admitted that he changed his mind several times regarding the appropriate policy and finally decided that the program should determine ahead of time what it aims to detect and only screen for those conditions (the “European model”). One Israeli interviewee (interviewee #3) indicated that there is an agreement among professionals that if a condition for which there is an effective treatment is detected, it should be reported to the medical home. In regard to how to convey the information, those are, in his words, “games between (policies of –S.Z) the UK, Germany, and Switzerland.” Another Israeli interviewee (interviewee #2) argued that the only conditions that should be reported are those diseases that are captured by
certain criteria, certain cut-off levels or combinations of peaks at the tandem mass spectrometry output.

This aspect, of the inchoate nature of the policies and the varying interpretations of those policies regarding basic programmatic aspects as practiced by different stakeholders becomes particularly clear within the framework I have employed. As data analysis portrays, the construction of social knowledge into the medical knowledge of policy makers that leads to their final decision making is particularly important in the case at hand for two reasons: First, newborn screening aims to detect rare genetic and metabolic conditions. Because they are rare, the natural history and etiology of many of those conditions is uncertain, sometimes even unknown. Furthermore, in regard to many of those conditions, a significant amount of clinical variation within the screened population exists. Next, the decisions regarding determination and detection of conditions by the technology are made by health professionals and policy makers while the minors’ interests are represented by their parents, who in most cases are uninformed. Given the complexity of interpretation of the screening results, as discussed earlier in this chapter, and the vulnerability of the screened individuals and their families, understanding the social influences on the “clinical” decision making process regarding various programmatic aspects is crucial.

I suggest that the story of the creation of the Israeli newborn screening program exemplifies the concepts of the social construction of the medical knowledge and biomedicalization. Data analysis showed that the rationale that drove the American parties to push for the creation of an expanded program in Israel was their concern regarding the great need for expansion and the view of the financial donors, that by
granting the money for this purpose they are actually doing a Mitzvah that will improve
the life of Israeli kids. The justification for expansion was the detection of a few positive
cases in the pilot testing. In my view, both the rationale for initiation of the program and
the justification using the pilot testing results are the social knowledge of the program
initiators in the U.S. and Israel. This social knowledge was co-produced with their
scientific knowledge in the decision - making towards expansion and influenced the final
decision to expand the panel. In other words, the idea that the establishment of an
expanded newborn screening in Israel, or better yet, a world center of genetics (which
was the original plan of the American Initiators as discussed earlier) will save lives or
that it is a mitzvah (or pikuah nefesh as one interviewee articulated) for Jews to help
other Jews, wherever they are, are components of a social knowledge of the initiators of
expansion. Similarly, the evidence base gathered by the initiators in the U.S. using the
electronic search prior to contacting the Israeli parties and the information obtained by
the pilot testing in New York newborn screening program are the technoscientific
component of knowledge. The social component in both cases influenced the launch of
the expanded program.

Once the program was established, the inchoate nature of the policies and the
varying interpretations of those policies regarding basic Programmatic aspects as
practiced by different stakeholders characterized four major aspects of the program: 1.)
the selected panel of conditions, 2.) the criteria for selection of conditions to be included
in the screening panel, 3.) the mechanism for detection and reporting of results for
conditions not included in the panel, and 4.) the involvement of American newborn
screening professionals in the evolution of the Israeli program. I argue that the unclarity
regarding all those issues is best interpreted using the perspective that physicians’ ways of knowing are influenced by their social knowledge; that is their moral and ethical, values, their socialization, the institutional and professional procedures and routines they use and, finally, in the broader perspective, the social structure of society. Just like for Nicolson (1987) and Brown (1995) there is no “objective” or “clinical” answer for “clinical” questions but rather the decisions of health professionals reflect their social knowledge, in the case at hand too, the responses of newborn screening program officials and other stakeholders’ views reflect their moral, institutional, and cultural, views. Furthermore, following Zola (1972) and Clark’s (2003) work on medicalization and biomedicalization; not only both kinds of knowledge (scientific and social) influence the final clinical decision making, but rather there is a process of co-production of social knowledge with technoscientific knowledge. In the case at hand, many pieces of social knowledge take a part in the process of social construction. Those include the peer pressure to adopt tandem mass spectrometry and expand the panel, the opportunity to expand the program following the anticipated financial support, the end of the years-long financial American support for Congenital Hypothyroidism screening, and the concerns regarding budget cuts following policy reforms in the health basket committee. All those factors, along with the growing scientific knowledge regarding incidence of candidate conditions, cost benefit analysis and the results of the pilot testing of newborn screening bloodspots conducted at New York State newborn screening lab influenced the final decision making regarding expansion. The next chapter discusses the social and ethical dimensions surrounding the operation of the program and the influence of the American experience.
Chapter 5: The Context of the Expanded Newborn Screening Program in Israel

Introduction

The previous chapter told the story of the creation and implementation of the expanded Israeli newborn screening program. In particular, it focused on the social and ethical aspects of the initiation of the program, the policies regarding determination, detection, and reporting of “screen positive” results and finally the lack of education and public awareness regarding the program. Recent literature suggests that the conduct of a detailed analysis of the social, political, and economic context and being sensitive to cultural differences may not solve ethical dilemmas but will allow avoiding mistakes in applying solutions originated in the U.S. to resource poor problems (Marshall et. al, 2004). In accordance with this view, a major research question was how the context within which the Israeli newborn screening program is embedded influences its creation and operation. This chapter completes the picture, by discussing the larger context within which the program flourished, and then moving to major ethical and social issues raised by the implementation of the expanded screening. This chapter, like the previous one, relies mainly on data gathered through in-depth interviews with Israeli program officials and with physicians, and international newborn screening experts who played a role in the process of expansion. The concepts of the social construction of medical knowledge, medicalization and biomedicalization, the technological imperative and McKinlay’s (1982) stages in the routinzation of a new technology, and the quest for a “perfect baby” in Israel, which were presented in the first chapter, framed the discussion in this chapter, as they did the previous one.

Legal Basis of the Expanded Program
Several American and European newborn screening programs served as a model for the design of the expanded Israeli newborn screening program in regard to various clinical and technical aspects, including analytes, assays, and cut-off levels. In contrast to the recognition of the influence of American and European practices and procedures on the programmatic aspects of the Israeli newborn screening, there is little discussion of the influence of the international legal models for guidance, perhaps because those legal guidelines are not seen as relevant to the Israeli context. One of the model European programs works under state-run guidelines. A European interviewee (interviewee #21) was highly critical of those guidelines which, he claims, were influenced by lobbying groups, written by lawmakers rather than physicians, and are therefore difficult to understand. In contrast to this model of state-run guidelines, the legal basis of the operation of the newborn screening program in Israel is closer to a regulation rather than a law. As discussed in chapter 2, a regulation of the Ministry of Health focused on the operation of the program came into effect in 2009 (regulation No. 17/2009 see chapter 2).

While an Israeli interviewee (interviewee #1) emphasized that the Ministry of Health is the entity in charge of the ethical and legal aspects of the program another one (interviewee #6) implied that program officials, on behalf of the Ministry of Health, are the ones who should make the decisions regarding the conditions included in the screening panel and the other ethical and legal issues.

I argue in this dissertation, that that the inchoate nature and lack of clarity regarding the responsibility over the various aspects of the program’s operation and functioning, and regarding other programmatic aspects discussed in chapters 4 through 6 is a reflection of what stage the tandem mass spectrometry is at in its “career” in the
developing newborn screening program. I suggest that the program is in the second stage of its adoption by professionals and organizations. Specific examples to strengthen my argument are provided throughout the different sections.

Economical Considerations in the Evolution of the Program

The main theme emerging from the interviews in regard to economic aspects of the program is the concern that the newborn screening program in Israel will find it difficult to compete with other health care needs when it comes to resource allocation. Currently, according to an Israeli interviewee (interviewee #6) the expanded newborn screening program is funded through the health basket under the rubric of “technological development”. However, several interviewees anticipated that in the future newborn screening will have a low priority in the process of resource allocation. One interviewee (interviewee #4) pointed out that newborn screening deals with children, who have no political clout, as opposed to adults who can more strongly demand care; moreover, the mandatory nature of newborn screening puts a relatively high burden on the public health system despite the rareness of the disorders for which screening is performed. As discussed in chapter 2, since the National Health Insurance Act of 1995 became effective in Israel, newborn screening has to compete with many other health care needs. Another interviewee (interviewee #9) explained that according to the law, the various healthcare needs, including preventive medicine; compete to be included in the “health basket” or medical care provided to all Israelis. Indeed, he noted, in contrast to cancer medications that have a stronger lobby, many vaccinations did not make it into the basket. My understanding from those interviews was that respondents worry that the current funding of newborn screening by the Ministry of Health could be taken away if lobbying for
other, stronger candidate health care needs, convinces the Health Basket committee that its inclusion in the basket overrides the need for newborn screening. I argue that the competition on the limited resources available for all healthcare needs may increase the efforts of program officials and other supporters of expanded screening by tandem mass spectrometry to praise the performance and advantages of the technology for the purpose of newborn screening, in order to keep the governmental funding. Following McKinlay’s (1982) model this enthusiastic report will be done by publicizing its effectiveness in professional journals, by the presentation of preliminary results of the expanded screening in and around the country, and by word-to-mouth conversations with other colleagues in Israel and internationally.

Another concern related to the economic aspect of the program is the massive dependence on external funding sources for the early phase of the program and its expansion. As discussed extensively in chapter 4, because of the tough competition for funds available at the Ministry of Health for various drugs and technologies, the newborn screening program managed to find at least two other venues for supporting its costs. First of all, interviews revealed that for thirty years the kits for Congenital Hypothyroidism screening were funded by a private American donation. This arrangement lasted until very recently (see discussion on Chapter 5). Secondly, an Israeli interviewee (interviewee #4) admitted that in 2005 he received a donation from a private source that allowed for the purchase of the tandem mass spectrometry device. An American interviewee (interviewee #18) explained the motivation of the donors was to grant the Israelis one-time assistance that would nonetheless be far-reaching and have an impact on generations of children. Other interviewees, both Israeli and American
(interviewees #6, 17, 18) were concerned about the pattern of economic dependence on the external funding sources that characterizes the newborn screening program. However, an Israeli interviewee (interviewee #5) explained that the plan was to start the program using the one-time donation of technology and diagnostic kits and once it was up and running the external financial support would be replaced by funding from the Ministry of Health.

This last observation clarifies the third theme that came out of the interviews-- the overarching consensus that newborn screening is cost-effective. Most of the interviewees (interviewees #2,3,4,6,13, 17, 18) stated in full confidence that using the tandem mass spectrometry device for screening an expanded panel of conditions is cost effective, as the same assay is used to detect all conditions at the same time and a for a similar cost. One piece of evidence to support this claim was that the public saves 5 million shekels (around $1.2M) for each child that is prevented from becoming severely retarded by early detection and intervention. Therefore, they argued, the benefit for society from screening is clear and significant. However, other than this estimated cost, no further evidence was brought up by interviewees to support their claims. The wide agreement among respondents regarding the cost-effectiveness of screening newborns in Israel using tandem mass spectrometry, despite the lack of evidence for this assertion, fits McKinlay’s description of the exploratory studies of the effectiveness of an innovation; a description that characterize his first stage in the career of the technology, the stage of “promising reports”. Finally, it is likely that at least some of the arguments in favor of the cost-effectiveness of screening (perhaps even the calculation of saving $1.2M by detecting affected children early enough that preventive treatment can start) rely on articles that
made an association of this promising report with “respected scientists” and with
prestigious institution (Mckinlay, 1982).

