

UNDERSTANDING SCIENTIFIC DECISION-MAKING AND UNCERTAINTY  
THROUGH GROUNDED THEORY:  
THE CASE OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

by

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(Under the Direction of Barry Bozeman)

ABSTRACT

The purpose of this study is to understand how decisions are made by members of a public agency that addresses scientific and technical issues under conditions of uncertainty. The primary research method used is grounded theory, a major qualitative research tool used in the social sciences for decades. Decision-making under conditions of uncertainty is an important topic because, despite the textbook approach to administrative decision-making where the steps involved in reaching a conclusion are relatively straightforward and linear, the reality is more complex.

This research project uses the Advisory Committee on Immunization Practices (ACIP) as an example of how decisions are made under conditions of scientific uncertainty. The ACIP is a fifteen-member group of physicians that meets periodically to review data on vaccines licensed for use in the United States by the U.S. Food & Drug Administration (FDA). Group members make recommendations to the U.S. Centers for Disease Control & Prevention (CDC) on vaccine uses and doses for specific populations.

Using semi-structured interviews with current and former ACIP members, the dissertation seeks to understand how ACIP members make recommendations to the CDC where a high degree of evidence exists (e.g., the primary age groups for which a new vaccine is needed and has been shown to be safe and effective) and where lesser (or no) evidence exists (e.g., interchangeability of vaccine brands) and poses questions about the bases of recommendations in these two circumstances. The conclusion is that where a high degree of technical consensus exists about the evidence and data, a decision generally is made according to a clear, relatively linear decision-making process. If a high degree of technical consensus does not exist, the decision is made based on a variety of criteria, including readily available resources, decision-process constraints, and the available knowledge base, among other things. In short, where a reasonably clear, consensus-based decision-making process is in place, decision-makers generally follow a long-established decision rule. In the absence of such a rule, decision-makers rely on a variety of contextual factors as well as familiar processes and analogies that are accepted practice within their professional community.

INDEX WORDS: scientific decision-making, uncertainty in decision-making, federal advisory committees, medical research

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## DEDICATION

I dedicate this dissertation to my mother, Laura M. Martinez (1939-2007).

had I come of age  
in another time, another place  
or tasted death in lesser days—  
had I bowed my head but once  
or turned my eyes an inward glance

I would not be so overwise  
to see a world or hear her sighs;  
I would not lose peace of mind  
to cast a thoughtful look behind

but time is short; life is dear—  
and whispers echo ancient fears;  
smooth caress, forgotten touch  
return to ash, and ash to dust—

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I also extend my heartfelt thanks to the persons who helped to identify, locate, and gain access to members of the Advisory Committee on Immunizations Practices (ACIP). My good friend M. Christine Cagle, Ph.D., Associate Director for Policy & Planning, Divisions of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, within the U.S. Centers for Disease Control and Prevention (CDC) spoke with me at length and ultimately directed me toward the appropriate CDC personnel. Jeanne M. Santoli, MD, MPH, Deputy Director, Immunization Services Division, National Center for Immunization and Respiratory Diseases at the CDC first suggested that I study the ACIP, and she referred me to Jean Clare Smith, MD, Medical Officer, Assistant to the Director for Immunization Policy, Immunization Services Division, National Center for Immunization & Respiratory Diseases at the CDC. Dr.

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I especially appreciate the time and attention of each current and former ACIP member who consented to be interviewed. In alphabetical order, I thank: Dr. Jon S. Abramson; Dr. Lance Chilton; Dr. Paul R. Cieslak; Dr. Janet A. Englund; Dr. Reginald Finger; Dr. Harry F. Hull; Dr. Franklin Judson; Dr. Tracy Lieu; Dr. S. Michael Marcy; Dr. Julie Morita; Dr. Kathy Neuzil; Ms. Patricia (Patsy) Stinchfield; and Dr. Jonathan Temte. These highly-trained and renowned medical professionals juggled hectic schedules and multiple commitments; it was no small matter to find time to be interviewed. Their participation and candor were essential to the success of the project.

