

**The Orphan Drug Act of 1983: A Case Study of
Issue Framing and the Failure to Effect Policy Change from
1990-1994**

Lynn Redington, M.P.H., M.B.A.

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Approved by,

Thomas C. Ricketts, Ph.D., M.P.H., Chair

Margaret B. Dardess, Ph.D., J.D.

Michael D. Murray, Pharm.D., M.P.H.

John E. Paul, Ph.D.

Pam C. Silberman, J.D., Dr.P.H.

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ABSTRACT
LYNN S. REDINGTON, M.P.H., M.B.A. The Orphan Drug Act of 1983: A Case Study of Issue Framing and the Failure to Effect Policy Change from 1990-1994 (Under the direction of THOMAS C. RICKETTS, Ph.D., M.P.H.)

Both low- and high-commercial-potential (LCP and HCP) orphan drugs are eligible for benefits provided by the Orphan Drug Act of 1983 (ODA). During 1990-1994, legislators attempted to amend the law to better target benefits to LCP drugs and “restore the spirit of the law” to promote the development of LCP drugs for rare diseases that might otherwise be abandoned, or “orphaned.” These amendment attempts were not successful.

This dissertation research examines: 1) how ODA stakeholders attempted to shape the debate about HCP orphan drugs in the 1990s, and, 2) potential factors that may have impeded or promoted ODA reform in the 1990s.

ODA reforms were debated in four Congressional hearings from 1990-1994. Hearing transcripts were obtained and thirty-eight statements were coded. The qualitative research method of memoing was used to construct four frames from the Congressional text: 1) ODA Reform as Economics and Access, 2) ODA Reform as Patient Relief, 3) ODA Reform as Rules of Participation, and 4) ODA Reform as Congressional Action.

Potential reform factors were proposed *a priori* and subsequently evaluated based on a review of over 100 documents and ten informant interviews.

The research offers a microcosmic window into how policy stakeholders define problems, propose solutions, and advance their interests in debates over social conditions and public policies. In the 1990s, legislators asked: does market exclusivity for HCP orphan drugs provide an unnecessary monopoly that leads to excessively high orphan drug prices, windfall

profits, and other problems? The research illustrates how disputants chose to define, or avoid defining, terms such as “unnecessary monopolies,” “excessively high drug prices,” “windfall profits,” and “problems” that result from these conditions.

The research demonstrates how policy development and framing theory can structure inquiry into attempted policy reform, aid in developing *a priori* hypotheses, and, shape analyses and recommendations. The dissertation includes a guide for analyzing policy development and a guide for constructing and deconstructing issue frames. These are applied to the historical case of attempted ODA reforms, but may be useful for other cases.

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LIST OF ABBREVIATIONS

ALS	Amyotrophic lateral sclerosis (Lou Gehrig's Disease)
BLA	Biologics License Application
DHHS	Department of Health and Human Services
EPO	Erythropoietin
FDA	Food and Drug Administration
FFDCA	Federal Food Drug and Cosmetic Act
hGH	Human growth hormone
HCP	High commercial potential
LCP	Low commercial potential
MS	Multiple Streams
NDA	New Drug Application
NIH	National Institutes of Health
NORD	National Organization for Rare Disorders
ODA	Orphan Drug Act of 1983
PEST	Political, economic, social, technological
Pharma	The pharmaceutical industry
PhRMA	The Pharmaceutical Research and Manufacturers of America
PL	Public Law
R and D	Research and development
SMO	Social movement organization
SWOT	Strengths, weaknesses, opportunities, threats

Introduction

The Orphan Drug Act of 1983 (ODA) provides the pharmaceutical industry with incentives to encourage development of drugs for rare diseases and conditions (conditions that affect fewer than 200,000 Americans). The law's incentives effectively reduce the costs of clinical testing, and ensure a seven-year monopoly on use of a particular drug compound for a specific rare disease. This latter "market exclusivity" provision is widely regarded as the law's most important incentive.

Congress's intent and rationale for creating the ODA are reflected in the law's text:

(1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States; (2) adequate drugs for many of such diseases and conditions have not been developed; (3) drugs for these diseases and conditions are commonly referred to as "orphan drugs"; (4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss; (5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and (6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.

The ODA has been considered "one of the most successful US legislative actions in recent history" (Haffner et al 2002). In the decade prior to the law's enactment, 10 orphan drugs were developed by pharmaceutical companies and approved for marketing by the Food and Drug Administration (FDA). Since enactment in 1983, approximately 1700 drugs have been designated as orphans, and 300 orphan drugs have received FDA approval.

Despite its apparent success, one aspect of the law has generated significant controversy for the past two decades. The law presumes that orphan drugs are unprofitable without government support. But means testing to determine a drug's financial (or "commercial") potential is not currently required as a condition for such support. Hence, both low- and high-commercial-potential (LCP and HCP) orphan drugs are eligible for ODA benefits. During 1990-1994, legislators attempted to amend the ODA to limit the conditions of eligibility or revoke certain benefits for HCP orphan drugs. These amendment attempts were not successful.

The issue of whether HCP orphan drugs should continue to receive ODA benefits, particularly the seven-year market exclusivity benefit, continues to stir debate and media coverage. A key question in the debate has been: does market exclusivity for HCP orphan drugs provide an unnecessary monopoly that leads to excessively high orphan drug prices, windfall profits, and other problems? Sub-questions that naturally arise from this larger question include: 1) when is a monopoly necessary; 2) at what point is a profit or price excessive; 3) what problems are created by excessive profits or prices; 4) how should these identified problems be addressed; 5) if an amendment to the ODA is warranted, how should this be done; and, 6) will the benefits of amending the ODA be worth the risk, if any, of diminishing industry interest in orphan drug development?

Many stakeholders are intensely interested in how the above sub-questions are addressed. Shaping opinion about market protections (e.g., patents or government-granted market exclusivity), drug prices, industry profits, healthcare financing, government subsidies for research and development (R&D), and patient access to medications is important, not just for the future of the ODA, but for the future of larger social, technological, economic, and political/legal issues.

An examination of how ODA stakeholders attempted to shape the debate about HCP orphan drugs and potential ODA reforms offers a microcosmic window into strategies that can be used to frame issues, influence the course of debates, and promote or impede policy development. Moreover, the literature on issue framing, political influence, and policy development is extensive, and offers the opportunity “to stand on the shoulders of giants” and use extant research and theory to structure and guide such an inquiry.

Utilizing the historical case of ODA developments and debates, along with extant theory and research, this dissertation research explored two general questions: 1) what factors seem to promote or impede policy development; and, 2) how does issue framing support policy development? This qualitative inquiry used mixed methods, including literature reviews, informant interviews, and a content analysis of Congressional transcripts.

The research demonstrates how policy development and framing theory can structure a case inquiry, aid in developing *a priori* hypotheses, and shape the analysis and recommendations that can be culled from the research. Kingdon’s (1995) Multiple Streams (MS) model provided the foundation to examine the ODA’s history and evolution, including how activities in the problem, policy and politics streams converged or diverged, and favored or disfavored policy changes. MS also provided foundational assumptions for successful policy development, such as the need for a “policy entrepreneur” and “windows of opportunity.” The MS model assumes the policy development world is fluid and ambiguous, and subject to multiple interpretations. Policy entrepreneurs use political acumen to promote selective interpretations and actions to further their interests. Framing theory was used to drill down into the political acumen aspects of the MS model. Detailed guidance on framing is lacking in the MS model, and framing theory complements the model well.

To *frame* is to “select some aspects of a perceived reality and make them more salient in a communicating text, in such a way as to promote a particular problem definition, causal interpretation, moral evaluation, and/or treatment recommendation for the item described” (Entman 1993, p. 52). Strategic framing is considered an important tool in influencing individual attitudes, knowledge, or behavior (Gandy 2003); exerting political influence (Entman 2007), exercising power (Reese 2003), instigating social change, and winning debates or adherents (Lakoff 2004, Pan 2003); mobilizing collective action (Snow, Rocheford, Worden and Benford 1986, Benford 1993, Benford and Snow 2000), and, expanding social and political actors’ realm of influence (Pan 2003).

Extant framing theory and research were used to develop *a priori* hypotheses about the function and utility of framing, and the characteristics of potent frames. The literature review provided optional methods for constructing frames from text, along with their strengths and weaknesses. This research utilized the method of a single researcher coding text and “memoing” to construct frames, a method that yields information-rich frames but risks having poor inter-coder reliability.

After an extensive review of the policy development and framing literature, two *a priori* guides were developed. The first guide identified factors that may impede or promote policy development and was used to assess why the proposed ODA reforms did not result in an amendment to the law. The second guide summarized factors that may be important in recognizing, understanding, and developing effective frames.

The research will be useful for students and practitioners of health policy and political communications. The dissertation culminates in lessons learned from the ODA case, and recommendations for using these lessons. Public health advocates often struggle to develop succinct messages that are rooted in a potent frame (Dorfman, Wallack and Woodruff 2005).

The ultimate goal of this research is to improve communications competencies that could advance health policy advocacy and instigate positive social change.

In addition to its general utility, this research generates new insights and strategies to address a policy controversy that has cast a shadow on a law that has otherwise produced many benefits for the public's health.

Chapter 1—Overview of Research

Utilizing the historical case of ODA developments and debates, along with extant theory and research, this dissertation research explored two general questions: 1) what factors seem to promote or impede policy development; and, 2) how does issue framing support policy development? This qualitative inquiry used mixed methods, including literature reviews, informant interviews, and a content analysis of Congressional transcripts. This chapter provides an overview of the dissertation research by describing the research approach, its importance, the conceptual model used to structure the research, some definitions, and the scope of the research that was conducted. For more detail on research methods, see Chapter 4.

Research Approach

This case study of the ODA was divided into four aims or steps: 1) describe the contextual backdrop and history of key ODA events and changes; 2) examine how issues were framed in Congressional hearings related to ODA amendments from 1990-1994; 3) identify factors that contributed to the failure of ODA amendments that were proposed from 1990-1994; and, 4) based on the analysis of findings and extant theory, develop practical guidance on framing analysis and strategy in policy development.

First, the general history, chronology and rationale of the ODA were summarized from a review of published research reports, articles and legal briefs. This provided context for the remaining research.

Second, a descriptive review of how issues were framed in ODA amendment proceedings from 1990-1994 was completed. Four Congressional hearings were held between

1990-1994 to discuss the issue of whether, and to what degree, HCP drugs should continue to receive ODA benefits. Thirty eight witnesses presented statements on this issue and/or proposed ODA reforms. Transcripts of these statements were obtained from a government documents library. These were coded using a list of variables and coding categories developed from theory and research in policy development, political communications and framing. Four frames were then developed using the qualitative research method of “memoing” (Miles and Huberman 1994).

Third, a descriptive review of factors that may have influenced the course of ODA reforms during 1990-1994 was completed. First, potential critical success and failure factors were proposed and assembled into a guide. The guide was derived from the framing and policy literature and conceptually structured using Kingdon’s (1995) multiple streams model. Using the guide along with a review of over one hundred documents and ten informant interviews, an assessment of which factors seemed to influence the course of ODA reforms that were proposed in 1990, 1992 and 1994 was made.

Fourth, the dissertation concludes with practical framing strategy recommendations and guidance. This was synthesized from Aims 1-3. The practical guide addresses strategies for advancing policy development amidst controversy and was informed by study findings as well as extant research and theory on frame reflection (Shon and Rein 1994), problem definition and issue framing (Rochefort and Cobb 1993, Kingdon 1995), taxonomies of policy language (Stone 2002), frame breaking and creativity processes (Fredin 2003), and strategic frame analysis (The FrameWorks Institute 2007).

Importance of Research

This dissertation research is innovative and significant because 1) it uniquely identifies and applies findings from framing theory and research, a field commanding ever-growing

attention; 2) it analyzes an important health policy issue; and, 3) it may aid public health advocates' understanding and competency in advancing difficult or contentious policy positions. Moreover, no research with similar aims has been published to date.

Framing has been touted as a key communications tool for instigating social change (Lakoff 2004). A number of studies have demonstrated the marked change in attitudes and behaviors that can result from subtle changes in the description of a social phenomenon (e.g., Tversky 1981). Hence, framing seems to hold promise for health policy advocates. But the literature review (see Chapter 2) points to a number of challenges in translating research into practice. By carefully applying extant theory to a real world problem, this research could demonstrate the promise and limits of framing theory, thereby providing important lessons for both framing scholars and framing practitioners.

Furthermore, the topic of the ODA is an important one because changes in the law could impact a number of stakeholder groups—either positively or negatively. ODA changes could affect: 1) many Americans, as approximately 1 in 10 has at least one of the 6000 known rare illnesses; 2) many firms, as dozens are in the process of developing orphan drugs; and, 3) many payers—as individuals, employers and government insurers indirectly support the ODA tax credits or pay for orphan drugs directly.

Moreover, this research heeds the call of Hertog and McLeod (2003) to conduct more research on:

... the framing of social concerns within public and private institutions of power and the social impact of such framing. Certainly, one of the assumed reasons for study of the framing of social concerns is that it has an impact on social policy and plays a role in the process of social control. Perhaps the analyses of congressional debates and hearings, corporate publications, and stockholder meetings can be combined with popular culture studies on the one hand and policy votes and investment decisions on the other. If, as we believe, framing is one of the most powerful forces in determining public and private social policy, this form of research could stand as some of the most important political and social communication research ever carried out. (p. 160)

Conceptual Model

Because the public policy development process is extremely complex, Sabatier (1999) urges the use of a conceptual model to focus and structure policy inquiries. He reminds researchers: “One simply cannot look for, and see, everything.” (Sabatier 1999 p. 4) A conceptual model enables individual researchers to surface assumptions and clarify the factors that are of importance to the study (Miles and Huberman 1994). Additionally, if multiple researchers use the same conceptual framework, cross-case analyses then become more possible (Miles and Huberman 1994). The ability to compare the case being studied to previous case studies improves the usefulness of the study. Rather than producing knowledge that is idiosyncratic, i.e., useful for and applicable to only the case at hand, study findings can be generalized or applied to other cases.

To structure parts of this research and enable analytic generalization, the Multiple Streams (MS) framework of Kingdon (1995) was used as a foundation to examine the ODA’s history and evolution, including how activities in the problem, policy and politics streams converged or diverged—favoring or disfavoring policy developments and modifications. MS also provided foundational assumptions for successful policy development, such as the need for a “policy entrepreneur” and “windows of opportunity.”

Kingdon developed the MS model from his study of 23 American federal policy cases in the fields of transportation and health. Since its dissemination in his original 1984 book, *Agendas, Alternatives and Public Policies*, Kingdon’s theory of policy development garners approximately 80 citations each year (Sabatier 1999). Such frequent referencing and use may enable greater cross-case analyses.

According to Zahariadis (1999), the MS model is suitable for examining the policy formation processes under conditions of ambiguity.¹ The model is also useful for analyzing factors that contribute to the failure of health policy (Kingdon 1995).

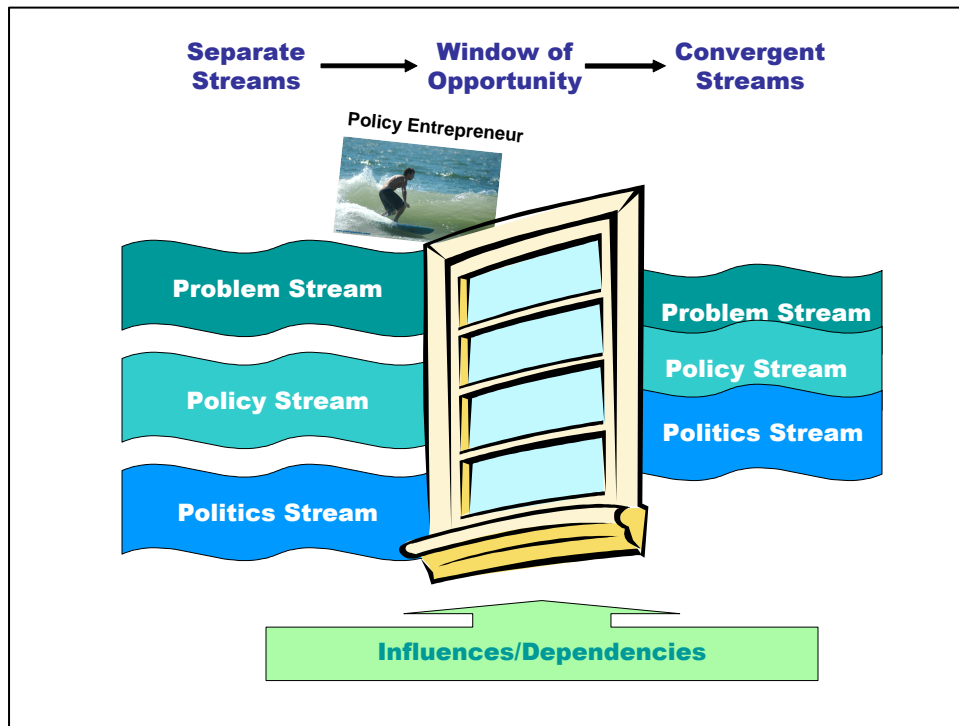
The MS model was selected for several reasons. First, the MS model is suitable for policies that develop under ambiguous conditions. The ODA seemed to develop in ambiguous conditions based on an exploratory review of the ODA. Second, the MS model's emphasis on agenda setting and policy formation seemed to be suited to the review of the early history of the ODA and ODA amendment processes from 1990-1994. (According to Longest (2002), the processes of policy modification and policy formation are similar.) Third, the MS model seemed to complement extant framing theory well. MS provided a broader roadmap of the policy development process, and framing theory enabled a drill down into a specific aspect of the process, i.e., how actors construct arguments that influence the course of policy developments.

As depicted in Figure 1, and described by Kingdon, MS theory asserts that policy changes typically occur if three “streams” converge. A policy entrepreneur and a window of opportunity are two key catalysts in this process. The three streams of actors and activities are described as 1) a problem stream, where problems are defined and solutions are implicated, 2) a policy stream, where solutions are advocated and matched with problems, and, 3) a politics stream, which includes elected officials and dominant ideologies, the public mood and pressure group trends. A policy entrepreneur paves the way for a proposal and takes advantage of the windows of opportunity to match their proposal to important problems of the day, and match problems to political preferences.

¹ Ambiguity is the capacity to have multiple meanings. According to Stone (2002) ambiguity is central to politics, and is an important feature of political symbols. Symbols, such as “civil rights” and Martin Luther King, can mean two or more things, e.g., to one social movement they symbolize racial injustice; to another social movement, they may symbolize discrimination against obesity, homosexuality, personal disabilities, etc. Ambiguity unites people who may benefit from the same policy but for different reasons.

The MS model is based on the “garbage can model” of decision making (Kingdon 1995) where organized anarchies prevail and decisions arise from a confluence of events. In complex, ambiguous and unstable contexts, the garbage can model asserts that decision makers don’t yet know their preferences and that they use trial and error to discover means, ends and underlying causes. According to the model, decisions will bubble up out of a stew of interaction, epiphanies and choice opportunities. (See Appendix A for more details)

**Figure 1. The Multiple Streams Model of the Policy Development Process
As Described by Kingdon (1995)**



The MS model addresses three issues: 1) how the search for solutions and problems is conducted; 2) how policymakers focus their attention; and, 3) how issues are framed (Zahariadis 1999). As mentioned, Kingdon’s MS concepts were complemented by a literature review of extant research and theory on issue framing (see Chapter 2) because, as Zahariadis points out, the MS model addresses the first two issues better than the last. Moreover, the MS model was originally developed more than two decades ago and the field of framing has developed significantly during this time.

In Kingdon’s research of 23 cases, policy entrepreneurs played a significant role in coupling the streams in all but 3 cases. Policy entrepreneurs champion a cause, solution or problem that they deem important or worthy. According to Kingdon, policy entrepreneurs are “advocates who are willing to invest their resources—time, energy, reputation, money—to

promote a position in return for anticipated future gain in the form of material, purposive or solidary benefits” (p. 179). To advance their cause, policy entrepreneurs get ready for the right moment, when a window of opportunity opens, to match their solutions to problems and find politicians receptive to their ideas. As depicted in Figure 1, and described by Kingdon, a policy entrepreneur is like a surfer that rides or carves the waves of opportunity. Kingdon asserts that policy entrepreneurs don’t create the waves. Instead, they wait for the right set of opportunities and carve them to the advantage of their cause.

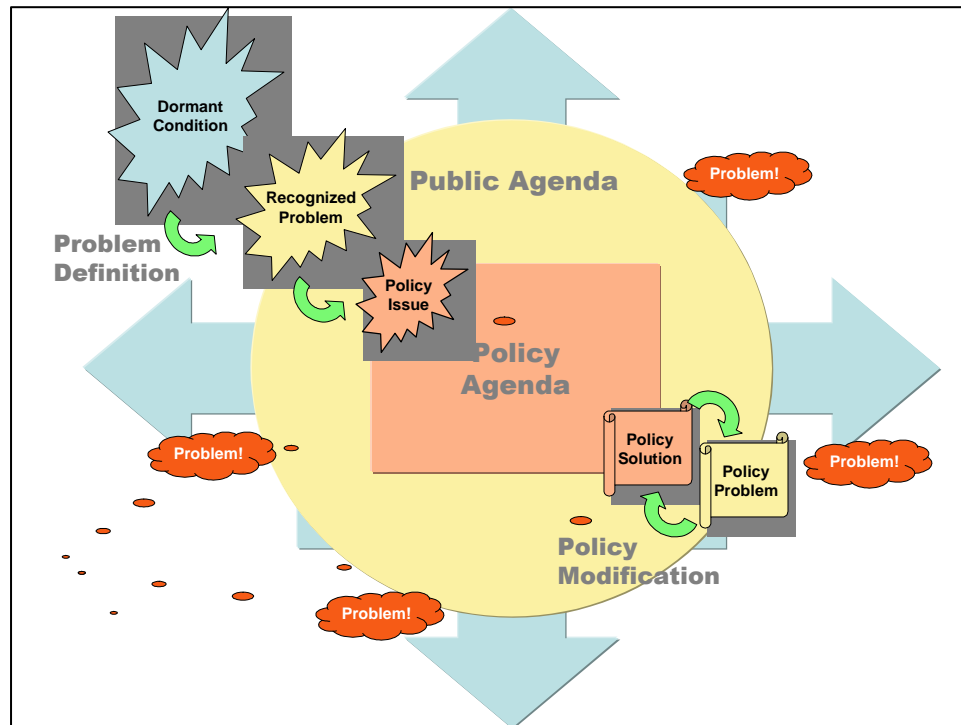
Qualities of effective policy entrepreneurs include persistence, technical expertise and political acumen (Kingdon 1995). Related to political acumen, policy entrepreneurs use issue framing in their attempt to couple the three streams (Zahariadis 1999). Language, word choice and symbols are important as they are used to promote selected interpretations, mobilize support, and influence the political environment. By using selected words, these actors highlight aspects of problems and make them salient, and connect how selected solutions can solve selected problems. When a selected problem diminishes in importance, for whatever reasons, the policy entrepreneur can repackage the description of their solution and attach it to a new problem. (Kingdon 1995)

According to Kingdon, windows of opportunity for policies can be opened in the problem stream, e.g., when the crash of a large passenger jet underscores the problem of airline safety and steps up the search for airline safety policies. They can also open as a result of changes in the politics stream, e.g., a change of presidential administration, a shift in national mood, or a shift in Congressional partisanship majority. While focusing events and political changes can create windows of opportunity for selected policies, ideas and perceptions of problems and solutions are also important factors. “Policy problems are not simply givens, nor

are they matters of the fact of a situation; they are matters of interpretation and social definition” (Rocheffort and Cobb 1993 p. 57, quoting Cobb 1983).

As conceptualized in Figure 2 and described by Kingdon, any number of conditions that lay dormant in the world could become problems. A problem is usually perceived as such only when there is pressure to do something about it. A lobbyist said to Kingdon, “If you have only four fingers on your hand, that is not a problem; that’s a situation” (Kingdon 1995, p. 109). Many problems and issues compete for the attention of policymakers. The victors that rise to the top of the policy agenda tend to benefit from a persuasive and compelling problem definition (Portz 1996). The media can play a role in galvanizing public and governmental attention on a problem or issue. However, in Kingdon’s research, the media were important in only 4 of the 23 cases studied.

Figure 2. Problem Definition and Policy Modification
Issues become problems when demands for action occur (Kingdon 1995)



Definitions

Agenda Setting: The process of placing issues on an agenda for consideration and intervention. In the framing literature, agenda setting is sometimes referred to as the process of emphasizing *what* issue to think about and framing described as *how* to think about the issue.

Amendment Failure: This is a short-hand term for describing reforms to the ODA from 1990-1994 that were discussed and proposed, but did not result in an amendment to the law. Proposed amendments addressed the issue of whether ODA benefits should be more restrictive for high commercial potential orphan drugs. Other issues, such as proposals to extend the ODA grants program, were included in these amendment proposals. However, unless otherwise stated, the focal issue referenced in this dissertation is that of the ODA reforms as they apply to HCP orphan drugs.

Cognitive Cultural Models: Deeply held understandings that motivate thought and behavior in largely unconscious and automatic ways. They are a kind of prototypical framing that includes several elements packaged together, and that are culture-specific – for example, what it means to be a neighbor, a leader, a parent, etc. The basic elements of a cognitive cultural model include “participants” (people, objects, activities that are associated with that concept or model), a “scenario” (a series of expected, standard events that show the relationships between the participants and are expected to occur in a particular sequence), “presuppositions” (assumptions), “entailments” (conclusions), and “evaluations” (assessments as to whether the model itself, as a whole, is a good thing or a bad thing). (FrameWorks Institute 2002)

Drug: Refers to a medication for a medical condition that is approved by the FDA or has potential to become FDA-approved. “Drug” may also refer to a general class of drugs, such as drugs generally or potentially useful for a medical condition. “Drug” also refers to medications that are derived using traditional chemical methods or via genetic engineering, and those that are considered biologics (derived from living organisms).

Frames: Organizing principles that are socially shared and persistent over time that work symbolically to meaningfully structure the world (Reese 2003). To frame is to “select some aspects of a perceived reality and make them more salient in a communicating text, in such a way as to promote a particular problem definition, causal interpretation, moral evaluation, and/or treatment recommendation for the item described” (Entman 1993, p. 52).

Frame Alignment: Linking interpretive frameworks, i.e., between that of an individual and a social movement organization (SMO). There are four frame alignment processes: frame bridging, frame amplification, frame extension and frame transformation. (Snow et al. 1986) (These concepts are further described in Chapter 3.)

Framing vs. Marketing: Framing and marketing are two related but different concepts.

Kotler and Armstrong (1989) define marketing as a “social and managerial process by which individuals and groups obtain what they need and want through creating and exchanging products and value with others.” (p. 5) Marketing has traditionally emphasized the end-goal of an exchange between a target audience and a firm that offers products and services. However, social movement organizations (SMO) can use the principles of marketing more broadly to help meet their goal of increasing support for the SMO’s cause. In either case, framing theory can inform and guide how organizations: 1) conduct research on target audiences and perceptions of products, services or social causes; 2) determine marketing strategies, such as segmentation, targeting, positioning, and messaging strategies; and, 3) craft, deliver and test specific messages.

Framing vs. Positioning: Framing structures the way we think about problems, and how we select and compare potential solutions to those problems. In this regard, framing complements an important marketing concept known as “positioning.” Positioning is the process of influencing target audiences to view a product or idea as superior to alternatives. Positioning is about establishing that Product A or Idea A is better, different, or special compared to B, C, and D. Positioning emphasizes the mental processes of comparison, while framing emphasizes the higher-level mental processes that organize and structure how comparisons are made. Marketers can use framing theory to better understand this higher-level “schemata of interpretation” (Goffman 1974), and explore how target audiences can think in new ways about problems, causes, and solutions. A frame analysis might reveal that an idea or product is perceived as superior to other solutions only when the problem is framed in a certain way. Reframing can change the set of alternatives that are evaluated, e.g., reframing can imply that Idea A should be compared to alternatives X, Y, and Z, rather than B, C, and D. Or, reframing can change the way that existing alternatives are evaluated—by using a new set of

criteria, or a different value and belief system. For example, reframing may imply that Idea A should be compared to B, C, and D using principles of social equity rather than principles of economic efficiency.

High Commercial Potential Drug: A drug that could potentially generate substantial financial returns for its sponsor. Consensus is lacking on what constitutes a HCP orphan drug.

Issue Frame: Descriptions of social policies and problems that shape understanding of how the problem came to be and the important criteria by which policy solutions should be evaluated. Issue frames usually originate from professional politicians, advertisers, spokespeople, editorialists, think-tankers and others who care about molding public opinion. Many issue frames can be summarized by a simple tagline, such as “reverse discrimination” and “right to life.” (Nelson and Willey 2003)

Orphan Drug: Refers to a drug that could potentially be developed to improve a medical condition, but no sponsor seems willing to support its development. In reference to the Orphan Drug Act, an orphan drug is a drug for a rare disease or condition.

Orphan Drug Act of 1983: By providing incentives to companies, the law encourages development of drugs to treat rare diseases affecting fewer than 200,000 Americans.

Orphan Drug Designation: Refers to the process by which a sponsor applies to the FDA to have a selected drug designated as an orphan drug.

Policy: A conscious and deliberate effort to influence behavior.

Policy Discourse: The verbal exchange, or dialogue, about policy issues; usually embedded within an institutional context. (Schon and Rein 1994)

Policy Forums: Institutional vehicles for policy debate; including legislative arenas, the courts, public commissions, councils of government and political parties, the editorial pages of

magazines and newspapers, academic settings, radio and television programs (Schon and Rein 1994) and internet blogs and chat rooms.

Policy Frame: The frame an institutional actor uses to construct the problem of a specific policy situation. (Schon and Rein 1994)

Priming: The process of consciously triggering a cognitive cultural model and then applying its reasoning to other issues. Priming can also mean the ability to affect the criteria by which political leaders or ideas are judged. (Iyengar and Simon, 1994)

Problem Definition: Pertains to what we choose to identify as a public issue and how we think and talk about the concern (Rocheffort and Cobb 1994). A problem definition is a malleable, strategic portrayal of a situation, aimed at accomplishing political goals (Kingdon 1995).

Public Policy: The sum of government activities, whether acting directly or through agents, as it has an influence on the life of citizens. (Birkland 2001, quoting Peters 1999)

Rare Disease: As defined in the text of the Orphan Drug Act, “any disease or conditions which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug.”

Reframing: Changing the lens through which people can think about the issue, so that different interpretations and outcomes become visible to them.

Sponsor: Refers to an individual or organization that takes responsibility for developing, manufacturing and marketing a drug. In the case of orphan drugs, the sponsor is like a parent that adopts a neglected drug or area of drug research. Sponsors are usually pharmaceutical or

biotechnology companies. But government agencies, individual academicians and others could serve as lead investigators and devote the resources necessary for development.

Stakeholders: Parties who are affected by or have a vested interest in the success of an initiative or policy.

Symbols: According to Stone (2002), a symbol is anything that stands for something else. Symbols are collectively created and their meaning depends on how they are interpreted, used or responded to. A good symbol captures the imagination and shapes perceptions. Metaphors are a common symbolic device that is used in text.

Scope of Research

Sabatier's reminder to researchers that "One simply cannot look for, and see, everything" (Sabatier 1999 p. 4) also applies to the scope of a research project. To ensure focus and feasibility of completing the dissertation, this research was limited by the following parameters.

Conceptual Model: As mentioned previously, Kingdon's Multiple Streams model guided and focused the proposed research. This was supplemented by extant theory and research on framing and policy discourse. The multiple streams model guided the identification and clarification of the issue and its place in the policy process. Framing theory was then used to further understand why the ODA was not amended and to help structure guidance for future policy arguments around the ODA.

Subtopics within the Orphan Drug Act of 1983: The emphasis of this research was on the ODA as it applies to medicines for rare health conditions. Since its original enactment in 1983, the ODA has been extended to apply to foods and medical devices for rare conditions. The ODA also provides incentives for firms to develop medicines for common conditions if the firm can demonstrate that research and development costs would likely exceed revenue that

would be generated by the medicine. However, the law's support of orphan foods, orphan medical devices, or unprofitable medicines for common illnesses was not the focus of the research.

Other countries have enacted legislation that is similar to the American orphan drug law. The adoption of such laws is mentioned briefly in the research, but the focus of this research is on the Orphan Drug Act legislation in the United States.

Frame Processes: The emphasis of this research is on producing frames strategically and intentionally to attract support for a social or political issue, and not on unintentional or subconscious frame production. The importance of how these strategic frames are consumed or disseminated is acknowledged. However, frame consumption and dissemination were not addressed to any extent in this research.