Disorganization, Informality, and Authoritative Biomedical knowledge

One challenge that was referred to repeatedly by interviewees and linked by them to
the Israeli culture was the disorganization and lack of planning of various programmatic
aspects of the expansion. Israeli Interviewees (interviewees #3,7,9) described basic
issues that were left unsettled in the preparation phase for expansion. These included the
critical issues of responsibility for funding newborn screening and conducting screening
that was discussed earlier as well as the physical location in which the repeat
testing/confirmatory diagnosis would take place (the emergency room or neonatal unit
were mentioned as a realistic alternatives.) One interviewee (interviewee #9) noted
sarcastically: “...What we are good at doing is buying the technology...and there is this
plan to have Sheba Tel Hashomer Medical Center do the testing. But what will the
government provide for follow-up and treatment. Here we have a bit of a problem...”
A
telling metaphor was used by an interviewee to describe the Israeli way of establishing
public health programs. The classic Israeli mistake, he claimed, is “to set up the booth
and then start looking for funding. ”

Interviewees associated some of the disorganization and lack of planning of the
program, which may be better described by the Hebrew word “balagan” ---with the
notion of the hardship of the day-to-day life in Israel (interviewees #3, 7, 9, 13). One
Israeli interviewee (interviewee #7), while referring to the need to inform parents about
screen positive results as soon as the newborns are detected in order to allow for a quick
confirmatory diagnosis, articulated the same thought in fewer words: “In Israel, today is
today, but tomorrow is not tomorrow...” In a similar vein, a practicing physician
(interviewee #9), while discussing the right timing to inform parents about screen
positive results, referred to the “hysterical and difficult average Israeli parent”. At the
same time, an Israeli interviewee (interviewee #3) justified this aspect of disorganization
of the Israeli newborn screening program by contextualizing it: the official praised the
country for succeeding in the plan to expand the newborn screening program, receiving
an external donation for developing the infrastructure, and shortly afterwards getting the
Ministry of Health to assume responsibility for funding, while all the while confronting
war and limited resources. Another interviewee (interviewee #7) similarly considered the
financial aspects of expanded newborn screening in light of the relatively scarce
economic resources in Israel, when he described the fundraising and reliance on aid from
U.S. benefactors as another example of “the culture of Schnor.” In Yiddish a shnorrer is
a person who lives by begging or sponging off others. In Hebrew slang the word
“schnor” also describes the efforts of receiving donations or grants.

Although interviewees conceded that the Israeli culture contributed to a lack of
systematic planning, they also highlighted how positive aspects of Israeli culture shaped
the expanded screening program. One such strength reflected by interviewees was the
direct contact and less formality characterizing the Israeli world of clinical genetics
(interviewees #3, 7, 16). As one Israeli interviewee (interviewee #3) explained, the
relationship between metabolic experts is more direct and less formal than in other
Westernized countries, as is the relationship between doctors and patients. Consequently,
it is easier to locate patients, even at unconventional times. Another Israeli interviewee
(interviewee #7) described a similar attitude towards patients, explaining that “once a
newborn is detected with a metabolic disorder, I go look for the Bedouin family in the
desert right away, and makes sure I do not leave before discussing treatment alternatives
with them”. This last point is of particular importance in Israel, as both Israeli and
American interviewees (interviewees #12, 18) noted the unique phenomenon of
consanguinity in both Arab and Jewish societies residing in Israel, a custom that increases
the prevalence of genetic mutations and metabolic disorders in those communities, which
in turn increases the need for newborn screening. Finally, the cultural atmosphere within
which the program is embedded is aptly summarized with a quotation from an Israeli
interviewee (interviewee #13): “...I am not trying to fight windmills as I have not got
enough energies for that...we are going for small fights, small victories, and trying to
survive this way...”

I argue that the cultural issues of lack of planning of programmatic aspects, along
with, less formality in delivery of results and follow-up reflect the concept of
authoritative knowledge in biomedicine, which according to Browner (1996) is
associated with the dominance of clinical technologies. Program officials feel that they
are in charge of the newborn screening process from start to an end. Therefore, they feel,
it is only natural that the decision when and how to publicize the expansion process and
to revisit the consent issue will be in their hands, even though they are aware of the
ethical implications of such policy. In similarity to the governance of technology in
Browner’s world of prenatal screening, I suggest that the central role tandem mass
spectrometry plays in newborn screening, as it is portrayed in the literature and the
empirical data gathered for this study, contributes to the authoritative nature of
biomedical knowledge in that it makes the medical team more knowledgeable about the
process of screening, while parents of newborns and the general public become far less educated about those issues. In this atmosphere, program officials’ sense of control over the increasing biomedical knowledge that is obtained by the technology is intensified. This, in turn, contributes to the deference of parents of newborns on the one hand and the paternalistic behavior characterizing newborn screening program officials on the other hand.

The Political Context of the Expanded Newborn Screaming Program

Given the complex and ever dynamic political situation in the Middle East, one of the questions this study wished to address was whether or not the Israeli program is directed towards including Palestinian newborns, and if so, how the screening of this sector is operated. The literature reports that screening of part of the population for Phenylketonuria (PKU) is conducted in the Gaza Strip (Abu Shahla et. al, 2004). Researchers have been optimistic in regard to the possibility of screening a high percentage of newborns in the West Bank for Congenital Hypothyroidism at a time that allows the provision of an effective treatment (Sack et. al, 2008).

Throughout the interviews, limited data was collected about this topic. One Israeli interviewee (interviewee #7) recounting the history reported that screening of Palestinian newborns by the Israeli newborn screening program started in 1988 in the West Bank, right before the initiation of the first Intifada. Palestinians were located and screened at the Maternal and Child Health Clinics rather than at hospitals as in Israel, because newborns do not stay at the hospital for more than one day in the West Bank. Following the Oslo agreement between Israel and the Palestinian authority signed in 1993, the Palestinians decided to conduct newborn screening by themselves. The program official
added that screening was also performed by Israel’s Ministry of Health at the hospitals of the Southern Lebanon Army.

According to a couple of the interviewees (interviewees # 16, 17), the pilot phase in 2005 that provided the main justification for the initiation of the program included blood spots of both Israeli and Palestinian newborns. As to the recent report about the conduct of newborn screening by the Palestinian authority in Gaza, one Israeli interviewee (interviewee #7) doubted that newborn screening is in fact being performed there. However, he noted that the information about screening in the West Bank is not accessible to the Israeli program directorship. An American interviewee (interviewee #17) expressed his doubts about obtaining parental consent of the Palestinians for using their newborn’s bloodspots at the pilot stage. While describing the pilot phase that preceded the initiation of the program, program officials did not discuss the issue of informed consent for newborn screening among Palestinians at all. To summarize this point, data analysis reveals the willingness of the Israeli newborn screening program to cooperate with the Palestinians in order to include their newborns in the expanded Israeli newborn screening program; however the political situation in the region, in particular after the attack of the Israeli Defense Force in Gaza in December 2008, seem to have impeded this good will.

A related theme that came out of the interviews was the importance of collaborative efforts to ensure successful implementation of the expanded program and to overcome the obstacles to achieving this goal. A continuum of views of interviewees appeared on this topic, ranging from a positive and optimistic American view about the possibility of collaboration with the international newborn screening community (interviewee #18), to
the skeptical view of an Israeli interviewee about the difficulty to collaborate with local newborn screening experts (interviewee #2), and up to a strong resentment articulated by Israeli interviewees who were not involved in the establishment of the program about collaboration with the program directorship (interviewee #8). The American informants (interviewees #17, 18) asserted that they have never seen a group of scientists and physicians who are so willing to share information and offer help, and added of their collaboration with Israeli scientists and physicians that “...if there is any place in the world that wants the help with Newborn Screening, we’re there. It is one of the most non-competitive, most collaborative groups you could possibly work with.”

An Israeli interviewee (interviewee #2) argued that all medical professionals in Israel see themselves as experts and as the center of each project they are involved with. In his view, the lack of collaboration has a negative impact on both the patients and the system. Physicians keep their patients close to their heart partially for academic reasons, so they can keep data –and therefore future publications, a vital currency in academia -- to themselves. That is, if a physician has only 5-6 patients affected by a rare condition, it is almost impossible to get a publication out of it. He noted that this is the reason why it is hard to locate Galactosemia patients in Israel. The least optimistic about the possibility of collaboration were two Israeli interviewees (interviewee #8, 11). Both expressed a deep resentment towards the centralization of the program at Sheba Tel Hashomer Medical Center and criticized not being included in the decision - making process regarding the development of the program. The ethical and social implications of this issue are discussed in chapter 5.

The Social Context of Routinization of Tandem Mass Spectrometry
A major concern arising from the routinization of advanced medical technologies such as tandem mass spectrometry relates to the technological imperative— that is, to the question of whether the availability of the technology necessarily means it should be used (see chapter 1). Should the simple availability of tandem mass spectrometry technology determine the uses to which it was put and the range of conditions it was used to detect? Interviewees were not as intrigued by the ethical issues surrounding the introduction and use of tandem mass spectrometry technology in newborn screening. In fact, they were more concerned about the cost of the machine, its performance, and the time-consuming training period. Rather than discussing whether or not the technology should drive the practice of newborn screening, interviewees discussed the advantages of using tandem mass spectrometry for an expanded panel of conditions in terms of time and cost saving. One interviewee (interviewee #9) noted that in Israel everything goes by technology as “we love technology.” Another (interviewee #5) noted that in Israel routinization of the machine is relatively easier because this is a small country. A European interviewee (interviewee #21) strengthened this point by saying that in his country, throughout the initial phase of using the tandem mass spectrometry, travelling of technicians between different cities to assist with its utilization was a major part of the routine. Significantly, two program officials (interviewee #2, 4) used the term “simplified” to describe the advantage of using tandem mass spectrometry instead of traditional testing methods. An interviewee at the management level of the Ministry of Health (interviewee #4) explained “here the question of technology is very simplified. We checked the cost, the utilization, there is an outstanding team, no problem.” In fact, American interviewees (interviewees 16,17,18) were more concerned about the important questions of “just because we can
test, does it mean we should?" than were the Israelis. In regard to the training period, Israeli interviewees acknowledged that they hadn’t received the official training required by most newborn screening programs before starting to use tandem mass spectrometry but did not seem very concerned about it. One interviewee (interviewee #9) pointed out that he was supposed to fly out of the country for a few days of training as part of the purchase of the device, but he had not yet had the chance to do it. However, an American interviewee (interviewee #16) recalled that one of the Israeli scientists spent four days in his laboratory, learning about the assays and how to use the tandem mass spectrometry device prior to the implementation of the program in Israel. It was implied by his response that four days is a sufficient training period for this technology.

I suggest that the routinization of tandem mass spectrometry in the expanded newborn screening program in Israel affords a good opportunity to examine the technological imperative (Koenig, 1988); that is to use the technology simply because it exists. As data analysis in this section reveals, in the past few years, along with the introduction of tandem mass spectrometry to newborn screening programs around the world (see chapter 2) the newborn screening program in Israel was facing many changes. The decision to expand the program in Israel in 2005 as opposed to the rejection of the same idea only few years earlier (see chapter 4) is only one example. This crucial decision, data shows, came along around the time of the purchase of the tandem mass spectrometry device by Sheba Tel Hashomer Medical Center. Indeed, other important developments were associated by interviewees with the establishment of the expanded program. These included the end of the long-lasting American donation that covered the costs of the diagnostic kits for Congenital Hypothyroidism, the American push to expand the existing
newborn screening program, and finally the opportunity that came up to receive additional funding from U.S. based resources dedicated for the process of expansion. Indeed, all those factors might have played a role in the decision to expand the program at this point in time. However, my analysis suggests that the purchase of the tandem mass spectrometry device played an important role in the decision of the advisory committee to approve the expansion of the program, thus strengthening the concern that the technological imperative was the main reason for the development of the program.