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## CHAPTER 1

### UNDERSTANDING DECISION-MAKING UNDER CONDITIONS OF UNCERTAINTY: THE CASE OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

The purpose of this study is to understand how decisions are made by members of a public agency that addresses scientific and technical issues under conditions of uncertainty. The primary research method used is grounded theory (GT), a major qualitative research tool used in the social sciences for decades. GT first emerged from the Chicago School of Sociology between the 1920s and 1950s, although it did not become a widely used research method until the 1980s (Glaser and Strauss, 1967, vii, 15-18; Holton, 2008; Singleton and Straits, 1999, 349). As discussed in Chapter 3, GT is a method well-suited to a research project that seeks to understand how decision-makers grapple with uncertainty.

Scientific decision-making under conditions of uncertainty is an important topic because, despite the textbook approach to administrative decision-making where the steps involved in reaching a conclusion are relatively straightforward and linear, the reality is far more complex. It is axiomatic that public servants inside administrative agencies make decisions that affect the populace to no small extent. If administrators did not have the authority to sift through data, weigh alternatives, formulate a plan, and pursue an appropriate course of action, a public agency would be, at best, a superfluous form of organization, and, at worst, a colossal waste of resources. Public agencies are created and maintained because they theoretically allow administrators to make informed decisions on a variety of technical and complex issues that might otherwise never be addressed by government (Kettl, 1990; Lindblom, 1959).

Decision-making can be more daunting than it sounds. Depending on the nature and scope of the policy, innumerable means may be sufficient for achieving the objective. Seasoned public servants must review all reasonable means, assess opportunities and potential obstacles, and determine whether one approach is preferable to another. Afterward, they must select the approach that achieves the organization's goals, generally in the most efficient and effective manner possible. In many cases, this calculation will involve a straight cost-benefit analysis. Accordingly, the preferred alternative will be an approach that bestows the greatest benefit with the least cost. In other cases, such as instances involving environmental quality or affirmative action, the calculation may involve broader goals that extend beyond a strict cost-benefit analysis. It may cost more money and tax businesses in the short-run to install pollution control devices on smokestacks, but the goal of improving the health of the natural environment and human beings in the long run may necessitate the implementation of such a policy. Similarly, while it remains a contested concept, ensuring that members of historically disadvantaged groups are afforded opportunities in jobs, housing, and education may require increased expenditures in the short run, but some policy-makers believe that the benefits of ensuring diversity in American life are worth the short-term costs (Burke, 1986, 79-99).

After public servants move through the process of identifying a goal, considering the range of options for implementation, and finally choosing the preferred option, the policy can be formulated and implemented. This description of the decision-making style is orderly, rational, and takes into account virtually every relevant factor necessary for arriving at a reasonable decision. Unfortunately, this rational explanation of the decision-making process for public administrators does not explain all the factors that influence decision-making, especially in areas involving scientific and highly technical issues where the evidence and data are complex and

consensus on the nature of the issues and/or the evidence and data is low or non-existent (Norberg-Bohm and Rossi, 1998, 225-226; Rosenbloom, 1993, 325-329).

Many public servants face decision points where a plan must be developed and implemented, but enormous uncertainty exists, especially when scientific or highly technical issues are involved. Scientific studies often produce contradictory evidence and conflicting results or provide incomplete information, which complicates decision-making. As mentioned above, to better understand how administrators make decisions when data are contradictory or incomplete, the purpose of this project is to explore scientific decision-making when uncertainty exists. Thus, the dissertation will examine how a specific public agency grapples with the uncertainties inherent in scientific research.

Exploring decision-making under conditions of uncertainty is a crucial enterprise because every decision-making process involves uncertainty to some extent. Scientific decision-makers accept the presence of uncertainty and develop heuristic tools for coping with unknown variables, but the general public is not so quick to accept the limits of scientific data. In fact, some citizens have expressed concern about the benefits of scientific innovation and the reliability of expertise, in part because they believe that experts are not always forthcoming with credible information. In a nation that professes to be based on democratic principles and encourages individual participation in the political process, no small level of skepticism exists about the inaccessibility of specialized opinion and the idea that experts enjoy a level of knowledge that is unavailable to the citizenry.