Direct Discourse over Mediated Discourse: Much of the framing literature addresses how the media frame issues. In contrast, this research focused primarily on unmediated discourse—as it attempted to construct frames from Congressional testimony. Although Congressional testimony is edited to some degree, it is assumed that the published testimony substantially reflects the original testimony. The fact that testimony may be carefully prepared and written by individuals, other than the speaker, is acknowledged.

Text over Structure and Images: Content analysis research sometimes focuses on the complete set of textual data as well as where and how certain elements of text are featured in written documents (e.g., coding for contents of the headlines and lead paragraphs). Such research also codes aspects of images that accompany the text. In contrast, this research only focused on the complete set of textual data and not on its structure or accompanying images.

Chapter 2—Overview of Orphan Drug Act of 1983

In 1983, the Orphan Drug Act was signed into law (Public Law 97-414) as an amendment to the Federal Food, Drug and Cosmetic Act.² The objective of the ODA has been to stimulate industry interest in developing drugs and biological products for the treatment of rare diseases and conditions. Rare diseases are currently defined in the law (See Appendix E) as diseases and conditions that affect fewer than 200,000 Americans. Such rare diseases include Huntington's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease), Tourette syndrome, Crohn's disease, and cystic fibrosis.

As of 2008, the benefits and assistance for designated orphan drugs include:³

- Tax credits for the costs of clinical research
- Annual grant funding to defray the costs of qualified clinical testing expenses (\$14 million total for 2008)
- Assistance in clinical research study designs
- Seven-year period of exclusive marketing after an orphan drug is approved
- Waiver of Prescription Drug User Fee Act filing fees (about \$1,000,000 per application in 2008)

To be designated as an orphan drug, the sponsor of the drug must submit an orphan drug application to the FDA. In the application, the sponsor must successfully demonstrate that fewer than 200,000 patients will be eligible for treatment under the drug's proposed indication. Orphan designation is specific to the indication of the drug that will be tested in subsequent clinical trials. Hence, one drug can have multiple orphan designations, and a drug may also be

² Information on the Orphan Drug Act was derived from a review of more than 80 articles that contained detailed discussions (i.e., greater than 4 paragraphs) of the ODA in the general, business and medical press. Approximately fifty federal government documents were also reviewed.

³ From <http://www.fda.gov/consumer/updates/oda020808.html>, accessed August 27, 2008

FDA approved for a common problem. For example, Botox (Botulinum toxin type A) has orphan designation for two indications: 1) treatment of strabismus associated with dystonia, and, 2) treatment of cervical dystonia. The drug is also widely used to temporarily improve the appearance of facial wrinkles, an indication that has FDA approval.

Multiple sponsors can obtain orphan designation for a single drug/indication. While sponsors of all designated orphan drugs can receive the tax credits, FDA assistance, and so forth, only one sponsor will receive market exclusivity. That sponsor is the one that is first to receive FDA clearance for the drug's use in a specific indication. For example, three corporations applied for orphan designation for use of their recombinant human growth hormone (hGH) product in children with short stature due to growth hormone deficiency. Genentech was first to gain FDA approval, and to gain ODA market exclusivity. As a result, Serono and Lilly were "blocked" from marketing their product for the next seven years. The FDA will not approve another similar orphan designated drug for use in this indication unless the sponsor can demonstrate that their drug is different in some way or that it has significant safety or effectiveness advantages. Early in the ODA's history, the criteria by which FDA would determine whether a drug is the same or different than other drugs in its class were not established. Lilly successfully argued that a structural difference in their hGH molecule met the criteria of being different. Based on this argument, the FDA approved Lilly's hGH product for short stature. Genentech and Lilly then shared market exclusivity for growth hormone for short stature. This action unleashed a firestorm of lawsuits and controversy over what "different" or "same" meant. FDA subsequently addressed this issue when final rules were approved and implemented in 1992.

The FDA approval process is nearly the same for non-orphan designated drugs and orphan designated drugs, e.g., rigorous clinical trials must be completed to the satisfaction of

FDA, whether the drug is an orphan or not. In the case of the drug approval process, the FDA must review and approve the sponsor's New Drug Application (NDA) before the drug is allowed to be marketed in the US. If the orphan product is a biologic, the FDA must review and approve the sponsor's Biologic License Application (BLA).

The entire process from FDA orphan drug designation to FDA approval has been described as a race where the winner takes all, because only the first sponsor to gain FDA approval will receive market exclusivity. Market exclusivity is widely regarded as the most attractive feature of the ODA. Hence, losing the race to approval can be devastating for small companies that have invested tens or hundreds of millions of dollars in drug development. Launching a “me-too” drug seven years later can be too little, too late for many sponsors.⁴

Market exclusivity can mean higher profits for a drug sponsor because: 1) in the absence of competitive bidding, the sponsor can charge a higher price; 2) in the absence of competing marketing campaigns, the sponsor with exclusivity can lower their marketing expenses when it is easier to command attention and interest in the product with 100% of the market “voice;” and, 3) market exclusivity means, by definition, having 100% of the sales in that product category. Capturing all of the market generally translates to a higher volume of sales (in units). Higher unit sales usually translate into lower costs per unit because of scale efficiencies and the ability to amortize costs over a greater number of product units.

As of early 2008, twenty-five years after the ODA's enactment, more than 300 orphan drugs and biological products received FDA approval, and 1700 orphan drugs received FDA orphan designation.

⁴ Since a drug's 20-year patent life begins from the time of the patent filing, the patent may expire during or shortly after FDA approval. Patent expiration opens the market to generic competition. Generic competitors usually enter the market at a fraction of the price of the branded drug's price before it went off patent. Waiting 7 years makes it difficult, if not impossible, to recoup the investments that were made to get the drug approved.

As can be seen in Table 1, it took nearly three years to get the ODA passed. Since 1983, the ODA has been amended five times in an effort to clarify terms, improve its implementation and effectiveness, and to convene a National Commission on Orphan Diseases to assess public and private sector activities related to rare diseases. In 1992, the FDA issued its final rules to implement the law. These key events in the ODA's history are further described in Chapter 5.

Table 1--Chronology of the ODA: Enactment, Amendments, and Final Rules

Date	Event or Change	Related Bills
June 1980-December 1982	Pre-enactment legislative activities included a June 1980 hearing about the issues, a survey of rare disease drug developments at pharmaceutical companies, and getting H.R. 5238 passed. H.R. 5238 was introduced in 1981	n/a
January 1983	The Orphan Drug Act (P.L. 97-414) amended the Federal Food, Drug and Cosmetic Act (FFDCA)	H.R. 5238 introduced by Representative Waxman
October 1984	P.L. 98-551 changed the definition of "rare disease or condition" to a numeric prevalence threshold of 200,000 Americans. Previously, orphan drugs were defined as drugs lacking profitability	S. 771 introduced by Senator Hatch
August 1985	P.L. 99-91 enabled all orphan drugs, patentable or not, to become eligible for seven years of market exclusivity. Previously, market exclusivity only applied to non-patented drugs. P.L. 99-91 also established a National Commission on Orphan Diseases, and made modifications related to antibiotic drugs and financial assistance for pre-clinical testing expenses	H.R. 2290 introduced by Representative Waxman, S. 1147 introduced by Senator Hatch
April 1988	The allowable timing of the orphan drug designation request was amended by P.L. 100-290. It requires that the application for designation be made prior to the submission of an application for marketing approval, New Drug Application (NDA) or Product License Application (PLA). Previously, the designation request could be filed at any time prior to FDA's approval to market the product. This amendment also made medical foods and medical devices for rare illnesses eligible for grants and contracts to support clinical studies	H.R. 3459 introduced by Representative Waxman
January 1991	FDA proposed regulations to implement ODA	n/a
December 1992	FDA issued final regulations to implement section 2 of the ODA, which added 4 sections to the Federal Food, Drug, and Cosmetic Act. Regulations were issued under the Code of Federal Regulations, Title 21 (21 CFR 316)	n/a
August 1997	The tax credit of up to 50% of clinical research performed for designated orphan drugs was made permanent by P.L. 105-34 (Taxpayer Relief Act of 1997, Title VI, Sec. 604)	H.R. 2014 introduced by Representative Kasich
November 2002	The available funding for FDA's Orphan Products Research Grant Program was increased to \$25 million for 4 years by P.L. 107-281 Rare Diseases Orphan Product Development Act	H.R. 4014

Chapter 3—Literature Review of Framing Theory and Research

The literature on framing theory and research, as it relates to political communication and influence, will now be reviewed. This chapter introduces the reader to the field of framing and includes a description of how frames organize thinking, where frames are located, and what frames do. To inform the methods part of this research, literature on constructing frames from text are then reviewed. Frame analysis and strategy literature are then reviewed, followed by a review of reframing and policy development literature. A guide for analyzing factors that may favor or impede the passage of legislation is then proposed. The chapter closes with foundational theories of the ODA that may be useful for understanding current and future ODA frames.

The Literature on Framing

As we often use *frames* in communication to better understand complex phenomena, it seems ironic that the literature on framing seems very complex and difficult to comprehend. Framing theory novices, such as this researcher, apparently are not alone in this assessment. Even framing scholars characterize the field as theoretically and empirically vague (Scheufele 1999). Terms in the field seem ill-defined, e.g., one scholar asserts that the term *frame* is being used to describe a “variety of disjointed and incompatible concepts” (Fisher 2003, p. 1). Differences in terms, such as *agenda setting* and *framing*, are disputed. Arguments over terms are characterized as “border disputes” (Maher 2003). Maher has commented, “When scholars who are doing framing research disagree to this degree, we must then wonder if they mean the same thing when they use the word framing” (p. 83).

Perhaps early scholars could have set clearer foundations for later work, e.g., Goffman's 1974 book, *Framing Analysis*, has been widely cited, yet Goffman's foundational definitions lack clarity:

I assume that definitions of a situation are built up in accordance with principles of organization which govern events—at least social ones—and our subjective involvement in them; frame is the word I use to refer to such of these basic elements as I am able to identify. That is my definition of frame. My phrase “frame analysis” is a slogan to refer to the examination in these terms of the organization of experience (Goffman 1974, p. 10-11).

Framing research programs can be found in a number of disciplines—from anthropology, cognitive psychology, economics, linguistics and discourse analysis, communication and media studies, sociology, and, political science and policy studies (Van Gorp 2007, Benford 2000). Hertog and McLeod (2003) have described this as a mixed blessing: “The range of approaches political scientists, sociologists, media researchers, and others bring to the study of frames and framing is both a blessing and a curse (p. 39).” The blessing is that of conceptual openness and creativity, the curse is that “findings, methodological insights and theoretical conclusions don't ‘add up’” (p. 40).

In 1993, Entman challenged communications scholars to improve theoretical clarity: “Despite its omnipresence across the social sciences and humanities, nowhere is there a general statement of framing theory that shows exactly how frames become embedded within and make themselves manifest in a text, or how framing influences thinking” (Entman 1993, p. 51). Fortunately, many authors have risen to the challenge and have proposed clearer definitions and theoretical propositions (e.g., Reese 2003).

To deal with the challenging task of summarizing the framing literature, this researcher first read through nearly 3000 pages of interrelated literature regarding issue framing, policy development, policy analysis and political debate. Concepts relevant to the aims of the proposed research were culled from this broad sampling of articles and books, and then organized into a

typology (See Appendix B).⁵ Fortunately, it was discovered *post facto* that this approach is endorsed by policy case study researchers. According to George (2004), typologies and typological theories that are coupled with case studies based on real world problems can be highly useful to policy makers because they help them identify patterns and conditions that can lead to outcomes of interest.

The terms *frame* and *framing* will now be defined, followed by a description of how frames work to provide meaning and structure to human experience. Next, the following aspects of the framing literature will be described: where frames are located, what frames can do, how frames are used strategically, what characterizes a potent frame, and what processes lead to frame alignment. Finally, the framing literature was reviewed in order to inform specific aspects of this research, i.e., methods to construct and analyze frames, and ways to devise framing strategies, were reviewed. The framing literature review was then synthesized and combined with related policy development literature.

About Framing and Frames

Entman (2007) defines framing as the process of culling a few elements of perceived reality and assembling a narrative that highlights connections among them to promote a particular interpretation. Fundamentally, framing theory assumes that our mental representations of reality are socially constructed, that complex social issues have multiple possible interpretations, and that these interpretations are malleable.

⁵ According to George (2004), typologies characterize variants of a phenomenon, whereas typological theories seek to identify the causal mechanisms and pathways that link the independent variables of each “type” with its outcome. George defines a typological theory as “a theory that specifies independent variables, delineates them into the categories for which the researcher will measure the cases and their outcomes, and provides not only hypotheses on how these variables operate individually, but also contingent generalizations on how and under what conditions they behave in specified conjunctions or configurations to produce effects on specified dependent variables. . .” (p. 235). Typological theories draw together in one framework the research of many social scientists.

Language is critical to the process of understanding complex social issues, i.e., we often look to others to describe “what is going on here?” Rhetoric can help lodge a particular understanding of issues in the minds of people (Rochefort and Cobb 1993) and frames are the rhetorical devices that privilege⁶ and promote particular points of view (Kinder 2007), render events meaningful, and thereby organize experience and guide action (Snow et al. 1986). Though several types of frames have been described in the literature, including collective action frames, decision frames, and news frames (Nelson and Willey 2003), this literature review focuses most on issue frames. Nelson and Willey define issue frames as “descriptions of social policies and problems that shape the public’s understanding of how the problem came to be and the important criteria by which policy solutions should be evaluated” (p. 247).

By providing a central, organizing idea or set of principles (Reese 2003), frames allow people to rapidly identify why an issue matters, who might be responsible, and what should be done about it (Nisbet 2007). Framing is used in ideological contests and political struggles where “participants maneuver strategically to achieve their political and communicative objectives” (Pan 2003, p. 40).

How Frames Organize Thinking

According to Reese (2003), cognitive frames invite us to think about social phenomena in a certain way, often by appealing to our basic psychological biases. Frames introduce or raise the salience of certain ideas and trigger mental schemas that work to help individuals understand the idea. In other words, people assimilate new information by fitting it into their existing way of viewing similar things (Entman 2007, Goffman 1974, Snow et al. 1986). Hence, our preexisting meaning structures or schemas influence how we interpret complex social issues (Scheufele 1999).

⁶ In the context of this sentence, *privilege* means to make important, dominant or to set as the de facto standard.

Using metaphors is a form of framing (Lakoff 2004) and illustrates the notion of cognitive frames. Using a single word, such as the word *epidemic* in the description *obesity epidemic*, invokes a schema of obesity as a contagious disease that is spreading and in need of urgent attention. Metaphors draw a comparison from one thing to another. But in a subtle way, metaphors can imply a whole narrative story and a prescription for action (Stone 2002).

According to Reese (2003), cultural frames also organize our thinking. But in contrast to cognitive frames, cultural frames invite us to summon a deeper, more persistent understanding of our world and enable us to apply broader constructs to account for our social reality.

Where Frames are Located

Frames seem to be everywhere in the “discursive universe” (Fisher 1997). Frames are found within communicators and receivers of information, and within text; but our most enduring frames are located in our culture (Entman 1993, Maher 2003 and Van Gorp 2007).

Frames Located in Culture

Schon and Rein (1994) describe cultural meta-frames as broadly shared beliefs, values and perspectives among societal members. In politics, institutions and interest groups derive their values and perspectives from cultural meta-frames. Van Gorp (2007) describes frames in culture as a sort of grand inventory of culturally guided ways of understanding and communicating about the world. Communicators and receivers constantly select frames from this inventory. Occasionally, a creative person or social movement organization will use a new frame that ultimately becomes widely shared and part of the cultural stock of frames.

The stock of cultural frames can serve as both resource and constraint in politics. According to Benford et al. (2000), the cultural stock of meanings, beliefs, ideologies, practices,

values, myths and narratives can constrain political opportunity if the political movement cannot create a frame that is resonant with the extant cultural stock.

Schon and Rein have described example cultural meta-frames as: 1) the market frame, where principles of economic exchange and self-interest serve as the guide to social actions; 2) the social welfare frame, where principles of societal obligation guide us to help people in need when other means, such as the market, have failed; and, 3) the social control frame, where principles of criminality and protection serve as guide. Each of these cultural meta-frames is, in essence, a theory about how the world works based on a set of beliefs.

In a similar vein, Benford et al. (2000) have described example “master frames.” These include rights frames, choice frames, human injustice frames, environmental frames, oppositional frames and hegemonic frames. Master frames are often created or referenced by innovative social movements and later used as a springboard in a different domain. For example, the *rights frame* was defined by the southern civil rights movement, later picked up by the women’s movement and other ethnic movements, and, further “diffused to gay rights, animal rights, abortion rights, fetal rights, and student rights” (Oliver 2000, p. 41).

Frames Located within Communicators

Communicators (e.g., writers or speakers) consciously or unconsciously select frames to help get their point across or to influence receivers to see the world as they do. Scholars have focused on how and why journalists, as communicators, present selected frames of events or persons (e.g., Maher 2003, Pan 2003). Other scholars have focused on framing in social movement organizations (Snow et al. 1986, Benford et al. 1993, 2000), public relations firms (Hallahan 1999), policy advocates (Schon and Rein 1994, Stone 2002) and a variety of other communicator types.

Frames Located within Receivers

Goffman (1974) refers to “schemata” as the frames or mental structures used by individuals as receivers (e.g., readers or listeners). Receivers may rely on their own schemata to make sense of a situation or event and may not rely on the frames offered or intended in messages (Entman 1993). Framing is a dynamic process as receivers can accept, modify, reject or ignore frames that are embedded in messages. An individual’s schemata or frame can act as blinders for new information because if new information does not fit into the receiver’s frame, the information may be rejected (Lakoff 2004). Van Gorp (2007) asserts that “. . . sometimes, a kind of shock is required for the receiver to be able to break through a persistent frame” (p. 69).

Frames Located within Text

Frames are manifested in text by the presence or absence of “certain keywords, stock phrases, stereotyped images, sources of information, and sentences that provide thematically reinforcing clusters of facts or judgments” (Entman 1993, p. 52). The ways in which frames can be constructed from text will be discussed later in this literature review.

How Socio-Cultural Interactions Create Meaning and Frames

Benford et al. (2000) describe how communicators, receivers and culture interact to create meaning and generate new or modified frames. Social groups are both consumers and producers of frames because they consume existing cultural meanings and produce new meanings. As frame communicators and receivers interact, receivers can affect the form and content of the message. In other words, receivers can precipitate frame transmission.

What Frames Do

So far, the discussion of framing has been fairly abstract. As this review turns to the function of frames and how they can be used to improve the way we communicate and influence others, concepts should become more concrete.

Stone (2002) asserts that typical policy arguments are politically constructed to advance certain definitions of goals, problems and solutions. Each construction then invokes a different set of rules or ways to solve social issues. Because framing is central to policy and political rhetoric, political elites and social movement organizations strategically use frames in their communications. Politics is about controlling interpretation because shared meanings motivate people to action. (Entman 2007, Benford et al. 2000, Snow et al. 1986, Stone 2002)

Benford (2000) categorizes frames by the tasks they can accomplish. *Diagnostic frames* articulate a cause or blame for a situation or event. *Prognostic frames* suggest the solution or remedy for a problem. *Motivational frames* articulate the rationale for action by describing the severity or urgency of a problem, or the efficacy or propriety of solving a problem.

How Frames are used to Mobilize Consensus and Action

Entman (2007) asserts that, if power is the ability to convince other people to do what you want, then framing is a critical communications tools in the exercise of political power. Convincing people what to think about, and how to think about it, is how power is exerted in non-coercive political systems.

Lakoff (2004) believes that reframing social issues is the way to achieve social change and has written a book on how American progressives need to better use framing theory to win debates, and attract adherents and votes.

Pan (2003) has described a number of ways that frames can be used strategically in social and political movements. Frames can be used to promote a new configuration of social and

political forces; unify a discursive community; promote a more deliberative democracy; promote political goals and attract more supporters; mobilize collective action; expand social and political actors' realm of influence; and, increase one's chance of winning debates or adherents.

Pan (2003) asserts that the key framing strategies that political actors must consider include which frame to sponsor; how to sponsor it; and, how to expand its appeal. In terms of which frame to sponsor, the choice can be based on a variety of criteria, e.g., potency and breadth of appeal. Benford et al. (2000) point out that collective action frames increase in potency if they are broad in their interpretive approach. Moreover, frames should be inclusive and flexible, and they should be culturally resonant. Cultural resonance can be enhanced when a collective action frame is connected to an historical movement, e.g., connecting gay rights frames to civil rights frames of the 1960s.

Van Gorp (2007) provides guidance on how to recognize a potent frame. A potent frame would activate a schema with just a single reference and trigger a causal chain of reasoning devices. Moreover, a potent frame is implied and hidden. Except for the evidence of framing devices (e.g., words, metaphors, exemplars, descriptions and arguments), the frame is not explicit in the text. Effective issue frames can be summarized by a simple tagline, such as "reverse discrimination" and "right to life" (Nelson 2003).

Dorfman et al. (2005) believe that effective framing is critical to advocate's ability to influence how issues are interpreted. They have advised public health advocates to emphasize the social context of issues when presenting their views and to craft messages that will trigger frames that connect to values. According to Dorfman et al., this is done by generating *Level 1 messages* to express the overarching values, i.e., why a particular stance on a social issue matters. *Level 2 messages* address the general issue at hand, while *Level 3 messages* address the details of the issue. Level 1 messages connect with the audience in the deepest way.

Pan (2003) believes that frames can become more potent if they link with societal values; use appropriate cultural attributes and symbolic devices; and, link with news values that are in current use in society.

Snow et al. (1986) have identified four processes that promote frame alignment, thereby attracting social movement adherents: 1) frame bridging; 2) frame amplification; 3) frame extension; and, 4) frame transformation. Frame alignment links the interpretive framework of an individual to that of a social movement organization (SMO).

Frame bridging is the linkage of two or more ideologically congruent but structurally unconnected frames related to a particular issue or problem.

Frame amplification is the process of clarifying and invigorating an interpretive issue frame. There are two varieties of frame amplification: value amplification and belief amplification. Value amplification is a type of frame amplification that clarifies the link between the target and the social movement. Values are defined as models of conduct or states of existence that are thought to be worthy of protection and promotion. Value amplification means identifying, idealizing and elevating one or more values that are presumed to be basic to potential supporters but, for whatever reasons, have yet to inspire their support. (Snow et al. 1986)

Belief amplification is another type of frame amplification. Here, beliefs refer to a particular tenet, or a body of tenets, that are held by a social group, e.g., “God is dead, the Second Coming is imminent, capitalists are exploiters, and black is beautiful” (Snow et al. 1986: p. 469). Belief amplification is a springboard for mobilizing support and clarifies and invigorates a belief frame of a particular issue. In the literature on social movements, there are five kinds of beliefs that are especially relevant: 1) beliefs about the seriousness of the issue at hand, 2) beliefs about the locus of blame or causality, 3) stereotypes about individuals or groups that are targeted

for influence or vilification, 4) beliefs about the probability that collective action will achieve results, and, 5) beliefs about the importance or moral imperatives of joining a cause. (Snow et al. 1986)

The third process of frame alignment is frame extension. This is a kind of grafting of interests and frames, which is necessary when potential adherents may not share the sentiments or beliefs of the social movement organization. In frame extension, the SMO extends the boundaries of its framework to appear congruent with that of potential adherents. For example, Snow et al have described a religious organization's use of frame extension in recruiting members: they would identify that a potential recruit was interested in meeting attractive women, and recruiters would use this fact in their recruitment. They would convince prospects to attend one of their meetings by emphasizing the fact that many "pretty girls" attended their meetings.

The fourth process of frame alignment is frame transformation, which is a time consuming and intense process of planting and nurturing new values and jettisoning old meanings or understandings (Snow et al. 1986). Oliver and Johnston (2000) argue that ideological transformation is the correct description for what Snow et al refer to as frame transformation, because the concept of ideology better describes the conversion process. According to Oliver and Johnston, ideology is "a system of meaning that couples assertions and theories about the nature of social life with values and norms relevant to promoting or resisting social change" (p. 43). Oliver and Johnston see a frame as an orientating principle that is easy to convey. In contrast, an ideology is a system of ideas that has to be adopted through concerted education, socialization and debate. Frames can be communicated with stock phrases or sound bites while ideologies are much more difficult to transmit. Once conversion to a new ideology occurs, elements of the new ideology can function as frames.

Benford et al. (2000) have described three factors that will increase the credibility of a frame: frame consistency, empirical consistency and the credibility of the frame articulators. Credibility is enhanced if the frame is consistent with receivers' beliefs, claims and actions. Credibility is also enhanced through empirical consistency, i.e., when there is a fit between the frame and some observable or understandable evidence. Lastly, credibility of the frame depends on the credibility of the person or institution using the frame in their speech or writing.

Benford et al. (2000) have also described the factors that influence frame salience: centrality, experiential commensurability and narrative fidelity. Centrality increases frame salience when the beliefs, values and ideas in the frame are also central to the targets of mobilization. Experiential commensurability means the salience of a frame is increased because it is congruent with the personal everyday experiences of the targets of mobilization. Narrative fidelity is achieved when the frame resonates with narratives or myths that exist within the target's culture.

Frames that Conflict

Scholars generally believe that framing is an important strategic tool to attract participation in social movements and support for political causes. Characteristics of "potent" frames and the processes that promote frame alignment have just been described. But frames do not always align; they often conflict.

Schon and Rein (1994) assert that when disputants hold conflicting frames, policy debates will often reach an impasse. Because disputants have "mutually incompatible ways of seeing the policy situation" (p. 29) they talk past each other and, as a result, the policy situation will cease to develop. In order to break a policy stalemate, Schon and Rein believe stakeholders must reflect on the frames that underlie political actors' values, beliefs and perceptions. But to do this, they must first become aware of their frames by constructing them "either from the

texts of debates and speeches or from decisions, laws, regulations, and routines that make up policy practice” (p. 34). One aim of this research was to use theoretical insights from Schon, Rein, and other framing theorists to construct and reflect on frames utilized during the described 1990-1994 ODA amendment hearings.

To guide this part of the research, the following topics were reviewed from the literature: 1) the frame construction process, along with its challenges and limitations; and, 2) the process of analyzing frames and developing policy development strategies related to framing.

Methods of Constructing Frames from Text

This section of the literature review informed portions of Chapter 4 that pertained to methods of text analysis and frame construction.

As mentioned, one aim of this research was to examine how issues were framed in Congressional hearings related to ODA amendments from 1990-1994. The reviewed literature indicates that constructing frames from text is a challenging process. Nelson and Willey (2003) have described frames as “slippery and hard to measure” (p. 245). Van Gorp (2007) has remarked, “Frames seem to be everywhere, but no one knows where exactly they begin and where they end” (p. 62). These challenges, and options for addressing them, will now be described.

One of the key problems of constructing frames from text is their “stealth” nature, i.e., frames are not literally outlined in the text (Van Gorp 2007). In fact, framing scholars assert that most elements of the frame reside in the receiver rather than the text, i.e., just one frame element in the text can trigger a much larger set of elements in the minds of the receiver/reader. (Van Gorp 2007, Fisher 1997)

Humor and frames seem to present similar challenges to text researchers. In Neuendorf’s *Content Analysis Guidebook* (2002), challenges to coding humor include: “It’s

subjective, so much so that some scholars say it resides in the receiver rather than the message. It's multidimensional, and multiple senses of humor (i.e., abilities to identify and appreciate humor types) may exist. It's primarily latent in nature rather than manifest, with the typical challenges that go along with latent content." (Neuendorf 2002, p. 147)

Frames are latent like humor. Neuendorf (2002) defines latent content as text consisting of "unobserved concept(s) that cannot be measured directly but can be represented or measured by one or more indicators" (p. 23). Inter-coder reliability is typically poor with latent content because constructs are difficult to conceptualize and operationalize so that two or more coders will look for and code the same values (Neuendorf 2002).

To improve inter-coder reliability of latent content, researchers seem to resort to tactics that diminish the usefulness and face validity of their research. One tactic is to use the presence, absence or frequency of selected words to indicate whether certain frames exist in text. As an example, Andsager and Powers (1999) used word counts and cluster analysis to determine how popular media framed breast cancer. Andsager and Powers concluded that three general frames emerged from the articles they examined: "basic information on breast cancer and its treatment; research on causes and prevention; and personal stories of cancer survivors or their relatives." Andsager and Powers did achieve acceptable inter-coder reliability with this word count approach. But, if frames suggest problem, cause, moral judgment and remedy (Entman 1993), then their three categories seem more characteristic of topics rather than frames. Indeed, Reese (2007) has found that many doctoral students at his university "find in framing a more compelling hook to hang their content analyses on. Often, it is simply a matter of substituting

‘frame’ for . . . ‘topic’ or ‘theme.’ If they cannot show how the frame does more ‘organizing’ and ‘structuring’ work,⁷ I prefer they not use the label.” (p.151)

In contrast to the Andsager and Powers study, Saguy and Riley (2005) used a purely qualitative approach in a study of obesity framing. Drawing on a mix of secondary and original data sources, the researchers read the selected documents several times and constructed theme sheets as different themes emerged. Three competing frames emerged: fatness⁸ as body diversity, obesity as risky behavior, and obesity as disease. These categories do fit Entman’s frame definition. The “fatness as body diversity” frame, for example, implies that being fat or thin is part of human diversity, much like having light or dark skin color. The frame further implies that, if the rights of all people should be supported or defended, then obese individuals’ rights should be supported (like civil rights). Various remedies can be implied from this. Society could make special concessions for the needs of the obese (e.g., by providing larger seats in planes) and reduce discrimination of obese individuals (e.g., by promoting tolerance and anti-discrimination through education and punitive means).

Tankard (2003) would likely describe the frame construction methods of Saguy and Riley as arbitrary, unsystematic and subject to confirmation bias. Tankard advocates a more replicable approach to frame construction, but this approach seems to yield frames that lack richness and usefulness compared to that of Saguy and Riley.

In an attempt to remedy the weaknesses of inductive and interpretive frame construction methods, such as that of Saguy and Riley, Tankard has several recommendations. Tankard assumes that defining characteristics of frames can be found in text and observers or coders can

⁷ Reese defines frames as “organizing principles that are socially shared and persistent over time, that work symbolically to meaningfully structure the social world” (Reese 2007 p. 150, Reese 2003 p.10).

⁸ Saguy and Riley use the seemingly derogatory words “fat” and “fatness” in their article. “Fat,” they explain, is a word that is commonly used by advocates for the rights of overweight or obese individuals.

recognize and agree upon these characteristics. He suggests that researchers be more precise about frame definitions, and more systematic about procedures used in identifying frames. He recommends that researchers a) identify a list of frames for the particular domain of interest; b) specify keywords, catchphrases and images that will help detect each frame; then, c) identify frames in a content analysis. However, when Tankard used this procedure to detect abortion issue frames in text, acceptable levels of inter-coder reliability were not achieved. An acceptable level of 89% agreement between coders was reached only when all six frames were collapsed to two frames—generally favorable to abortion and generally unfavorable to abortion. While Tankard’s procedure would likely reduce the problem of bias in constructing frames from text, his method seems to raise validity issues (i.e., are pro and con positions validly considered frames?).

Frame construction procedures outlined by Van Gorp (2007) and McLeod (2003) seem attractive for their multi-pronged, 360 degree approaches. However, some scholars assert that one should not do both inductive and deductive frame construction because one approach may bias the other (personal communications with Felicia Mebane, August 2007).

Van Gorp (2007) recommends that researchers first inductively construct an inventory of frames based on media content, public discourse and a literature review. The researcher should then list framing and reasoning devices that are most indicative of the identified frames (these can be placed in a matrix: where the rows include the frames, and the columns include the devices). Last, the researcher should deductively determine to what extent these framing devices are present in the complete data set.

McLeod (2003) believes that researchers should do some preparatory work before constructing frames from text by reading widely among ideologically divergent sources to gain awareness of an array of potential frames for the topic under study. From this he advises

researchers to develop some preliminary models of frames and sub-frames (the more, the better, he says). Next, the researcher should a) match the frames to sponsor groups; b) become sensitive to symbolic representations; and, c) then determine hypotheses about the relationships among frames, ideologies and narrative structures. Last, the researcher should identify methods appropriate to studying frames in the context of the selected topic.

Van Gorp (2007), Fisher (1997), and Nelson and Willey (2003) caution that frame construction from text is labor intensive and there is no guaranteed yield. These scholars also caution that researcher subjectivity is inevitable and that researchers may need to be a member of the culture to find the storylines that characterize cultural frames. As can be seen in Chapter 4, this research used an inductive approach to constructing frames. Compared to word counts or the deductive approach of Tankard, this is a more interpretive approach that would likely have poor inter-coder reliability. However, the richness of this approach seemed preferable to a rigor that would yield little substance or usefulness.