**Newborn Screening, Equity, and Stigmatization**

One ethical issue that was widely discussed in the interviews was equity. When asked about the benefits of newborn screening, a considerable amount of interviewees (interviewees #3, 6,8,9,18) discussed how every child deserves of a healthy start, and praised the universality of newborn screening for its contribution in improving equity among different sectors of the Israeli population. Most of them thought that the Arab population in Israel, including Druze and Bedouin, are the main benefactors from the universality of this public health service, given the high consanguinity in those communities.

In contrast to the dominant theme that newborn screening, being a public health service, improves equity, the issues of stigmatization by larger society and discrimination by insurance and other public organizations of newborns detected by screening were not addressed by interviewees. In fact, both issues were discussed briefly by only a couple of interviewees (interviewee #8, 10) as a potential harm rather then an existing challenge. Given the concept of the quest to the “perfect baby” and the intolerance towards disability in the Israeli society (Remmenick, 2006) that was discussed extensively
throughout this work, I would anticipate to hear from interviewees more about the fear of stigmatization and discrimination of newborns with the expansion of the panel. I believe, that the little concern raised by interviewees regarding those issues is more a reflection (or a by–product) of the public ignorance regarding the practice of newborn screening, its current expansion, and its social implications than it is a significant say on the attitudes of Israeli society towards those possible harms.

Benefit for the Baby, the Family, and Society from Screening

Following the extensive discussion in the international newborn screening literature regarding the changing perspectives on the benefit of newborn screening, to include not only medical treatment that results in improved physical health of the baby, but additional perceived benefits for the baby, family, and society as well (Alexander et. al, 2006; Bailey et. al, 2006 and see chapter 2 for a discussion) I was interested in finding out, whether the interviews would reflect this shift in the notion of benefit that is currently taking place in Westernized countries. Two questions were posed to the interviewees in order to understand their attitudes regarding this issue. First, was the question “What, in your view, is the purpose of screening?” Second, interviewees were asked “what are the benefits for the baby, family, and society from screening?”

In regard to the first question, there were no big surprises. Most interviewees, Israelis and international, repeated the standard traditional criterion “early detection and effective treatment.” (interviewee #6) although each one articulated this theme slightly differently. Some talked in general about presymptomatic treatment to prevent complications (interviewee #8), or detect a disease before it is too late (interviewee #20) while others were more specific about the outcome and talked about prevention of mental retardation.
or anticipated that in the future we would be able to prevent death or other diseases (interviewee #4, 21). Still others considered saving a child’s life or preventing disability as the main purpose of newborn screening (interviewee #18). One Israeli interviewee, being more aware of the connection between the philosophical and non-philosophical aspects of newborn screening, explained that because the aim of newborn screening is prevention of mental retardation we only screen for primary (congenital) hypothyroidism and not for secondary and tertiary forms of the disease (interviewee #7).

As to the second question, when asked specifically about the benefactor of screening, the vast majority of interviewees, both Israeli and American (interviewees #2, 3, 7, 8, 10, 11, 13, 17, 18) focused on the benefit for the baby. Specific benefits discussed by interviewees included early treatment and the chance to prevent irreversible harm or fatality. More specifically, interviewees talked about prevention of death from sepsis or neurological harm in the case of Galactosemia (interviewee #2). Other benefits brought up by interviewees included allowing the child to have a normal life and less hospitalizations (interviewee #11), as well as a shorter period of time before diagnosis and also sparing the baby the ordeal of going through the evaluation, a process referred to in the literature as the “diagnostic odyssey” (interviewee #2, for a theoretical discussion on the topic see chapter 2). One interviewee focused on the improvement of IQ levels in newborns detected as being effected in Congenital Hypothyroidism (interviewee #7).

For the family, many interviewees indicated the benefit of genetic counseling and its contribution to informed parental reproductive decision making (interviewees #2, 7, 8, 10, 17, 18, 21). One Israeli interviewee pointed out that the provision of information to parents, early enough in the child’s life, is advantageous to them if they wish to make
reproductive choices and have access to treatment, even at the cost of elevated anxiety (interviewee #8). However, she emphasized that this is a secondary benefit, while the primary benefit is to improve the health of the newborn. Others discussed the stronger bonding to the child and having a better attitude towards him following early detection, as opposed to detection after symptoms arrive (interviewee #2).

For society, the main benefits pointed out by Israeli interviewees were the contribution to the public’s health and improved quality of life for all citizens (interviewees # 6) the reduced cost of care provided to disabled newborns (interviewee #4), and in particular, the difference between the cost of caring for a severely retarded child as opposed to a mildly retarded child, or a child with no retardation at all (interviewee #2). The disadvantage of ineffective screening which does not allow for using the resources for other purposes was brought up by one respondent (interviewee #1).

Only two interviewees discussed the benefit of the increased public understanding about genetic inheritable conditions gained by the performance of newborn screening (interviewees #2, 18). One American interviewee (interviewee #18) went beyond the traditional criterion of early detection and the existence of effective treatment to the purpose of learning through newborn screening about the natural history of the disease. She explained that “When you really want to know the reality of the situation, the only way often is to do a population-based program, and there are examples you know of biases ascertainment again and again, especially in Genetics, when we looked at too focused a pool; and then when you go into broader base, we’ve learned a great, great deal.” This response reflects the view that one of the goals of newborn screening is to
increase knowledge about the diseases included in the screening panel, or in other words, that newborn screening has a public health/epidemiological research purpose. From a broader perspective, the ultimate goal of epidemiological research is the same-- to treat and cure disease in individuals by gaining knowledge about population health. This broader point of view, however, was less common among interviewees. In my view, the reason for this is that in the narrow sense a broader notion of benefit does not commensurate with respondents’ view the goals of medicine; that is the goal of improving health and providing treatment for the sick individual.

Only one Israeli interviewee explicitly discussed the broadened notion of benefit to include the family, even if there is no direct benefit to the baby from screening (interviewee #1). Finally, one Israeli interviewee (interviewee #14) stated that the notion of benefit in newborn screening is in fact narrower than it may seem at first glance. For him, in the case of newborn screening, there is a benefit for the newborn and family only and there is no societal benefit whatsoever because of the rarity of disorders screened for by newborn screening.

I suggest that this emphasis on the benefit to the baby also reflects the notion of the Israeli quest for the “perfect baby”. As discussed in chapter 2, just as in Israeli society the fear of having to care for a disabled child leads to the uncritical acceptance of prenatal screening for an expanded panel of conditions, the same fear leads providers of newborn screening to emphasize the importance of neonatal screening that will minimize the number of severely retarded children as the major reason for screening. The same rational makes broadening the notion of benefit to include the family in society, only a secondary consideration, if at all.
Informed Consent for Screening, Storage and Future Use of Bloodspots

Internationally, informed consent for screening and for the future use of residual bloodspots has been among the most controversial issues in newborn screening in the past two decades (see chapter 2). Consequently, I was particularly interested to learn how interviewees view the current process of obtaining consent for screening, the nature of their attitudes regarding the existing consent process, and their perspectives on what the appropriate model for obtaining consent for screening and for future use of specimens might be, once screening for the expanded panel of conditions is up and running.

Data analysis reveals that unlike their attitude regarding other ethical and social aspects of the program, interviewees were sincerely concerned about the issue of informed consent, and advocated strongly for improving and regulating it. One Israeli interviewee (interviewee #1) emphasized that the first essential questions that must be addressed throughout the process of expansion are informed consent issues and in particular, the justification for the mandatory basis for screening.

The following themes emerged from the interviews in regard to informed consent for newborn screening. First, the majority of the interviewees agreed that a higher standard of informed consent for the expanded newborn screening panel is needed, yet there was no agreement regarding the appropriate form the informed consent should take. While some interviewees discussed the ethical obligation to inform parents orally about the plans for expansion and upgrading of the program, or alternatively required that a letter summarizing the testing and its significance be provided to mothers post screening (interviewees #5, 8,9, 18), other interviewees were satisfied with the existing situation in
which there is no requirement for either written or oral informed consent for screening, but rather there is an opt-out option (interviewees #1, 6, 16, 17).

One Israeli interviewee (interviewee #11) argued that by arriving at the hospital to have a baby, the woman implies that she agrees to receive all examinations and services included in the “health basket”, including newborn screening, and therefore consent can be assumed. If parents object to screening, they should inform the hospital about it before the delivery. Yet another Israeli interviewee (interviewee #9) claimed that the information should be disseminated publicly rather than individually. In his view, parents do not have the necessary tools to understand the process of newborn screening and its implications. Therefore, the media should be used to publicize the general concept of identifying conditions before symptoms arrive, rather then “providing details and horrifying data” about the diseases to parents upon hospitalization and requiring them to sign consent forms.

Still others required, or to be more accurate, compromised on a lesser level of consent for screening. They stated that in the current situation, informed consent is impossible to achieve. As one interviewee (interviewee #5) put it, he would like very much to have a requirement for informed consent for newborn screening, but he does not think, realistically speaking, that this will happen. He implied that the reason for that is, again, the ignorance of parents and complained about the vagueness of the system, which takes uninformed consent for granted, or allows for no informed consent de-facto, only de-jure. Along these lines, an Israeli interviewee (interviewee #8) commented sarcastically, that when she had her baby in an Israeli hospital, nobody asked for her consent. Had she not been a physician, she noted, she, too, would most probably be
ignorant about the testing. Finally, an American interview (interviewee #16) articulated this obstacle of parental understanding nicely by saying “how are you going to educate a person to the level that they can make a truly informed consent about the things they can’t even pronounce?”

The second theme reflected by the interviews was the paternalistic position expressed by program officials regarding the right timing for revisiting and modifying the practice of informed consent for screening. This position was articulated, for example, by the statement of an Israeli interviewee (interviewee #1), according to which it was agreed that the program directorship would leave the current mechanism for informed consent, or more accurately the non-existing mechanism for consent, as is, including the availability of opting out, and instead focus its efforts on developing public education about newborn screening. However, the interviewee acknowledged that this is opting out of the worst kind, because the new mother who can choose to opt out doesn’t even know about the testing and therefore does not have a real choice. This program official reported that the directorship of the program agreed to work on creating a genuine opt-out mechanism that will ensure that women know about the heel-prick of their baby and understand the purpose and broader social and ethical implications of newborn screening. He added that he is in favor of NOT obtaining women’s signatures, at least during the first stage of the expansion of the panel, because in his view, the system is unable to handle this and it would not ensure an appropriate informed consent anyway. Most surprising and disturbing in this regard was the response of another Israeli interviewee (interviewee #7), who explicitly noted that he purposefully “was very discreet about the testing” for one of the conditions in the old panel, in order to avoid any questioning about
it. As of the day of the interview (September 2007) he thought that nobody knew about the existing screening program that has been running since 1978, but declared that the plan was to educate the public about it through the internet.

A third theme, and positive one for a change, was the notion that Israel is less strict than the U.S. in terms of delivery of newborn screening results to parents and follow-up of detected newborns. The same Israeli interviewee that testified about keeping the screening a secret (interviewee #7) described how once a Bedouin newborn is detected with a metabolic disorder, he goes to look for that Bedouin family in the desert right away, and makes sure he doesn’t leave before discussing treatment alternatives with them. Less positive implication of this notion, though, is the flexible mechanism reported for obtaining informed consent. In the words of one Israeli respondent (interviewee #3) “I pick up the phone and say I signed them up on taking blood, although this is not really necessary as this is for clinical purposes…” Another Israeli interviewee (interviewee #13) who was involved in the decision making process towards implementation of the expanded program confirmed that in Israel’s health care system there is no need for consent for clinical purposes as opposed to research for the purpose of epidemiological study. In other words, the wide rubric ‘clinical purposes” that encompasses most bloodwork taken from newborns, provides a mechanism to obtain blood samples without requiring informed consent.

An Israeli interviewee (interviewee #6) made the distinction between invasive actions that require a special informed consent form defining the advantages and disadvantages of the clinical action, and non-invasive actions, which do not require a special consent procedure. According to this interviewee, newborn screening belongs to
the latter and therefore there is no need for a specific consent form for it. Finally, one interviewee (interviewee #12) declared that he does not think health care professionals should have parents sign consent forms for each and every blood drop taken, but rather only general information about the process should be disseminated to prospective parents.

Fourth, there was an agreement among the vast majority of interviewees regarding various aspects of education for newborn screening. In general, Israeli and international interviewees thought this aspect of the program should be further developed (interviewees #1, 5, 6, 7, 9, 10, 11, 13, 17, 18, 21). In particular, interviewees thought that the best time for provision of education would be during pregnancy (interviewees #10, 18) and the parties responsible for providing parents with education about the process should be the ob-gyns (interviewee #2, 17).

As to the actual policy of the expanded program towards consent for screening, an Israeli interviewee noted that the plan is to have women sign a consent form at some point during pregnancy, but not around the time of labor (interviewee #2). He explained that at this point (the interview was performed in September 2007), according to the draft of the Ministry of Health regulation document, gynecologists would be required to explain to a pregnant woman all she needed to know about newborn screening. In addition, the educational materials were to be posted on an internet website from which gynecologists could get the information. The doctor would have to indicate in the pregnancy follow-up file whether or not she talked to parents and informed them about the testing and its purpose. In some places, the Maternal and Child Health Clinics of the Ministry of Health (Known in Israel as “Tipat Chalav” -S.Z.) or the doula accompanying the woman can provide the information. The head of the pediatric department or someone
on her behalf will double check that the mother who delivered knows about the conduct of newborn screening. If someone still does not know about it, there are accessible educational materials on the website. The question of how the woman would know that there is a website with screening information remained unanswered. The interviewee anticipated that the process of obtaining consent is going to be very complicated if not impractical. Another Israeli interviewee (interviewee #9) admitted that it would be impossible for the neonatologist or nurse to provide all necessary information to parents while she is performing the heel prick. As mentioned earlier, another Israeli interviewee (interviewee #11) argued that there is no time to explain the procedure to each and every prospective or new mother in her own language. Therefore, in order to prevent legal proceedings, the plan to expand the panel and its purpose should be publicized in the media. This would result in better outcomes than interviewing parents during pregnancy and requiring parental signatures on consent forms.

As expected, all American interviewees (interviewees #16,17,18) were clear and unified about the best time to educate parents about newborn screening. In their view, too, education should take place throughout pregnancy and consent should be reinforced when the woman comes in to have the baby. They refer to the American College of Gynecologists recommendations from 2003 but they, too, note that provision of education at this time is problematic considering that in many U.S. states, New York for instance, as many as a third of the mothers receive no prenatal care before the beginning of labor. Fortunately, in that sense, Israel is advantageous in that prenatal care is provided for a higher percentage of prospective mothers. Another aspect of consent relates to the policy regarding reporting uncertain results or results with unknown clinical significance.
It is noteworthy, that when asked about this topic, interviewees (interviewees #6,13) thought that if parents gave their consent for screening, program officials are obligated to report back to parents all available information including uncertain results or results with unknown clinical significance.

Finally, the issue of storage and future use of residual bloodspots collected for newborn screening was hardly discussed by interviewees. When pushed to express their opinions on those issues, an Israeli interviewee (interviewee #1) informed me that despite the fact that biobanking of bloodspots is not currently a part of the expanded program, a decision was made to keep specimens for quality control purposes for at least one or two years without asking for the approval of the Helsinki Committee (the national ethics committee in charge of clinical research). The question remains whether quality control issues are separate from research.

In regard to saving the bloodspots for more than two years, the program official indicated that the future plan is to refer the question back to the Ministry of Health and follow its decision. He noted that his personal opinion is that bloodspots should be saved for “programmatic purposes” such as studies of prevalence of diseases and introduction of technologies to the program, as well as for potential future needs of the newborn herself, such as diagnosis and treatment of infectious diseases later in life, which would require blood samples from the time of birth for comparison purposes. In the latter case, he claimed, parental consent should be obtained. One Israeli interviewee (interviewee #2) noted that saving specimens will make sense only after the reformation of the program to identify the bloodspots by the newborn’s identification number, as opposed to the previous method that identified newborns solely according to their mother’s information.
An Israeli interviewee (interviewee #4) thought that storage of blood samples is appropriate only for anonymous use for research purposes. Another interviewee (interviewee #5) emphasized that use for research requires the approval of the national ethics committee (Helsinki Committee) as it makes use of genetic material, an action regulated by the Genetic Information Act of 1994.

Significantly, issues of storage and future use of bloodspots for research were hardly acknowledged by interviewees. For example, only three interviewee (interviewees #1,5,13) were concerned about the issue of consent for the storage of bloodspots for future use. The immediate reason for this may be that currently, biobanking is not a high priority on the Israeli newborn screening program agenda. One repeating theme in respect to biobanking did emerge from the interviews, however, and can be summed up succinctly: let’s collect and keep newborn screening data first, and decide how to use it later. While one interviewee (interviewee #4) stated this opinion explicitly, for others it was implicit in their comments. A European interviewee (interviewee #21) contributed the international perspective on this topic. He explained how in his country residual bloodspots are retained for five years. Within six months from collection of blood samples billing issues are resolved; after this time the blood spots are pseudomonized -- that is, the blood is separated from the patient’s name -- and the spots are kept for another four and a half years. Because most diseases that are screened for will show up within five years, it is considered appropriate to dispose of the spots after that time.

I argue that the concepts of biomedicalization, authoritative medical knowledge, and the quest for the “perfect baby” clarify the findings regarding the issue of informed consent in this study. First, the paternalistic view expressed by program officials
regarding their plan to revisit and modify the current practice of informed consent for screening at the right time, and only after the program is up-and-running for a while, fits with the concepts of biomedicalization and authoritative medical knowledge. The Israeli newborn screening policy-makers’ interviews consider the process of obtaining informed consent for screening to be a clinical decision, rather than a moral or ethical one. Consequently, they view it as a subject to their own control. As one of them (interviewee #2) articulated it “It depends on us when we are ready to provide the public with knowledge. It is a matter of six months...” According to Clark (2003) with the utilization of an innovative clinical technology – in this case tandem mass spectrometry—the clinical practice (newborn screening) becomes more technoscientific in nature. Following Browner (1996), this dominance of the clinical technology strengthens the hegemonic efforts of biomedicine in this area. Since the knowledge required to assess what is best for the screened individuals is in their exclusive authority, and it is not accessible to lay people, the requirement for a higher level of consent than the existing opt-out option seem to be unnecessary at this point.

Secondly, the quest for the “perfect baby” in the Israeli society is reflected in public officials’ attitudes towards the process of newborn screening. As discussed in chapter 1, according to Remmenick (2006) there is an inherent deep intolerance of physical and mental disability in Israeli Jewish culture that leads pregnant women to fear they might have to care for a sick child, in a society that prioritizes the health of babies above all else. The reflection of this fear on the health providers’ end is their motivation to expand the panel to include as many disorders as possible in order to avoid malpractice suits. Following Remmenick’s findings, in the case of newborn screening, even when the
public is better informed about the process and its consequences, and even if there is a requirement for a signed consent form or provision of an oral consent for screening, it is very unlikely that a mass refusal of newborn screening will occur. Given the authoritative nature of biomedical knowledge in genetic screening, I anticipate that only a minority of new mothers/parents will refuse testing, even following the addition of disorders to the existing newborn screening panel. As long as the disorders screened for are described by the medical authority as having effective treatment if detected earlier in the baby’s life, an expanded panel would be perceived by mothers as taking one more step towards achieving the desired goal of having a “perfect baby”. Just as in the case of prenatal screening, the genetic anxiety among Ashkenazi women in particular, I suggest, will accelerate the acceptance of an expanded newborn screening panel, once it is publicized. Moreover, the fact that the expanded screening is performed by a sophisticated, powerful, and sensitive medical technology such as tandem mass spectrometry will increase the public deference towards the authority of medical knowledge and the consequent control of the medical team over the whole process, including the decision of whether or not it should be conducted.

American Influence on the Evolution of the Israeli Program

A major research question was how the expanded program in Israel was influenced by the American newborn screening experience. Even before I started data collection it was clear to me that there was a significant American influence on the creation and implementation of the new program. In fact, I originally became aware of the plan to expand newborn screening in Israel by an American colleague who turned out to be a key informant in this study.
Throughout data gathering it became clear that the American influence played a major role in the creation of the program at various levels. To begin with, as previously discussed, the initiative to expand the program was an American one. Secondly, the expansion was approved by the Ministry of Health following a pilot testing performed at an American newborn screening lab and interpreted with the assistance of American newborn screening specialists. In addition, the scientific consultation by American experts was meant to be an ongoing one, at least at the early stages of implementation (interviewee #16). Moreover, the purchase of the tandem mass spectrometry device and the initial training of program personnel were all funded by a donation from American resources (interviewee #17,18) and the provider of the testing kits is an American company, PerkinElmer (see chapter 4).

American influence on the expanded newborn screening program in Israel was analyzed at three different levels. First is the influence of the American experience on the design of the program in terms of conditions selected for screening, analytes, assays, cut-off levels, and other procedures used by American newborn screening programs. Secondly, American funding resources were taken advantage of throughout the process of expansion. Third, American experts provided professional consultation and advising to the developing program. The following section will discuss the findings regarding all three levels.

The American influence on the design of the Israeli program clearly emerges from most interviews, although interviewees differ in their opinions regarding the extent of its impact. While some Israeli and American interviewees, mainly those who were not directly involved in the creation of the program, suggest that the program is highly
influenced by its American counterparts (interviewee #2,3,8,5,14,16,18), other Israeli interviewees prefer to talk about the “Israeli adaptation of International models” rather then on the “American influence.” (interviewee #4,6). Either way, all interviewees reflect the high impact of the American influence on the design of the Israeli program.

In terms of the panel of conditions and policy of determination and reporting of results, the Israeli newborn screening program seems to be highly influenced by U.S. practices. An Israeli interviewee (interviewee #2) testified that the American trend of expansion of the newborn screening panel clearly influenced the decision making process in the Israeli program. The future plan of the program directorship is to include all American College of Medical Genetics core conditions on the newborn screening panel.