Frame Analysis and Strategy

This section of the literature review informed the approach to Aim 4, which was to analyze issue frames used in the ODA amendment hearings from 1990-1994 and provide strategy guidance to ODA stakeholders. Analysis and strategy were guided by theories and research pertaining to frame reflection (Schon and Rein 1994), political language (Stone 2002), frame potency (Pan 2003, Van Gorp 2007, Benford et al. 2000, Lakoff 2004), and frame breaking and creativity (Fredin 2003). Theories that have not been previously addressed in the literature review will now be discussed briefly.

To recap, frames strategically portray a situation and imply problem definition, causation, moral judgment and remedies (Entman 1993). Frames are used in political communications to persuade others to understand a situation in terms that favor the frame sponsor's position.

Schon and Rein assert that political debates reach an impasse when disputants hold conflicting frames. Schon and Rein have described four basic ways to address policy controversy and, possibly, advance policy development: 1) do nothing to intervene, and allow the controversy to continue, escalate or wane; 2) devise and implement a marketing strategy to better advance one's policy position and attract adherents; 3) negotiate to arrive at a mutually satisfactory compromise, i.e., turning a win-lose proposition into one of win-win; and, 4) co-design new policy, i.e., contending parties would use collaboration and frame reflection to redesign the policy object.

Reframing is one way to change the debate and attract political support (Lakoff 2004) and would likely be an important part of Schon and Rein's marketing strategy alternative. Reframing means changing the lens through which people can think about an issue, so that different interpretations and outcomes become visible to them.

Many reframing options are usually available for consideration. Fredin (2003) has urged journalists to create a web-based environment that would allow readers to explore alternative views of a news story. Because aspects of this "frame breaking and creativity" environment were useful to consider for this research, some of its principles will now be described.

Fredin asserts that individuals can build a new understanding of a situation or event through browsing, creativity, and imagination. Creativity involves sorting through a large number of alternatives to find those with potential. Because many alternatives can become overwhelming, it is necessary to organize them in a web-based digression format that allows an individual to explore choices at different levels. By using links and the ability to drill down to get more information, individuals can browse and imaginatively explore "first a little, then a lot." Fredin offers suggestions for developing a frame database that would help individuals creatively invent new frames. The database could be visualized as having the different frames listed in the

rows, and key elements of the frames listed in the columns. Column elements might include the frame's roots, core position, appeals to principle, metaphors, exemplars, catchphrases and depictions. Using this database, with the addition of pertinent facts, new frames could be created by recombining elements or exploring counter frames.

Another interesting approach to reframing would be to use Stone's (2002) policy taxonomy to explore different ways of viewing and describing a political situation or event. Stone asserts that politics is a creative process that helps us see from different perspectives. In her book, *Policy Paradox*, she argues that policy goals, problems, causes and solutions have a generic structure to them. Political actors promote one way of looking at policy situations to advance their causes. In response, Stone created a "rhetoric of policy argument" to equip readers to continually re-envision problems and solutions. See Appendix B for a summary.

To illustrate the ways in which an argument can be dissected and reframed, Stone gives an example of sharing a cake with her class. The idea of dividing the cake equitably so that, by definition, everyone would get the same amount is challenged by Stone's multiple definitions of equity. For example, if Stone gave everyone in the class an equal slice, those that missed class that day would lose out. Also, students working close by might object to being left out. Stone offers several other scenarios that challenge the seemingly simple notion of equal slices for everyone. For example, there are multiple ways to define *everyone*. Does everyone mean those invited into the class, or should the notion of everyone be based on rank or some other definition of membership in a group. By understanding the different possible interpretations of equity and other equally important concepts, one can use Stone's policy taxonomy to consider different vantage points by which to view a situation. From this exploration, different frames and political arguments can be crafted.

Reframing and Policy Development

This section of the literature review guided the analysis of the failed ODA amendments and how reframing can be used to influence future ODA policy development.

As already mentioned, policy debates can reach an impasse because disputants have “mutually incompatible ways of seeing the policy situation” (Schon and Rein, p. 29). Reframing can change the rules and perspectives by which policy issues are judged and debated. Framing advocates believe that reframing is a way to move policy issues forward and break the impasse. This dissertation research explored how framing supports policy development. Given this, it seemed logical to close this literature review by relating framing theory back to theories of policy development, especially the Multiple Streams model. Hence, how advocates might frame their messages to promote passage or blockage of legislation will now be explored.

Critical success and failure factors for the passage of legislation have been synthesized from the literature review and are listed in Table 2. Note that these factors resemble Kingdon’s MS model streams (problem, policy, politics streams) and other important MS factors, such as the skill and activities of policy entrepreneurs.

Based on the Table 2 synthesis, the MS model and framing theory appear to intersect in several important ways. First, a competent and persistent policy entrepreneur is needed to raise awareness of issues, and frame them in a way that promotes a selective understanding. This means the policy entrepreneur must successfully use framing to define social conditions “out there” as tractable problems that are appropriate and feasible for government action, e.g., because the problem is a social (not a private) problem and it affects a powerful minority that is important to political actors.

Second, the policy entrepreneur must be vigilant and creative in scoping out emerging trends and windows of opportunities. The policy entrepreneur can use previously described

framing theories to generate framing options and choose the frames that are most likely to succeed in shaping policy in a preferred direction. The policy entrepreneur has many options for portraying their pet causes, problems and solutions. Framing research can provide guidance on selecting potent frames or frames that can easily bridge to multiple political groups.

Third, the policy entrepreneur must know when the time is ripe to couple the streams and portray a problem in a way that advances their cause and suggests the entrepreneur's preferred policy solution. This means the entrepreneur must also frame problems and solutions in terms that will resonate and activate important political allies.

Table 2—Guide for Analyzing Factors that Favor or Impede Passage of Legislation
Some Constructs and Propositions from the Policy and Framing Literature

Construct	Factors Favoring Passage of Legislation	Factors Impeding Passage of Legislation
Problem Definition	<ul style="list-style-type: none"> -Defined as a social problem -Problem is getting worse -Suggests a solution that is tractable -Cause or blame is attributable to a source that is disliked -Problem was caused intentionally -Problem was caused secretly -Suggests problem has exciting qualities or is urgent -Problem affects a powerful minority or it affects the majority of people -Affected people are aware of problem -Defined so individuals can see they are or might become the next victim -Defined ambiguously to appeal to more people and leave wiggle room -Problem fixers gain resources, power, status 	<ul style="list-style-type: none"> -Defined as a private problem -Problem is getting better w/o policy -Suggests a solution that is intractable -Cause or blame is attributable to a source that is liked or favored -Problem was unintended/accidental -Problem was not created in secrecy -Suggests problem is not exciting or no longer seen as exciting; not urgent -Problem affects silent minority -Affected people are not aware of problem -Suggests a remote chance of becoming a victim in the foreseeable future -Defined explicitly and precisely, narrowing appeal and revealing specifics that can be disagreed upon -No one gains from fixing problem (or costs exceed benefits)
Policy Promotion	<ul style="list-style-type: none"> -Government action is only way to solve problem -Solution has obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to important interests -Policy is not seen as complex -Easy to communicate features -Policy sponsors are popular -Policy opponents are unpopular 	<ul style="list-style-type: none"> -Government action is one possible way to solve problem -Solution has no obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to unimportant interests -Policy is complex, risks are unknowable -Not easy to communicate features -Policy sponsors are unpopular -Policy opponents are popular
Political Milieu	<ul style="list-style-type: none"> -No major competing political issues -New political forces (e.g., new president) w/ compatible interests -Organized interest support or lack of opposition 	<ul style="list-style-type: none"> -Competing issues command attention, pushing issue/solution off agenda -No major changes in political stream that would favor legislation -Strong, organized interests opposed
Events	<ul style="list-style-type: none"> -Focusing event galvanizes support 	<ul style="list-style-type: none"> -Focusing event detracts from problem and/or solution
Climate/mood	<ul style="list-style-type: none"> -Economic, political, social, technological currents favor problem definition or solution 	<ul style="list-style-type: none"> -Economic, political, social, technological currents do not favor problem definition or solution
Policy Entrepreneur	<ul style="list-style-type: none"> -Persistent, credible, resourceful 	<ul style="list-style-type: none"> -No policy entrepreneur

Foundations for Framing the ODA

At the heart of framing theory is the idea that a situation or event can be interpreted and described in a number of ways. The text of the ODA contains many assumptions about a situation of rare diseases, a lack of treatments for these diseases, and the need for government intervention. These concepts will now be explored as a foundation for developing alternative views, or frames, of the ODA. Alternative frames of ODA reforms that were proposed during 1990-1994 are discussed in Chapter 8.

The ODA as Promoting Equity in Orphan Drug Access

As can be seen in the following excerpt of the law, Congress recognized or assumed that companies did not invest in orphan drug development because such investments would be unlikely to yield profits. Rare disease patient advocates asserted that this created inequities: If companies continued to invest in drugs for common illnesses, this meant that the medical needs of patients with common illnesses would be attended to while the medical needs of patients with rare illnesses would continue to be ignored. In other words, the needs of the many were taking precedence over the needs of the few.

- (1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States;
- (2) adequate drugs for many of such diseases and conditions have not been developed;
- (3) drugs for these diseases and conditions are commonly referred to as "orphan drugs";
- (4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss;
- (5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and
- (6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.

Theories of Efficiency vs. Equity and Markets vs. Government

Arguments for initial passage of the ODA implied that 1) drugs were being developed based on principles of economic efficiency, and, 2) this situation had created inequities because the needs of individuals with common illnesses were being addressed before the needs of individuals with rare health conditions. Later, arguments for reform of the ODA implied that the market exclusivity provision of the ODA, the law's primary "tool" to equitably distribute research and development resources, had created inefficiency in the market. This suggests a tradeoff between efficiency and equity. Potential theories that may help explain the role of markets and government in promoting efficiency and equity, and the potential tradeoffs between the two values, will now be discussed.

Market economists believe that markets—where buyers and sellers complete voluntary transactions and sellers compete for customers on the basis of price and quality—are the most effective way to meet the needs of a population. Market proponents believe that government intervention is warranted only when markets fail to efficiently meet the needs of individuals and society.

Economists assert that markets are efficient when scarce resources are allocated to producing the right type and amount of goods and services for the right price for the right consumers. Under theoretically perfect market conditions, supply and demand of goods and services reach an equilibrium where the cost of producing an extra unit (marginal cost) is equal to the value gained from consuming that unit (marginal benefit), and resources are used optimally. The text of the ODA implies that companies did not allocate resources to orphan drugs because it was not economically efficient to do so.

Markets fail to allocate resources efficiently and equitably when market power is too concentrated, i.e., when either a monopoly or monopsony is in effect. When markets are

monopolized, a firm is better able to charge a price that exceeds its cost by more than a normal profit. Inefficiency is created when the marginal benefit to the consumer does not match the marginal cost, and when the firm restricts output to maintain prices. When government acts in the public's interests, actions are taken to reduce monopoly power by preventing price collusion, reducing barriers to market entrance, and improving consumer information. In the case of the ODA, however, government acted in the interests of rare disease patients by increasing monopoly power.

Market economists also accept the need for government intervention when consumption and production create externalities for the greater community, and when the good produced is a public good. Additionally, most economists acknowledge that the market model is an ideal because government is needed to provide fundamental enablers of commerce, such as a stable currency and enforcement of property rights. These concepts are also important in better understanding principles of the ODA.

Markets can become inefficient when there are externalities. Externalities are created when the market transaction has “spillover” effects to parties that were not part of the transaction. The classic example of a negative externality is when a manufacturer is located on a river and, in the course of producing a product, dumps chemical pollutants into the river. Because no individual or entity owns the river water, normal market forces will not work to stop the polluting. Though the producer and consumer may benefit from the production of the good, the community as a whole suffers the consequences (pollution) of producing that good. Government's role in this case is to levy a fine or tax so that those who enjoy the benefits of producing and consuming a product pay all of the costs of its production. Governments can also use laws, regulations and jail sentences to deter pollution, as well as developing clearer ownership rights for the resources that are being polluted.

Externalities can also be positive. If producing a product has positive spillover effects for society or the community at large, then governments may consider subsidizing or otherwise encouraging its consumption, production, or both, so the value of the external benefits are included in the market price and output level of these products. Public education, for example, is subsidized because it is regarded as having substantial external benefits. Rare disease patient advocates extol the virtues of the ODA's positive externalities when they emphasize that investment in rare disease R and D tend to simultaneously result in developments for common illnesses. For example, Alpha-1 antitrypsin deficiency is a genetic lung disease that produces a form of emphysema that develops 10 to 30 years earlier than the more prevalent form found in smokers. Because it affects young people, it can be studied separately from all the complicating factors of the aging process. (Maeder 2003)

Public goods are different from products such as oranges or computers because people do not pay for each unit they use. Instead, public goods, such as national defense, are purchased collectively for the entire nation. National defense is a public good because no private business could sell defense services to those who want them. In fact, national defense services are provided even if individuals do not use them or want them. Everyone pays for national defense whether they want it or not. A uniform mandate for payment of a public good avoids what economists call "the free rider problem" where some may want the benefits of a public good without having to pay for it. The US has a long history of allocating government funds for fundamental R and D. For example, basic research on biomedical diseases has been conducted at the National Institutes of Health for the better part of the last century. The public good benefits of the ODA have been advocated as a justification for the law.

Governments play a critical role in creating and enabling commerce by assuring the conditions within which people and organizations can use, buy and sell goods and services. For

example, providing a stable currency obviates the need for cumbersome and inefficient systems of barter, and establishing a set of property and contract laws, via legislation or judicial precedent, establishes the complex set of do's and don'ts, and liabilities and privileges, that are needed as a foundation in our modern society. As further discussed below, patents enable inventors to exclude others from using their intellectual property and “appropriate” returns on their investments. Patents enable knowledge sharing, so patents also promote positive externalities. Knowledge is also considered a public good because it is not exhausted when it is used. The ability to use knowledge beyond specific inventions and applications is the foundation for the US patent system.

The Advanced Technology Program (2005) asserts that investments in research and development produce benefits to society as a whole that are greater than the benefits that can be captured by the person or organization financing the work. Patent laws strongly influence the pace of technological progress and the structure of industry because they establish ownership of knowledge and ideas and enable patent owners to convert that into salable property. Patents permit the creator of an idea to exclude others from making, using, selling, offering to sell, or importing into the United States the patented invention—generally for a period of 20 years from the date of filing. In exchange for the patent, the patent holder places the information associated with the invention within the public domain. Hence, the patent system has dual policy goals—providing incentives to the inventor to invent and disseminating technical information to spur further invention. The intent of this information sharing is to stimulate further creativity in meeting similar and expanded demands in the marketplace.

In the early 1980's, many biotech drugs were not patentable because they consisted of proteins and peptides that were copied from those found naturally in the body. As a proxy for a

patent, the ODA's market exclusivity provision gave biotech companies property protection for their drugs, enabling them to appropriate the benefits of their investments.

The usefulness of patents in protecting the inventor's investment varies by industry. Some industries gain competitive advantage by using non-patent tactics, such as superior customer relations and being first to market with products that better meet customer needs. Patents, however, are seen as critical to the pharmaceutical industry. The cost to bring a novel pharmaceutical product to market has been estimated to exceed one billion dollars. Patents and other exclusivity provisions better enable the inventor to recoup this expense.

Congress has supported patent and market exclusivity protections for pharmaceutical and biological therapies on numerous occasions in the past two decades. The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417), commonly known as the Hatch-Waxman Act, made it easier for generic copies of brand name drugs to gain FDA approval and enter the marketplace after the brand's patent expires. But, at the same time, the Act introduced several significant changes to patent laws in order to preserve investors' interests in drug R&D. These include methods for extending the term of a drug patent up to five years to reflect property rights lost during the long FDA review process. The Act also uses marketing exclusivity provisions to protect drugs from competition if, for example, the drugs are new chemical entities or are being clinically studied in new ways. Moreover, several bills were recently introduced in Congress to provide additional patent protection or FDA-administered marketing exclusivities as a tool to encourage development of bioterrorism countermeasures.

Federal government actions relating to property protection, positive externalities, and public goods are generally recognized as important in promoting innovation. In this light, the ODA can be viewed as an expression of the federal government's commitment to promoting innovation.

In addition to using patents and market exclusivity provisions to protect private interests in innovations, the government supports R&D directly through grants, tax credits and other financial incentives. As described by the Advanced Technology Program of the federal National Institute of Standards and Technology (2004), externalities or “spillovers” from R and D investments are the primary justification for government support. For example, when a firm generates new knowledge to produces an innovative product or process, not all of the economic benefits of that knowledge accrue to the firm. Other firms can reverse engineer the innovator’s products, and benefit from knowledge shared via the firm’s patent disclosures, publications and employees (that migrate to other firms). Suppliers and other collaborators that work with the firm may also benefit from knowledge sharing.

The Public Interest vs. Self-Interest View of the ODA

In theory, the US government is “of the people and for the people” and is designed to respond to the demands of citizens. Hence, promoting sound health policy is the responsibility of all citizens. However, some political scientists (e.g., Wilson 2003 and Feldstein 2001) contend that the benefits of promoting policy change should equal or exceed the costs (in time, effort, political capital, or money) of doing so. Hence, groups with concentrated interests that expect concentrated benefits are more likely to lobby for policy change than individuals that would have to expend considerable effort to promote change.

The specific benefits of the ODA to patients with rare diseases are obvious and have been previously described. But more generally, the ODA encouraged a reallocation of resources toward rare diseases, enabling more equitable allocation of R&D funds. This was a fundamental change, as it implied that the health needs of the many should not take precedence over the health needs of the few. In this light, the ODA symbolizes the tangible results that a disenfranchised, minority group can achieve if they organize and advocate their cause effectively.

Congressional hearings are a forum for collective expression and protest, and legislation is a means to exert power.

Feldstein (2001) contends that political markets are no different than economic markets, where individuals and groups act to further their own self-interests. Like a market exchange, legislators supply legislation and interest groups demand legislative benefits in exchange for providing political support. According to this theory, legislators act in their own self interests to get reelected and carefully weigh the political benefits (i.e., campaign contributions, votes and volunteer time) vs. the political costs of not supporting legislation.

Government actions can also improve the economic conditions of individuals, firms, industries, states or countries. The passage of the ODA increased the value of firms that had vested interests in orphan drug research, production and marketing. Increased value of a firm can translate into 1) increased wealth for an individual, e.g., when an individual owns stock in an orphan drug producing firm; 2) increased wealth of an industry, i.e., when similar firms collectively increase in value; 3) increased wealth of a region, i.e., when wealth of the firm's employees (and their families) translates to an increase in the overall economic activity, or "base," of a geographical area; and, 4) increased wealth of a nation, e.g., when a nation has concentrated expertise that is valued by other nations, exports improve its economic position relative to other countries.

The ODA enhanced the value of firms that developed and marketed orphan drugs in a number of ways. First, the law provided tax credits, grants and FDA assistance. These provisions reduced the size of the required research and development investment. Second, the law provided market exclusivity. By reducing or eliminating alternative sources of orphan drugs, firms are better able to charge higher prices. Higher prices translate into increased revenue and profit per unit sold. Market exclusivity could also translate into reduced marketing and product

production costs. Without competing advertising, sales personnel, etc., firms would not have to spend as much on marketing and sales to get the attention and interest of prescribers, patients and other stakeholders. Moreover, market exclusivity means, by definition, the firm is supplying 100% of the market. Based on the theory of experience curves, operating costs should decline when production increases. Hence, serving 100% of the market should be more profitable than serving less than 100%.

Because drug companies focused on developing drugs for common illnesses, individuals with less common conditions did not get an equal or fair chance at accessing new, more effective therapies. Reportedly, rare disease patient advocates demanded legislation to equalize their rights and enable them to access drug treatments just as patients with more common illnesses were able to do.

Chapter 4—Research Design and Methodology

Utilizing the historical case of ODA developments and debates, along with extant theory and research, this dissertation research explored two general questions: 1) what factors seem to promote or impede policy development; and, 2) how does issue framing support policy development? This qualitative inquiry utilized mixed methods, including literature reviews, informant interviews, and a content analysis of Congressional transcripts. The research was divided into four aims.

After describing the researcher's perspective and background, an overview of the four aims of this study will be presented in this chapter. Next, methodological details of each of the aims will be described.

Researcher Perspective and Background

Because portions of this dissertation research required interpretation and judgment, it is important to be explicit about this researcher's background and potential biases. Awareness of potential biases can inform and guide different stages of the dissertation research—from research design, to analysis and reporting.

Lynn Redington has worked in various aspects of the pharmaceutical and biotechnology industries for many years. She has also worked for a managed care organization. Though Redington has master's degrees in both business administration and public health, and tends to look at complex health issues through market and social justice frames, her business and market perspectives sometimes dominate.

Redington has never directly worked on the ODA legislation, but she has worked to prepare orphan drugs for market launch. While Redington may be most adept at adopting an industry perspective of the ODA, applications of the proposed research will not be limited to industry. Redington is equally interested in addressing the perspectives of other ODA stakeholders, e.g., patients with rare health conditions, legislators and payers.

Research Design by Aim

To recap, this dissertation study had four aims: 1) to provide a history and overview of the ODA for context setting; 2) to describe how issues were framed in ODA amendment hearings; 3) to identify factors contributing to ODA amendment failures from 1990-1994; and, 4) to analyze how issues were framed and provide framing strategy guidance for ODA stakeholders. Briefly, Aim 1 entailed identifying a set of published information and extracting and synthesizing specific information and themes. Aim 2 entailed extracting and synthesizing original, unpublished text from government documents. Aim 3 utilized mixed methods and several data types, including document reviews, informant interviews and theory-mediated analyses. Aim 4 utilized selected data from Aims 1-3 and used framing theory and policy development theory to analyze and devise strategies. How data were sourced, collected and analyzed is summarized in Table 3. This is further described in Appendix C. Details on the research design for each aim will now be discussed.

Aim 1: History and Overview of the ODA

The first aim was to describe the context and history of the ODA and to provide an overview of its successes and challenges. Completing this aim depended on collecting secondary data found in published articles, archived records and websites. The information that was sought is outlined in Appendix C. Generally, documents were identified via use of

computer search engines using the key words, “orphan drug.” To cover the period leading up to the ODA’s enactment to the present, searches were restricted to documents produced between 1980 and 2008. Documents were reviewed. Desired information was highlighted on the documents, and then described in the form of a historical analysis. Themes emerged with repeated readings of the documents. For further description of inclusion criteria and sourcing of these documents, see Appendix C.

Table 3--Data Collection and Analysis by Aim

	<i>Aim 1: ODA History & Overview</i>	<i>Aim 2: Issue Frames 1990-1994</i>	<i>Aim 3: ODA Reform Factors</i>	<i>Aim 4: Issue Frame Analysis & Strategy</i>
<i>Data Sources</i>	Published articles, archival records, websites	Congressional testimony re: ODA amendments	Informant interviews + preliminary data from Aim 1 and Aim 2	Findings from Aims 1 through 3
<i>Data type</i>	Secondary: documents	Secondary: documents	Primary: one-on-one phone interviews	Mixed: reduced and interpreted data from Aims 1-3
<i>Data Sampling</i>	Using key words “orphan drug;” search article databases: PubMed & Factiva; government records: Thomson databases, physical scan at government library; Google search of gray literature	All records were used; no sampling	Purposive sampling; included interviewees that represented different stakeholder groups: Industry, Government, Patients, Payers, Policy Advisors	Based on relevance to Aim 4
<i>Data collection instrument</i>	Outline	MS Excel spreadsheet, Iterative memos	Interview guide	n/a
<i>Data analysis</i>	Qualitative, descriptive	Qualitative, descriptive and interpretive	Qualitative, descriptive	Qualitative, theory-mediated analysis, interpretive

Aim 2: Issue Framing in ODA Reform Debates during 1990-1994

The second aim was to describe how issues were framed in ODA reform debates that occurred at four Congressional hearings during 1990-1994. Transcripts from four hearings were obtained from a government documents library. All testimony was included in the sample. The information that was sought from testimonies is outlined in Appendix C. Microsoft Excel was used to collect and descriptively analyze the data.

Aim 2 was conducted in two steps. In Step 1, the Congressional testimony was coded using the data collection and classification scheme described in Appendix C. The testimony from each individual constituted the unit of analysis.

In Step 2, issue frames were constructed from Step 1 data using a process called memoing. “A memo is the theorizing write up of ideas about codes and their relationships as they strike the analyst while coding . . . it can be a sentence, a paragraph or a few pages . . . it exhausts the analyst’s momentary ideation based on data with perhaps a little conceptual elaboration. . .” (Miles and Huberman 1994, p. 72, quoting Glaser 1978). More information on the memoing process can be found in Appendix C.

Aim 3: Factors Affecting ODA Reform from 1990-1994

The third aim was to identify factors that may have impeded or promoted ODA reform attempts from 1990-1994. Primary and secondary data were collected and analyzed to complete this aim. Secondary data included articles from the business, consumer, and medical press, as well as gray literature documents. The Congressional testimony from the 1990-1994 hearings also provided data and insights. Primary data were derived from ten informant interviews. The informant interview guide can be found in Appendix C.

Aim 3 was semi-structured based on the Multiple Streams model (Kingdon 1995) of policy development. This meant that the following elements and factors in the development and failure of the ODA amendments were explored: 1) Problem definition, i.e., how the problem defined, and whether stakeholders agreed that a problem existed; 2) policy solution; 3) politics; 4) the broader climate (political, social, economic climate), and, 5) individuals that were influential in the process. (Kingdon refers to these individuals as *policy entrepreneurs*, but this term was not used in the informant interviews, nor was it used in the reviewed documents.) Hypotheses about what might impede or favor passage of legislation were developed in the proposal phase of this research (see Table 2). Having these hypotheses in mind *a priori* served as a reminder of what to look for in the reviewed documents, as well as what to probe for in the informant interviews.

Selected articles and reports that informed Aim 3 were also used to inform Aim 1. These were described previously in this chapter. A description of the Congressional testimony informed Aim 3 and Aim 2, and have already been described in this chapter. The informant interviews and the process of gaining Institutional Review Approval to conduct these interviews will now be described. A description of the sample, as well as the recruitment and interviewing process, will follow.

In June 2008, an application was submitted to University of North Carolina's Office of Human Research Ethics Institutional Review Board (IRB) for "Determination Whether Research or Similar Activities Require IRB Approval." After one resubmission, the application was approved in July 2008. It was determined that IRB approval was not

required because the submitted list of potential informants were considered “elected officials.”⁹

In late October 2008, 16 potential informants were sent an email or mailed letter that contained a request for a 20-30 minute phone interview. For a copy of the correspondence, see Appendix D.

Ten (63%) informants agreed to an interview, and the interviews were completed by phone in the month of November 2008. One potential informant responded to the interview request, but declined the interview. The remaining 5 simply did not respond to the interview request. Informants were told that their responses would remain anonymous and confidential. Hence, the sample will be described in general terms.

The purposive sample of 10 informants was drawn from an initial target list of 16 potential informants. Purposive sampling is useful for gathering opinions from specific predefined groups. Hence, the target list included individuals from four different ODA stakeholder groups: 1) federal government, 2) industry, 3) patients, and 4) payers. The list also included three health policy experts that advised multiple stakeholder groups. The process of creating the initial target list of 16 included identifying individuals that met most of the following criteria: 1) individuals that were leaders of relevant organizations or initiatives, e.g. leaders of the stakeholder groups listed in Appendix F, members of congress that chaired the hearings and sponsored the proposed ODA reforms in the 1990s, or presidents of the companies that were involved in the debate of the 1990s reforms; 2) individuals that spoke at the 1990-1994 hearings; and, 3) individuals that have advised key stakeholder groups on the proposed ODA reforms as a consultant or researcher. Targeted informants also had to be locatable, which generally meant that they were not deceased or

⁹ The targeted informant list was not limited to officials elected to government service. The preliminary list that was sent to the IRB included leaders of companies, and patient- and industry-advocacy organizations.

retired. The target list of 16 informants was reviewed and approved by the dissertation committee chair before anyone was contacted.

One to two informants from each of the four stakeholder groups were interviewed. All of the three targeted health policy experts were interviewed. Characteristics of the informants included: three of the ten informants had testified at one or more ODA hearings. Three had published articles on the ODA. At least two had participated in drafting the ODA legislation. Of note, most informants had worked in multiple capacities throughout their careers, e.g., some informants started in the federal government (e.g., Food and Drug Administration and the Office of Management and Budget) but later worked in industry, or as health policy advisors.

That interviewees may not remember events of 14 to 18 years ago was anticipated by this researcher. Before each scheduled interview this researcher reviewed publications, quotes and Congressional testimony by, and about, the individual interviewee. This background preparation enabled the researcher to jog the interviewee's memory when necessary, and focus the interview around the given "facts" of the situation. While 14-18 years ago remained difficult for informants to remember, about a third of informants seemed to readily recall details of the players and events surrounding the 1990-1994 ODA amendments. Others qualified their answers with caveats such as, "that was a long time ago, but I think . . ."

Generally, informants repeated facts, statements, and themes that were already available in several articles that reviewed the 1990-1994 amendments. Hence, results from the interviews seem to validate the published reports and vice versa. Note that findings from the informant interviews are combined with that of the document reviews and discussed in Chapters 5 and 6

Aim 4: Frame Analysis and Framing Strategy Guidance

The fourth aim was to analyze the frames derived from Aim 2 and to provide framing strategy guidance. Findings from Aims 1 through 3 were used to complete this aim. Data relevant to this aim were selected and interpretively analyzed. Analysis and strategy were guided by theories and research pertaining to frame reflection (Schon and Rein 1994), political language (Stone 2002), frame potency (Pan 2003, Van Gorp 2007, Benford et al. 2000, Lakoff 2004), and frame breaking and creativity (Fredin 2003).

Chapter 5—History of the ODA

The Development and Enactment of the ODA

Based on the reviewed literature and informant interviews, rare disease patient advocates were the lead champions of the 1983 ODA legislation. Patient advocates were apparently proactive and purposeful in defining problems, crafting solutions, finding legislators that would champion those solutions, and creating a climate that favored ODA passage. It is not clear whether the media were initially encouraged to publicize the need for drugs for rare diseases, or whether they decided on their own to focus on the issue. In the year or two prior to the ODA's enactment, it does seem clear from the literature and interviews that patient advocates were actively involved in enlisting the support of key opinion leaders and engineering an effective media campaign.

As mentioned in Chapter 1, Kingdon (1995) developed the Multiple Streams Model from his study of the development of 23 different federal policies. The process of creating and enacting the ODA appears to differ from the cases that Kingdon studied. Unlike Kingdon's cases, the ODA's underlying problem and solution streams seemed highly coupled and interdependent, and policy entrepreneurs (patient advocates and select legislators) seemed very influential in creating a climate that favored change. Also, the media were very important in galvanizing support for the ODA, whereas the media were important in only 4 out of the 23 cases that Kingdon studied.

Events Leading to the Law's Enactment

The problem, that drugs for rare diseases and conditions were needed and lacking, captured the attention of legislators starting in the late 1970s. First, former New York Representative Elizabeth Holtzman responded to this problem by drafting legislation that created a pool of money that could be used to develop orphan drugs. The bill was not well received, especially by industry, because it proposed that profits from any drug developed with these monies be returned to the government. Despite opposition, the bill was re-introduced by former New York Representative Ted Weiss. It went no further. Prospects for an orphan drug bill seemed bleak until the issue gained public visibility and support after it was widely publicized in the consumer media.

In early 1980, Adam Seligman, an American victim of Tourette syndrome, was obtaining drugs from Canada to treat his condition. The drugs were seized at the border and Adam's treatments were stopped. In response, Adam's mother sought the help of Representative Henry Waxman of California. Waxman was interested in the Seligman's plight. As Chairman of the House Energy and Commerce Committee's Subcommittee on Health and the Environment, Rep. Waxman held a preliminary hearing in mid-1980 to learn more about the problems that rare disease patients faced in seeking treatment. Adam testified at the hearing.

The hearing was sparsely attended, but one article that followed the hearing generated substantial interest in the issue. A Los Angeles Times reporter attended the hearing and wrote an article about the dearth of treatments for rare diseases, the lack of industry interest in developing these treatments, and how patients were suffering as a consequence. The article captured the interest of Jack Klugman, the lead actor of a popular TV series called *Quincy M.E.* (medical examiner). Klugman offered to help the cause by raising awareness of the issue in a special show. In March 1981, the show, *Give Me Your Weak*, aired on TV.

Thousands of viewers of the television show sent letters to Klugman voicing their support and asking how they could help. With a window of public support, Representative Waxman held a second hearing. This time Klugman testified. The hearing was attended by a variety of media and the story of the plight of rare disease patients was widely publicized.