A related issue brought up by interviewees, was the tension between American and European attitudes in the developing Israeli program regarding the policy of determination and reporting of results. Another Israeli interviewee (interviewee #3) recalled that throughout the development of the expanded program, some clinicians pushed for the “American model” of “tell all you can find out” while others advocated for the “be more conservative and less informative” European model. He brought up as an example the Swiss, German, and UK newborn screening programs. The first does not report conditions detected on the screening panel if they are not part of the panel, the second only screens for Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD) on top of the PKU and Congenital Hypothyroidism, and as to the third “…nobody really knows exactly what they are doing.”

In similarity to many U.S. newborn screening programs, the program official argues, the Israeli program’s official position is that as much as can possibly be known about the
newborn’s metabolic and genetic condition following screening should be reported back to parents and the medical home. In his view, the reasons for the U.S. model of disclosing all available information are based on medical and ethical considerations as well as on the issue of transparency. In terms of the policy regarding reporting of results back to the medical home and parents he noted that the Israeli program directorship locates itself between the Americans and the British and added that “this is not a bad place to be.” The respondent used the term “taking the best of all worlds” to describe the attitude of the Israeli newborn screening policy makers to the job of developing an expanded program.

In the U.S. a variety of panels are used by different programs although the future plan of most states is to adopt the American College of Medical Genetics core panel (see discussion in chapter 2). One Israeli interviewee (interviewee #10) linked the variety of U.S. state-run program panels to the different genetic make-up of the populations and ethnicities residing in those states. Similarly, he indicated, the typical backgrounds and ethnicities of people living across the State of Israel necessitate a different newborn screening panel than the panels offered by U.S. states. However, his response was not indicative of the common response. The vast majority of interviewees, including those who claimed they were not directly involved in the design of the expanded screening program (interviewees #2, 3, 5, 6, 11, 16, 17, 18), thought that the influence of the American experience is very dominant. Therefore, they assumed that the final panel of conditions would follow the American College of Medical Genetics recommended core panel of 29 conditions and anticipated that the technologies, methods, analytes, and cut-off values used by U.S. screening programs will serve as the model for Israel’s expanded
newborn screening program. It is noteworthy that Israeli interviewees (interviewees #2, 3) indicated that screening for the full American College of Medical Genetics core panel is more of a future goal than a present plan. At the first stage, they explained, the panel will include less than half the conditions included in the recommended panel, as discussed in details in the “Criteria for Disease Selection” section in chapter 4.

In terms of technological influence, an Israeli interviewee (interviewee #2) reported that the plan is to use U.S. standards, including graphs of the Center for Disease Control, in the Israeli system. In addition, the program is using German quality control measures that allow the program directorship to be confident about their analytes and results. Finally, he indicated, algorithms compatible with American College of Medical Genetics ACT Sheets (i.e., a U.S. educational instrument that provides information about the analytes and algorithms recommended for detection of metabolic and genetic diseases included in the panel) are used.

The following observation sheds light on the cultural context within which the program was designed. An Israeli interviewee (interviewee #3) indicated that while the discussion regarding the warranted panel of conditions was taking place, people questioned the less expanded panel in the Israeli program in comparison to the wide panel of some U.S. States, which includes 30 conditions or more. The interviewee argued that this question evolves from the view that screening for more conditions shows the advanced developmental stage of the state of Israel. While this view of “the more-the better” is very typical of the Israeli society, it has also been the subject of extensive dialogue in the international newborn screening literature in the past few years (see chapter 2) and was explicitly expressed by American interviewees (interviewees #17, 18).
when asked about their motivation to push for the expansion of the screening panel in Israel. It could be associated, then, with the technology-driven philosophy that both Americans and Israelis share rather than with a direct American influence. Interestingly, this view of “we need expanded newborn screening” as a prominent newborn screening policy maker titled a recent editorial article (Howell, 2006), was not reflected in the views of the European interviewees who seemed more conservative about the need to expand the panel. A European interviewee (interviewee #20) disapproved of the term “expansion” and related to it as an American definition that does not apply to Europe. In his view, the important difference between current and traditional screening is not that the current panel is expanded, a process that have been taking place in Europe for three or more decades, but rather the use of tandem mass spectrometry for the screening of the majority of the conditions on the panel rather than using traditional screening methods.

Not surprisingly, not everybody praised the Americans involvement in the expansion of the Israeli program. The criticism of American involvement on the Israeli end was in some cases extremely explicit. An Israeli interviewee (interviewee #11) came across as highly defensive in this regard. He suggested that the U.S. should not have served as a role model for the Israeli program, considering that 40 million people lack health insurance in the U.S. In his eyes, the weakness of the American health care system makes its newborn screening programs an unwarranted role model for the developing Israeli program. Another Israeli interviewee (interviewee #3) was critical of the excessive sense of fairness and the high weight given to ethical concerns in the American universe of newborn screening. He recalled that throughout the development of the Israeli program, people who took part in the process criticized the American paternalism that
makes the Americans think they can decide for other people just because they have the financial resources. He also noted “not everything is America is better...we, Israelis, are smarter. We’ll only take what’s good in the American system...”

This brings us to the second level of influence, the role of the American funding resources in the creation and implementation of the expanded program. A major aspect of the American influence in that sense stems from the history of newborn screening in Israel, years before the initiative for expansion was even considered. In response to the question about funding resources of newborn screening in Israel, couple of interviewees (interviewees #4, 7) noted that for almost thirty years, since the very beginning of newborn screening for Congenital Hypothyroidism in Israel in 1978 and until a few years ago, screening for this disorder was enabled by a donation of a private American foundation that provided all diagnostic kits (As noted earlier, Israel was then a pioneer in newborn screening for Congenital Hypothyroidism). An Israeli interviewee (interviewee #1) noted that it was not until the past few years that the Israeli program “achieved independence” as the long-lasting donation of diagnostic kits for Congenital Hypothyroidism was over. From now on, he proudly declared, screening will be fully funded by the Ministry of Health. Nonetheless, he added, when an expansion of the Israeli newborn screening program is under consideration, American financial support may take a different form, yet it would still play a major role in the decision making process and in the implementation of the program.

The third level of influence of American experience on the Israeli program is related to consultation and advising roles of American experts in the developing newborn screening program. In this regard, the American footprints are undeniable, at least on the
early stages of the program development. An Israeli interviewee (interviewee #4) commented that he first became aware of the benefits of expanding the existing newborn screening panel when one of the American physicians approached him and described the state of newborn screening in the U.S. Other Israeli interviewees (interviewees #2, 3) confirmed the crucial role the American physicians played in the earlier phase of conceptualizing the idea of an expanded program.

On the American end, the presentation of the role Americans played in the design, funding, and consultation for the program is more modest but the interviews convey the same message. The American interviewees talk about the “pivotal role” the American experts played in the development of the new program (interviewee #18), the pride they take in the fact that the expanded program did actually take off (interviewee #17), how the Americans were encouraging the program from the side rather than from inside, and how they used networking and connections to make the idea of expansion in Israel become reality (interviewee #18).

Although not in so many words, however, all American interviewees admitted that they felt that after their job was done (i.e., making the connection to potential funders and arranging for a pilot project of the Israeli specimens in their own U.S. state lab) the Israelis took over the project completely and the American colleagues have not been included in the decision making process anymore. According to an American interviewee (interviewee #16), when the Americans were involved in the early stages of initiation of the program, newborn screening experts around the world were asked, through his mediation, to chaperon the program by serving in a scientific advisory committee. They all agreed to serve, but the committee has never met. The interviewee
thought that the involvement of the American people who helped the program start, both ideologically and practically, was deliberately minimized once the program took off and the Israeli directorship took over. Similarly, one American interviewee (interviewee #18) admitted subtly that once it became very that the Israelis involved in the project were highly capable, she took a step back, and let the Israelis make the decisions based on their knowledge, expertise, and what they felt would be most valuable to the population. Another interviewee (interview #17) recalled that he was not contacted by Israeli program officials for a long period of time. H, too, testified that he pulled back once the first few donors were approached. Both noted that their efforts to initiate a connection with the Israeli directorship to learn about the progress of the project have failed.

In short, a major theme that emerged from the interviews was that American interviewees, who played a key role at the initiation of the program, felt disappointed to be left out of the developing program once the Israeli directorship took a leading role. Nonetheless, regardless of those feelings, all American interviewees felt that their input on the design of the program was influential, either by marketing the idea of an expanded newborn screening program in Israel or by offering professional assistance in the pilot testing needed for the justification of the expansion process (interviewee #16, 17, 18).

Finally, there are two areas in which the American influence on the Israeli program seems to be far less significant. The first one is public awareness about newborn screening in general and the process of expansion in particular. As discussed in depth in the section about education and public awareness regarding newborn screening in Israel, several program officials pointed out that newborn screening is rarely discussed by the Israeli public, unlike the situation in the U.S. in which the global process of expansion of
newborn screening flamed a heated debate among geneticists, advocates for expansion, and family members of individuals affected by genetic diseases in the past five years (see chapter 2). One Israeli interviewee (interviewee #1) raised the question of why the public in Israel remains unfamiliar with the existence of the program, let alone the plan to expand it. The lack of public awareness is particularly unexpected given the high popularity of prenatal screening in Israel (see chapter 2) and the high diffusion of U.S. “health care politics” to the Israeli media.

Another issue in which the American influence seems less significant is the concern that genetic information obtained by newborn screening will contribute to the discrimination of individuals by insurance companies, which is a widely discussed issue in the American newborn screening literature. Perhaps this is less of an issue in Israel, given the existence of universal health care that ensures that the medical care of each and every citizen is covered by the state (see chapter 2). However, as one interviewee (interviewee #13) notes, Israel is on the move from “humanistic medicine” to “economy medicine.” Once the latter form takes over, disclosing genetic information to insurance agencies could become an obstacle.

The last two chapters showed how the American clinical and social experiences were pulling the strings behind the expanded newborn screening program in Israel from its early beginning. The whim of two American Jews is what initiated the program in the first place. Then, an influential American manufacturer of newborn screening testing kits provided the enthusiastic report that led the initiators to try and make the whim come true. Soon enough the Israeli Ministry of Health got involved and became a catalyzer for the new initiative. Next, the institutional home for the program was found at Sheba Tel
Hashomer Medical Center; a prestigious hospital and the historical home of the old newborn screening program. Around the same time this institution also managed to purchase the tandem mass spectrometry device. The American assistance continued in the pilot testing to justify the program that was performed at the top-notch New York State Newborn Screening Program facilities. From that point on, the pattern of the American influence was transformed. Once the Israeli team of newborn screening experts and Ministry of Health agents realized the potential of the new initiative to update Israel’s public health services they became catalyzers for the initiative themselves.

From this point on the American influence on the Israeli program shifted gears. Now, the ideology and philosophy behind the American newborn screening experience took over. For example, one Israeli interviewee (interviewee #3) noted that his U.S. based metabolic education most likely influenced his viewpoints regarding the warranted panel of conditions, methodologies, and procedures in the expanded program. Indeed, the future goal of the program directorship is to implement the American College of Medical Genetics core panel of 29 conditions. In addition, another Israeli interviewee (interviewee #2) indicated that the Center for Disease Control measures are used for quality control along with European standards. Finally, at least on paper, American consultation is considered by program directorship an integral part of the early phase of operation of the new program.