Representative Waxman redesigned the orphan drug bill and introduced it to the House in 1981. Former Senator Nancy Kasselbaum introduced a similar bill in the Senate. The bill passed the House but then stalled in the Senate. In response, Klugman produced another television show on the issue. But this time he emphasized the holdup in Congress and included 500 “extras” that were patients with rare diseases and conditions. The bill passed the Senate after the show aired.

The bill had a final hurdle to overcome. Rare disease patient advocates had heard that President Reagan planned on vetoing the bill. To apply pressure just before Christmas 1982, they purchased full-page advertisements in Washington D.C. newspapers. The ads urged Reagan to sign the bill and suggested that Reagan could become the “Grinch that stole Christmas” for victims of rare diseases. Klugman also offered support should a veto occur. Reportedly, Reagan responded to the public pressure and signed the bill in January 1983.

Stakeholder Interests and Roles

A number of interest groups had a stake in the ODA, including rare disease patient advocacy organizations, legislators, FDA, and the pharmaceutical and biotechnology industry. (See Appendix F for further details)

According to multiple sources, the lead proponents of the ODA were associated with patient advocacy groups and Congress. FDA and industry also participated in drafting the ODA. The media raised awareness and public interest regarding the need for rare disease treatments. Members of Congress and President Reagan were final decision makers of the ODA’s fate.

Patient Advocates

While the Seligmans were noted as early patient advocates, Abbey Meyers, a mother of 3 children with Tourette syndrome, soon emerged as the face of rare disease patients in the orphan drug cause. Initially, Meyers became involved as a volunteer with the Tourette Syndrome Association. Later, she founded and led the National Organization for Rare Disorders (NORD), a federation of voluntary health organizations focused on rare diseases.

Voluntary, non-profit organizations that advocate for specific patient interests have a long history in the US. Many of these organizations have a disease focus, and often these organizations are founded by someone that has been personally affected by the disease. For example, the March of Dimes was founded in 1938 by President Franklin Delano Roosevelt to “fight” polio, a disease that he personally contracted.

There are many disease-focused organizations that advocate for the needs of patients with specific rare illnesses. As a federation of over a hundred sub-organizations, NORD provided a unified voice in urging the passage of the ODA to develop treatments for multiple rare diseases. In advocating for treatments for rare diseases, NORD uses collective terms to emphasize the magnitude of the problem, i.e., instead of referring to the prevalence or incidence of selected rare illnesses, NORD emphasizes that there are 5000-7000 rare illnesses and that, collectively, these affect 1 in 10 Americans. This seems consistent with the political strategy to present a policy solution as having diffuse rather than concentrated benefits.

Government Officials

Legislators that have been persistent and credible in the orphan drug cause include Henry Waxman, a House of Representatives Democrat representing California’s 30th congressional district since 1975. In addition to the ODA, Waxman has drafted many legislative proposals that have focused on improving cost, quality and access to health services. From

1979-1995, Waxman used his position as chair of the Subcommittee on Health and the Environment, which is part of the Energy and Commerce Committee, to investigate a number of high-profile health and environmental issues. Waxman has co-authored a number of health-related bills with Senators Ted Kennedy and Orrin Hatch, who are also highly visible in the health legislative arena.

President Ronald Reagan was in office when the ODA was on the policy agenda. His initial resistance to signing the ODA seemed consistent with his presidential campaign promises. For example, one of the tenets of Reagan's campaign was to reduce the size of the federal government, whereas the ODA represented increased government involvement. Nevertheless, a veto carried the risk of negative publicity.

Since the FDA would become responsible for administering the ODA, the FDA has also had an influence on the design and approval of the law.

Industry Advocates

According to patient advocates and newspaper articles, the Pharmaceutical Research and Manufacturers of America¹⁰ (PhRMA) originally opposed passage of the ODA. But this assertion has been contested by PhRMA. PhRMA apparently opposed parts of the initial ODA drafts, such as an early proposal to give rare disease treatments priority FDA review. Industry advocates did not want new drug applications for rare disease treatments to leapfrog over drug applications for common illnesses because this would extend the elapsed time from submission of the NDA to FDA approval. Waiting for FDA approval can be expensive. If a drug can potentially generate \$300 million in sales, each day of waiting for approval can represent nearly a million dollars of lost revenue to the drug's sponsor.

¹⁰ The organization was originally called the Pharmaceutical Manufacturers of America (PMA). Since the 1990s amendment hearings, the organization changed its name to the Pharmaceutical Research and Manufacturers of America (PhRMA).

Window of Opportunity and Coupling of Streams

Paraphrasing Kingdon (1995), the ODA's development and passage could be described as follows: A window of opportunity opened up in the problem stream as a result of the media attention and public support for the issue (i.e., the plight of rare disease patients, and the lack of treatments and industry interest). A policy solution had been in the works for a couple of years, which meant that a solution had been crafted, socialized and refined. Hence, not only was a solution ready to be matched to the problem, but legislators had been exposed to the issue for some time and, as a result, had some time to "soften up" to the idea.

The overall macro-environment in late 1982 and early 1983 did not seem to contain any major forces that might derail passage of the ODA. It is interesting to note, however, that many of the political, economic, social and technological trends and forces of the time certainly were not consonant with the tenets of the ODA. But, as Kingdon (1995) points out, issues of healthcare cost, quality and access are "hardy perennials" on political agendas.

On the economic front, the nation had just emerged from a severe recession. Though Reagan promised American voters that he would shrink government, he had actually increased government expenditures and the nation's deficit increased markedly. The deficit notwithstanding, Reagan was applauded for his handling of the difficult economy of 1981-1982, which included recession, inflation, and job losses. If anything, Reagan's association with pulling America out of the recession could have been used as political capital to push back on the ODA. On the other hand, the ODA was a "feel good" proposal that could enhance Reagan's public image as being caring and attentive to the needs of Americans in a difficult situation.

In the months preceding ODA enactment, America was still in a "Cold War" with the (former) Soviet Union. That time was marked by increased military expenditures and Reagan's "Evil Empire" speech. The Cold War was a continuing saga, rather than a new chapter in

American history. Hence, it was unlikely to effect legislation such as the ODA. Moreover, orphan drug legislation's importance probably paled by comparison with America's political preoccupation with the USSR.

In terms of social forces or trends specific to the early 1980s, nothing in particular seems to stand out as favoring or detracting from ODA passage. The plight of Adam Seligman and other rare disease patients resonated with the public, but the public seems perennially interested in and sympathetic to individual hardships. According to one informant interview, Reagan also had a "soft spot" for individual hardship. Reportedly, Reagan created the Medicaid waiver process in response to the plight of Katie Beckett and her parents. At the time, Medicaid paid for Beckett's hospital care but would not pay for care at home. In 1982, Reagan signed the "Katie Beckett Waiver" law, so that states could ask the Health Care Financing Administration (now the Centers for Medicare and Medicaid Services) to waive specific requirements of the Federal Medicaid law. The informant further emphasized that "the bigger the issue, the more that ideology kicks in." In other words, a problem may be more ideology neutral if it is seen as affecting individuals that you can name and visualize.

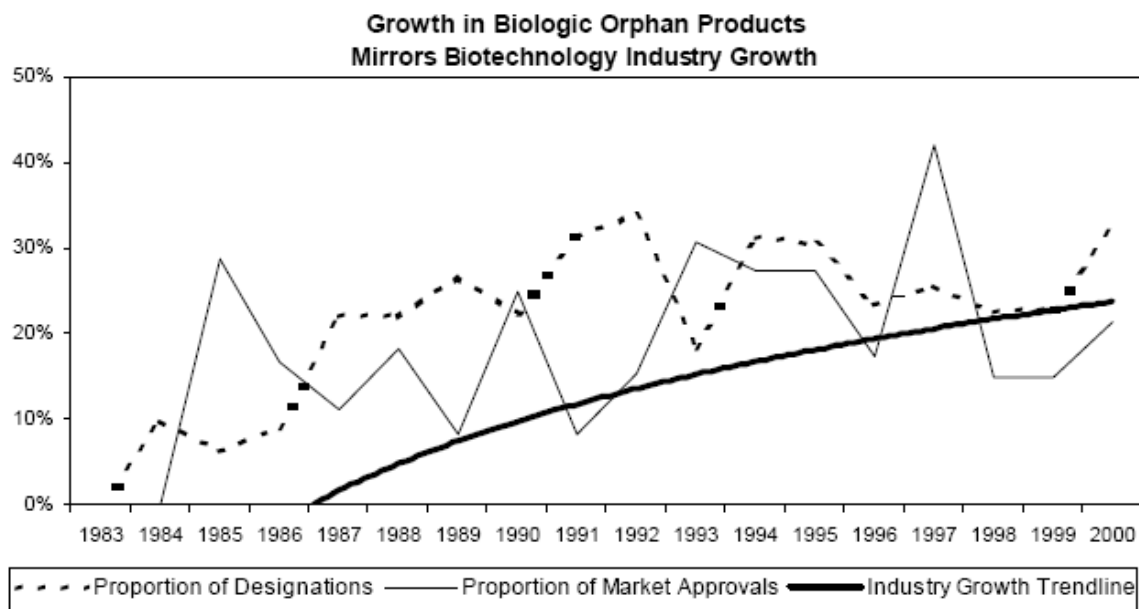
Perhaps the ODA was seen in an ideology neutral light. Certainly, the following aspects of the ODA did not seem consistent with conservative Republican ideologies of the early 1980's. The ODA: 1) provided industry subsidies and government protection (via market exclusivity) in a time when deregulation and small government were emphasized; 2) influenced the choice of which products were developed, manufactured and marketed by private companies in a time when the USSR's command economy principles were criticized; and, 3) attempted to equalize the rights of rare disease patients to have access to medical treatments just as patients with more common illnesses do. This occurred in a time when Reagan opposed some of the tenets of the 1964 Civil Rights act.

Technological factors may have played a role in enactment of the ODA. Patient advocates must have believed that the pharmaceutical technologies and know-how of the time could yield treatments for their rare illnesses. Otherwise, creating government-sanctioned incentives to invest in researching and developing these treatments might be meaningless. It is noteworthy that ODA enactment coincided with the “birth” of the biotechnology industry. The first genetically engineered biological treatment, human insulin, was launched in 1982. There is no evidence to suggest that legislators anticipated that the ODA would support a large portion of these emerging biotechnologies (“biotech”). This is important because biotech drugs are substantially more expensive than drugs made with traditional chemical methods. If projected cost impacts of the legislation were important, then this faulty assumption would favor passage of the ODA because the projected cost to society of such a bill would be presumed to be minimal.

As a side note, growth trends in FDA approvals for biotech drugs and FDA approvals for orphan drugs seem to parallel each other. (See Figure 3) Because ODA enactment coincided with the birth of biotech, it is difficult to parse out the degree to which technology drove the growth in orphan drugs versus the degree to which legislation drove growth. In most reviews of the ODA, authors imply that legislation has been the primary driver of growth in FDA approvals of orphan drugs since 1983. An alternative explanation is that the ODA coincided with the birth of the biotechnology industry and that the ODA may have had an additive effect, but wasn’t the primary cause of orphan drug development. If one were to explore this alternative explanation, the following observations are relevant: 1) half of the drugs launched by the biotech industry have been designated as orphan drugs. 2) As mentioned, the pace of biotech orphan drugs mirrors that of non-orphan drugs from the biotech industry. 3) Eighty percent of rare diseases have a genetic basis (Lavandeira 2002). Biotechnology drugs are well

suited to address conditions with genetic underpinnings, so rare diseases were a natural target of biotech—with or without the ODA.

Figure 3--Growth in Orphan Drugs vs. Biotechnology Industry Growth
 From: Office of Inspector General Report on the ODA's Implementation and Impact, May 2001



In summary, several factors seemed to favor passage of the ODA. In accordance with propositions made in Table 2, many “problem definition” factors were favorable. These included a surge in the problem stream, where the needs of rare disease patients gained visibility in a popular medium of the time (television and newspapers). The story of the plight of patients had some exciting qualities, including the life threatening and debilitating nature of many rare illnesses, the well-developed characterization of the victims (i.e., personalized stories in the news media and “real” people appearing in Klugman’s TV show), and the identification of tangible villains (resistant companies and legislators). According to numerous accounts, no one faulted the victims. Their plight was not of their doing, as in lung cancer caused by smoking. Instead, an act of nature had inflicted these rare conditions upon them (a majority of rare diseases are

congenital). That certain members of Congress and industry became villains in the story probably resonated with the public imagination. Congress- and industry-bashing seems to be an enduring cultural theme.

How rare illnesses were defined as a problem also seemed to favor support for ODA legislation. Rare diseases and conditions are, by definition, rare. But, collectively, these conditions are not rare. There are as many as 7000 recognized rare conditions. Collectively, 25 million Americans are potential victims of a rare illness. To gain widespread support for a public policy, it is important to define a problem so that: 1) individuals can see that they could become the next victim of the problem, and, 2) it is seen as a social problem (although putting a face on the problem makes it simultaneously a private problem). Wisely, defining the magnitude of rare illnesses and conditions in collective terms is a tactic that has been used by many rare disease patient advocates—in pre- and post-ODA enactment times.

The lack of rare disease treatments seemed to be defined as a problem that had broad appeal and that justified government intervention. To gain broad support, patient advocates described their problem as one of a violation of rights. They contended that they had the right to access effective drug treatments just as victims of more common illnesses did. This problem definition would likely resonate with a broad base of individuals that felt marginalized or who supported the rights of minorities that were marginalized.

Pro-ODA advocates also contended that normal market forces had failed to produce needed rare disease drug treatments, so it was the government's responsibility to intervene in order to ensure social justice. This frame justifies Congressional intervention.

Evolution of the ODA during 1983-2008

After the ODA was signed into law in January 1983, new proposals to change the law circulated nearly every year. Proposals that were successful, i.e., resulted in an amendment,

tended to increase the reach and effectiveness of the law. Proposals that were not successful tended to decrease the benefits of the ODA, either by reducing the value of the ODA incentives or by reducing the number of drugs that would qualify for the incentives. Other factors that may have favored or impeded changes in the law will be discussed in the next section.

The first two successful amendments will now be discussed because of their particular relevance to Aim 3 of this research. Other amendments are described in Table 1.

In late 1984, the original definition of “rare disease or condition” was changed by P.L. 98-551 by giving drug sponsors the option of using *either* a prevalence standard *or* a profitability standard to obtain orphan designation for their drug. The law currently states, “the term rare disease or condition means any disease or condition which (a) affects less than 200,000 persons in the U.S. or (b) affects more than 200,000 persons in the U.S. but for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for such disease or condition will be recovered from sales in the U.S. of such drug.” Prior to October 1984, orphan designation was based entirely on the profitability standard. To receive orphan designation based on the profitability standard, potential orphan drugs are means tested and sponsors have to provide financial projections that demonstrate development costs will exceed sales.

Several sources assert that this amendment was proposed and passed because stakeholders were disappointed by the dearth of orphan designation applications in the first year of the ODA’s existence. Reportedly, companies did not want to share financial information, and the FDA was not well equipped to judge the soundness of financial projections provided by companies. The profitability standard remains unpopular. Most orphan designations are based on the prevalence standard.

The August 1985 amendment extended ODA provisions to drugs that were patentable. Previous to P.L. 98-551, only drugs that were not patentable were able to receive the market exclusivity provision of the ODA. This amendment significantly benefited the biotechnology industry, because many biotech drugs were not patentable. The ODA market exclusivity provision became a surrogate for a patent because it effectively allowed inventors of biotech drugs to appropriate the financial benefits of their inventions. As a result of this amendment, biotech entrepreneurs were better able to raise financial capital for orphan drug development because the ODA market exclusivity provision increased the potential commercial value of orphan drugs.

ODA Reform Attempts during 1990-1994

As mentioned previously, the text of the ODA suggests that Congress assumed that orphan drugs are unprofitable without government support. But means testing to determine a drug's financial (or commercial) potential is not currently required as a condition for such support. Hence, low- and high-commercial-potential (LCP and HCP) orphan drugs are eligible for ODA benefits. During 1990-1994, legislators attempted to amend the ODA to limit the conditions of eligibility or revoke certain benefits for HCP orphan drugs. These amendment attempts were not successful.

Overview of the 1990-1994 Congressional Hearings

During 1990 to 1994, four Congressional hearings were held to discuss whether problems with the Orphan Drug Act (ODA) existed, and, if so, whether the ODA should be amended to address these problems. As can be seen in Table 4, the hearings were held in February 1990, July 1990, March 1992, and June 1994.

Two alleged problems were discussed in the February 1990 hearing. The first, and most widely discussed problem, was that the ODA was too inclusive, i.e., that certain orphan drugs would have been developed without ODA incentives, meaning the ODA incentives were not needed to spur orphan drug development. According to presiding Congressman Henry Waxman, market exclusivity for these drugs resulted in “an unnecessary monopoly and higher prices to consumers.” Three orphan drug categories¹¹ were identified as problems to be investigated in the hearing: 1) human growth hormone (hGH), 2) aerosol pentamidine, and, 3) Erythropoietin (EPO). Indications that ODA incentives were not needed included: 1) development of these drugs commenced years prior to the 1983 enactment of the law, hence the prospect of ODA incentives was presumably not a factor in the decision to develop the drugs; 2) sales of the drugs seemed to far exceed the limits of what would constitute a low-commercial-potential drug (LCP); and, 3) multiple companies sought orphan drug designation and FDA approval within each of the above drug categories. This also indicated that these were HCP drugs and that ODA incentives were not necessary to spur development of these drugs.

A second disputed issue discussed in February 1990 was that drugs for AIDS should no longer qualify as orphan drugs because the prevalence of the condition had grown beyond the 200,000 patient cut off. Note that this issue is not the focus of this dissertation research.

In July 1990, Waxman submitted a bill¹² (H.R. 4638) to address these problems. Waxman’s proposal to solve the problem of unnecessary monopolies was to allow “shared exclusivity” under situations where multiple sponsors were pursuing FDA approval of similar orphan drugs. The bill also proposed to revoke orphan drug status if the candidate population

¹¹ The term “orphan drug categories” refers to a class of drugs or biological agents rather than a specific brand in that category.

¹² The ODA bills submitted between 1990 and 1994 were titled “Orphan Drug Amendments,” e.g., H.R. 4638 was titled “Orphan Drug Amendments of 1990.” Hence, ODA bills submitted between 1990 and 1994 are often referred to in this dissertation as ODA amendments. Unless otherwise stated, “amendments of the 1990s,” or “proposed amendments of the 1990s” refers to bills that were submitted to amend the ODA from 1990 to 1994.

for the drug became greater than 200,000. In October 1990, the bill received the unanimous vote of Congress. But in November 1990, President Bush pocket vetoed the bill. For a copy of the President's Memorandum of Disapproval, see Appendix G.

The purpose of the two 1992 hearings was to address the notion that the ODA was, according to Senator Howard Metzenbaum, "being used as a legal loophole to block competitors from a lucrative market for a drug of tremendous commercial value." Similar to the 1990 hearing, the ODA was criticized as being too inclusive. Critics contended that drug categories with HCP did not need the ODA incentives, and that providing incentives for HCP drugs violated the spirit of the law. Moreover, critics believed that selected companies were abusing their market exclusivity position as a way to "block" competition and charge "excessive" prices.

Bills introduced in the 102nd Congress (H.R. 3930, S. 2060) addressed these issues by proposing that an orphan drug's market exclusivity could be withdrawn once the product reached cumulative sales of \$200 million. The bills presumed that a cumulative sales threshold was a defining characteristic of an HCP drug, and that such a drug could stand on its own and compete without the protections of the ODA market exclusivity provision. The bills did not pass.

The purpose of the June 1994 hearing was to hear testimony on H.R. 4160, which aimed to limit the ODA-granted market exclusivity provision to LCP drugs. As written, all drugs that received orphan drug designation would be granted four years of market exclusivity upon FDA approval. In order to extend the market exclusivity another three years, applicants would have to apply for approval from the Secretary of Health and Human Services and demonstrate "that the drug has a limited commercial potential, as determined under regulations of the Secretary, on the basis of total sales revenue for such drug during the 4-year period of exclusivity . . . or factors other than total sales revenue identified by the Secretary." In other words, the bill would

leave it up to the Secretary to define how to differentiate a LCP drug from a HCP drug. The criteria by which an orphan drug would have LCP were not included in the text of the bill. Instead, the bill specified that criteria would be developed and codified in the regulations within the six months following the bill's passage into law.

In all, 38 statements were heard at the four hearings. Thirty-one individuals provided the 38 statements. Five individuals testified at more than one hearing. Most notably, Abbey Meyers, Executive Director of NORD, testified at all of the four hearings. Four others testified at two of the four hearings.¹³ Testimony, statements and supporting documents consumed a total of 881 pages.

Based on statements made by members of Congress and the witnesses present, several differences among the four hearings seemed apparent: 1) whether the hearing focused on a particular bill or not; 2) the amount of Pro vs. Con testimony heard in each of the hearings; and, 3) the proportion of witnesses that represented government, industry or patient interests in each of the hearings.

The first hearing did not mention a specific bill or amendment. The stated purpose of the first hearing was to determine if there was a problem, i.e., whether the ODA might be too inclusive. The second and third hearings had a more specific focus on Senate bill 2060 and its proposition to revoke an orphan drug's market exclusivity once its cumulative sales reached \$200 million. The fourth hearing also had a specific focus on a pending bill, H.R. 4160.

Each of the four hearings also had differing compositions of witnesses and testimony. As seen in Table 5, the majority (7 out of 11) of witnesses at the first hearing were affiliated with the industry sector. The 7 witnesses worked in six firms. Representatives of industry advocacy groups, such as the Association for Biotechnology Companies, did not testify. Four of the 7

¹³ Wiggans testified at the first and fourth hearing; McLaughlin testified at the second and third hearing; and, Dresing and Hodel testified at the second and third hearing.

industry witnesses were in favor of a change to the ODA, while both witnesses from the government sector, i.e. FDA, were against change. One representative of a patient advocacy group was for change, while the other (Abbey Meyers) was against change.

The second hearing had a greater proportion of patient advocates (7 out of 11) and the testimony indicated more favorable views toward changing the ODA (8 witnesses were Pro and 3 were Con). Nearly all (6 out of 7) patient advocates were in favor of changing the ODA. Four of eleven witnesses were from industry, and none of the witnesses represented the government sector.

The third hearing offered a greater witness-perspective balance compared to the other three hearings. There were 1, 5 and 6 representatives of government, industry and patients, respectively. Moreover, 5 witnesses were against changing the ODA while 7 were Pro change.

Only four witnesses testified at the 1994 hearing. One was from the government sector, 2 represented patients and 1 represented industry. Of the four witnesses, 2 were in favor of changing the ODA. One witness was in favor of some aspects of the proposed amendment and another witness didn't voice his opinion either way. The testimony of this latter witness (Brad Margis) seemed off topic. Margis's testimony was about promoting the need for more research to help patients with A-T disorders (ataxia telangiectasia), and not about his position on the proposed ODA amendment.

Table 4--Summary of 1990-1994 ODA Amendment Hearings

<i>Item</i>	<i>Description</i>
Number of hearings from 1990-1994	4
Number of people that testified	38 total witness statements 31 total witnesses
Number of pages of hearing text	881 total
Dates of each hearing	February 7, 1990 January 21, 1992 March 3, 1992 June 16, 1994
Description of Feb. 1990 Hearing	Title: "Orphan Drug Act" House of Representatives Committee on Energy and Commerce, Subcommittee on Health and the Environment, Henry A. Waxman presiding Stated Purpose of Meeting: "When Congress adopted the act, it recognized that there was a possibility the act might be too inclusive, that is, it might give exclusivity to drugs that would have been developed without the incentives of the law. The result is an unnecessary monopoly and higher prices to consumers. The purpose of this hearing is to gather information to determine whether this has happened. We also will hear testimony on whether Congress should reauthorize the grants program for next year. In particular, we will hear testimony about three drugs: Human growth hormone, aerosol pentamidine, and EPO."
Description of Jan 1992 Hearing	Title: "Anticompetitive Abuses of the Orphan Drug Act: Invitation to High Prices, U.S. Senate, Subcommittee on Antitrust, Monopolies and Business Rights, Committee on the Judiciary, Howard Metzenbaum presiding. Stated Purpose of Meeting: "We are here because the orphan drug law, which was passed to encourage one company to develop a rare treatment that will result in only small sales and modest profits, is being used as a legal loophole to block competitors from a lucrative market for a drug of tremendous commercial value."
Description of Mar 1992 Hearing	Title: "Orphan Drug Amendments of 1991" U.S. Senate, Committee on Labor and Human Resources, Sen. Howard Metzenbaum presiding. Stated Purpose of Meeting: "Today the committee will hear testimony on the Orphan Drug Amendments of 1991 . . . amendment addresses issue that "Tragically, the act has also allowed a handful of profiteers to use their seven-year monopoly as a shield to block competition and charge absurdly high prices for blockbuster orphan drugs."
Description of June 1994 Hearing	Title: "Orphan Drug Reauthorization" House of Representatives, Committee on Energy and Commerce, Subcommittee on Health and the Environment, Henry Waxman presiding. Stated Purpose of Meeting: "hear testimony on H.R. 4160. . . we will begin what we hope will be the final chapter in the 7-year controversy over amendments to the Orphan Drug Act. . . . by allowing highly profitable drugs to have the full 7 years of market exclusivity, the law has unwittingly allowed drug manufacturers to charge unreasonably high prices without the constraints of price competition."
Valence of testimony, e.g., Pro = in favor of changing the ODA	Pro: 22 Con: 14 Both: 1 Neither: 1
Affiliation of witness	Government: 4 Industry: 17 Patients: 17

Table 5--Summary Data on Witnesses and Their Testimony

Last Name	First Name	Organization	Other Org Info	Affiliation	Date	Valence
Benson	James	FDA	Acting commissioner	Government	Feb 90	Con
Bernard	Edward	Fisons Partner	Research associate	Industry	Feb 90	Pro
Foulds	Richard	Fisons Corp	Medical affairs VP	Industry	Feb 90	Pro
Haffner	Marlene	FDA	Orphan products	Government	Feb 90	Con
McGuire	Jean	AIDS Action	Exec Director	Patients	Feb 90	Pro
McLaughlin	John	Genentech Inc	General counsel	Industry	Feb 90	Con
Meyers	Abbey	NORD	Exec Director	Patients	Feb 90	Con
Rathman	George	Amgen Inc	Chairman of board	Industry	Feb 90	Con
Schmergel	Gabriel	Genetics Inst.	CEO	Industry	Feb 90	Pro
Tambi	Brian	Lyphomed Inc	SVP	Industry	Feb 90	Con
Wiggans	Thomas	Serono Labs	President	Industry	Feb 90	Pro
Hire	Pam	None	(Personal situation)	Patients	Jan 92	Pro
Smith	Cindy	None	(Personal situation)	Patients	Jan 92	Pro
Nathan	Mary	None	(Personal situation)	Patients	Jan 92	Pro
Hodel	Derek	PWA Group	People w/ AIDS	Patients	Jan 92	Pro
Jacobson	Herb	None	(Personal situation)	Patients	Jan 92	Pro
Dresing	Robert	Cystic Fibrosis	President, CEO	Patients	Jan 92	Con
Meyers	Abbey	NORD	Exec Director	Patients	Jan 92	Pro
McLaughlin	John	Genentech Inc	General counsel	Industry	Jan 92	Con
Termeer	Henri	Genzyme	Chair, CEO	Industry	Jan 92	Con
Castello	John	Ares-Serono	American headquarters	Industry	Jan 92	Pro
Simpson	Bruce	Fisons Corp	Exec Vice President	Industry	Jan 92	Pro
Kessler	David	FDA	Commissioner	Government	Mar 92	Con
Gasparini	Dixie	None	(Personal situation)	Patients	Mar 92	Pro
Meyers	Abbey	NORD	Exec Director	Patients	Mar 92	Pro
Hayes	Catherine	HD Society of America	President, Huntington's disease	Patients	Mar 92	Pro
Hodel	Derek	PWA Group	People w/ AIDS	Patients	Mar 92	Pro
Dresing	Robert	Cystic Fibrosis Foundation	President, CEO	Patients	Mar 92	Con
Stinson	Phil	None	(Personal situation)	Patients	Mar 92	Con
Penner	Harry	Novo Niordisk	President	Industry	Mar 92	Pro
Anthony	Forest	ABC	President	Industry	Mar 92	Pro
Sayare	Mitchel	ABC	CEO, Director	Industry	Mar 92	Pro
Duzan	Steve	IBA	Chair IBA, Chair/CEO	Industry	Mar 92	Con
Mossinghoff	Gerald	PMA	Immunex Chair PMA	Industry	Mar 92	Con
Corr	William	Dept of HHS	Pub Health Service	Government	Jun 94	Both
Meyers	Abbey	NORD	Exec Director	Patients	Jun 94	Pro
Wiggans	Thomas	BIO	President	Industry	Jun 94	Pro
Margis	Brad	A-T Children's Project	President	Patients	Jun 94	Neither

Table 6--Comparing and Contrasting the Four Congressional Hearings

<i>Date of Hearing</i>	<i>Feb 1990</i>	<i>Jan 1992</i>	<i>Mar 1992</i>	<i>June 1994</i>
<i>Valence of Testimony</i>	6 Con 5 Pro	3 Con 8 Pro	5 Con 7 Pro	0 Con 2 Pro 1 Both 1 Neither
<i>Composition of Witnesses</i>	2 Government 7 Industry 2 Patients	0 Government 4 Industry 7 Patients	1 Government 5 Industry 6 Patients	1 Government 1 Industry 2 Patients

Cross tabulation of Table 6 data:

	<i>Stakeholder Group</i>		
	Government	Industry	Patients
<i>Valence by Date:</i>			
<i>Feb 1990: Pro</i>	0	4	1
<i>Con</i>	2	3	1
<i>Jan 1992: Pro</i>	0	2	6
<i>Con</i>	0	2	1
<i>Mar 1992: Pro</i>	0	3	4
<i>Con</i>	1	2	2
<i>June 1994: Pro</i>	0	1	1
<i>Con</i>	0	0	0
<i>Both</i>	1	0	0
<i>Neither</i>	0	0	1

Chapter 6—Factors Affecting ODA Reform from 1990-1994

This chapter will focus on the ODA amendments that were proposed during 1990-1994 and factors that may have promoted or impeded their passage.

As mentioned previously, in July 1990, Representative Henry Waxman submitted a bill (H.R. 4638) that would amend the ODA, address the problem of “unnecessary monopolies” and allow “shared exclusivity” in situations where multiple sponsors were developing similar orphan drugs. The bill also proposed to revoke market exclusivity if the candidate population for the drug became greater than 200,000. This addressed a sub-issue that the AIDS population had grown beyond 200,000 and that AIDS drugs should no longer receive orphan designation. In October 1990, the bill received the unanimous vote of Congress. But in November 1990, President George H. W. Bush pocket vetoed the bill.

Waxman convened a hearing in 1990 to determine if the ODA was too inclusive, and if so, what should be done about it. Spokesmen from three companies testified that they wanted a change in the ODA to enable them to gain FDA approval to market their rare disease treatments. Competitors had been granted ODA market exclusivity, and the companies argued that the ODA should not apply to the drug markets that they were targeting because these were lucrative markets that did not need government incentives and government-granted monopolies. Moreover, some of these companies had been doing the studies necessary for FDA approval before the ODA was enacted. Enactment of the ODA had changed “the rules in the middle of the game.” As a result, several companies claimed that their drug development investments would now be wasted and their expected returns, in the form of product revenue, would now

vanish because they were blocked from the market. Arguments were made that the ODA was intended to support development of drugs with low commercial potential and that the ODA was never intended to support lucrative drug markets. Moreover, critics argued that market exclusivity was resulting in higher prices to patients and payers, and this situation was not warranted in highly lucrative drug markets, and several companies were ready to compete to bring prices down.

Based on informant interviews and published accounts of the February 1990 hearing and H.R. 4638 (ODA Amendments of 1990), factors that may have impeded or favored passage of the proposed 1990 amendment are listed in Table 7. Factors that seem to favor the amendment included: 1) pro-reform industry spokesmen created a bridge to show how the problem that faced their companies was also a public or social problem, i.e., the monopoly blocked them from competing, which then caused the public to pay higher orphan drug prices; 2) the problem of being blocked from competing affected a powerful minority (companies that had considerable resources to rally for reform); and, 3) companies negatively affected by this situation were acutely aware of it and its consequences.

Informants and published sources asserted that the 1990 amendment did not gain the support of President Bush because the policy solution was not workable. Reasons for this included: 1) the policy violated the takings clause of the constitution, i.e., the proposed change in the law took away a property right (market exclusivity) without compensation; and, 2) the change in the law would be difficult to administer. The amendment “creates additional exceptions from the protection of exclusive approval, certification, or license for drugs for rare diseases for . . . drugs which were developed simultaneously.” FDA was responsible for determining how this would be carried out, and questioned how this could be done. 3) Shared exclusivity appeared to be a contradiction in terms, an oxymoron; and, 4) that the amendment carried the risk of making

the ODA less effective because it “diluted the benefits of the law.” Anti-reformers most often used the fourth point in their 1990 Congressional testimony. The fourth point relates to the ODA Reform as Economics and Access Frame, which is described in Chapter 7.