I suggest that the social aspect of the American influence on the developing newborn screening program is best understood through the social constructionist framework. The social knowledge that led to the creation and implementation of the new program was constructed into the clinical or scientific knowledge of program initiators and policy
makers in Israel. On the American end, the social knowledge included the views of American initiators that newborn screening is a great need of Israel, the views of financial donors that their investment will help save generations of children in Israel, and the attitudes of the American manufactures of the newborn screening testing kits as well as New York State Newborn Screening program officials regarding the purpose of newborn screening and the appropriate methodology to achieve those goals. On the Israeli end, the social knowledge included the need to expand the program at this point in time, the views of newborn screening experts and Ministry of Health agents regarding the purpose of screening, the required evidence base for selection of conditions to the panel, the warranted policy regarding determination, detection, and reporting of results, and finally, their attitudes regarding informed consent for screening and education of parents and health professionals. The combination of all those pieces of knowledge with the technoscientific knowledge regarding disease prevalence, cut-off values, analytes, testing algorithms and other practices that best fit the Israeli population resulted in a dominant American flavor of the design and functioning of the expanded program.

From a social science point of view, while most social constructionists have limited their consideration of social factors to the same society in which the science is being conducted, what is interesting and special about this case is the influence of international social and political themes. Those pieces of local and international social knowledge I have discussed are being included in the construction of a biomedical policy in Israel, as part of the co-production of social knowledge and clinical information. In the next chapter, I summarize the major findings of data analysis and conclude by tying it to the conceptual framework underlying this project.
Chapter 6: Conclusion

Introduction

This dissertation discusses the ethical and social dimensions of the development of the expanded newborn screening program in Israel. Analysis of policy guidelines, brief observation at the newborn screening lab in Israel, and 21 in-depth interviews provided the empirical basis of this dissertation. The interviewees were conducted with program officials, practicing physicians involved in the process of newborn screening in Israel, and international interviewees who either served as consultants for the developing program or whose programs’ practices and procedures served as a model for the Israeli program. I open this concluding chapter by presenting three issues that proved problematic in the development of the Israeli expanded newborn screening program. I show how those challenges are not unique to the Israeli newborn screening program, but rather reflect a global problem. The international policy analysis provides a chronological, geographical, and conceptual context to support my claims. The first problematic issue identified in this study is the inchoate nature of the policies and the varying interpretations of those policies regarding basic programmatic aspects as practiced by different stakeholders; the second is the insufficient evidence-base used to justify various programmatic aspects. The third challenge is the minimal involvement of the community in the process of making the decisions that shaped the implementation of the program. In order to ground each one of these in the context of this work, I will return to the conceptual framework I drew on in the introduction. Finally, I will discuss the social and ethical dimensions of the international perspective on the expanded Israeli newborn screening program. In particular, I will analyze the dominant influence of the
American experience on various stages and aspects of the expanded Israeli newborn screening program.

**Challenges of the Israeli Program**

**Obstacle #1: Varying opinions of Stakeholders and Inchoate Policy regarding Various Programmatic Aspects**

The first and most apparent obstacle revealed by this study is the *inconclusive policy regarding various programmatic aspects* in the Israeli developing newborn screening program. As discussed extensively in chapter 4 inconclusiveness surrounded various programmatic aspects including the reasoning of the selection of conditions to the screening panel; the mechanism for determination of cut-off levels for the selected condition; the programmatic policy regarding the detection of conditions not included in the screening panel and the reporting of those incidental findings back to parents of newborns and the medical home.

One major topic characterized by inconsistent and at times conflicting perspectives held by those involved with the program is the issue of informed consent for screening. While the majority of the interviewees agreed that a higher standard of informed consent for the expanded newborn screening panel is needed, there was no agreement regarding the appropriate form the informed consent process should take. Several respondents advocated for keeping the existing opt-out option. Among those, some argued that since newborn screening is a non-invasive procedure it does not require a special consent process. Others, however, called for requiring written consent once the expanded panel is up-and-running. Still others thought that in the current situation, informed consent is impossible to achieve. In addition, the debatable issue of storage and future use of
residual bloodspots collected for newborn screening was hardly discussed by interviewees.

In the global perspective, the policy analysis showed that only modest attention was paid by authors of guideline documents to the practical or “non-philosophical” dimensions of the program. Thus, issues that are relevant to the day-to-day functioning of screening programs, including the provision of information to parents and health care professionals before screening; description of staff training, description of genetic counseling following transmission of screening results; discussion of the roles of program personnel, and ensuring the availability of facilities for diagnosis and treatment are briefly discussed and variably addressed by the documents.

The social perspective on the inchoate nature of the policies and the varying interpretations of those policies regarding basic Programmatic aspects as practiced by different stakeholders I find most relevant is derived from the concept of the social construction of medical knowledge. Because medical knowledge is inseparable from social knowledge, physicians’ moral and ethical values, their socialization, the institutional and professional procedures and routines they use affect their knowledge (Atkinson at Lock, 1988; Shiloh, 2002). In the policy analysis (chapter 3) the modest attention to the non-philosophical dimensions of newborn screening demonstrates how social forces and ethical views influence the understanding of the techno-scientific standards and procedures. While for some policy-makers, various programmatic aspects seem important enough that they should be settled prior to the operation of the program, at least half of the investigated documents do not discuss those issues.
The development of the Israeli program, too, is best interpreted using the concept of the social construction of medical knowledge. In my view, the rationale for the initiation of the program (the great need identified by program initiators), the justification for expansion (mainly, the pilot testing results), and the motivations of the American donors to invest in this initiative (“Pikuah Nefesh” or saving lives of many future generations) are all components of the social knowledge that was constructed with the medical knowledge of the people involved in the development of the program. This combined body of knowledge has influenced the final decision to move along with the expansion. In the next stage of development, following the establishment of the program, the inchoate nature of the policies and the varying interpretations of those policies regarding basic Programmatic aspects as practiced by different stakeholders characterized three major aspects of the program: 1.) the determination of how conditions would be selected for the panel 2.) the mechanism for detection and reporting of results for conditions not included in the panel, and 3.) the involvement of American newborn screening professionals in the evolution of the Israeli program.

Again, the vagueness regarding all those issues would be best interpreted using the social constructionist view. In the Israeli case, many pieces of social knowledge take part in the process of the social construction of knowledge. Those include, for example, the peer pressure of the program directorship’s colleagues in the field to adopt tandem mass spectrometry and expand the panel, the end of the agreement with a U.S. private donor regarding the provision of Congenital Hypothyroidism screening kits, and the concerns regarding budget cuts following possible policy reforms in the health basket committee (see chapter 4 and 5). All those factors, I suggest, represent the social knowledge that was
combined with the scientific knowledge and led to the final decisions regarding various aspects of the process of expansion.

Obstacle #2: Insufficient Evidence Base for Decision making

The second obstacle is the insufficient evidence base for decision-making regarding various aspects of the Israeli newborn screening program. The essentiality of a strong evidence base to justify various programmatic practices and procedures has been discussed extensively in the literature (see chapters 2, 3 and 4). However, the policy analysis showed a variable and mainly minimal requirement of an evidence base for the various aspects of newborn screening programs. Apart from the earliest document in the field that was authored by the Committee on Fetus and Newborn in 1965 (Rule, 1965), most of the other documents have implicitly stated the importance of a solid evidence base with respect to one or several criteria required by the documents as a condition for the implementation of the program; only the American College of Medical Genetics document contains a definition of how gathering and evaluation of the evidence should be performed. Similarly, in regard to the Israeli newborn screening program, the description of the dynamics that characterized the committee’s decision-making process provided by one of the committee members of the advisory newborn screening committee showed a considerably questionable evidence base.

The need for a strong evidence base to support the decision-making process regarding the expansion of the panel and the introduction of tandem mass spectrometry fits nicely with McKinlay’s (1982) model of how medical innovations become a part of established medical practice. In addition, the concepts of medicalization (Zola, 1972; Vailley, 2008) and biomedicalization (Clark et. al, 2003) clarify the essential role the tandem mass spectrometry plays in the expansion of the panel and the introduction of tandem mass spectrometry.
spectrometry device played in the evidence base presented to justify the process of expansion.

The concept of medicalization focuses on the social process by which individuals (and conditions) are labeled as either healthy or ill and considers such labeling an increasing part of the human existence. Biomedicalization is a related concept in which medicalization increases and become more complex, multisited, multidirectional and more techno-scientific. The concept of biomedicalization is defined in part by the growing techno-scientific nature of the biomedical practices and innovations. As described in chapter 4, the evidence presented by committee members to justify the expansion process included the estimated values of prevalence of the candidate conditions in other countries, the extrapolation of those numbers, and some other “extremely random” considerations. This line of reasoning, I suggest, fits with the concept of biomedicalization and can also be applied to McKinlay’s model of routinization of an innovative technology. The heavy reliance on techno-scientific information -- in this case the international estimated values of prevalence and its extrapolations to the Israeli population -- as the justification for expansion reflect the process of biomedicalization. At the same time, its adoption by powerful institutional structures also symbolizes the second stage in McKinlay’s career of the innovation. McKinlay also discusses the motivations for this adoption. He mentions the peer pressure which is very dominant among physicians as a main reason, but also notes as other motivations the wish to improve care, to be seen up-to-date or helpful. Chapter 6 discusses how all of the above motivations are expressed, either explicitly or implicitly, by interviewees.
Obstacle #3: Role of the Community in the Process of Newborn Screening

The third problematic issue relates to the role of the community in the process of newborn screening. The involvement of the public in the newborn screening process was investigated in the policy analysis through the discussion of two separate categories. The first was the community’s approval of the screening test. This follows the Wilson and Jungner (1968) criterion that the “test should be acceptable to the population” that is a central concept of population-based screening programs. In the policy analysis, only two thirds of the documents discussed this criterion. I argue that the reason for this low percentage was the vagueness of the criterion. What does “acceptable” mean and how should it be measured? Who is the target population? The other aspect of the role of the community in the newborn screening process that was evaluated in the policy documents was the question of who should be making newborn screening policies and the process by which such policies should be made. Less than half of the documents required public participation in the decision making process. Thus, the public was essentially invisible in this sense.

In regard to the Israeli program as it was portrayed in the interview analysis and brief observation period, the invisibility of the public became a genuine obstacle to the appropriate functioning of the program. The relevant community in the case of Israel’s newborn screening program includes both parents of screened newborns and health professionals who provide newborn screening services. Data analysis revealed parents’ almost complete ignorance regarding the process of newborn screening in general and its current expansion in particular. Analysis reveals that the major party responsible for this ignorance is the newborn screening program directorship. The comparison between
newborn screening and prenatal screening in this regard brought about a similarity and a difference. The directorship of the newborn screening program and providers of prenatal screening alike influenced the approach of the public to the genetic service. However, their approaches were the total opposite. While providers of prenatal genetic services drove the uncritical public acceptance of prenatal screening, the newborn screening directorship made a deliberate decision not to call attention to the process of expansion, while awaiting the right timing to publicize it among parents of newborns, newborn screening providers and the general public.