Popular stakeholders, including patient advocates and FDA, were also against a change in the ODA’s market exclusivity provision. One informant asserted that if NORD had been behind this change in the law it would have had a good chance of passing. NORD opposed the change in the 1990 Congressional hearing. NORD seems to be regarded as a popular voice in ODA affairs and they are very organized, so lack of support from NORD may have been an important factor.

Informants and published reports did not mention shortcomings in the problem stream as significant to the failure of the 1990 amendment. However, in the view of this researcher, as many as 9 factors in the problem stream may have detracted support. (The “problem” that is being referred to here is that selected companies were blocked from FDA approval and market returns.) 1) The problem was often defined as a private problem. Pro-reform companies claimed that the law took them by surprise, was not fair, and caused them financial harm. This is a quasi-private problem because the law affected individual company’s interests, and some companies benefited while others did not. 2) The problem might get better without a policy change. The enactment of the ODA was a one-time event.¹⁴ Companies caught at a disadvantage did not anticipate the ODA and had already invested substantial resources in R and D. They were unable to recoup this investment because a competitor was first to gain FDA approval and ODA market exclusivity. 3) The problem suggests a solution that is intractable. The problem seemed ill-defined, difficult to measure or recognize, or at odds with the fundamentals of the ODA. A solution that addresses a moving target and lacks some kind of

¹⁴ The 1984 and 1985 amendments also had an important effect on Pro-reform companies. It may be more accurate to look at the 1983 enactment and the subsequent 2 amendments collectively as a one-time event.

link to a problem would be difficult to design. For example, in the 1990 Congressional hearing Waxman defined the problem as providing “exclusivity to drugs that would have been developed without the incentives of the law. The result is an unnecessary monopoly and higher prices to consumers.” How would a government official determine what made a sponsor decide to investigate a new drug? Information about the degree to which ODA incentives affected a company’s decision to develop an orphan drug is not available to government officials. 4) The cause or blame is attributable to a source that is liked or favored. The ODA was considered a successful law, a good law. The ODA enabled a “handful of drugs” to become “excessively profitable” (note, excessive was never defined), but the law otherwise was “working well.” Other factors that could have dampened support for the amendment, or at least did not favor passage of it, included: 5) the problem was unintended. In the 1990 hearing, anti-reform witnesses contended that a) no law is perfect, b) laws always create unintended effects, c) if the intended effects of the law are sound and if unintended effects are infrequent or have little impact on the law’s total effects then an amendment to address these unintended effects is not warranted—particularly if the costs or risks of amendment outweigh the benefits of correcting these unintended effects. Pro-reformers did not argue with these contentions to any significant degree. 6) The problem wasn’t created in secrecy or from a hidden agenda. Problems that were created covertly and with ill intentions seem to better capture attention and incite action. In the case of the ODA, companies followed the rules of the law as it was written. Orphan drugs that were first in gaining FDA clearance benefited from the law. Competitors that did not get there first were at a disadvantage. There was nothing secretive or illegal about this. 7) That the ODA offered a competitive advantage to some companies and a disadvantage to others wasn’t the kind of story that would be exciting enough to, for example, attract media attention; 8) the problems were seen as infrequent, i.e., the ODA was working well most of the time; and, 9) that

problem companies were those that were “abusing the law” and were “excessively profitable.”

The accusation that companies were abusing the law was disputed because companies were following the law. Designing an amendment that curtailed excessive profitability seemed problematic because this term begged for a definition. No definition of what was acceptably profitable and excessively profitable was offered by reformers, and if a definition were offered, it would probably be disputed. In the 1990s, the US healthcare system did not have explicit standards or upper limits that could be used to differentiate an excessively profitable medical product from one that was acceptably profitable. Moreover, in the 1990 Congressional hearing, there was no agreement about how to measure the profits of a single drug. The text of the ODA (see Page 1) suggests that an unprofitable orphan drug is one that would “generate relatively small sales in comparison to the cost of developing the drug and consequently (a pharmaceutical company would expect) to incur a financial loss.” In the 1990 hearing, disagreements over the “cost of developing the drug” included a) that there are many other costs in bringing an orphan drug to market besides drug development costs, e.g., administrative costs and manufacturing costs; and b) disputes about whether the cost of drug development should include the “dry holes” or not. For every drug that reaches the market, there may be hundreds or thousands that did not succeed in doing so. Some contended that drug development costs had to include the costs of the unsuccessful drugs (dry holes) as well as the successful drugs. In other words, the costs of the dry holes had to be factored or amortized into the costs of the successful drugs. This point was disputed. Remarks included, “the ODA is designed to subsidize orphan drugs, not to subsidize the pharmaceutical industry.” Or, “the drugs that never made it to the market have no bearing on the costs of those that did.”

Table 7--Factors Favoring or Impeding Passage of 1990 ODA Amendment
Factors Proposed *a priori* from Policy and Framing Literature and Color-Coded Based on Research Findings

<i>Dimension</i>	<i>Factors Favoring Passage of Legislation</i>	<i>Factors Impeding Passage of Legislation</i>
Problem Definition	<ul style="list-style-type: none"> -Defined as a social problem -Problem is getting worse -Suggests a solution that is tractable -Cause or blame is attributable to a source that is disliked -Problem was caused intentionally -Problem was caused secretly -Suggests problem has exciting qualities or is urgent -Problem affects a powerful minority or it affects the majority of people -Affected people are aware of problem -Defined so individuals can see they are or might become the next victim -Defined ambiguously to appeal to more people and leave wiggle room -Problem fixers gain resources, power, status 	<ul style="list-style-type: none"> -Defined as a private problem -Problem is getting better w/o policy -Suggests a solution that is intractable -Cause or blame is attributable to a source that is liked or favored -Problem was unintended/accidental -Problem was not created in secrecy -Suggests problem is not exciting or no longer seen as exciting; not urgent -Problem affects silent minority -Affected people are not aware of problem -Suggests a remote chance of becoming a victim in the foreseeable future -Defined explicitly and precisely, narrowing appeal and revealing specifics that can be disagreed upon -No one gains from fixing problem (or costs exceed benefits)
Policy Promotion	<ul style="list-style-type: none"> -Government action is only way to solve problem -Solution has obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to important interests -Policy is not seen as complex -Easy to communicate features -Policy sponsors are popular -Policy opponents are unpopular 	<ul style="list-style-type: none"> -Government action is one possible way to solve problem -Solution has no obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to unimportant interests -Policy is complex, risks are unknowable -Not easy to communicate features -Policy sponsors are unpopular -Policy opponents are popular
Political Milieu	<ul style="list-style-type: none"> -No major competing political issues -New political forces (e.g., new president) w/ compatible interests -Organized interest support or lack of opposition 	<ul style="list-style-type: none"> -Competing issues command attention, pushing issue/solution off agenda -No major changes in political stream that would favor legislation -Strong, organized interests opposed
Events	<ul style="list-style-type: none"> -Focusing event galvanizes support 	<ul style="list-style-type: none"> -Focusing event detracts from problem and/or solution
Climate/mood	<ul style="list-style-type: none"> -Economic, political, social, technological currents favor problem definition or solution 	<ul style="list-style-type: none"> -Economic, political, social, technological currents do not favor problem definition or solution
Policy Entrepreneur	<ul style="list-style-type: none"> -Persistent, credible, resourceful 	<ul style="list-style-type: none"> -No policy entrepreneur

Color Code Legend:

Red = Highly Probable Factor (meaning, this factor was mentioned in interviews or documents, and there was little or no evidence to refute its importance)

Green = Somewhat Probable Factor (meaning, this factor was mentioned in interviews or documents, but the evidence that would support its importance was weak or mixed)

In 1991, Senators Kassebaum and Metzenbaum introduced S. 2060, a bill that would amend the ODA to establish a “\$200 million sales trigger.” “If cumulative net sales of an orphan drug exceed \$200 million, marketing exclusivity will be withdrawn from the sponsor.” Testimony on the bill was heard in two 1992 Senate hearings. Senators Kassebaum and Metzenbaum created the bill to preserve the original intent of the ODA to spur rare disease drugs that had little commercial potential and to curtail use of the law to “shield extremely profitable drugs from competition.”

The bill had several factors in the problem stream (See Table 8) that seemed to favor its passage, including an increase in the number of orphan drugs that were generating substantial sales or being priced at a point that patients and Congress were reacting negatively and with greater alarm. While NORD had not supported the 1990 amendment, the 1991 bill had the support of NORD, which was important. One informant said the reason for the change in attitude was because NORD and others were shocked at the price of Ceredase¹⁵, a drug for Gaucher’s disease that was made by Genzyme Corporation. NORD reportedly was concerned that, if they did not push back on industry in some way, more orphan drugs would become available at prices similar to that of Ceredase (averaging \$200,000 per patient per year, but as high as \$1 million per patient per year). Also, instead of emphasizing that the ODA had put selected companies at a disadvantage, as in the 1990 amendment, the emphasis of the 1991 amendment was on vilifying selected companies and emphasizing how their pricing practices were hurting patients and payers. Companies were accused of exploiting patients that were in desperate need of these therapies, suggesting that problem of high prices was being created knowingly and intentionally by companies. A story of powerful villains and weak victims is one

¹⁵ Ceredase was launched by Genzyme Corporation in 1991. Cerezyme was launched by Genzyme in 1994 to largely replace Ceredase. The former was extracted from human placentas; the latter was derived by methods of biotechnology. If Ceredase or Cerezyme are mentioned in this dissertation, assume that one or the other is being referenced, and that collectively these 2 drugs refer to Genzyme’s orphan drug for Gaucher’s disease.

that has exciting qualities to it, i.e., it is one that could gain the attention of legislators and attract media coverage. Rare disease patients were acutely aware of the problem of paying for expensive orphan drugs. Witness testimony included chilling tales of the financial burden of expensive orphan drugs. Though a small number of patients are affected by rare diseases, patients suggested that high orphan drug prices were just the tip of the iceberg and that if something wasn't done to push back on industry pricing practices that this problem would expand beyond orphan drugs.

Factors that may have impeded the 1991 bill's passage were similar to that of the 1990 bill, e.g., the ODA was popular, and proposed changes were seen as risky. Also, opponents of the 1991 bill asserted that government action was just one possible way to address the problem and there were alternative, and possibly more effective, ways to address the problem of patient access to high-priced drugs. For example, industry-sponsored medication assistance programs (MAPs) were advanced as a viable solution. To garner support for this solution, a dozen companies wrote letters affirming that they had a MAP, and that patients that could not afford their drugs would qualify for the MAP. Some companies provided written assurance that no patient would be denied access to one of their marketed drugs for financial reasons.

Table 8--Factors Favoring or Impeding Passage of 1991 ODA Amendment
Factors Proposed *a priori* from Policy and Framing Literature and are Color-Coded Based on Research Findings

Construct	Factors Favoring Passage of Legislation	Factors Impeding Passage of Legislation
Problem Definition	<ul style="list-style-type: none"> -Defined as a social problem -Problem is getting worse -Suggests a solution that is tractable -Cause or blame is attributable to a source (industry) that is disliked -Problem was caused intentionally -Problem was caused secretly -Suggests problem has exciting qualities or is urgent -Problem affects a powerful minority or it affects the majority of people -Affected people are aware of problem -Defined so individuals can see they are or might become the next victim -Defined ambiguously to appeal to more people and leave wiggle room -Problem fixers gain resources, power, status 	<ul style="list-style-type: none"> -Defined as a private problem -Problem is getting better w/o policy -Suggests a solution that is intractable -Cause or blame is attributable to a source (ODA) that is liked or favored -Problem was unintended/accidental -Problem was not created in secrecy -Suggests problem is not exciting or no longer seen as exciting; not urgent -Problem affects silent minority -Affected people are not aware of problem -Suggests a remote chance of becoming a victim in the foreseeable future -Defined explicitly and precisely, narrowing appeal and revealing specifics that can be disagreed upon -No one gains from fixing problem (or costs exceed benefits)
Policy Promotion	<ul style="list-style-type: none"> -Government action is only way to solve problem -Solution has obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to important interests -Policy is not seen as complex -Easy to communicate features -Policy sponsors are popular -Policy opponents are unpopular 	<ul style="list-style-type: none"> -Government action is one possible way to solve problem -Solution has no obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to unimportant interests -Policy is complex, risks are unknowable -Not easy to communicate features -Policy sponsors are unpopular -Policy opponents are popular
Political Milieu	<ul style="list-style-type: none"> -No major competing political issues -New political forces (e.g., new president) w/ compatible interests -Organized interest support (NORD) or lack of opposition 	<ul style="list-style-type: none"> -Competing issues command attention, pushing issue/solution off agenda -No major changes in political stream that would favor legislation -Strong, organized interests opposed
Events	<ul style="list-style-type: none"> -Focusing event galvanizes support 	<ul style="list-style-type: none"> -Focusing event detracts from problem and/or solution
Climate/mood	<ul style="list-style-type: none"> -Economic, political, social, technological currents favor problem definition or solution 	<ul style="list-style-type: none"> -Economic, political, social, technological currents do not favor problem definition or solution
Policy Entrepreneur	<ul style="list-style-type: none"> -Persistent, credible, resourceful 	<ul style="list-style-type: none"> -No policy entrepreneur

Color Code Legend:

Red = Highly Probable Factor (meaning, this factor was mentioned in interviews or documents, and there was little or no evidence to refute its importance)

Green = Somewhat Probable Factor (meaning, this factor was mentioned in interviews or documents, but the evidence that would support its importance was weak or mixed)

In 1994, Representative Waxman introduced H.R. 4160 and Senator Kassebaum introduced S. 1981, similar bills that would have lowered the term of ODA market exclusivity from seven to four years, but permitted products with demonstrated “limited commercial potential” to continue to qualify for an additional three years. This proposal seemed to have many impeding factors, as seen in Table 9. Notably, the proposal required that the Department of Health and Human Services (DHHS) define “limited commercial potential” within six months of the bill’s enactment. The FDA would have input on this issue and oversee its implementation, a responsibility for which the FDA was reportedly ill-equipped and reluctant to carry out. One informant thought that the requirement to define “limited commercial potential” within six months was the most significant impeding factor. In years of debates, Congress had not agreed on a definition for LCP, so it seemed an impossible task for DHHS to do it in six months.

Impeding factors that seemed common to the 1990, 1991 and 1994 bills were that the problem was due to a flaw in the ODA, assailing a law that was otherwise perceived as very good and very popular; and, that the proposed solution was perceived as risky, i.e., that proposals would reduce sponsor interest in orphan drugs, which would mean fewer orphan drugs would ultimately become available to patients.

Unique to the 1994 bill was the fact that another bill was competing for congressional attention, and, offered the possibility of making ODA grievances irrelevant. The Clinton Health Security Act had been debated in Congress for months and some members of Congress shared Representative Bliley sentiment, “why are (we) spending these critical days in June holding hearings? This is the time when we should be in mark-up considering the most important issue of this session—health care reform!”

Table 9--Factors Favoring or Impeding Passage of 1994 ODA Amendment
Factors Proposed *a priori* from Policy and Framing Literature and are Color-Coded Based on Research

Construct	Factors Favoring Passage of Legislation	Factors Impeding Passage of Legislation
Problem Definition	<ul style="list-style-type: none"> -Defined as a social problem -Problem is getting worse -Suggests a solution that is tractable -Cause or blame is attributable to a source that is disliked -Problem was caused intentionally -Problem was caused secretly -Suggests problem has exciting qualities or is urgent -Problem affects a powerful minority or it affects the majority of people -Affected people are aware of problem -Defined so individuals can see they are or might become the next victim -Defined ambiguously to appeal to more people and leave wiggle room -Problem fixers gain resources, power, status 	<ul style="list-style-type: none"> -Defined as a private problem -Problem is getting better w/o policy -Suggests a solution that is intractable -Cause or blame is attributable to a source that is liked or favored -Problem was unintended/accidental -Problem was not created in secrecy -Suggests problem is not exciting or no longer seen as exciting; not urgent -Problem affects silent minority -Affected people are not aware of problem -Suggests a remote chance of becoming a victim in the foreseeable future -Defined explicitly and precisely, narrowing appeal and revealing specifics that can be disagreed upon -No one gains from fixing problem (or costs exceed benefits)
Policy Promotion	<ul style="list-style-type: none"> -Government action is only way to solve problem -Solution has obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to important interests -Policy is not seen as complex -Easy to communicate features -Policy sponsors are popular -Policy opponents are unpopular 	<ul style="list-style-type: none"> -Government action is one possible way to solve problem -Solution has no obvious relative advantage to current situation or alternative solutions -Benefits of solution accrue to unimportant interests -Policy is complex, risks are unknowable -Not easy to communicate features -Policy sponsors are unpopular -Policy opponents are popular
Political Milieu	<ul style="list-style-type: none"> -No major competing political issues -New political forces (e.g., new president) w/ compatible interests -Organized interest support or lack of opposition 	<ul style="list-style-type: none"> -Competing issues command attention, pushing issue/solution off agenda -No major changes in political stream that would favor legislation -Strong, organized interests opposed -Focusing event detracts from problem and/or solution
Events	<ul style="list-style-type: none"> -Focusing event galvanizes support 	<ul style="list-style-type: none"> -Focusing event detracts from problem and/or solution
Climate/mood	<ul style="list-style-type: none"> -Economic, political, social, technological currents favor problem definition or solution 	<ul style="list-style-type: none"> -Economic, political, social, technological currents do not favor problem definition or solution
Policy Entrepreneur	<ul style="list-style-type: none"> -Persistent, credible, resourceful 	<ul style="list-style-type: none"> -No policy entrepreneur

Color Code Legend:

Red = Highly Probable Factor (meaning, this factor was mentioned in interviews or documents, and there was little or no evidence to refute its importance)

Green = Somewhat Probable Factor (meaning, this factor was mentioned in interviews or documents, but the evidence that would support its importance was weak or mixed)

Chapter 7—Issue Frames Used in ODA Reform Hearings 1990-1994

The method for constructing frames was described in Chapter 4. Briefly, frames were constructed by repeated readings of the Congressional testimony and by looking at patterns in selected data that were extracted, coded, and placed into a table using Excel. Summarized data can be found in Appendix C.

Four frames were constructed and named: 1) ODA Reform as Economics and Access, 2) ODA Reform as Patient Relief, 3) ODA Reform as Rules of Participation, and, 4) ODA Reform as Congressional Action. Each frame has distinctive elements, but some overlap is expected since each describes aspects of the same situation or phenomena.

ODA Reform as Economics and Access to Frame

The ODA Reform as Economics and Access (to orphan drugs) Frame (Economics and Access Frame) emphasizes the importance of output of the ODA and its potential reforms. Witnesses using this frame emphasized that proposed amendments must be judged based on how a change might effect the number of new orphan drugs that would be researched, developed, produced and marketed in the future (“output”). This frame was frequently used by witnesses that were anti-reform. They argued that a change in the ODA might negatively affect the effectiveness of the law in spurring new orphan drug development. Assumptions underlying this argument were that 1) the ODA is a set of economic incentives to encourage industry to develop new orphan drugs; 2) that better economic incentives should lead to more orphan drug research activity and, consequently, more orphan drugs, and, 3) that patients with rare diseases

and conditions were in need of new orphan drugs, hence, more orphan drugs meant greater patient access and the potential for health improvements.

Many witnesses began their testimony by using this frame. They would first point to the success of the ODA in producing new orphan drugs. They did this by citing two numbers: the number of drugs that been designated as orphans by the FDA and the number of designated orphan drugs that had received FDA approval since the law was enacted in 1983. These numbers were compared to the dearth of orphan drugs that were approved in the decade prior to 1983. Opponents of reform would argue that the law has been a success and that either 1) change was not needed because it was a success, or, 2) they were against reform because change could negatively affect the law's effectiveness in the future. In other words, this frame emphasizes the *consequences* of any action that might, as witnesses said, “undermine the ODA’s incentives,” or “dilute the benefits of the law.”

To gain support for their views, opponents of reform emphasized the tangible successes of the ODA in increasing access to orphan drugs, and the fear and uncertainty inherent to proposed ODA reforms. Some opponents referred to a recent drop in the number of applications for orphan drug designations as evidence that industry had already reacted negatively to the idea of ODA reform. In 1991, the number of applications had dropped significantly, so it was suggested that just the possibility of ODA reform was causing industry uncertainty about the future of the law. This uncertainty had led to a drop in industry’s orphan drug development activities.

Proponents of ODA reform contended that the ODA needed to change because the future of the entire ODA policy was being endangered by a few companies, i.e., that if Congress didn’t act to institute change now, public support for the law could dwindle to a point where the

law would be repealed. Proponents also argued that aspects of the ODA were decreasing access to orphan drugs rather than increasing access as intended.

ODA Reform as Patient Relief Frame

Where the Economics and Access Frame relied on enumeration (of orphan drugs), the Patient Relief Frame relied on anecdote and emotional appeal. The Patient Relief Frame suggests that an amendment's merits should be judged based on whether it acknowledges and addresses the hardships that rare disease patients endure. In the two 1992 hearings, thirteen patient advocates testified. Many of them recounted the hardships of having a rare disease and how an orphan drug had helped control the disease. Proponents of ODA reform then described the burden of financing the needed orphan drug. Proponents argued that the ODA market exclusivity provision allowed companies to charge unreasonable prices because there was, by definition, an absence of competition. Patient advocates claimed that granting market exclusivity so that companies could command high prices and generate substantial sales was not consistent with the intent of the ODA. Patient advocates used metaphors to depict targeted companies as evil, exploitive, and less than human. The emphasis of the frame was on the alleged victims and villains, and the need for "something to be done." Reform proponents argued that ODA reform would result in lower orphan drug prices and reduced financial burden. The testimony suggested that the act of reform is perhaps more important than the substance or consequences of the reform. If this is the case, ODA reform would symbolize the importance of patient relief and social justice, thereby signaling to industry that patient welfare is more important than corporate welfare.

Opponents of ODA reform responded to patient appeals by arguing that, yes, something should be done to help relieve the financial burden of orphan drugs. But opponents argued that ODA reform was not the right solution for the problem. Opponents proposed other solutions,

including: 1) patient assistance programs that provide free orphan drugs to the financially needy; 2) health insurance reform; or, 3) national health reform. Opponents further argued that changing the ODA could result in a reduction in orphan drugs, and that having expensive drugs was better than not having drugs at all.

ODA Reform as Rules of Participation Frame

The ODA Reform as Rules of Participation Frame (Rules of Participation Frame) emphasizes the importance of how “the game is played” and not necessarily the game itself. This frame centers on social etiquette and fairness, and emphasizes the do’s and don’ts of participating in the social process of developing, producing and marketing orphan drugs. This frame is based on the idea that the right set of rules can be developed to effectively dictate fair and correct participation in the orphan drug process. The challenge of this frame is on defining what is “right” and “fair.”

Users of the Rules of Participation Frame tended to be witnesses that spoke on behalf of individual companies. Proponents of ODA reform claimed that the rules of the ODA needed to change so that one company didn’t become the “winner that takes all.” The market exclusivity provision of the ODA had created a situation where multiple companies had pursued development of an orphan drug, e.g., human growth hormone, and the first company to get FDA approval “won” the entire market. For companies that had to wait 7 years to market their version of the drug, they felt this situation was unfair because waiting 7 years meant effectively losing their entire investment in the drug. This winner-takes-all situation was also unfair for patients, these companies argued, because the “winning” company was able to charge monopoly prices, and the situation denied patients the ability to choose among different company brands. Proponents argued that an orphan drug category that attracts multiple companies is likely a high

commercial potential market. Hence, proponents further argued, such orphan drug categories didn't need the help of the ODA, so the ODA should not apply to them.

To gain adherents, ODA reform proponents morally condemned companies that were first to gain market exclusivity, i.e., proponents contended that these companies were using the incentives to block competition and were “blatantly subverting the intent of the law.”

Opponents of reform claimed that they had done nothing wrong, that they legally and rightfully obtained market exclusivity, and that they should not be punished for effectively and efficiently gaining FDA approval. Reform opponents (companies) depicted their critics as “sore losers,” and emphasized that everyone knew the “rules,” and, that the rules shouldn't be changed in the “middle of the game.”

ODA Reform as Congressional Action Frame

The ODA Reform as Congressional Action Frame (Congressional Action Frame) focuses on whether government involvement is appropriate or not. In the context of the proposed ODA reforms from 1990-1994, appropriate government involvement mainly refers to attempts by legislators to use ODA amendments as a way to contain industry prices and profits. Based on documents, Congressional testimony and informant interviews, anti-reformers asserted that the 1990s ODA amendments were a thinly veiled attempt by Congress to exert increased government control over pharmaceutical industry pricing practices. Whether government involvement is appropriate or not also refers to opinion about legislators' (e.g., Rep. Waxman and Sen. Metzenbaum) efforts to amend the ODA in the 1990s, and whether these efforts were welcomed or not. For example, anti-reformers contended that the ODA was a good law that was working and that amendments would make it less effective.

The challenge of the Congressional Action frame is in defining “appropriate.” This frame invokes long-held American cultural themes of the role of government vs. the role of

markets in creating goods and services for unmet needs. When and how government should act in the interest of the public is central to progressive vs. conservative tenets, as well as a number of other political and economic philosophies.

Proponents of ODA reform argued that Congressional action was needed to help patients or companies because the market had failed to provide the right orphan drugs at the right price. When advocating for Congressional intervention, reform proponents depicted Congress in a positive light, e.g., as a hero and saint.

Opponents of ODA reform thought that Congress should not act on the controversies that prompted amendment proposals because 1) this was not Congress's responsibility (e.g., controlling drug prices was not Sen. Metzenbaum's responsibility); 2) they felt Congress had better things to do, i.e., this should not be a priority because the law was working well; 3) Congress did not have the knowledge or expertise to intervene in the situation (e.g., Rep. Waxman was accused of trying to manipulate market forces to control prices, a job he was not trained to do); and/or 4) this was duplicating the work of other Congressional committees or other sectors of government (e.g., containing health costs was being addressed by Clinton when the 1994 ODA amendment was proposed). To denigrate the actions of Congress, reform opponents described them as "tinkering" or "meddling." This invoked the idea that these actions were frivolous, intrusive or ill-informed. Moreover, a couple of opponents suggested that Congressional actions could become a slippery slope, i.e., reforms in the ODA that effectively moderated orphan drug prices could set a precedence for government price controls in other drug markets or industry sectors.

Table 10--Four Frames Constructed From Congressional Testimony

	1. Economics and Access	2. Patient Relief	3. Rules of Participation	4. Congressional Action
Basis for judging ODA amendment proposals	By how it will impact the future number of orphan drugs that will be accessible to patients	By how it will acknowledge and address patient hardship	By how well it encourages appropriate participation in the orphan drug development process	By whether governmental involvement is appropriate or not
Pro/Con Assertions	Amendment will increase/decrease the # of future orphan drugs	Amendments will/won't better recognize suffering & provide relief	Amendments will/won't encourage the right participation	Congress should/shouldn't intervene in situation
Values	Efficiency, Security	Security, Equity	Equity, Liberty	Security, Liberty, Equity
Underlying Assumptions	ODA is a set of incentives. Better incentives lead to more orphan drugs, which means more rare disease patients can be helped	The legislative process is a way for citizens to raise awareness of perceived injustices, seek retribution, and better balance power	ODA is a set of rules. The right rules will be fair and result in the right companies doing the right things to help patients with rare diseases	Certain situations require Congressional involvement, others do not
Challenges	Relationship between incentives, new drugs and unintended effects	Who should be helped and how?	What is "right" and "fair" participation?	Who and what is "appropriate" involvement?
Amendment Proponents' Claims	--Reform will increase patient access to orphan drugs -- Reform will preserve patient access to orphan drugs	Something must be done because . . . --Patients are suffering from rare diseases --Patients have been exploited or abandoned	Rules should be changed so the law won't: --Apply to HCP drugs --Help one company by hurting another --Take something away that rightfully belongs to a company --Allow companies to subvert the intent of the law	We need Congress to help us because . . . --The market has failed to provide the right drugs at the right price
Amendment Opponent Claims	--We don't know how reform will affect patient access to drugs, so we shouldn't do it --Overall the ODA is working as intended, so leave it alone --Reform will decrease patient access	--Something should be done to help patients in need, but reform could hurt them not help them	--ODA isn't perfect, but no law is --No law can control every possible behavior or outcome --Changing the law could create new, unforeseen problems	--Congress should not take this action b/c: --This is not their responsibility --They have more important things to do --They lack knowledge or expertise in this area --They are duplicating the work of others
Metaphors	Hydrology: Flow of new orphan drugs; Geology: "undermine incentives"	A physical struggle between good and evil, weak and strong	A game with rules, fair play vs. cheating ("abusers")	Congress as: hero and savior; child "tinkering;" intruder "meddling"
What Law Symbolizes	Law as inducement	Law as social justice	Law as etiquette	Law as paternalism
Cultural Themes	Ecology; Black box with inputs and outputs	Dualism, conflict, civil rights	Gamesmanship vs. sportsmanship	Government vs. market controls, progressives vs. conservatives
Stakeholder Roles	Producers, consumers, suppliers (of incentives)	Victims, villains, heroes	Winners, losers, cheaters, rule makers, referees	Legislators, regulators, capitalists, civilians
Motivational Tactics Used	Instill fear and uncertainty that action, or lack of action, could have negative consequences in the future	Foster pity for patients and disdain for companies. Personalize the problem: have patient or parent tell story of individual plight. Depict "evil" companies as less than human (eg. "parasites")	Foster pity for the "cheated" and disdain for the "cheaters." To discourage reform, portray the "cheated" as "sore losers." Instill doubt that action is needed; Instill fear.	Discredit Congress, e.g., use "meddling & tinkering" to describe their actions. Instill fear: depict their actions as a "slippery slope." Pro reform: Depict Congress as hero and savior

Values or Goals of Frames

Stone (2002) asserts that political arguments usually have one of four generic goals or values: security, equity, liberty, and efficiency. This researcher expected that each frame would clearly rely on one of these values. Yet, as can be seen in Table 10, each frame seemed to suggest 2 to 3 of these values or goals. For example, the Patient Relief Frame implied that security and equity were important goals. Moreover, trying to “fit” the goal of the frame to one or more of these four goals was not without difficulty. For example, the Economics and Access Frame was deemed as having efficiency and security as its primary goals. However, efficiency is likely a crude way of expressing that the frame emphasizes the importance of the impact of ODA reform on the number of orphan drugs that will be produced and marketed in the future.

Of note, all patient advocates used arguments that advanced the importance of security, i.e., that rare diseases and conditions were often life threatening and debilitating, and, orphan drugs were needed to ensure patients’ minimum requirements for biological survival and activities of daily living. When patients were described as being victimized or treated unfairly by drug companies, equity as a value or goal was implied.

The Economics and Access Frame seemed to have a foundation of efficiency. As described by Stone, efficiency is about getting a greater output out of a given input, or “getting a bigger bang for the buck.” The frame promotes efficiency in that it emphasizes the importance of inputs (ODA incentives and uncertainty about reform) in optimizing outputs of the social system (people, processes and things that are related to orphan drugs). Of note, ODA efficiency was often tied to the value of security, because greater efficiency (more orphan drugs) meant that a greater number of rare disease patients could be helped.

The Rules of Participation Frame seems to be based on the values of equity and liberty. In fact, testimony suggested that there was a trade-off between the two values, i.e., greater equity

might result in less liberty, and vice versa. For example, ODA rule changes that ensure more equal treatment of individual companies (equity) might reduce the ability of one company to choose a course of action that suited their self-interests (liberty).

The Congressional Action Frame appears to be based on the values of security, equity and liberty. Congress coming to the aid of patients means security for patients. Equity is promoted when Congressional action redistributes resources, e.g., when one party gets more of something (patients get more orphan drugs) and another gets less (taxpayers get a reduction in their assets when taxes are increased). Congress “meddling” in self-organizing markets suggests a derogatory reference to Congress interfering with the liberty of market participants. Of note, “laissez-faire capitalism” literally translates to “hands off” capitalism, as in the government keeping their hands out of market or business practices.

Chapter 8—Framing Strategy and Guidance

Strategic framing is considered an important tool in influencing individual attitudes, knowledge or behavior (Gandy 2003), exerting political influence (Entman 2007); exercising power (Reese 2003), instigating social change and winning debates or adherents (Lakoff 2004, Pan 2003); mobilizing collective action (Snow, Rocheford, Worden and Benford 1986, Benford 1993, Benford and Snow 2000); and, expanding social and political actors' realm of influence (Pan 2003).

This case study research explored the question of “How does framing support policy development?” This chapter begins by addressing this question in the context of the proposed ODA reforms of the 1990s. A summary and analysis of the four ODA frames are then included. General recommendations to help public policy stakeholders better consider how they and others think about complex issues and advance public policy change are then provided. The chapter closes with a practical guide for how to use framing theory in public health practice.

How Does Framing Support Policy Development?

This research indicates that framing was an important part of promoting or impeding ODA policy developments during 1990-1994, and supports Stone's contention that the struggle over ideas is the essence of policy making in political communities. “Ideas are a medium of exchange and a mode of influence even more powerful than money and votes and guns. Shared meanings motivate people to action and meld individual striving into collective action. Ideas are at the center of all political conflict.” (Stone 2002, page 11)

Potential policy developments, such as the 1990-1994 ODA reforms, are complex and ambiguous, and people rely on others to interpret and translate for them “what is going on here?” By definition, ambiguous situations can be interpreted in a multitude of ways. For example, the ODA reform case could be described as a case of a disenfranchised minority group arguing for their rights and attempting to rebalance power with capitalist exploiters, or a case of government meddling in private affairs. Each of these frames implies a different problem, solution, and set of criteria for evaluation. Ambiguity provides the opportunity for interpreters to frame the situation in a way that is positive or negative, clear or confusing, inspiring or disempowering.

Frames are organizing constructs that help simplify and guide understanding of a complex reality. At the same time, frames force us to view the world from a particular, and limited, perspective, and thereby limit the options we can see. Reframing could be used to diffuse a conflict and help combatants constructively explore how they can reach accord. Reframing could also help a teenager find the inner courage and justification for becoming a suicide bomber. In other words, framing can be used for constructive and destructive purposes. While this is an unfortunate fact, this research lends support to the idea that framing is critical for those interested in shaping the future of health policy.

As Russo and Shoemaker (2001) point out, every decision is embedded within a frame. The question is whether you control the frame—or the frame controls you.

Strategic Assessment of ODA Reform Frames

The case of how issues were framed during attempted ODA reform hearings in 1990-1994 is an interesting one. Advocates were highly skilled in framing their arguments, so there is much to be learned from this case.

To recap, frames constructed from the text of the debates were named ODA Reform as . . . : 1) Economics and Access, 2) Patient Relief, 3) Rules of Participation, and, 4) Congressional Action. The frame analysis suggested that each frame evoked different values, beliefs and systems of logic, and that the criteria by which to evaluate the merits of proposed reforms varied from frame to frame. For example, the Economics and Access Frame asserts that reforms should be judged by how they might impact the future number of orphan drugs that will become available. The Patient Relief Frame asserts that reforms should be judged based on how it acknowledges and addresses hardships experienced by rare disease patients. Reform would be judged in the Rules of Participation Frame based on how well it encourages appropriate behavior or participation in the orphan drug process. In the Congressional Action Frame reform would be judged based on whether Congressional involvement is deemed appropriate or not.

The Economics and Access frame was most often used by anti-reformers. Using this frame, anti-reformers would cite statistics on the marked increase in orphan drug development that occurred after ODA enactment, compared to years prior. This frame depends on fostering fear of the unknown and reform's potential for negative effects. Arguments that invoked this frame emphasized potential causes and effects of reform, and how these might ultimately affect the future number of orphan drugs that might be accessible to patients with rare illnesses.

The Patient Relief Frame depended on fostering pity for patients with rare diseases and disdain for greedy companies. This frame suggested that “something should be done,” but “something” was not usually identified.

Those using the Rules of Participation Frame often used the metaphor of a game, i.e., winning and losing, cheaters and the cheated, inequity and fairness, competition, and, rules being changed in the middle of the game. Competitive companies argued about whether the ODA

had given them a fair or unfair advantage in competing in their respective orphan drug markets. To discourage reform, companies said their accusers were “sore losers.” To encourage reform, companies said that the advantaged competitor was not acting in the spirit of the law.

The Congressional Action Frame was more dominant in the 1994 amendment hearing, although use of the frame was sprinkled throughout 1990-1994. In 1994, congressional action was questioned by members of Congress because representatives of patient, industry, and governmental groups testified that they would support the 1994 bill in order to put an end to the prolonged threats of Congress to change the ODA. Attempts to discredit the bill’s creators were implied by comments such as the bill’s supporters were “putting the rabbit in the hat,” “meddling” or “tinkering” with issues that they were not qualified or welcomed to deal with.

Using principles that were summarized in Chapter 3 and Appendix B, potential strengths and weaknesses of the frames are assessed in Table 11. This armchair assessment indicates that all four frames contained elements that could promote frame resonance. For example, users of the Rules of Participation frame used the simple to understand metaphor of a game, and denigrators of Congressional Action described the actions as “meddling” and “tinkering.” Each of these examples fit into cultural myths and common narratives.

It is difficult to assess the degree to which the frames might elicit what Lakoff calls, Level 1 values (Dorfman 2005). While all frames suggest Level 1 values, users of the Rules of Participation Frame tended to devote most of their arguments to Level 3 values, while users of the other frames tended to focus on Level 2 values. According to Dorfman (2005), Level 1 is the expression of overarching values, such as fairness, responsibility, equality, equity, and so forth, the core values that motivate us to change the world or not change it. Level 2 is the general issue being addressed, such as housing, the environment, schools, or health. Level 3 is about the nitty gritty of those issues, including the policy detail or strategy and tactics for

achieving change. Messages can be generated from any level, but Level 1 is most important because it is at Level 1 that people connect in the deepest way. Level 1 is uncovered in the second of the following three questions that advocates should ask themselves before constructing their messages. 1. What's wrong? 2. Why does it matter? 3. What should be done about it?

Arguments rooted in the Economics and Access Frame appeared to be effective in discouraging ODA reform because the frame tended to emphasize the bigger picture, or landscape, and emphasize the potential impact of ODA reforms on the total "system." The call to action of this frame was clear (e.g., do nothing, do not reform the ODA), because users of this frame tended to assert "it ain't broke, so don't fix it." The frame was also flexible in that it was easy to bridge from the other frames to this one, and the frame was inclusive so many stakeholders could see the benefit of thinking in this frame.

The Patient Relief Frame seemed to have the strengths of consistency and credibility. Patient advocates provided empirical evidence that supported the frame (e.g., cost of the medications as a percent of their salaries, difficulties in obtaining medical insurance, etc.), and listeners would likely have similar experiences and opinions if they were in the situation of patients that were described. The weakness of the Patient Relief Frame was that it did not seem to leave the listener with a sense of what to do, or a call to action. Users of the frame seemed to evoke emotion and a feeling of "how awful," but listeners were probably left with a feeling of inadequacy when it came to devising or evaluating remedies. As informants suggested that rare disease patient advocates were not overly enthused about the prospect of reforming the ODA in the 1990s, lack of an action orientation may have been purposeful.

The Congressional Action Frame did seem to clearly support an action, but that action seemed clear only when anti-ODA reformers used the frame. The action suggested was to stop “meddling” with a successful law and don’t reform it.

Table 11—Strengths and Weaknesses of Four ODA Reform Frames

<i>Frame Element</i>	<i>1. Economics and Access</i>	<i>2. Patient Relief</i>	<i>3. Rules of Participation</i>	<i>4. Congressional Action</i>
<i>Level 1 Message?</i>			-	
<i>Emphasize Landscape?</i>	+	-		
<i>Frame Resonance?</i>	+	+	+	+
<i>Action Oriented?</i>	+	-		+
<i>Flexible?</i>	+			
<i>Consistent?</i>		+		
<i>Credible?</i>		+		
<i>Frame Devices?</i>			+	

Legend:

“+” means this seemed to be a strength of the frame

“-” means this seemed to be a weakness of the frame

These evaluations were based on the researcher’s judgment and interpretation of the framing literature as it applied to the four ODA reform frames.

For a description of why each of these frame elements are considered important, see Chapter 3 and Appendix B

Framing Strategy Recommendations

As discussed in the next chapter, it is unlikely that there will be strong demand in the near future for ODA reforms of the type seen in the 1990s. Hence, there is little need to reframe the ODA debate to further encourage or discourage ODA reforms that address how, and to what extent, sponsors of high commercial potential drugs should benefit from ODA provisions. Instead, the following recommendations are general in nature, and not limited to the ODA.

As previously stated, this research supports the importance of using potent frames in political communications. It is highly recommended that health policy practitioners learn more

about the art and science of framing, and explore opportunities to use framing principles to craft messages that instigate positive social change. However, *caveat emptor*. There are no guarantees that it will help. The field of framing is arcane and more art than science. Moreover, message framing is just one factor in the complex political equation to promote positive change. And finally, framing is not easy. Based on the experience of conducting this dissertation research, it is difficult to become self-aware of the frames that limit your own perspectives of the world, and it is difficult to train your mind to recognize frames in a communicating text. It is also a challenge to evaluate the degree to which frames are working as intended and to create new ones if they are not.

The Typology of Framing (Appendix B) can serve as a preliminary guide and reduce the difficulties of applying framing theory to practical problems. Further development of this is needed.

Since framing theories are a challenge to apply to real world situations, framing novices would benefit from expert guidance. Fortunately, guidance is already available, although the quality of such guidance has not been evaluated by this researcher. For example, The FrameWorks Institute provides training and resources on framing to non-profit organizations in order to “change the public conversation about social problems.” FrameWorks has developed a proprietary approach, called “Strategic Frame Analysis,” that can be found at <http://www.frameworksinstitute.org/sfa.html>.

This dissertation research also points to the importance of systems thinking in framing research. Chapter 3 includes a preliminary exploration of alternative views of the ODA as a first step toward deconstructing and reconstructing how we view a complex social issue in order to change the social dialogue. Systems theories and approaches may facilitate such a process and guide how we might introduce interventions into a social system to instigate change.

For example, Meadows (1999) has outlined a potentially useful systems approach. She identifies twelve basic ways to intervene in a complex social system to cause positive change. The least effective of the twelve is to change parameters in the system, such as subsidies, taxes and standards, and the most effective are to change the system's paradigms, or even transcend the paradigms. Changing paradigms is a powerful way to change a system because they are the shared social agreements about the reality of the system, and hence, ultimately govern the structure, rules and goals of the system. Assuming that the world of laws, people, illnesses, treatments, etc. is a social system and that we can intervene in this system in a number of ways, it would be informative to better understand the goals of this system and the alternative ways to meet these goals. Questions that could be asked include, what are the goals of this system, e.g., to eliminate or alleviate every rare illnesses at any cost? What are the social agreements that we have about participating in this system? Can we use framing to change the paradigm of this social system? Or should we intervene with leverage points that operate at a lower, and possibly less effective, level? Some of the social agreements and potential tools of intervention were described in Chapter 3 (Foundations for Framing the ODA)

Table 12—Leverage Points in a System

Adapted from Leverage Points, Places to Intervene in a System, Meadows (1999 p. 2)

Effectiveness	Leverage Point
Least Effective	<p>Constants, parameters, numbers (such as subsidies, taxes, standards)</p> <p>The size of buffers and other stabilizing stocks, relative to their flows</p> <p>The structure of material stocks and flows (such as transport network, population age structures)</p> <p>The length of delays, relative to the rate of system changes</p> <p>The strength of negative feedback loops, relative to the effect they are trying to correct against</p> <p>The gain around driving positive feedback loops</p> <p>The structure of information flow (who does and does not have access to what kinds of information)</p> <p>The rules of the system (such as incentives, punishment, constraints)</p> <p>The power to add, change, evolve or self-organize system structure</p> <p>The goal of the system</p> <p>The mindset or paradigm that the system — its goals, structure, rules, delays, parameters — arises out of</p>
Most Effective	<p>The power to transcend paradigms</p>

Note: stocks and flows could relate to the number of orphan drugs; parameters might include the number of rare diseases measured against the number of drugs that substantially alleviate suffering from these diseases; stabilizing stocks relate to inventory of drugs or monies to pay for them; length of delays could relate to the time it takes to discover and develop new drugs or receive an accurate disease diagnosis. . . rules might include laws and regulations for developing and paying for orphan drugs, etc.

How to Use Framing Theory in Public Health Practice

Framing theory can be used to enhance the way that public health practitioners advocate for change, as it can inform and guide how organizations: 1) conduct research on target audiences and perceptions of products, services or social causes; 2) determine marketing strategies, such as segmentation, targeting, and positioning; and, 3) craft, deliver and test specific messages. Based on this dissertation research, as well as the researcher's experience in strategic planning, this section provides practical advice for applying framing theory throughout the advocacy planning process. Note that framing theory tips are highlighted in green.

If advocacy is about changing “what is” into “what should be,” a strategic plan is the roadmap for getting from the current state of “what is” to the desired state of “what should be.” Like the evolutionary plan that inspires a flock of birds to fly in close formation as they travel from north to south for the winter, a clear strategic advocacy plan will inspire a pattern of organizational activities that are aligned, aimed in the right direction at the right time, and result in reaching organizational goals. Accordingly, public health organizations should ask the following questions: Where are we now? Where do we want to be? How do we get there? And, are we getting there?

Framing theory will now be described in the larger context of a strategic planning process. To simplify terms, assume that a public health organization is advocating for “Idea A.” Idea A could be one of a number of innovations that improves health, e.g., a health reform policy, a vaccine for HIV, or, an anti-smoking educational campaign.

Where are we now?

Public health advocates can assess “where they are now” by using business strategy techniques such as a PEST analysis (Kotter and Schlesinger 1991), competitive assessment (Kotler 1997), and SWOT analysis (Kotler 1997). A variety of data sources can be used for this

current-state analysis, including published articles and reports, web sites, informant interviews, focus groups, and surveys.

A PEST analysis is an organized way to scan the broader environment and identify political, economic, social, and technological (P-E-S-T) factors and trends that may favor or impede an organization's ability to shape and create a desired future. PEST analysis can also include a historical analysis to better understand "how we got here."

Many important snapshots can be derived from the PEST analysis. At minimum, the following summaries from the PEST analysis should be developed: 1) opportunities and threats (the O-T of SWOT) for the organization; and, 2) a stakeholder analysis or a community map that identifies and describes the players in the Idea A social system, how they interact, and what motivates and satisfies them.

A competitive assessment identifies alternatives to Idea A. Among other things, it includes a summary of Idea A's competitive strengths and weaknesses (the S-W of SWOT). To set the stage for reframing, it is important to identify current and potential criteria that can be used to compare competitive alternatives.

Framing theory tip: Do a deep dive into how target audiences think and communicate about Idea A and the competition. What criteria do target audiences use to compare and evaluate Idea A? What problem does Idea A (or B, C and D) solve (for target audiences)? Why does solving the problem matter? What is causing the problem? How does one Idea solve the problem better than another? What is the target audience's mental model for how an Idea works in the social system? Or, how does one Idea effect a change on the current state of the social system and lead to some desired or undesired state? Under which mental model(s) does Idea A stand out as superior?

Think broadly and creatively about potential alternatives to Idea A, i.e., use a systems thinking framework to uncover potential public health levers and leverage points in the social

system of interest (see Table 12 for an example). Note that alternatives could include “do nothing, stay the course, or, continue with existing behaviors.”

Analyze current and potential frames, and summarize them in a format similar to Table 10. This will improve the organization’s ability to understand and deflect current frames, as well as inform the creative process of creating new frames. Table 10 was created from extensive debate and dialogue on a public policy issue, as found in Congressional testimony. Depending on the nature of Idea A, other sources for conducting a frame analysis include articles and blogs that review and opine about Idea A and alternatives, paid advertisements and other collateral materials, observing conversation and live debate, and, primary target audience research.

Summarize findings in the form of a SWOT (Strengths-Weaknesses-Opportunities-Threats) analysis. Strengths are internal attributes which can be leveraged to your advantage. Weaknesses are internal attributes which should be protected or improved to keep competitors from using them against you. Opportunities are external events or conditions that may allow you to strengthen your position, or weaken your competitors’ position. Threats are external events or conditions that could adversely impact your position.

Where do we want to be?

A strategic roadmap is of little use if an organization is not clear about where they want to be in the future. Hence, it is important to articulate the organization’s vision of this ideal or achievable future, and the organization’s goals and role in creating that future.

Framing theory tip: Do a deep dive into how your organization thinks and communicates about where it wants to go. What assumptions underlie the organization’s vision and mission? What do these assumptions reveal about dominant organizational perceptions and judgments about Idea A target audiences, problems, causes and solutions? Self-examination of the organization’s frames may be an important first step toward breaking away from legacy mindsets and creating new ways to frame a complex reality.

How do we get there?

An Idea A strategic roadmap will define how the organization intends to focus its resources to accomplish its goals. All public health organizations have limited resources and must therefore focus on carrying out organizational initiatives that build on strengths and opportunities, and minimize weaknesses and threats. The communications campaign is one such initiative. Hence, organizations need to devise a communications plan that will effectively and efficiently use organizational resources to communicate the value of Idea A and elicit a desired response, such as an increase in demand for Idea A. Framing theory can inform the communications plan and, hence, is the focus of this section.

A communications plan specifies: 1) the primary target audiences that will be reached; 2) the desired response the communications intend to elicit; 3) the primary messages to be used; 4) the vehicles that will be used to deliver messages; 5) the source of the messages; and, 6) the plan for evaluating the success of the communications campaign. For advocates who want to fundamentally change the way target audiences view social conditions, define problems, identify causes and solutions, and formulate relevant judgments, framing theory can inform and guide many of these communications plan elements.

Once advocates determine who they want to reach and what response they want to elicit, they will be ready to craft and test messages that can potentially reframe problems, causes, and solutions; and, help target audiences see new possibilities for public health innovations.

The FrameWorks Institute (2002) has created a checklist¹⁶ to evaluate whether messages are on point and capitalize on framing theory and research. This checklist assumes that the innovation is a public policy, but many of the FrameWorks questions are potentially relevant to other public health interventions. In addition to using such message development tools, framing

¹⁶ From the FrameWorks Institute Toolkit on Framing Public Issues. Accessed March 1, 2009 at <http://www.frameworksinstitute.org/assets/files/PDF/FramingPublicIssuesfinal.pdf>

theory novices may want to seek the help and advice of framing theory experts such as the FrameWorks Institute. A few example questions from the FrameWorks Institute checklist are shown below.

Framing theory tips for developing effective messages:

(from FrameWorks Institute Toolkit on Framing Public Issues (2002)

<http://www.frameworksinstitute.org/assets/files/PDF/FramingPublicIssuesfinal.pdf>

- *Based solely on the material you have provided, are you confident that an ordinary reader/viewer could answer the critical question: What is this about? Is it about prevention, safety, freedom, etc.?*
 - *In your attempt to frame for the reader “what is this about,” did you begin at Level One, by introducing a value like responsibility, stewardship, or fairness?*
 - *Did you reinforce your Level One message by using words, images, and metaphors that support your frames?*
 - *Did you signal early in your message that solutions exist? Do the solutions “fit” the problem as defined?*
 - *Did you establish the cause of the problem, and did you assign responsibility? Reviewing your material, can you tell who created the problem and who should fix it?*
 - *Did you effectively put the problem in context, explaining long-term consequences, trends and opportunities to resolve the problem, so that your story is not episodic?*
 - *Did you anticipate and deflect the default frame? Did you avoid arguing with it directly and, instead, substitute a new frame?*
 - *Did you use credible and unlikely messengers? Are they likely to be perceived as overly vested in the issue or a sole solution?*
 - *Is your message strategically oriented to the intended audience, i.e. if addressing business leaders, did you frame your issue as appealing to managerial competence and responsibility?*
-

Chapter 9—Discussion and Conclusions

This historical case study of the Orphan Drug Act (ODA) explored two general questions: 1) what factors seem to promote or impede policy development; and, 2) how does issue framing support policy development? Factors that may have favored or impeded ODA policy change in the 1990s were proposed and evaluated. The literature on framing was reviewed to help evaluate how ODA reform stakeholders framed their arguments and to provide framing strategy guidance. The research provides many useful insights that may benefit policy stakeholders and academicians who want to better understand or influence public policy developments. At the same time, there are limits to how these research findings can be used.

This chapter discusses the opportunities and challenges of conducting this dissertation research and the future of ODA reforms.

Conducting Historical Case Study Research

Historical policy studies often inform what could or should be done in the future (George 2004, Hacker 2001, Schon and Rein 1994). But it is difficult to cull lessons from the past to predict or guide potential courses of action in the future. Although “history often repeats itself,” history is a natural experiment with a vast world that is complex, dynamic and often chaotic. Unlike experiments in physics, where variables can be isolated and manipulated in controlled conditions to determine their effect on some outcome, the interacting social systems of business, politics, and medicine are not amenable to reductionism, determinism and other tidy scientific principles. But, paraphrasing Voltaire, health policy students should not let the perfect

be the enemy of the good. Some understanding of what happened in the past and what might happen in the future is better than ignorance justified by futility.

One general approach that might be particularly useful in applying health policy lessons of the past to the future is scenario analysis. Scenarios could be constructed a number of ways and include scenarios that are based on extending trends that are already occurring, that use new paradigms for how people and things could interact in a system, or envision how the future might look if something unexpected might occur. Scenario analysis is useful to understand the range of possible futures, evaluate how one might influence or react to those possible futures, and become aware of the early signals that portend those futures.

Applying Theory to Policy Practice

This research began with an extensive review of framing and policy development theory. The literature on framing theory is vast, abstract, and buried within many related disciplines, e.g., psychology, sociology, political science, linguistics, philosophy, economics, and decision science. In order to evolve from a state of “eyes glazed over” to that of understanding, this researcher needed to 1) summarize the key points into a typology or guide (see Appendix B); 2) develop *a priori* hypotheses (e.g., see Table 2); 3) discover and review alternative methods for extracting frames, and select the one that seemed least problematic (see Chapter 4); and, 4) apply these concepts, hypotheses and methods to a real-world case.

Certainly, there are no guarantees that a theory will provide a more accurate analysis than research using no theory at all. But the benefits of using theory for research, especially dissertation research, seem to far outweigh the risks.

Moreover, “One simply cannot look for, and see, everything.” (Sabatier 1999 p. 4) A model elucidates the variables that will be explored, and provides focus to the inquiry and structure for the research findings. This can increase efficiency and prevent “boiling the ocean.”

That a model forces the researcher to make variables and assumptions explicit is also a benefit. However, there is a certain irony to using theory to structure a study that has a primary focus on framing. The conceptual model frames the research. Conceptual models, like issue frames, “are organizing principles that are socially shared and persistent over time that work symbolically to meaningfully structure the world” (Reese 2003). Frames can introduce certain biases into the research, and potentially blind the researcher to important data that fall outside the scope of the frame. At the same time, conceptual models urge the researcher to make his or her assumptions and focal points explicit, making the researcher more conscious of the limitations they place on the research.

But what if the model does not help explain the case? For example, some of the assumptions in the MS model did not seem to apply to development of the ODA in the early 1980s. The garbage can model (see Appendix A) did not seem to explain the problem and policy streams. The policy (the ODA) seemed to be directly linked and rationally developed as a way to solve a particular problem. The streams did not seem to be independent, nor were they chaotically and opportunistically linked to each other by “organized anarchies.” However, the MS model did help explain aspects of the 1990-1994 amendments. Private and public payers, as well as patients, were concerned about high drug prices specifically and healthcare costs generally. The debates over ODA reform seemed to morph into an airing of grievances over drug prices and high-cost treatments. Hence, the ODA reform debate seemed independent, but related, to the problem of health care costs.

Another challenge of the MS model is determining how to identify factors in the larger political, economic, social and technological environment that may have favored or impeded policy development. To get a sense of major events and trends, this researcher reviewed every December and January issue of *Time Magazine* that was published from 1980 to 2000 (covering

pre-ODA enactment to post-ODA reforms of 1990-1994). The December issues included a photographic “year in review,” and the January issue often included predictions and concerns about the year ahead. Though efficient, this was obviously a very limited historical review.

It is interesting to note that none of the informants interviewed for this research seemed to use a comprehensive theory¹⁷ to evaluate whether a proposed policy has what it takes to get successfully passed or adopted, or to evaluate what conditions should change to better ensure that a policy succeeds or fails. Comments about the idea of using theory included, 1) “I’m aware of different political science theories about policy development, but I’m not a political scientist and I don’t think about policies in that way.” 2) “No one knows why a policy succeeds or fails . . . (policy development) theories are for academics and pretty much useless;” 3) “You have to get enough votes in the Senate, that’s the most important thing;” and, 4) “The policy has to be workable. You have to be able to implement it.”

Finally, if the purpose of a doctorate is to take one’s capacity to think about complex issues to a new level, then theory-mediated dissertation research is very beneficial. It points to how malleable our views of the world are, and how we can break out of our usual ways of framing issues to generate novel, creative, and sometimes more compassionate insights.

Factors that may have Promoted or Impeded Policy Reform

From 1990 to 1994, several amendments to the ODA were attempted but failed to gain passage. Though several issues were addressed in these amendments, one reform issue dominated and was the focus of this study: the law was intended to provide government incentives for development of drugs that had low commercial potential (LCP). Pro-reformers thought the law should be amended to reduce support of high commercial potential (HCP)

¹⁷ Informants were asked, “Do you have a favorite theory that helps you evaluate whether a public policy will get passed or not. . . . or, perhaps, a checklist of important things that a policy must have in order to get passed?”

drugs. Anti-reformers thought the law was working well and that reforms to address this issue carried the risk of reducing the effectiveness of the law.

Arguments for reform seemed less developed and defensible.¹⁸ Anti-reformers also had many factors in their favor including: 1) the ODA was a popular, feel-good law that was considered a success; 2) anti-reformers had inertia on their side; 3) patient advocates didn't initially support ODA reform, and their later support may have been tepid; 4) the amendment's initial backers were a handful of companies that felt cheated by the law, and they were in zero-sum opposition with another handful of companies; 5) the proposed solution was difficult to administer; 6) the problem seemed amorphous;¹⁹ and, 7) what constituted a HCP drug, "excessive" profitability, and ill-intent in using the law was never defined or, even worse, feasibly definable.

The Future of ODA Reform

According to multiple sources, and based on a series of unsuccessful attempts in the 1990s, it is unlikely that attempts will be made in the near future to reform the ODA to better limit benefits of the law to low commercial potential drugs.

Patient advocates that were interviewed think the ODA is working well, and doesn't need to be amended. Moreover, amendments could have undesirable consequences. One informant commented, "If it ain't broke, don't fix it." Another said, "We don't want amendments (to the ODA). Amendments invite mischief. People try to Christmas tree their other issues on to amendments."

¹⁸ For example, patients wanted "something to be done" about the financial burden of orphan drugs, but "something" wasn't clearly articulated. Or, legislators urged amendments to the ODA that would solve the problem of excessive drug prices and profits, but the way in which this would be defined and measured was unclear.

¹⁹ For example, one definition of the problem in 1990 was that it was not fair that the ODA had created a situation where one company benefited from the ODA at the expense of another. Using the ODA to "block competitors" from entering a market was described as a problem. This seems like an amorphous problem because the market exclusivity provision, by definition, blocks competitors from entering a market.

Several informants believed the ODA amendments of the 1990s were about drug prices, not about high profits or sales. Some contended that high-priced orphan drugs like Ceredase are what brought so many to the table to discuss ODA reform in the 1990s. But, most informants thought that the issue of high-priced drugs is larger than prices of orphan drugs. Comments included, “Orphan drugs are not going to drive the discussion. The issue is bigger than that”; and, “It’s not that *orphan* drugs are expensive, *drugs* are expensive.”

One informant commented that pricing a drug at \$200,000 to \$1 million per year per patient is “unconscionable.” Another said, “There’s a sea of public hostility building toward pharma and biotech companies about their prices.” But, as an informant from a large health maintenance organization said, “drugs like Cerezyme that cost \$200,000 a year for a patient are irritating, but we only have 12 patients on it (out of 8 million HMO members), so it (pushing back on such prices) is not a high priority for us.”

Accusations that orphan drug sponsors “abused” the ODA market exclusivity provision to block competition, charge “unreasonable” prices, and generate “excessive” profits were frequently heard in during the ODA reform hearings from 1990 to 1994. It is interesting to note that these same accusations can be found in discussions about drug company practices outside of the realm of orphan drugs. Drug companies with patent protections that enable market exclusivity for their drugs have also been accused of abusing their patent rights to block competition, charge “unreasonable” prices, and generate “excessive” profits.

Evidence that would support the need for 1990s-like ODA reforms is mixed. In the 1990s, the rationale behind reducing the length or degree of market exclusivity was that this action would increase competition and lead to lower orphan drug prices. However, expiration of market exclusivity is not always followed by increases in competition and lower prices. For example, market exclusivity has expired for Cerezyme, an orphan drug that is frequently the

poster child of price “gouging.” Yet, Cerezyme remains the sole orphan drug for Gaucher’s disease and its price has remained high. (According to Anand (2005), Cerezyme can cost up to a million dollars per year per patient.) Biologics like Cerezyme are currently protected from competition because of the way that biologics are currently regulated.

Prices of many biologics, meaning drugs that are derived from living organisms, have been under particular scrutiny. Legislation to encourage generic versions of biologics that no longer have patent protection is under consideration. The FDA does not yet have a regulatory pathway to approve biologics that are therapeutically equivalent (“bio-generics” or “bio-similars”). Hence, makers of many biologic products continue to hold market monopolies. Because competition from generic drugs can have a significant effect on drug pricing, and many orphan drugs are biological²⁰, this legislation could help contain biologic drug prices and lessen the need for ODA reforms that try to contain orphan drug prices.

As health care costs continue to rise, there will be continued interest in developing public policies that promote health care cost containment. As demand for new, improved health technologies continues, demand for public policies that promote innovation will continue as well. According to Saloner and Ranji (2008), availability of more expensive, state-of-the-art drugs can fuel health care spending not only because the development costs of these products must be recouped by industry but also because they generate consumer demand for more intense, costly services even if they are not necessarily cost-effective. Simultaneous demand for policies that promote cost containment and innovation will likely create tensions and frame conflicts that were similar to that found in the ODA reform hearings of 1990-1994.

Patents, and other forms of market exclusivity, are seen as critical in promoting innovation in the pharmaceutical industry (Schacht and Thomas 2005). In 2003, the cost to

²⁰ According to Anand (2005), more than half of the drugs produced by biotechnology companies are orphan drugs.

bring a novel pharmaceutical product to market topped \$800 million (DiMasi et al 2003).

Patents and other exclusivity provisions better enable the inventor to recoup this expense.

Congress has supported patent and market exclusivity protections for pharmaceutical and biological therapies on numerous occasions in the past two decades. The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417), commonly known as the Hatch-Waxman Act, made it easier for generic copies of brand name drugs to gain FDA approval and enter the marketplace after the brand's patent expires. But, at the same time, the Act introduced several significant changes to patent laws in order to preserve investors' interests in drug R&D. These include methods for extending the term of a drug patent up to five years to reflect property rights lost during the long FDA review process. The Act also uses marketing exclusivity provisions to protect drugs from competition if, for example, the drugs are new chemical entities or are being clinically studied in new ways. Market exclusivity continues to be a popular tool for encouraging selective health interventions, i.e., several bills were recently introduced in Congress to provide additional patent protection or FDA-administered marketing exclusivities as a tool to encourage development of bioterrorism countermeasures (Schacht and Thomas 2006).

Informants believed that drug prices will continue to be an important political issue because prescription drugs are now covered under Medicare Part D, meaning the federal government is now an even larger payer of prescription drugs. Moreover, many believe the pressure for government to wield its purchasing power will grow as baby boomers age into Medicare, costs continue to rise, and Democrats increase power in Washington DC. Other policy means to moderate drug prices include increasing the use of "comparative effectiveness" evaluations in drug purchasing decisions, and, promoting re-importation of drugs from Canada and other countries that better negotiate lower drug prices.

The increased creation and promotion of Medication Assistance Programs (MAPs) or patient assistance programs appear to have taken some of the wind out of the 1990s ODA reform argument. Pro-reformers contended that high prices were affecting patients' ability to access orphan drugs. Many pharmaceutical companies administer, support, or donate to MAPs, and claim that no patient will go without one of their drugs for financial reasons. PhRMA offers a single point of access to public and private MAPs, as do many voluntary, non-profit organizations. According to PhRMA (2008), there are more than 475 public and private patient assistance programs, including more than 180 programs offered by pharmaceutical companies. MAPs are likely available for all or most orphan drugs.

Lifetime caps on insurance policies continue to challenge patients on expensive orphan drugs. According to NORD, a lifetime cap of \$1 million is sometimes inadequate for rare disease patients. The challenge of these caps is that they apply to the entire family, i.e., if medical costs for one family member exceed the policy's lifetime cap of \$1 million, then all family members become ineligible for medical coverage under the plan. The Health Insurance Coverage Protection Act, a bill that was recently introduced to Congress, proposes to phase in an increase in minimum lifetime caps in private insurance plans to \$10 million with an annual inflationary index thereafter.