In regard to the future, based on the analysis of Remmenick (2006) who discussed the quest for the “perfect baby” and its relation to prenatal care and pregnant women’s deference to biomedical hegemony in Israel, I suggest that appropriate education of parents and health professionals will change the state of parental indifference towards the process of expansion of newborn screening. I anticipate just as there is uncritical acceptance of prenatal screening, once the newborn screening program directorship starts publicizing the process of expansion among parents, prospective parents, and health professionals, all those sectors will actively support the process of expansion, despite the uncertainty inherent to many disorders included in the expanded screening panel. Newborn screening, I expect, will be perceived by both health professionals and parents as taking one more step towards achieving the ultimate goal of having a perfect child. Indeed, this practice may be considered a baby step, in comparison to prenatal screening, as the alternative of abortion in case of detection of an affected baby does not exist and yet, on the big scheme of things, the practice will likely be perceived as a desirable preventive medicine measure.
The other sector in the Israeli community that was not consulted by the program directorship in regard to the development of the program includes members of the medical community who do not serve as program officials; yet they are or most likely to be involved in the outcomes of the expanded screening. Those include geneticists, metabolic experts, and pediatricians who will be responsible for communicating screen positive results to parents of screened newborns and discussing its clinical significance with them. Several interviewees expressed their strong disappointment regarding not being included in the decision making process regarding expansion of the panel in different ways. These feelings of resentment were so strong that one practicing physician refused to be audiotaped once she realized that the purpose of the interview was to discuss the expansion of newborn screening in Israel, a process she has never been involved with despite her status as an expert in the field of newborn screening in Israel. In addition, the fact that the program is highly centralized and located at one prominent hospital in the center of the country, a medical center that also owns the tandem mass spectrometry device used for the expanded screening, increased the sense of resentment and disconnect between program directorship and other members of the newborn screening community.

I suggest that those responses can be the product of the structural, institutional, and political context within which the program is embedded. I think this issue reflects the fact that the Israeli public health culture does not emphasize the importance of collaboration for a successful operation of public health services as much as its American counterpart. In particular, when an innovative technology is involved in the development of a public health service, its first stages of operation necessitate high levels of both national and
international collaboration in order to become effective and successful. This leads us to
the final insight I will discuss in this project, the significant influence of the American
newborn screening experience on the Israeli program.

**Unique Characteristic of the Israeli program: Significant American Influence**

The fourth insight evolving from this study is the *clear influence of the American
ewborn screening experience on various stages and aspects of the developing newborn
screening program in Israel.*

The first contribution to this significant influence is focused on the economical
aspect. As discussed in chapters 2, 4 and 5, in Israel, a gap exists between the high
scientific capabilities and the availability of financial resources to support the technology
required for this scientific progress. On the one hand, the State of Israel is not considered
a developing country. In terms of technological advancement and scientific
achievements, its standards resemble those used in most western countries. More
specifically, in the field of medical genetics alone, in Israel the number of geneticists per
capita is among the higher in the world if not the highest (interviewee #3, 18). When it
comes to the governmental budget available for the implementation and operation of
public health programs, however, Israel certainly can not be regarded as a resource-rich
country.

As data analysis reveals, given the limited annual budget of the country,
governmental agencies in general and the Ministry of Health in particular, are constantly
seeking external, mainly international, funding opportunities. The major target funding
source is the Jewish American community. Indeed, the story of the evolution of the
Israeli newborn screening program portrays the strong affiliation of American Jews to the
first and only Jewish state and the increased motivation or sense of obligation of the former to improve the health and well-being of the latter. As a public health service directed towards the health and well-being of future generations of Israeli children, newborn screening provides an attractive opportunity to achieve this goal. A related aspect is the professional, academic, and social affiliation of many Israeli clinicians, in particular, newborn screening experts, to their American colleagues. Many Israeli metabolic, genetic, and pediatric specialists received a U.S. based education and keep close connections with their American colleagues even after they move back to Israel.

Therefore, it is not surprising that various aspects and stages of the evolving Israeli program have a clear American component. These include the initiative to expand the panel, the provision of financial support for the establishment of the program, the determination of the ultimate panel of conditions, protocols, algorithms, and quality control and quality assurance measures, and finally, the technological and physical assistance in conducting the pilot testing that provided the main justification for the establishment of the program. In particular, the American influence was dominant in the early stages of the creation of the program, that is, in bringing up the concrete plan to expand, in locating funding sources, in the Israeli institutional home for the new imitative, and finally in the conduct of the pilot testing to justify the project.

I argue that McKinlay’s stage of promising reports could be applied to all these early stages of the creation of the program. In particular, American program initiators’ testimony that the evidence base supporting the need for an expanded panel in Israel came primarily from the manufacturer of the diagnostic kits fits McKinlay’s model very well. Another stage that reflects McKinlay’s point about the enthusiastic or promising
report is the stage of fundraising. In order to convince the potential donors that their investment in this project would be justified, fund raisers ought to present a persuasive cost-benefit analysis. The investigation of the motivations of the financial donors of the program strengthens this point. According to an American interviewee (interviewee #18), the American donors viewed their financial support as a fulfillment of the Jewish Mitzva of “pikuach nefesh” (a matter of life and death). They believed that allowing for expansion of the program would save the lives of Israeli babies detected with genetic and metabolic disorders. The respondent’s own description of the rationale for the donation was “donation helps set up the program only once but the impact on saving lives of generations of babies will be huge.” In other words, in order to achieve the ultimate goal of receiving financial support for the purchase of the device and/or establishment of the infrastructure, the fund raising campaign could not present the performance of tandem mass spectrometry as a risky procedure that can produce a significant amount of uncertain or inconclusive genetic and metabolic information. Similarly, the presentation of the possible increase in parental anxiety following a detection of screen positive baby, the costs of confirmatory diagnosis and other related burdens and finally the growth in knowledge the clinical significance of which is unknown would most likely not serve as a good advertisement for the expanded program. Rather, fund raisers were compelled to use a rosy picture of an efficient, powerful, time and money saving device, even if they were aware of the ethical dilemmas and economical difficulties related to it.

The other component of the conceptual framework I have drawn on in this part of the story is the social construction of medical knowledge. The motivations of the financial donors for the creation and implementation of the program indicate how existing social
values in the Jewish American community are coproduced with the clinical knowledge of Israeli public health providers to inform policy making regarding the new program. In particular, I suggest that the Jewish obligation of pikuach nefesh on the one hand, the technological imperative driven philosophy on the other hand, and finally the oversimplified assertion that newborn screening saves lives were among the major social forces influencing the American donors to select the developing newborn screening program in Israel as the subject of their financial investment. In order to justify (either to the financial donors or to themselves) the “great need” for the establishment of an expanded screening program, the initiators used the scientific knowledge regarding high incidence of genetic mutations in the Israeli society resulting from the consanguinity in traditional communities of Arabs and Ultra Orthodox Jews, their social knowledge about the talented group of genetic and metabolic experts in Israel who could take over this project and continue its successful implementation, and their own social experience regarding the availability of American technical and professional assistance that they assumed would play a pivotal role in the implementation of the new program.

**Concluding Remarks**

In Mckinlay’s model of seven stages, the third stage of public acceptance and state endorsement is the result of the exposure to the promising or enthusiastic reports about the technology (stage 1) and more clearly the result of the organizational and professional adoption (stage 2). This third stage involves a general approval of the innovation by the public. The public acceptance is translated to a public belief that the innovation is a “good thing” and should be available for use. However, this support of the community
can only evolve from professional interests that are already committed to the innovation. At the same time, according to McKinlay, professionals and medical organizations may use public acceptance to legitimate their association with the innovation.

McKinlay suggests that the state does not act on the basis of reliable evidence but rather on the basis of a combination of professional, organizational, and public pressure. Therefore, he argues “an innovation at this highly public third stage in its career usually remains without formal evaluation. Usually it still awaits a study that meets even minimally acceptable methodological criteria...once the state acts to support an innovation and social policy is implemented, the career of an innovation can be viewed as having passed the point of no return” (McKinlay, 1982:245). In his model, the stage of “standard procedure” and observational reports comes next. Most of those reports make it difficult to decide if the innovation is actually effective. At this point of the career, the utilization of the technology is so deeply rooted that questioning its effectiveness or desirability is almost impossible.

Drawing on McKinlay’s model I argue that the expanded newborn screening program in Israel is approaching the “point of no return”. The “promising reports” stage (including the pilot testing), the adoption by organizations and professionals (including support of the Ministry of Health, the program directorship, and practicing physicians) have all passed. The stage of public acceptance that precedes state endorsement has not arrived yet, mainly due to internal programmatic and institutional considerations that are unjustified, in my view. However, McKinlay himself admits that in real life oftentimes the order of stages is mixed and some stages never take place. Nevertheless, data analysis
clearly shows the support and commitment of the state of Israel to use tandem mass spectrometry for expanded newborn screening.

At this point, McKinlay model does not clarify the current social situation surrounding the utilization tandem mass spectrometry for expanded newborn screening in Israel. I believe that at this critical point in the “career” of the tandem mass spectrometry the making of social policy could in fact direct to an appropriate and socially responsible use of tandem mass spectrometry for expanded newborn screening in Israel rather than to entrench an undesirable or ineffective program, which is many times the case according to McKinlay. In other words, McKinlay’s model describes nicely the current stage in the routinization of tandem mass spectrometry for expanded newborn screening; that is that this technology is approaching the point of no return. However, there is one element in the data that McKinlay’s model does not explain very well. I argue that there is still time, with adequate knowledge, to ensure that the utilization of this new technology is performed under ethical and socially acceptable standards. However, for the development of a warranted policy, it is crucial to understand the social and ethical dimensions of the evolution, the larger context, and the obstacles in regulating various programmatic aspects of the expanded newborn screening program in Israel. I hope that this dissertation has shed light on the major social factors and ethical issues that influence this policy in the making.
APPENDIX 1
THE CONDITIONS INCLUDED IN THE FIRST STEP OF THE EXPANSION OF
NEWBORN SCREENING IN ISRAEL (May 2009)

1. Phenylketonuria
2. Congenital Hypothyroidism (primary)
3. Congenital Adrenal Hyperplasia
4. Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)
5. Very long chain Acyl-CoA Dehydrogenase Deficiency (VLCADD)
6. Maple Syrup Urine Disease (MSUD)
7. Homocystinuria
8. Tyrosinaemia type 1
9. Glutaric Aciduria type 1
10. Methylmalonic Acidaemia
11. Propionic Acidaemia
APPENDIX 2

In-depth Interview Guide

A. Background Information

1. What is your scientific/clinical background?
2. What is your role in the expanded newborn screening program?
3. How did you come to be involved with the expanded NBS program?
4. Do you feel your input was influential?

B. Expanded Panel

5. When, by whom and on what basis was the decision to expand the panel made?
6. Can you tell me more about the timing of the expansion?
7. Which conditions/disorders will be included in the expanded panel on the first phase (other than CH, PKU)?
8. When will the program start testing for the expanded panel?
9. How were the conditions/disorders to be included in the panel chosen?
10. By whom were the conditions/disorders included in the panel chosen?
11. Do you agree with this process? Would you have done this differently?
12. Are you familiar with the methods, markers and cutoff values you will use for the expanded panel?
13. How were those methods, markers and cut off values determined?
14. Do you anticipate that other candidate conditions will be included in the expanded panel in the future?
15. Do you support this process of expansion? Would you have done this differently?
16. In your view, is a decision to stop the testing for a condition following a pilot stage possible?

C. Secondary Conditions

17. Testing for an expanded panel of conditions using tandem mass spectrometry is characterized by the ability to detect secondary conditions; conditions that are not part of the panel. (Probe: For example, there is one variant of MCAD which was only recognized when newborn screening by tandem mass spectrometry started. There is a chemical phenotype and gene mutation but they are not symptomatic and will never develop the disease. As for SCAD, some argue that there is no connection between clinical findings and pathology) What is your opinion regarding scaling the tandem mass spectrometry device to identify secondary conditions?