Most sources seem to accept the idea that prices of drugs for small populations are expected to be higher than drugs used by large populations. As it seems the number of orphan drugs will only increase in the future, one can expect that concerns about orphan drug prices will grow accordingly. According to FDA, 325 orphan drugs were approved for marketing by May 2008, and approximately 1500 additional orphan drugs are in the development pipeline. Though millions of rare disease patients have been helped by these drugs, there are as many as 7000 different rare illnesses, so millions more are likely in need of more effective therapies.

Technological advances in genetics and drug discovery, as well as the trend toward personalized medicine, are likely to drive further increases in the number of future orphan drugs. Pharmacogenomics, the study of how variations in the human genome affect how individuals respond to drugs, will continue to enable development of drugs that are more targeted and better tailored to the genetic makeup of individuals. (Haffner 2002 and 2006, Loughnot 2005)

If a resurgence of interest in ODA reform were to occur, it is unclear who would drive this debate. In 2001, the Office of Inspector General conducted a survey of rare disease patient advocacy organizations and firms that were developing orphan drugs. The study concluded that these stakeholders were highly satisfied with the ODA and that no amendments were needed. Moreover, two informants thought ODA reform had its day in Congress, and that it would be difficult to get traction for future ODA reforms because of issue fatigue.

Appendix A: Decision-Making and Policy Development Paradigms

Eisenhardt and Zbaracki (2002) have characterized three strategic decision-making paradigms: 1) the cognitive paradigm, which assumes that decisions are information driven; 2) the politics and power model, which assumes that decisions are socially driven, and the 3) garbage can model, which assumes that decisions arise from a random confluence of events via organized anarchies. Many experts on policy analysis and political decision making refer to or invoke one or more of these paradigms in their writings (e.g., Allison and Zelikow 1999, Bardach 2005, Feldstein 2001, Feldstein 2003, Hendersen 2002, Kingdon 1995, Longest 2001, Longest 2002, Sabatier 1999, Shi 1997, Stone 2002, Veney and Kaluzny 1998, and, Weissert and Weissert 2002). Hence, a summary of these paradigms follows.

As mentioned in Chapter 1, a model related to the garbage can model was selected to guide portions of this research (the Multiple Streams Model by Kingdon 1995). In the final analysis of this research, this assumption was challenged, i.e., the question of whether the MS model seemed appropriate or useful for describing and predicting the outcomes of the Orphan Drug Act amendments was be addressed.

The Cognitive Paradigm

According to Eisenhardt and Zbaracki (2002), the cognitive paradigm of decision making assumes that decisions are made based on mental processing of information. This paradigm recognizes that decisions can be fully rational or boundedly rational. Fully rational decision making means that, given adequate time and resources, decision alternatives can be known and understood, and that a systematic process of evaluating the alternatives will point the way to the right decision. The rational model predicts that decision makers will know and/or understand the goal of the decision, then follow a sequential process that basically includes steps

to: 1) gather information, 2) develop a set of alternatives, and, 3) select from the alternatives based on some set of considerations and analyses.

Based on the work of Herbert Simon in the mid-20th century, Eisenhardt and Zbaracki also describe a less idealistic cognitive paradigm where decision making is boundedly rational. In this paradigm, decision making is still information-driven, rational and logical, but cognitive limitations of decision makers are assumed and acknowledged. Simon described people as partially or “boundedly” rational agents that experience limits in formulating and solving complex problems and in processing (receiving, storing, retrieving, transmitting) information. This view of decision making acknowledges that goals can be unknown, unclear and/or inconsistent across people and time, and goals and choices can be simultaneously discovered. The model predicts that: 1) decision-making processes may be haphazard, opportunistic, iterative and non-sequential; 2) actions may be dictated by what has been done in the past, rather than what should be done; and, 3) alternatives may be eliminated by objection one by one, rather than considered simultaneously, exhaustively and systematically. Complex and/or contentious decisions, threatening environments and high uncertainty can make decision making more boundedly rational.

The cognitive paradigm is reflected in, for example, Shi's (1997) description of policy analysis where a decision maker “lays out goals, identifies alternatives that can meet the goals, uses logical and rational processes to evaluate identified alternatives, and chooses the best or optimal way to reach the goals” (page 189). Shi acknowledges the bounds of rationality in the statement, “Policy analysis is typically performed with constraints on time, information, and resources.” Policy analysis is further described as a five-step framework that includes 1) establishing the context, 2) identifying the alternatives, 3) predicting the consequences, 4) valuing the outcomes, and 5) making a choice.

Bardach (2005) offers an eight-step framework for policy analysis that is also rooted in the cognitive paradigm. The eight steps in his framework are to 1) define the problem; 2) assemble some evidence; 3) construct the alternatives; 4) select the criteria; 5) project the outcomes; 6) confront the trade-offs; 7) decide; and, 8) tell your story. This is described as an iterative process.

The Bardach and Shi descriptions of policy analysis resemble an assembly line, invoking a machine metaphor with subassemblies, and inputs processed into outputs. In similar fashion, Longest (2001) describes the component parts of the policy making process in a machine-like model. The process is circular, where policy arises, if successful, out of the formulation and implementation phase. A policy modification phase ensues after stakeholders have had experience with the policy, or as conditions change. If policy change is needed or demanded, the process circles back to the formulation phase, and so forth.

The Politics and Power Paradigm

The politics and power paradigm of decision making assumes that organizations are political systems and that conflict is inherent in decision making (Eisenhardt and Zbaracki 2002). The paradigm implies that decisions are based on their anticipated social impacts, that goals are known and actions are calculated, and, that power prevails in decision making. War or sports metaphors are often invoked as decisions are portrayed as a conflict with winners and losers. This paradigm predicts that conflict will arise because of differing self-interests, assumptions and places in the power ladder; decisions will culminate from a process that involves people with conflicting interests and where the powerful triumph; and, in order to change the power structure in their favor, decision makers will engage in political tactics, e.g., coalition formation, cooptation and engagement of outside experts. One can view this paradigm in a negative light, i.e., that politics are dirty or bad, signal dysfunctional decision making, or, that politics are power

and conflict driven. In a positive or accepting light, political decision making can be seen as inherent to social interaction and that political maneuvering, such as advocacy and lobbying, can raise awareness, understanding and commitment to causes that can have broad public benefit.

Policy creation and evolution is prompted by changes in the macro-environment, such as political-legal, economic, socio-demographic and ecological or technical changes, and changes in what people want or demand. Longest (2002) invokes the politics and power paradigm of decision making in describing social demands. He describes a political marketplace where, using Feldstein's economic view (Feldstein 2001, 2003) there are demanders and suppliers of policies that seek to further their objectives. Power and influence are the models by which they accomplish their objectives. Influence in political markets is the process of persuading others to follow. Power is the potential to exert influence and can be mustered through legitimate means, as in having formal power or authority in a social system. Power can also be obtained through rewards, which can materialize in the form of political capital, e.g., favors that can be provided or exchanged, or influence that can be used now or at a later time. Coercive power is the flip side of reward power, where rewards are prevented or directly withheld. (Longest 2002)

The Garbage Can Paradigm

In the garbage can paradigm, decisions arise from a random confluence of events via organized anarchies (Eisenhardt and Zbaracki 2002). The garbage can model of organizational choice was first described by Cohen, March and Olsen (1972). Cohen et al described organized anarchies as organizations or decision situations that had three characteristics: 1) problematic preferences, where organizations have ill-defined and inconsistent preferences and a loose collection of ideas; 2) unclear technology, i.e., where the organizational processes are unclear to its members and where trial and error, learning from past accidents and pragmatic inventions based on necessity prevail; and, 3) fluid participation, meaning participants meander in and out

of decision situations or organizational activities, hence, the audiences and decision makers for any organizational choice change constantly and capriciously. Cohen et al posit that traditional decision making and management theories fail to work in situations where goals are unknown, processes (technologies) are hazy and participation is fluid.

In the garbage can model, decisions in an organization are made in a complex interplay of factors including: problems in the organization, deployment of personnel, the production of solutions and the opportunities for choices. Cohen et al state, “Although it may be convenient to imagine that choice opportunities lead first to the generation of decision alternatives, then to an examination of their consequences, then to an evaluation of those consequences in terms of objectives, and finally to a decision, this type of model is often a poor description of what actually happens. In contrast, a decision in the garbage can model is an outcome or interpretation of several relatively independent streams within an organization.” (Cohen et al 1972, p. 2)

Based on his research in health and transportation policy, Kingdon (1995) determined that the garbage can model best characterized public policy making in the 23 cases he studied. Kingdon also thought the federal government operated similarly to Cohen et al’s description of organized anarchies. In Kingdon’s “Multiple Streams” model of policy development, he adopted many of the features of Cohen et al’s garbage can model, i.e., that many conditions are ambiguous and that the meaning of solutions or problems can change over time; that solutions/choices search for a suitable problem; and that the amount of time participants have is a major constraint on where they focus their attention (“agenda setting”). Kingdon did change some of Cohen et al’s concepts. For example, rather than applying the model to an organization, Kingdon applied the garbage can model to policy actors that are not under one organizational

umbrella; and, Kingdon reduced and renamed some of Cohen et al's "streams"²¹.” Also, Kingdon introduced the idea of the policy entrepreneur into the MS model. While Cohen et al described different types of decision makers or structures, e.g., hierarchical, specialized and unsegmented, they did not discuss the notion of a single person, or small set of people, championing a choice and matching that to a problem and political/social situation. For a further description of Kingdon's MS model, see Chapter 1.

Hybrid Paradigms

Stone (2002) portrays policy development and decision making with elements of both the politics and power paradigm and the garbage can paradigm. As described by Stone and summarized in Table A1, the rational-analytic model fails to capture how decisions are analyzed and made in the “polis.” The polis is Stone's conception of society where problems and decision processes are ambiguous and strategically portrayed or manipulated by political actors. Stone asserts that the rational-analytic model of solving a problem by having explicit and consistent goals, and rationally evaluating many alternatives to achieve those goals, is not suitable for complex social issues that are to be addressed in political arenas. Instead, in Stone's polis model, goals are ambiguous and changing, and alternatives are purposely ignored and evaluated by criteria that favor the political actor's preferred solution.

²¹ In 1972, Cohen et al characterized and named four streams: 1) a stream of choices that contains choice opportunities, 2) a stream of problems, 3) a rate of flow of solutions, and 4) a stream of energy from participants. Kingdon reduced the four streams to three and modified their names slightly to: 1) a problem stream, 2) a policy stream, and 3) a politics stream. Kingdon then uses the concept of a window of opportunity for policy decisions in his model. This seems to replace Cohen et al's first stream, “a stream of choices.”

Table A1: Stone's Polis Model, A Hybrid Decision-Making Model

<i>Stages in Decision Process</i>	<i>Decision-Making Model in the Polis</i>	<i>Rational Decision Making Model</i>
<i>Define Goals</i>	<ul style="list-style-type: none"> Goals are stated ambiguously Some goals may be kept secret or hidden Goals may shift and be redefined as political situation dictates 	<ul style="list-style-type: none"> Goals are explicit and precise The same goal is used throughout the analysis
<i>Identify Alternatives</i>	<ul style="list-style-type: none"> Purposely keep undesirable alternatives from being considered Use rhetorical devices to blend alternatives and define them ambiguously to avoid triggering opposition 	<ul style="list-style-type: none"> Try to generate and imagine as many alternatives as possible Define each alternative clearly as a distinct course of action
<i>Evaluate Alternatives</i>	<ul style="list-style-type: none"> Make your preferred alternative seem most feasible or possible Selectively represent the costs and benefits of your preferred alternative 	<ul style="list-style-type: none"> Accurately and completely evaluate the costs and benefits of each alternative and course of action
<i>Decide</i>	<ul style="list-style-type: none"> Choose the course of action that hurts powerful interests the least Portray your decision as creating maximum social good for a broad public 	<ul style="list-style-type: none"> Choose the alternative that best meets your defined objectives/goals Choose the alternative that maximizes total welfare

Adapted from Stone, D. (2002). *Policy Paradox: The Art of Political Decision Making*. New York, NY: Norton, page 256

Appendix B: A Typology of Framing

*“Categorization is, in fact, the necessary condition of abstract thought and of the utilization of symbols.”
(Edelman 1993 p. 232, as quoted in Durham 2003 p. 125)*

Author	Phenomenon	Components
Entman 2007, 1993	How framing is defined esp. with regard to political communication and issue frames	The process of culling a few elements of perceived reality and assembling a narrative that highlights connections among them to promote a particular interpretation
Nelson (2003)	What types of frames there are	<ul style="list-style-type: none"> • Collective action frames • Decision frames • News frames • Issue frames
Entman (2007), Reese (2003), Goffman (1974), Snow et al. (1986)	How frames “organize” thinking	<ul style="list-style-type: none"> • Frames introduce or raise the salience of certain ideas, activating schemas that encourage target audiences to think, feel or decide in a particular way • People assimilate new information by fitting it into their existing way of viewing similar things. Goffman: frames interact with an individual’s “schemata of interpretation.” • Cognitive frames—invite us to think about social phenomena in a certain way, often by appealing to basic psychological biases (Reese) • Cultural frames—invite us to marshal a cultural understanding that is deeper, more persistent and extends past the immediate information. . . a broader way to account for social reality (Reese)
Entman (1993), Maher (2003) Van Gorp (2007)	Where frames are located in communications process	<ul style="list-style-type: none"> • Communicator (where frame is selected/sponsored) • Text (where frame is manifested) • Receiver (where frame is accepted, modified, rejected or ignored) • Culture (where enduring frames are generated, where the grand inventory of frames is located)
Gamson and Modigliani (1989), Fisher (1997)	How people understand issues	<ul style="list-style-type: none"> • People use cultural tools to make sense of both the original discourse and media translations of that discourse • Original discourse --produced by interested parties about a topic • Media—translates debates between proponents of different original discourses. Media are central in production of meaning as well as the place where social movements compete
Benford et al. (2000)	How communicators, receivers and culture interact to create meaning and frames	<ul style="list-style-type: none"> • Social groups consume existing cultural meanings and produce new meanings • Frame communicators and receivers interact • Receivers can affect the form and content of the message . . . Receivers can precipitate frame transformation
Entman (2007), Benford et al. (2000), Snow et al. (1986), Stone (2002)	Why political elites and social movement organizations (SMOs) use frames	<ul style="list-style-type: none"> • They care what people think because they want them to behave in ways that support, or at least tolerate, their activities • There are multiple ways of seeing a complex social issue. Politics is about controlling interpretation. Shared meanings motivate people to action

Author	Phenomenon	Components
Goffman (1974), Entman (2007, 1993), Maher (2003)	What frames do	<ul style="list-style-type: none"> • Frames enable individuals to “locate, perceive, identify and label” events and situations in their world • Fully developed frames function to: <ul style="list-style-type: none"> ◦ Define problems ◦ Diagnose causes ◦ Imply moral judgments ◦ Suggest solutions
Benford et al. (2000)	What tasks can be accomplished by which types of frames	<ul style="list-style-type: none"> • Diagnostic frames articulate cause or blame • Prognostic frames suggest solutions to problems • Motivational frames provide the rationale for action—severity, urgency, efficacy, propriety
Pan (2003)	How frames can be used strategically	<ul style="list-style-type: none"> • Promote configuration of social and political forces • Unify discursive community • Promote deliberative democracy • Promote political and discursive goals • Attract more supporters • Mobilize collective action • Expand actors’ realm of influence • Increase chances of winning
Snow et al. (1986)	To whom frames are intentionally or strategically targeted (esp. to promote social movements)	<ul style="list-style-type: none"> • Adherents • Constituents • Bystander publics • Media • Potential allies • Antagonists or Counter movements • Elite decisions-makers or Arbiters
Pan (2003)	What framing strategies to consider	<ul style="list-style-type: none"> • Which frame to sponsor • How to sponsor it • How to expand its appeal
Snow et al. (1986)	What factors influence social movement participation	<ul style="list-style-type: none"> • Contingent on frame alignment between individual and social movement organization (SMO) • Grievances • Four processes promote frame alignment (see below) • Frame alignment can be temporary because it is subject to reassessment and renegotiation • Frame alignment is a crucial aspect of adherent and constituent mobilization
Snow et al. (1986)	What processes promote frame alignment (thereby attracting social movement adherents)	<ul style="list-style-type: none"> • Frame bridging • Frame amplification • Frame extension • Frame transformation
Dorfman et al. (2005)	How advocates can influence issue interpretation	<p>Trigger frames that connect to values. Generate Level 1 messages that address “Why does it matter?”</p> <ul style="list-style-type: none"> • Level 1: expresses overarching values • Level 2: the general issue being addressed • Level 3: details of the issue <p>Emphasize the context:</p> <ul style="list-style-type: none"> • Context is in “landscape” messages • . . . not “portrait messages”

Author	Phenomenon	Components
Entman (1993, 2007), Snow et al. (1986) Lakoff (2004)	What proponents say about frame potency	<ul style="list-style-type: none"> • “the concept of framing consistently offers a way to describe the power of a communicating text” (Entman 1993, p. 51) • “Reframing <i>is</i> social change” (Lakoff 2004, p. xv) • “agenda setting, framing, and priming fit together as critical tools in the exercise of political power”. . . the “succinct definition of power is the ability to get others to do what one wants, ‘telling people what to think about’ is how one exerts political influence in non-coercive political systems” (Entman 2007) • The power of a given frame to attract & mobilize constituents is dependent on frame resonance
Pan (2003)	What increases the potency of frames	<ul style="list-style-type: none"> • Linkage with societal values • Cultural attributes of frames used • Symbolic devices used • Sociological: size & depth of web of subsidies • Linkage with news values in society • Adoption of frame in policymaking community
Van Gorp (2007)	What characterizes the potency of a frame	<ul style="list-style-type: none"> • Activates a schema with a single reference to it • Triggers a causal chain of reasoning devices • Stealth: Except for framing device, nothing is explicit in the text
Benford et al. (2000)	What characteristics a potent frame should have	<ul style="list-style-type: none"> • Broad in interpretive approach • Inclusive • Flexible • Culturally resonant, especially connecting to other historical movements (eg, gay rights, civil rights)
Benford et al. (2000)	What features characterize collective action frames	<ul style="list-style-type: none"> • Action-oriented core framing tasks • Interactive, discursive processes
Fisher (1997) referencing Triandafyllidou (1995)	What master frames are	<ul style="list-style-type: none"> • Higher-level deep structural frame that subsumes and shapes lower level deep structural frames
Benford et al. (2000)	What examples illustrate “master frames”	<ul style="list-style-type: none"> • Rights frames • Choice frames • Human injustice frames • Environmental justice frames • Sexual terrorism frames • Oppositional frames • Hegemonic frames • “Return to democracy” frame
Lau and Schlesinger (2005)	What dominant frames are used describing medicine and the role of government	<ul style="list-style-type: none"> • Health care as a societal right • Health care as a community obligation • Health care as an employer responsibility • Health care as a marketable commodity • Health care as a professional service

Author	Phenomenon	Components
Benford et al. (2000)	What factors influence frame credibility	<ul style="list-style-type: none"> • Frame consistency (congruence between beliefs, claims, actions) • Empirical consistency (fit between framing and observable/understandable evidence) • Credibility of the frame articulators or claimsmakers
Benford et al. (2000)	What factors influence frame salience	<ul style="list-style-type: none"> • Centrality (beliefs, values, ideas are central to targets of mobilization) • Experiential commensurability (congruent w/ personal, everyday experience of targets) • Narrative fidelity (resonate w/ cultural narratives or myths)
Benford et al. (2000)	What contextual constraints and facilitators affect frames	<ul style="list-style-type: none"> • Political opportunity—affected by cultural opportunity. Contingent on how they are framed • Cultural opportunity—extant stock of meanings, beliefs, ideologies, practices, values, myths, narratives, etc. • Audience effects—a dynamic interaction between social movement, frames and audience
Van Gorp (2007)	What frame breakthroughs do	<ul style="list-style-type: none"> • “ . . . sometimes, a kind of shock is required for the receiver to be able to break through a persistent frame” (p. 69)
Van Gorp (2007)	Why the notion of a cultural repertoire of frames is important	<ul style="list-style-type: none"> • # in repertoire > than # currently applied • Frames exist in culture and are persistent • Not the same as personal/individual mental structure (“schemata”) • Selected frame (in journalism) depends on media routines, organizational factors, external power forces . . . as well as frame sponsor influence
Van Gorp (2007)	What constituent elements are in a frame package	<ul style="list-style-type: none"> • Manifest framing devices—words, metaphors, exemplars, descriptions, arguments, visual images that point at the same core idea • Manifest or latent reasoning devices—explicit and implicit statements that deal with justifications, causes and consequences in a temporal order • Implicit cultural phenomenon that displays the package as a whole—meta-communication, ties into shared cultural phenomena • All elements need not be present in text
Van Gorp (2007)	How frames embedded in text can be reconstructed	<ul style="list-style-type: none"> • Inductively construct an inventory of frames based on media content, public discourse, literature review • List framing and reasoning devices that are most indicative of the identified frames (matrix: rows are the frames, columns are the devices) • Deductively determine to what extent these framing devices are present in the complete data set

Author	Phenomenon	Components
Van Gorp (2007), Fisher (1997), Nelson and Willey (2003)	What limits and challenges framing research	<ul style="list-style-type: none"> • Labor intensive • No guaranteed yield • Researcher subjectivity is inevitable • Frames are not literally outlined in the text • Frames lack fixed and quantifiable markers <ul style="list-style-type: none"> ◦ Cannot identify frames by counting key words or phrases, or specific argumentative structures • Just one frame element in the text can be enough to suggest or recall the whole set of elements <ul style="list-style-type: none"> ◦ one part can stand for the whole • May need to be a member of the culture to find the storylines that characterize cultural frames • Frames are slippery and hard to measure
deLeon (1998)	What approach to policy analysis makes sense	<ul style="list-style-type: none"> • Positivistic—disaggregates, produces predictions, more empirical, feeble with “wicked” problems • Post-positivistic—views holistically, produces understanding and insights, more normative
McLeod (2003)	How frame analysis should be done methodologically	<ul style="list-style-type: none"> • Prepare: Read widely among ideologically divergent sources to gain awareness of an array of potential frames for the topic under study • Develop Frame Models: Develop preliminary models of frames and sub-frames (the more, the better) • Analysis: Match frames to sponsor groups, sensitize yourself to symbolic representations, develop hypotheses of relationships among frames, ideologies, narrative structures • Methods: Identify methods appropriate to studying frames in the context of selected topic
Tankard (2003)	How frame construction can be done with a list of frames approach	<ul style="list-style-type: none"> • To determine how an issue or event is portrayed (in the news) • Attempts to be precise about frame definitions and systematic about procedures used in identifying frames • More systematic than quantitative • Assumes there are defining characteristics of media frames and that different observers/coders can recognize and agree upon them • How to: <ul style="list-style-type: none"> ◦ Identify a list of frames for the particular domain of interest ◦ Specify keywords, catchphrases and images that will help detect each frame ◦ Identify frames in a content analysis
Tankard (2003)	How inter-coder reliability can be achieved	<ul style="list-style-type: none"> • Collapse frame categories into 2, e.g., those pro and those con • Narrow the conception of framing to one dimension, such as causation

Author	Phenomenon	Components
Schon and Rein (1994)	How policy controversy can be addressed	<ul style="list-style-type: none"> Continuation or escalation—improve strategies for attack or defense Marketing strategy—better understand wants and needs of object and reshape policy object to better meet needs, wants Negotiation—find a compromise; convert win-lose to win-win by finding situations of joint gain Co-design—cooperative policy design (requires frame reflection)
Schon and Rein (1994)	How a “policy ladder” can help us see the hierarchy of frame concepts	<ol style="list-style-type: none"> 1. Policy practices—regulation, screening, verification 2. Policy object—set of rules, laws, prohibitions, entitlements, resources allocations 3. Policy-making process—includes its debates and struggles 4. Policy frames—positions and arguments used by advocates and opponents; pertains to specific policy issue 5. Institutional action frames—values, perspectives held by particular institutions and interest groups; #4 derived from these 6. Meta-cultural frames—broadly shared beliefs, values and perspectives among societal members; #5 derived from these
Schon and Rein (1994)	How meta-cultural frames can be understood	<ul style="list-style-type: none"> Action frames can be mapped to these Examples w/ typical responses: <ul style="list-style-type: none"> Market frame—when market fails, state should restore the market Social welfare frame—when market fails, state has obligation to help people in need; individuals are just the starting point for understanding the problem Social control frame—society must protect itself against criminals etc./ social problem defined in terms of problem people (victimizers)
Schon and Rein (1994)	How frame reflection should be done	<ul style="list-style-type: none"> Recognize discrepant frames from which conflicting policy positions arise Subject them to critical reflection

Author	Phenomenon	Components
Stone (2002)	What the typical policy argument entails	<ul style="list-style-type: none"> • Goals, problems and solutions • Each construction is often politically constructed and invokes a different set of rules
Stone (2002)	What the generic goals are in policy making	<ul style="list-style-type: none"> • Equity—everyone gets the same; distributive justice <ul style="list-style-type: none"> ◦ Recipients—who is everyone? Distribute by membership, rank, group? ◦ Items—what is the division? Divide by boundary of item, value of item? ◦ Process—how to divide? Divide by competition, lottery, or voting? • Efficiency—getting the most out of a given input <ul style="list-style-type: none"> ◦ Who gets the benefits and bears the burdens of a policy? ◦ How should we measure the values and costs of a policy? • Security—Minimum requirements for biological survival <ul style="list-style-type: none"> ◦ Valuation—how to assess need; by satisfaction derived or material value? ◦ Standards—how to measure need; by a fixed or relative standard? ◦ Purpose—for immediate survival or higher purpose? ◦ Time—for current needs or needs in the future? ◦ Unit of analysis—needs of individuals or needs of people in relation to society • Liberty—People free to do what they want as long as no harm is done <ul style="list-style-type: none"> ◦ Defining harm to individual—material, risk, aesthetic, emotional/psychological, spiritual/moral ◦ Defining harm to group/community—structural/capacity, accumulative, extent (harm to 1 or all), harm by omission ◦ Whose liberty should be curtailed
Stone (2002)	How policy problems can be defined or portrayed	<ul style="list-style-type: none"> • Symbols • Numbers • Causes • Interests • Decisions
Stone (2002)	What generic strategies can be used in policy solutions	<ul style="list-style-type: none"> • Inducements • Rules • Facts • Rights • Powers

Appendix C: Data Collection and Analysis for Each Aim

As mentioned in Chapter 4, the research had four aims and the data collection and analysis process varied from aim to aim.

To recap, the following data collection instruments were used for each aim. Aim 1 used an outline; Aim 2 used a Microsoft Excel spreadsheet and iterative memos; and, Aim 3 used an interview guide. These are shown in the following pages. More information on data sourcing, collection and analysis is also presented in this Appendix.

Data Collection and Analysis for Aim 1

To provide a history and overview of the Orphan Drug Act of 1983 (ODA), an outline of key elements was developed and used as the data collection instrument. Though not typically considered a “data collection instrument,” the outline did serve as a reminder of what data needed to be collected to complete the aim. As data were discovered and analyzed, each section of the outline was completed.

A summarized version of the outline is shown below.

1. Summary and Overview of the Orphan Drug Act of 1983
2. Early history of ODA—Leading up to Enactment
3. Evolution of ODA post-enactment
4. Unintended Effects of ODA (focusing on the issue that incentives were intended for drugs of limited commercial value)

Aim 1 data included peer-reviewed articles, articles found in the general and business press, government documents and reports, and information found on key stakeholder websites. In mid-2006, a comprehensive search for literature regarding the ODA’s history and evolution was conducted. This search yielded 79 articles. Between mid-2006 and 2008, articles and other

gray literature reports were added to this initial base of 79 articles if they provided new information. The mid-2006 literature search method will now be described.

2006 Literature Search Methods

The first step of this review was to identify a set of peer-reviewed articles, from a credible health science database, that contained a discussion of ODA problems. These articles formed the initial core of the review. From this core, additional articles were added to help explain and verify points made in the core articles. The core articles were identified via an electronic database search of PubMed. Additional articles were identified via the literature review method known as snowball sampling. This sampling technique is like a chain reaction, in that one article leads to another. Leads to additional articles were primarily derived by reviewing references in articles and reviewing those references for relevance to the study.

PubMed Search for the Core Articles

PubMed includes over 16 million citations from MEDLINE and other life science journals for biomedical articles dating back to the 1950s.

After considerable experimentation with search terms, Medical Subject Headings (MeSH) were found to be most efficient and effective. The MeSH term “Orphan Drug Production” was used in the PubMed search. This term is defined as “production of drugs or biologicals which are unlikely to be manufactured by private industry unless special incentives are provided by others.” The MeSH search was restricted in 3 ways: 1) By using Limits that restricted the output to publications written in English and publications that were dated from 1980 to 2006 (including commentary just prior to ODA enactment to the present); 2) By restricting the search to Major Topic Headings Only; and, 3) By limiting the MeSH search to

selected Orphan Drug Production subheadings. Subheadings were “economics,” “legislation and jurisprudence,” and, “ethics.”

Of the 110 article summaries retrieved using this PubMed search, 39 articles were included in this literature review. Included articles had to address the history and outcomes of the ODA, or include a discussion of needed modifications or shortcomings, and, focus on orphan drugs over other orphan products, focus on the U.S. over other countries, and be published in English between 1980 and 2006, inclusive. All titles of the 110 articles were reviewed and, when available, all abstracts were reviewed. Approximately 50 articles were targeted for inclusion in the literature review. For each of these 50 articles, full content was subsequently obtained and reviewed. Eleven of the 50 articles were then found to be off the mark, leaving the 39 final PubMed articles.

Factiva Database Search

Factiva provides tools for searching and monitoring general news and company, industry, and other business information. Factiva content is drawn from more than 10,000 sources from 152 countries in 22 languages, including more than 120 continuously updated newswires. The aim of using Factiva was to do a check to make sure that the PubMed articles adequately covered issues of interest (e.g., history and outcomes of the ODA, or discussions of needed modifications or shortcomings). Articles included from the Factiva search were provided only if they included new information. In other words, Factiva articles complemented the core PubMed articles. The Factiva search was not restricted by date of publication, but was restricted to articles that were published in English.

The “More Like This” search feature in Factiva had the highest yield of articles that met the inclusion criteria. A 2006 article by Haffner seemed most representative of the desired articles so the “More Like This” link was used to find Factiva articles like the Haffner article. In

Factiva, the More Like This link selected keywords from the headline and lead sentences of the Haffner article. These terms were then connected by the "OR" operator to run a new search. A More Like This search was also conducted using an article that discussed how Orphan Drug costs were straining budgets. As the most relevant documents are presented first in a More Like This search, only the first 50 documents in each of these two searches (a total of 100 articles) were read by this researcher. Approximately 10 articles were duplicates from the PubMed search. Duplicates from each of the two Factiva searches were also eliminated. Ten new articles met the Factiva inclusion criteria and were included in this review.

Snowball Search

The references in nearly all 39 PubMed-found articles were reviewed for leads to articles that would provide broader context or explain concepts addressed in the PubMed articles. From this approach, 15 articles were added to the literature database.

Personal Knowledge

Fifteen articles were discovered by means other than the above—mainly through this researcher's prior knowledge of the article. For example, this researcher had prior knowledge of five 2005 articles from a Wall Street Journal series on specialty drugs (four articles by Anand 2005 and one by Horowitz 2005). Four of these articles did not appear in the Factiva search, but were included in the 2006 literature review because they contained relevant information about development of drugs for rare diseases.

This researcher also had previous knowledge of a number of relevant articles based on her extensive experience in the pharmaceutical and biotech industries and previous graduate public health coursework. Included articles addressed drug patents (Barton et al 2005), drug pricing (Gregson et al 2005 and Arnst 2006), drug sales revenues (Grabowski and Vernon 2000),

drug company ethics (Hatch 2003), and drug research and development costs (Cockburn 2004 and DiMasi et al 2003). Also, this researcher discovered an Office of the Inspector General report (2001) during a search for government studies on orphan drugs. The report was found via a Google search. This particular report was not cited in the PubMed search.

Literature Search Results

A summary of the results from this initial 2006 literature search is shown in Table C2. An annotated bibliography of the 79 articles can be found under separate cover.