18. What do you know about the program's policy of reporting secondary conditions? Do you agree with this policy? Would you have done this differently?

D. Ethical, Social, and Cultural Concerns

19. What is the significance of newborn screening from a broad public health perspective?

20. What is the significance of newborn screening from a social perspective?

21. Who should benefit from newborn screening?

22. What do you think about the current informed consent process in the newborn screening program?

23. Should the informed consent process be modified following the expansion? If so, how?
24. What do you think about the plan to create a bio bank of the newborn screening bloodspots?

25. What is your view regarding using residual bloodspots for research?

26. I heard that the original plan was to expand newborn screening in Israel through a private firm. What was/is your view about privatization of newborn screening?

27. What do you think about the fact that the program is centered at Tel Hashomer Medical Center?

28. How do you think endocrinologists, metabolic experts, neonatologists and pediatricians, and other professional should be involved in the expanded program?

29. What do you think is the cultural, political, social, institutional context in which the program in Israel is embedded in?

30. How will this context effect the design and implementation of the expanded program?

31. What do you think are the unique characteristics of the expanded program?

32. What is the impact of the American experience on the formation and implementation of the expanded program?

33. What do you think are the challenges the expanded program is/will be facing?

34. Do you think the initiation and implementation of an expanded panel of conditions in Israel at this point is warranted?
APPENDIX 3

Participant Observation Guide

Laboratory Staff Routine Work

1. Who is working at the lab? (no names, titles, job descriptions, and responsibilities)
2. Who does what at the lab?
3. Who are the dominant people at the lab?
4. What are the dynamics between the different technicians?
5. What are the routines at the lab?

Use of Tandem Mass Spectrometry

6. Who operates the tandem mass spectrometry machine? Is it always the same person or different technicians?
7. If several people operate the machine, how does their techniques/customs differ?
8. How comfortable with the use of tandem mass spectrometry do the various operators of the machine seem?
9. Does the staff seem knowledgeable about the capabilities and limitations of the device?
10. Where and what kind of training on tandem mass spectrometry did the staff receive? How much experience do they have in utilizing the device?

Detection and Reporting of Screen Positive Results

11. What happens when a peak is detected for a certain condition?
12. How is a “screen positive” result for a primary or secondary condition determined?
13. How are peaks for conditions with uncertain/unknown clinical significance handled?

14. Who is reported about a screen positive/uncertain result?

15. How is the reporting being done?
APPENDIX 4

THE CONDITIONS INCLUDED IN THE FIRST STEP OF THE EXPANSION OF
NEWBORN SCREENING IN ISRAEL (May 2007)

The Israeli panel of experts decided to add the following diseases, in addition to PKU and Hypothyroidism:

1. Phenylketonuria
2. Congenital Hypothyroidism (primary)

Amino acid disorders
3. Maple syrup urine disease (MSUD)
4. Homocystinuria
5. Tyrosinaemia type 1

Organic acid disorders
6. Glutaric aciduria type 1
7. Methylmalonic acidaemia
8. Propionic acidaemia

Disorders of fatty acid oxidation
9. Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
10. Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)
11. Very-long-chain acyl-CoA dehydrogenase deficiency (VLCAD)
12. Carnitin palmitoyltransferase deficiency II (CPT)

Endocrine disorders
13. Congenital adrenal hyperplasia
APPENDIX 5

THE CONDITIONS INCLUDED IN THE FIRST STEP OF THE EXPANSION OF
NEWBORN SCREENING IN ISRAEL (May 2008)

1. Phenylketonuria
2. Congenital Hypothyroidism (primary)
3. Congenital Adrenal Hyperplasia
4. Maple Syrup Urine Disease (MSUD)
5. Homocystinuria
6. Tyrosinaemia type 1
7. Glutaric Aciduria type 1
8. Methylmalonic Acidaemia
9. Propionic Acidaemia
10. Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)
APPENDIX 6

Interview Coding Guide

1. Evolution of program

a. description

Ad hoc committees
Adding conditions gradually
Advocacy groups are not active in newborn screening

History
No sufficient evidence base for justification
Advisory committee role and consistency
Biochemistry and DNA banking
The history of
Computization and website
Non-identifiable barcode

b. ambiguity and inconclusiveness

Decision making re implementation
Panel of conditions
Reporting of results
American consultation
Decision making mechanism re implementation
Diagnosis and follow up

Of schedule

c. Pilot testing
Details about
Is unnecessary
Was unethical
Economical purpose
Hard to go back
Reasons to stop
d. Centralization of program
In favor
Not good for follow up
Against
In Germany: the opposite
e. Privatization
Against it in newborn screening
And freedom of choice
And voluntary screening
With governmental inspection
f. Expansion
Bottom up
Need for
Timing
g. Involvement in Decision/Policy-making
Feeling I am not included
Feeling my input was influential
Towards implementation
Consumer/parents’ involvement
Ministry of Health should make the decisions re: operation of the program, informed consent and storage

2. Criteria for screening

a. Description
False positive is a reason to start with few conditions
Early detection and effective treatment, severity
False positive caused delay in reporting and lack of trust in the community
Good assay, reliability
Importance of quick diagnosis and confirmatory testing
International
Low percent false positive
Move from prevalence to severity and psychological stress
Move from treatment to counseling
Pilot study
Rarity of conditions complicates justification
Specificity and sensitivity
Different panels to different populations
Donors' interests

b. Determination and Reporting of results
Mechanism for determination of conditions in panel
Different strategies for different conditions

Mechanism for reporting of results

Mechanism for reporting/follow-up: tipat chalav (maternal and child health clinics) involvement

Changes in cut-off level in order to detect certain variants

Cut off level as technical issue?

Differences of cut-off levels between states/countries

c. Prevalence

Important for better understanding of disease

Important for decision making

Important to epidemiologists

High because of continuity in Bedouins/orthodox Jews

High justifies the screening panel

Knowledge about effects the screening panel

Justification for screening

Obligation of reporting

Purpose of screening

d. Technology

Technologies used by the Israeli program

Technology drives policy

Routinization of new technologies

3. Ethical and Social Issues
a. Benefit to the baby, family and society

To the baby

To the family

To society

To the family: reproductive decision making

To society: not in rare conditions

To society: public awareness of genetic disorders

Broadening the concept of benefit

Philosophical aspect neglected

Pikuach nefesh

b. Informed Consent

Currently no requirement

Is not a realistic requirement

It depends on us when we are ready to provide the public with knowledge

Less strict than the U.S.

Liability

Need for consent for epidemiological purposes

Need for

No need and eradication of disease

No need for changing the opting out option

Opt-out

Reporting even if results uncertain

The program will require it when it is time
When should we obtain it?

Who should obtain it?

With uncertain conditions and for future use for research we'll need a better mechanism

c. Purpose of screening

Diagnosis and treatment

Reorganize the chaos of metabolic specialty

Financial profit

Learn about natural history

Prevent mental retardation

d. Social aspect

Newborn screening improves equity

Stigmatization

Parental anxiety

e. Storage of bloodspots

For quality control

For future medical treatment of the newborn

Collect and keep data first, decide how to use it later

Future use only for newborn screening research purposes

Non-identifiable bloodspots

Requires consent

4. The larger Context
a. Cultural aspect

Awareness in prenatal vs. no interest in post natal

Deliberate unplaning

Donation for a state in war situation, limited resources

Less formality, direct contact

Raising external financial support

Setting up the booth and then deciding what to sell

Consanguinity leading to high prevalence

Hardship of life in Israel

The more (conditions in the panel) the better

Impact of religiosity

b. Legal aspect

Legal and ethical responsibility of Ministry of Health

National Health Insurance Law, 1995

Child sues parents for wrongful life

Implications for insurance

The statute for genetic information

Guidelines in Germany

b. Economical aspect

Financial support for the program

Use of money for other purposes

Screening is cost effective

c. Political aspect
Need for consultants for the screening directorship

Screening for Palestinians

Frustration of consultant who lost contact

Impact of the program director

Need for collaboration

Resentment of interviewee

5. Education and Public Awareness

a. Education for Parents

Is necessary

Obtained gradually

Hard to achieve for multiple conditions

Screening rather than testing

b. Education for professionals

c. Public awareness

Gene-environment interaction

Neonatal vs. prenatal

Public interest more important than the individual

6. International Influences

a. American influence

Consultation role

Criticism of
Discrimination insurance
Donation and financial support
Panel of conditions
Paternalism
Soliciting creation of program?
Take a step back

b. International experience
We are following
We should follow

7. Challenges and Uniqueness
a. Challenges of program
Adapting the screening to the state and data
Avoiding over treatment
Dealing with uncertainty by international experience
Handling false positive
Maximal treatment and minimal parental stress
No metabolic specialty
Uniform panel
Follow up after detection
Higher standard of ethics
Need for consultation to deal with uncertainty
Need for resources
Resources for follow up

No complicated questions as opposed to personalized medicine

Locating patients

Comparison to vaccination

Program functioning: disorganization

Program temporality

Treatability of conditions detected

Uncertainty of results

b. Uniqueness of program

Advantages of program

Universal screening covered by the state

Gaps between the center and periphery

Heterogenic communities

Pioneers in screening

Quick delivery of bloodspots

Small country and single lab

Tailored to different regions/communities

Team work rather than routine laboratory

Accuracy of results

Better follow-up

Caution in testing

Highest no. of metabolisms/geneticists/pediatricians

High burden of metabolic disease
High quality and dedicated people

No responsible pediatrician for newborn

Part of public health system

Quick delivery of results

Separation between ambulatory medicine and hospital medicine

Starting a fresh program

Program will take a leadership role
APPENDIX 7 - TABLES

**TABLE 1: DOCUMENTS, AUTHORS, AND SCOPE OF GUIDELINES**

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<th>Doc No</th>
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<th>Authors</th>
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**Accepted/effective treatment:** the availability of an accepted or effective treatment was required as a precondition for inclusion of a condition in the screening panel

**Benefit/significance to family/society:** the topic was discussed and the position of the document was generally in favor of such a benefit

**Benefit/significance to the diagnosed individual:** the topic was discussed and the document required or at least strongly supported it as a precondition for inclusion of a condition in the screening panel

**Birth prevalence known/Natural history understood:** the topic was required as a precondition for inclusion of a condition in the screening panel

**Latent/presymptomatic phase:** the topic was discussed and the position of the document was generally in favor of such a phase as a requirement for screening
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**Acceptability of test or program**: refers to acceptability of test or program to parents, physicians, or the general public.

**Consent to participate is discussed**: the document discusses parental consent in newborn screening programs; M indicates that the document specifies that informed consent is necessary.

**Confidentiality or privacy**: the document specifies that protection/maintenance of privacy is required.

**Resources/ benefits equitably distributed**: these issues are discussed in the document.

**Alternative uses of resource considered**: these issues are discussed in the document.
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**Description of purpose/scope:** document discusses the purpose or scope of the screening program

**Provision of information:** refers to provision of information before testing
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Cost of test: The document discusses the consideration of cost of the test

Continuous evaluation of screening program: This refers to the requirement for regular assessment of the functioning of the program
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<td>22</td>
<td>Joint Working Group of the Human Genetic Commission and the UK National screening committee, 2005</td>
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<td>23</td>
<td>Health Council of the Netherlands, 2005</td>
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<td>24</td>
<td>International Society of Neonatal Screening</td>
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*Need for research regarding effectiveness:* this refers to any aspect of programmatic effectiveness (diagnostic, follow up, reducing mortality)
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