Results of 2006 Literature Search:

Total Number of Articles Found (Hits) vs. Total Number of Articles Included

<i>Strategy</i>	<i>Total Number of Hits</i>	<i>Number Included</i>
<i><u>1--Electronic Databases</u></i>	<i><u>210</u></i>	<i><u>49</u></i>
<i>PubMed</i>	110	39
<i>Factiva</i>	100*	10
<i>2--Snowball Method</i>	n/a	15
<i>3--Personal Knowledge</i>	n/a	15
<i>TOTAL</i>		<i>79</i>

*(1st 50 articles in each of two searches)

Characteristics of the 2006 Literature Search Articles

Most of the 79 articles could be characterized as narrative reviews or opinion pieces regarding the ODA and related issues. The data to support expressed opinions were typically in the form of single case descriptions or single scenarios. The history of ODA and related events were often described in the articles, along with selected contextual factors. Supporting data were typically derived from informant interviews, legislative and regulatory publications, corporate records and a variety of other sources.

Cross-sectional data were also used to support claims in the articles. The latest FDA data on the number of orphan drugs approved and the number in development were most often quoted. The latest FDA count of orphan drugs was usually compared to the pre-1983 count to support the claim of ODA success in spurring industry development of orphan drugs. Other cross-sectional data included prevalence counts of selected rare diseases and conditions, and dollar revenue and pricing data on selected drugs.

Data Collection and Analysis for Aim 2-Step 1

To investigate issue frames used in the ODA amendment hearings from 1990-1994, data were collected in accordance with the following variable and coding descriptions. Data were recorded in a Microsoft Excel spreadsheet.

Data Collection and Classification

Variable	Description	Coding Categories
Speaker	What is the name of the speaker?	Open code: insert speaker's name
Organization	What is the name of speaker's organization?	Open code: insert organization name
Authority	In whose name are statements made?	Industry, Public, Patients/family, Government, Payers, Academia/Research, Other (specify)
Subject	What is the testimony about, i.e., which bill in Congress?	H.R. 4638, S. 2576, S. 2060, H.R. 4959, H.R. 3930, H.R. 4160, H.R. 4865
Valence	How is the subject treated?	Positive/supportive; Negative/opposed; both; neither
Rationale	What is rationale for valence?	Open code: insert verbatim excerpt
Evidence	What evidence is presented to support the speaker's position?	Open code: insert verbatim excerpt
Values	What values, goals, or wants are revealed in rationale?	Equity, Efficiency, Security, Liberty, other (specify)
Values Verbatim	What leads the coder to conclude the basis for "Values" coding?	Open code: insert verbatim excerpt or insert coder explanation
Level 1 Problem	Why does speaker's position matter? What problem(s) is to be solved by support or opposition to amendment? (implied or stated)	Open code: if problem is implied, coder to insert implication. If problem is stated, coder to insert verbatim comment
Cause	What is the cause of the problem to be solved—that is implied or stated?	Open code: if cause is implied, coder to insert implication. If cause is stated, coder to insert verbatim comment
Rules	What rules or belief system would be used to solve the problem?	Ethical/moral, economic, legal, clinical/medical, other
Rules Verbatim	What leads the coder to conclude the basis for "Rules" coding?	Open code: insert verbatim excerpt
Remedy	What remedy to the problem does the speaker suggest? (implied or stated)	Open code: if remedy is implied, coder to insert implication. If remedy is stated, coder to insert verbatim comment
Metaphors	Does the speaker use metaphors to explain phenomena? Specify.	Open code up to 5 metaphors
Categories	Does the speaker use categories to explain phenomena? Specify.	Open code up to 5 categories

The codebook that guided data entry for selected items in Aim 3—Step 1 follows.

Data Collection Codebook

Variable	Coding Categories	Specifications
Speaker	Open code: insert speaker's name	Column 1: Assign ID# starting with 001 Column 2: Input last name Column 3: Input first name
Organization	Open code: insert organization name	Column 4: Input org name Column 5: Input department name if applicable
Authority	Industry, Public, Patients/family, Government, Payers, Academia/Research, Other (specify)	Column 6: Industry, i.e., pharmaceutical or biotechnology firms or industry group (e.g., PhRMA, BIO) representatives Public, i.e., all Americans Patients/Family, i.e., individuals directly affected by rare health conditions Government, i.e., Executive, Legislative, Judicial branches, federal, state or local Payers, i.e., 3 rd party that pays for medications on behalf of patients such as Insurance companies, managed care organizations, employers, Medicare, Medicaid Academic/Research, i.e., organizations that study the ODA to inform decisions or devise policies (include GAO or OMB here?) Other Column 7: Specify "other"
Subject	H.R. 4638, S. 2576, S. 2060, H.R. 4959, H.R. 3930, H.R. 4160, H.R. 4865	Column 8: Input Bill #
Valence	Positive/supportive; Negative/opposed; both; neither	Column 9
Rationale	Open code: insert verbatim excerpt	Column 10
Evidence	Open code: insert verbatim excerpt	Column 11
Values	Equity, Efficiency, Security, Liberty, other (specify) See definitions from Stone (2002)	Column 12 Column 13 (specify "other")
Values Verbatim	Open code: insert verbatim excerpt or insert coder explanation	Column 14
Level 1 Problem	Open code: if problem is implied, coder to insert implication. If problem is stated, coder to insert verbatim comment	Column 15
Cause	Open code: if cause is implied, coder to insert implication. If cause is stated, coder to insert verbatim comment	Column 16
Rules	Ethical/moral, economic, legal, clinical/medical, other	Column 17 Column 18 (specify "other")

Data Collection Codebook (continued)

Variable	Coding Categories	Specifications
Rules Verbatim	Open code: insert verbatim excerpt	Column 19
Remedy	Open code: if remedy is implied, coder to insert implication. If remedy is stated, coder to insert verbatim comment	Column 20
Metaphors	Open code up to 5 metaphors	Columns 21-25
Categories	Open code up to 5 categories	Column 26-30

Examples of five coded testimonies are shown on the following two pages. Note that not all sought after data points were included in every witness statement. For example, some witnesses made claims but did not provide evidence to support these claims. In this case, no data were entered in the cell for “evidence.” Or, only a few witnesses used a metaphor in their statement. When metaphors were used, the metaphor was input into its designated cell. If a metaphor was not used in the witness’s statement, the cell was left blank.

The name, organization, and subject of the testimony associated with each of the four example witnesses are described below.

1. James Benson, Acting Commissioner of FDA, HR 4638
2. Tom Wiggans, President Serono Labs, S 2060
3. Herb Jacobsen, Representing self (personal situation), S 2060
4. Abbey Meyers, President NORD, S 2060
5. Tom Wiggans, President of BIO, HR 416

Example Testimony as Coded Per Data Collection Specification for Aim 2-Step 1

ID	Valence	Rationale	Evidence	Values	Values Quote
1	Con	ODA has worked well to accomplish its objectives; any change to the law (eg. exclusivity) would likely make the law less effective which would hurt pts	The reasons for changing from profitability to prevalence standard in the 1985 ODA amendment were b/c the profitability standard didn't work. . . Current standard works-based on # of drugs developed	Efficiency, security	Efficiency: Prevalence standard better than profitability standard in producing desired results. No program eligibility standard will be 100% effective. Security: change in ODA could deprive patients of desperately needed therapies
2	Pro	ODA shouldn't apply to hgh	hgh already available before ODA, 5 companies were developing rHGH before ODA, hgh has always been commercially viable, the 85 ODA amendment changed rules of game for firms that had already invested in hgh	efficiency, equity	"the rules shouldn't be changed in midstream"
3	Pro	high cost of Ceredase due to lack of competition	Genzyme's pricing and the burden of paying for Ceredase	efficiency, security, equity	pts being victimized, assaulted by the deadliest weapon in this era, unbridled greed
4	Pro	"Ceredase is the Orphan Drug that broke the camel's back"	High prices of ODs as examples of unscrupulous companies	security, liberty, equity	pts need Congress's protection from unscrupulous companies who charge beyond what the market can bear
5	Pro	Put an end to controversy, provide greater certainty for industry to make investment decisions re: ODs	Congress has threatened amendments for several years. Uncertainty is compounded by proposed health care reforms--later mentions support for "joint development" amendment will "make sure it is not a winner-take-all game any more"	security, liberty	

Example Testimony as Coded Per Data Collection Specification for Aim 2-Step 1 (continued)

ID	Lev1 Problem	Cause	Rules	Rules Quote	Remedy	Metaphors
1	(there is no problem) OD therapies are desperately needed by pts, the more that get Rx, the better; pt needs outweigh risk of changing a law that works pretty well	If law is changed, pts may get fewer Ods	Legal, economic, medical	Legal: law creates inducements which work well; economic: altering exclusivity could lower firms' profit potential and decrease OD development; medical: pts need help	leave ODA alone	n/a
2	ODA blocked Serono from market causing them to lose money	rules were changed for hgh mfrs	Legal, economic, medical	GNE's exclusivity is an abuse of the law, "a billion dollar drug is no orphan".....let competition work where it was intended to work, eliminate this blatant circumvention of Congressional intent.. The ODA was enacted by Congress to help pts, not companies	change rules so that they are fair	"if Protropin is an 'orphan drug', it has found its Daddy Warbucks."
3	not fair, pts in desperate need	"given them a monopoly w/ no accountability" "incredible abuse of sick and defenseless human beings"	Economic, legal, moral	give it a dose of medicine--the free enterprise system, competition	legislation	victims, assault by pharma
4	unfair, companies "feed on the desperation of families"	Unscrup-ulous companies	Economic, legal, moral	"only the rich will live and the poor will die"	Congress needs to take responsibility for rare disease pts "our lives are in your hands"	"feed on desperation" parasite
5	Uncertainty	Congressional threats compounded by health reform debate, lack of compromise solution to ODA amendments	Legal, economic	n/a	n/a	game

Data Collection and Analysis for Aim 2-Step 2

In this step, frames were constructed from Step 1 data using a process called memoing.

“A memo is the theorizing write up of ideas about codes and their relationships as they strike the analyst while coding . . . it can be a sentence, a paragraph or a few pages . . . it exhausts the analyst’s momentary ideation based on data with perhaps a little conceptual elaboration. . .”

(Miles and Huberman 1994 p. 72, quoting Glaser 1978). In the proposal stage of this research, it was thought that the researcher would simply begin writing a memo for each frame. It was proposed that a reminder of what the researcher should look for be written at the top of the memo as shown below.

<p style="text-align: center;">Frame Construction Memo</p> <p><i>Objective:</i> To construct a frame from the Congressional Testimony</p> <p><i>Reminder:</i> Frames are <u>organizing principles</u> that are socially shared and persistent over time that <u>work symbolically</u> to <u>meaningfully structure</u> the world (Reese 2003). To frame is to “select some aspects of a perceived reality and make them more salient in a communicating text, in such a way as to promote a particular <u>problem definition</u>, <u>causal interpretation</u>, <u>moral evaluation</u>, and/or <u>treatment recommendation</u> for the item described” (Entman 1993, p. 52).</p>
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However, the memoing process for this research was much less structured. As Miles and Huberman suggest, the memoing process began as a loose collection of notes that were made during the process of coding the Congressional testimony. However, once the coding was

completed, this researcher still had not formulated the idea that there were X frames and, therefore, X memos needed to be written. Instead, the researcher began her seven-day journey of constructing frames with no particular frames in mind at all.

Much of the first and second day of the 7-day frame construction process were spent reviewing framing fundamentals and exploring basic questions such as “what is a frame,” “what does it look like,” and, “what clues should I use to find it?” Appendix B and Chapter 3 were reviewed, and selected books and articles were reread. In the first day or two, the researcher attempted to use some of the coding categories to create frames. For example, the idea of using Stone’s (2002) 4 categories of values or goals was explored, meaning, the idea of creating a “security frame”, a “liberty frame,” an “equity frame,” and an “efficiency frame” was explored. Other explorations included constructing frames from the metaphors that were mentioned in the testimony, or constructing frames from the coded “rules” categories (e.g., constructing legal, moral, and economic frames). The ideas of constructing frames based on stakeholder groups, or based on whether witnesses emphasized the ODA reform process, structure or outcomes were also explored.

Frames began to emerge in day 2 or 3 when the researcher used the latter part of Nelson and Willey’s (2003) definition of an issue frame, i.e., descriptions of social policies and problems that shape understanding of how the problem came to be and the important criteria by which policy solutions should be evaluated. In various Congressional testimonies, witnesses made assertions about how proposed ODA reform should be judged. A list of these assertions was made and elements of their arguments were noted. These were put into a matrix, similar to one that Van Gorp (2007) has described. Frames were put into the columns of the matrix and “framing and reasoning devices” (Van Gorp 2007) were put into the rows. Four frames had

emerged by day 4, and days 4 through 7 were spent revising the frame matrix, which is now Table 10, until no other revisions seemed necessary or compelling.

The frame construction process was done by a single researcher without input from others. The frames were informally tested out in the informant interviews (Aim 3), when different positions on ODA reform were discussed and evaluated. The frames seemed to help “organize and structure” (Reese 2003) arguments for and against ODA reform, and were not edited at all until this dissertation was reviewed by this researcher’s dissertation committee members. In response to committee suggestion, the frame names were edited slightly and an error in logic on the Congressional Action frame was corrected.

Committee members agreed with the researcher’s contention that frames constructed from the Congressional testimony would likely differ from researcher to researcher. But as agreed to in the proposal stage of this dissertation research, an information-rich frame construction method that might have poor inter-coder reliability was chosen over one that might yield frames with good inter-coder reliability but limited usefulness.

Data Collection Instrument for Aim 3

To investigate ODA amendment failure from 1990-1994, an interview guide was developed and used as the data collection instrument during one-on-one telephone interviews with 10 informants. The following preliminary interview guide was customized for each interview:

1. How have you been involved in the Orphan Drug Act of 1983 (ODA)?
 - a. When were you involved?
 - b. What was your role?
 - c. What was your affiliation?
2. What did you think of the 1990-1994 amendments . . . did events unfold as you expected? Why/Why not? (This is a “warm-up” question and is purposely open-ended.)
3. What factors may have impeded ODA reforms that were proposed from 1990-1994?
 - a. Use Table 2 to develop probes (e.g., whether there were problem definition, policy, or political issues that impeded reform)
4. What are your thoughts about the future of the issue these amendments attempted to address (i.e., use of incentives for high-commercial-potential drugs)?
 - a. Probes: Is this issue being addressed now? Or, since 1994?
 - b. Probes: What would you like to see happen with regard to this issue?
 - i. Do something . . . what? Why?
 - ii. Do nothing . . . why?
5. Do you have a favorite theory about why some public policies get approved and others don't? Or, perhaps, a checklist of important things a public policy must have in order to get approved?

Appendix D: Informant Correspondence

At the end of October 2008, a letter or email with the following information was sent to a list of 16 potential informants. Ten interviews were completed during the month of November 2008.

Dear X:

I would like to conduct a 20-30 minute phone interview with you as part of my doctoral dissertation research. I am interested in hearing your perspectives on the Orphan Drug Act, a public law that encourages development of drugs for individuals with rare diseases and conditions. I am particularly interested in issues that prompted amendment attempts in the 1990s, and why the attempts were not successful.

My dissertation, The Orphan Drug Act of 1983: A Case Study of Issue Framing and the Failure to Effect Policy Change from 1990-1994, is being completed as part of the health policy and management doctoral program in the School of Public Health, University of North Carolina, Chapel Hill.

Please let me know a good time to call you at your earliest convenience. I would greatly appreciate it.

By the way, your answers and comments would remain confidential and anonymous, and I would not audio record the interview.

Thank you in advance for your help.

Sincerely,

Lynn Redington, MPH, MBA, DrPH Candidate
(contact information was provided)

Appendix E: The Orphan Drug Act (as amended)

The text of the current law is included below. This was accessed and copied September 10, 2007 from <http://www.fda.gov/orphan/oda.htm>

CONGRESSIONAL FINDINGS FOR THE ORPHAN DRUG ACT

The Congress finds that---

- (1) there are many diseases and conditions, such as Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy which affect such small numbers of individuals residing in the United States that the diseases and conditions are considered rare in the United States;
- (2) adequate drugs for many of such diseases and conditions have not been developed;
- (3) drugs for these diseases and conditions are commonly referred to as "orphan drugs";
- (4) because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss;
- (5) there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and
- (6) it is in the public interest to provide such changes and incentives for the development of orphan drugs.

RECOMMENDATIONS FOR INVESTIGATIONS OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 525 [360aa].

(a) The sponsor of a drug for a disease or condition which is rare in the States may request the Secretary to provide written recommendations for the nonclinical and clinical investigations which must be conducted with the drug before---

- (1) it may be approved for such disease or condition under section 505,
- (2) if the drug is an antibiotic, it may be certified for such disease or condition under section 507, or

(3) if the drug is a biological product, it may be licensed for such disease or condition under section 351 of the Public Health Service Act.

If the Secretary has reason to believe that a drug for which a request is made under this section is a drug for a disease or condition which is rare in the States, the Secretary shall provide the person making the request written recommendations for the nonclinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request under this section, would be necessary for approval of such drug for such disease or condition under section 505, certification of such drug for such disease or condition under section 507, or licensing of such drug for such disease or condition under section 351 of the Public Health Service Act.

1. The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

DESIGNATION OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 526 [360bb]. (a)(1) The manufacturer or the sponsor of a drug may request the Secretary to designate the drug as a drug for a rare disease or condition. A request for designation of a drug shall be made before the submission of an application under section 505(b) for the drug, the submission of an application for certification of the drug under section 507, or the submission of an application for licensing of the drug under section 351 of the Public Health Service Act. If the Secretary finds that a drug for which a request is submitted under this subsection is being or will be investigated for a rare disease or condition and---

(A) if an application for such drug is approved under section 505,

(B) if a certification for such drug is issued under section 507, or

(C) if a license for such drug is issued under section 351 of the Public Health Service Act, the approval, certification, or license would be for use for such disease or condition, the Secretary shall designate the drug as a drug for such disease or condition. A request for a designation of a drug under this subsection shall contain the consent of the applicant to notice being given by the Secretary under subsection (b) respecting the designation of the drug.

(2) For purposes of paragraph (1), the term "rare disease or condition" means any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made.

(b) A designation of a drug under subsection (a) shall be subject to the condition that---

(1) if an application was approved for the drug under section 505(b), a certificate was issued for the drug under section 507, or a license was issued for the drug under section 351 of the Public Health Service Act, the manufacturer of the drug will notify the Secretary of any discontinuance of the production of the drug at least one year before discontinuance, and

(2) if an application has not been approved for the drug under section 505(b), a certificate has not been issued for the drug under section 507, or a license has not been issued for the drug under section 351 of the Public Health Service Act and if preclinical investigations or investigations under section 505(i) are being conducted with the drug, the manufacturer or sponsor of the drug will notify the Secretary of any decision to discontinue active pursuit of approval of an application under section 505(b), approval of an application for certification under section 507, or approval of a license under section 351 of the Public Health Service Act.

(c) Notice respecting the designation of a drug under subsection (a) shall be made available to the public.

(d) The Secretary shall by regulation promulgate procedures for the implementation of subsection (a).

PROTECTION FOR DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 527 [360cc]. (a) Except as provided in subsection (b), if the Secretary---

(1) approves an application filed pursuant to section 505(b),

(2) issues a certification under section 507, or

(3) issues a license under section 351 of the Public Health Service Act for a drug designated under section 526 for a rare disease or condition, the Secretary may not approve another application under section 505(b), issue another certification under section 507, or issue another license under section 351 of the Public Health Service Act for such drug for such disease or condition for a person who is not the holder of such approved application, of such certification, or of such license until the expiration seven years from the date of the approval of the approved application, the issuance of the certification or the issuance of the license. Section 505(c)(2) does not apply to the refusal to approve an application under the preceding sentence.

(b) If an application filed pursuant to section 505(b) is approved for a drug designated under section 526 for a rare disease or condition, if a certification is issued under section 507 for such a drug or if a license is issued under section 351 of the Public Health Service Act for such a drug, the Secretary may, during the seven-year period beginning on the date of the application approval, of the issuance of the certification under section 507, or of the issuance of the license, approve another application under section 505(b), issue another certification under section 507, or, issue a license under section 351 of the Public Health Service Act, for such drug for such disease or condition for a person who

is not the holder of such approved application, of such certification, or of such license if--

(1) the Secretary finds, after providing the holder notice and opportunity for the submission of views, that in such period the holder of the approved application, of the certification, or of the license cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated; or

(2) such holder provides the Secretary in writing the consent of such holder for the approval of other applications, issuance of other certifications, or the issuance of other licenses before the expiration of such seven-year period.

OPEN PROTOCOLS FOR INVESTIGATIONS OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 528 [360dd]. If a drug is designated under section 526 as a drug for a rare disease or condition and if notice of a claimed exemption under section 505(i) or regulations issued thereunder is filed for such drug, the Secretary shall encourage the sponsor of such drug to design protocols for clinical investigations of the drug which may be conducted under the exemption to permit the addition to the investigations of persons with the disease or condition who need the drug to treat the disease or condition and who cannot be satisfactorily treated by available alternative drugs.

GRANTS AND CONTRACTS FOR DEVELOPMENT OF DRUGS FOR RARE DISEASES AND CONDITIONS

SEC. 5. [360ee](a) The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in (1) defraying the costs of qualified clinical testing expenses incurred in connection with the development of drugs for rare diseases and conditions, (2) defraying the costs of developing medical devices for rare diseases or conditions, and (3) defraying the costs of developing medical foods for rare diseases or conditions.

(b) For purposes of subsection (a):

(1) The term “qualified testing” means---

(A) human clinical testing---

(i) which is carried out under an exemption for a drug for a rare disease or condition under section 505(i) of the Federal Food, Drug, and Cosmetic Act (or regulations issued under such section);

(ii) which occurs after the date such drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 506(b) or 507 of such Act or under section 351 of the Public Health Service Act; and

(B) preclinical testing involving a drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 505(b) or 507 of such Act or under section 351 of the Public Health Service Act.

(2) The term “rare disease or condition” means

(A) in the case of a drug, any disease or conditions which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug,

(B) in the case of a medical device, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical device for such disease or condition will be developed without assistance under subsection (a), and

(C) in the case of a medical food, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical food for such disease or condition will be developed without assistance under subsection (a).

Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under section 526 of the Federal Food, Drug, and Cosmetic Act is made.

(D) The term “medical food” means a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

(c) For grants and contracts under subsection (a) there are authorized to be appropriated \$10,000,000 for fiscal year 1988, \$12,000,000 for fiscal year 1989, \$14,000,000 for fiscal year 1990.

(d) STUDY.---The Secretary of Health and Human Services shall conduct a study to determine whether the application of subchapter B of chapter V of the Federal Food, Drug, and Cosmetic Act (relating to drugs for rare diseases and conditions) and section 28 of the Internal Revenue Code of 1986 (relating to tax credit) to medical devices or medical foods for rare diseases or conditions or to both is needed to encourage the development of such devices and foods. The Secretary shall report the results of the study to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate not later than one year after the date of the enactment of this Act. For purposes of this section, the term “rare diseases or conditions” has the meaning prescribed by section 5 of the Orphan Drug Act (21 U.S.C. 360ee).

ORPHAN PRODUCTS BOARD

SEC. 227 [236]. (a) There is established in the Department of Health and Human Services a board for the development of drugs (including Biologics) and devices (including diagnostic products) for rare diseases or conditions to be known as the Orphan Products Board. The Board shall be comprised of the Assistant Secretary for Health of the Department of Health and Human Services and representatives, selected by the Secretary, of the Food and Drug Administration, the National Institutes Health, the Centers for Disease Control and, any other Federal department or agency which the Secretary determines has activities relating to drugs and devices for rare diseases or conditions. The Assistant Secretary for Health shall chair the Board.

(b) The function of the Board shall be to promote the development of drugs and devices for rare diseases or conditions and the coordination among Federal, other public, and private agencies in carrying out their respective functions relating to the development of such articles for such diseases or conditions.

(c) In the case of drugs for rare diseases or conditions the Board shall---

(1) evaluate---

(A) the effect of subchapter B of the Federal Food, Drug, and Cosmetic Act on the development of such drugs, and

(B) the implementation of such subchapter;

(2) evaluate the activities of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration for the development of drugs for such diseases or conditions,

(3) assure appropriate coordination among the Food and Drug Administration, the National Institutes of Health, the Alcohol, Drug Abuse, and Mental Health Administration, and the Centers for Disease Control in the carrying out of their respective functions relating to the development of drugs for such diseases or conditions to assure that the activities of each agency are complementary,

(4) assure appropriate coordination among all interested Federal agencies, manufacturers, and organizations representing patients, in their activities relating to such drugs,

(5) with the consent of the sponsor of a drug for a rare disease or condition exempt under section 505(i) of the Federal Food, Drug, and Cosmetic Act or regulations issued under such section, inform physicians and the public respecting the availability of such drug for such disease or condition and inform physicians and the public respecting the availability of drugs approved under section 505(c) of such Act or licensed under section 351 of this Act for rare diseases or conditions,

(6) seek business entities and others to undertake the sponsorship of drugs for rare diseases or conditions, seek investigators to facilitate the development of such drugs, and seek business entities to participate in the distribution of such drugs, and

(7) reorganize the efforts of public and private entities and individuals in seeking the development of drugs for rare diseases or conditions and in developing such drugs.

(d) The Board shall consult with interested persons respecting the activities of the Board under this section and as part of such consultation shall provide the opportunity for the submission of oral views.

(e) The Board shall submit to the Committee on Labor and Human Resources of the Senate and the Committee on Energy and Commerce of the House of Representatives an annual report---

(1) identifying the drugs which have been designated under section 526 of the Federal Food, Drug, and Cosmetic Act for a rare disease or condition,

(2) describing the activities of the Board, and

(3) containing the results of the evaluations carried out by the Board.

The Director of the National Institutes of Health and the Administrator of the Alcohol, Drug Abuse, and Mental Health Administration shall submit to the Board for inclusion in the annual report a report on the rare disease and condition research activities of the Institutes of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration; the Secretary of the Treasury shall submit to the Board for inclusion in the annual report a report on the use of the credit against tax provided by section 44H of the Internal Revenue Code of 1954; and the Secretary of Health and Human Services shall submit to the Board for inclusion in the annual report a report on the program of assistance under section 5 of the Orphan Drug Act for the development of drugs for rare diseases and conditions. Each annual report shall be submitted by June 1 of each year for the preceding calendar year.

<http://www.fda.gov/orphan/oda.htm>

Accessed and copied September 10, 2007

Appendix F: Stakeholder Organizations

The following information on important ODA stakeholder organizations was accessed and copied on September 10, 2007 from <http://www.fda.gov/orphan/rdid/index.htm>

Office of Orphan Products Development

Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 827-3666 or 1-800-300-7469
<http://www.fda.gov/orphan/index.htm>

The Office of Orphan Products Development (OOPD) is dedicated to promoting the development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions since 1982. OOPD interacts with the medical and research communities, professional organizations, academia, and the pharmaceutical industry, as well as rare disease groups. The OOPD administers the major provisions of the Orphan Drug Act (ODA) which provide incentives for sponsors to develop products for rare diseases.

Office of Rare Diseases

National Institutes of Health
6100 Executive Boulevard, 3B-01
Bethesda, Maryland 20892-7518
Telephone: (301) 402-4336
ord@od.nih.gov

The Office of Rare Diseases (ORD) was established in 1993 within the Office of the Director of the National Institutes of Health (NIH). On November 6, 2002, the President established the Office in statute (Public Law 107-280, the Rare Diseases Act of 2002). The goals of ORD are to stimulate and coordinate research on rare diseases and to support research to respond to the needs of patients who have any one of the more than 6,000 rare diseases known today.

National Organization for Rare Disorders (NORD)

55 Kenosia Avenue
P. O. Box 1968
Danbury, CT 06813-1968
(800) 999-NORD(6673) or (203) 744-0100
TDD Number (203) 797-9590
E-mail: orphan@rarediseases.org
www.rarediseases.org

The National Organization for Rare Disorders is the federation of voluntary health organizations dedicated to helping people with rare “orphan” diseases and assisting the

organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and service.

Biotechnology Industry Organization

1225 I Street NW, Suite 400

Washington, DC 20005

(202) 962-9200

FAX (202) 962-9201

E-mail: bio@bio.org

www.bio.org

The Biotechnology Industry Organization (BIO) is the largest trade organization to serve and represent the emerging biotechnology in the United States and around the globe.

Pharmaceutical Research and Manufacturers of America

1100 15th Street, NW

Washington, DC 20005

(202) 835-3400

1-800-762-4636 Patient Assistance Program

www.phrma.org

The mission of the Pharmaceutical Research and Manufacturers of America is to help the research-based pharmaceutical industry successfully meet its goal of discovering, developing, and bringing to market medicines to improve human health, patient satisfaction, and the quality of life around the world, as well as to reduce the overall cost of healthcare.

Appendix G: President's Disapproval of 1990 ODA Amendment

Background information on the Orphan Drug Act Amendment of 1990 (H.R. 4638) follows, along with a copy of the Memorandum of Disapproval that was issued from the office of President George H.W. Bush.

H.R. 4638 would have permitted simultaneous licensing of the same orphan product for the same indication if 1) the second company requested orphan designation within 6 months of publication by the FDA of its action to designate the drug for the first company; 2) the second company initiated human clinical trials not more than 12 months after the first company initiated clinical trials; and 3) the second company submitted an approvable new drug application to the FDA no more than one year after the first company submitted its new drug application.

A hearing to discuss the need for H.R. 4638 was conducted in February 1990. H.R. 4638 was introduced to Congress in July 1990. The House and Senate unanimously passed 4638 in October 1990. President George H.W. Bush pocket vetoed 4638 in November 1990, i.e., the President had until November 8, 1990 to act on the bill, but he did not. On November 9th, he released the following memorandum explaining his decision.

(<http://www.presidency.ucsb.edu/ws/?pid=19023> accessed and copied September 10, 2007)

Memorandum of Disapproval for the Orphan Drug Amendments of 1990

November 8, 1990

I am withholding my approval of H.R. 4638, the "Orphan Drug Amendments of 1990." This legislation would make substantive changes to the orphan drug provisions of the Federal Food, Drug, and Cosmetic Act and the Orphan Drug Act.

Enacted in 1983, the Orphan Drug Act created economic incentives for drug companies to develop drugs for rare diseases and conditions -- so-called "orphan drugs." Typically, these drugs would not be profitable to develop because of their small patient populations.

By any measure, the Orphan Drug Act has been a tremendous success. A total of 49 new drugs for rare diseases have been approved under this program, and 370 others are in the development stage. These drugs have provided lifesaving treatments for such terrible diseases as enzyme deficiency, which affects adversely the immune system of about 40 children nationwide. Until the orphan drug was developed to treat these children, they had to spend their entire lives in the protection of an isolation bubble. One of the first orphan drugs is another example of a triumph. The most difficult form of leprosy affects only 4,000 people. A drug known for over 14 years to be effective in treating this condition was not being marketed by any drug company, because it was considered unprofitable -- until the Orphan Drug Act provided the marketing incentive. In a similar manner, orphan drugs provide treatment for terrible diseases for which there is usually no alternative therapy.

I have serious concerns about the effect that H.R. 4638 would have upon the incentive of drug companies to develop orphan drugs. I believe we must not endanger the success of this program, which is due in large measure to the existence of the "market exclusivity" provision in the Orphan Drug Act that allows companies to have exclusive marketing rights to an orphan drug for 7 years. Weakening the current 7-year exclusivity provision would certainly discourage development of desperately needed new orphan drugs.

Under current law, firms may apply to develop the same orphan drug, but only the first firm to have its drug approved receives market exclusivity. The certainty of this 7-year period is the basis of the economic incentive to attract drug firms to invest in orphan drugs.

The bill would make two major changes to the market exclusivity provisions of the Orphan Drug Act. First, the bill provides for "shared exclusivity." Firms that can demonstrate that they have developed the orphan drug simultaneously would be allowed to share the market with the firm initially awarded the market exclusivity. Second, the bill requires the Food and Drug Administration to withdraw the marketing exclusivity as soon as the patient population exceeds a 200,000 patient limit. Both of these changes have the effect of weakening the marketing incentives provided by the Act. Under this bill, the length of the market exclusivity period will depend on how quickly the patient population grows and whether other firms file claims for simultaneous development.

In addition, as currently constructed, the 200,000 patient population limit would be applied to orphan drugs approved prior to the enactment of the bill as well as to those approved in the future. This retroactive rule change would send a troublesome signal to all those who might wish to develop orphan drugs that the Federal Government may change unilaterally the rules for firms that made investment decisions based on the expectation of 7 years of market exclusivity.

I am aware that this bill was passed after a number of compromises among Members of Congress. I am extremely concerned, however, that individuals with rare diseases may suffer because of changes that this bill would make in the incentives to develop new drug treatments. Accordingly, I am withholding my approval of H.R. 4638.

George Bush
The White House,
November 8, 1990.

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<http://www.frameworksinstitute.org/assets/files/PDF/FramingPublicIssuesfinal.pdf>

<http://www.fda.gov/orphan/oda.htm>

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