Ironically, as life expectancy has increased and overall risks in American society have declined, sensationalistic stories about risk and generally irrational fear about potentially calamitous scientific consequences have driven many members of the public to question the

veracity of experts. The qualification of expert opinion and the caveats about uncertainty and research assumptions that invariably accompany scientific publications frustrate laypersons seeking clear-cut, easily-understood answers to complex questions. Thus, a paradox has arisen in recent decades: As overall risks have declined owing to scientific advancements, public concern over remaining risks has been heightened. The public expects science to banish all doubt, and do it quickly, efficiently, and affordably. When uncertainty persists and the limits of science become apparent, tolerance for uncertainty decreases with frustrated cries such as, “if we can put a man on the moon, why can’t we solve this issue?” (Lankshear, *et al.*, 2005).

Certainty is a rarely-achieved epistemological ideal; therefore, it is instructive to study decision-making processes where little uncertainty exists compared with decision-making processes where a great deal of uncertainty as part of the effort toward developing a model. Providing a model of the decision-making process where uncertainty exists can assist other decision-makers in understanding and improving their own decision-making process. To develop such a model, this research project specifically focuses on the Advisory Committee on Immunization Practices (ACIP) as an example of how decisions are made under conditions of scientific uncertainty.

The ACIP is a fifteen-member group of physicians that meets periodically to review data on vaccines licensed for use in the United States by the U.S. Food & Drug Administration (FDA). Group members make recommendations to the U.S. Centers for Disease Control & Prevention (CDC) on vaccine uses and doses for specific populations by developing written recommendations for routine vaccine administration to the pediatric and adult populations, along with vaccination schedules regarding appropriate periodicity, dosage, and contraindications. ACIP statements are official federal recommendations for the use of vaccines and immune



globulins in the U.S., and are published by the CDC (Blazek, 2008; Meadows, 2007, 25; Preboth, 2001; Thompson, *et al.*, 2003).

The overall goals of the ACIP are to provide advice to government agencies for reducing the incidence of vaccine preventable diseases and to increase the safe usage of vaccines and related biological products. In the United States, immunizations have resulted in the eradication of a variety of diseases, including smallpox, polio, measles, and rubella. Disease rates from vaccine-preventable diseases have been reduced by 99 percent (Blumenthal, 2004; Henley, 2003; March, 2004; McCaffrey, *et al.*, 2007; Meadows, 2007, 25-26; Ramsey, 2008; Schmidt, *et al.*, 2004; Smith and Shay, 2007).

Regularly-scheduled ACIP meetings are held three times a year. Notices of each meeting, along with agenda items, are published in the *Federal Register* in accordance with the requirements of the Federal Advisory Committee Act (FACA). A vote on vaccine recommendations may be taken when a quorum of at least eight eligible ACIP members are present. Eligible voters are those members who do not have a conflict of interest. If eight eligible voting are not members present, the ACIP executive secretariat can temporarily designate *ex officio* members as voting members, as provided in the committee charter. In some cases, the full ACIP may choose to designate a smaller working group to study a vaccine in depth, although the working group must report back to the ACIP so the entire 15-member committee can vote on recommendations to the CDC. In fact, in most cases the practical investigation of vaccines relies heavily on the working groups (ACIP Home Page). Working groups are discussed in more detail in Chapter 4.

The ACIP decision-making process includes review of labeling and package inserts; review of the scientific literature on the safety and efficacy of vaccines; assessment of cost

effectiveness; review of the morbidity and mortality associated with the disease; review of the recommendations of other groups; and consideration of the feasibility of vaccine use in existing programs (Blumenthal, 2004; Bridges, 2004; Gentile, 2008). At meetings, the ACIP may vote to include new vaccines into the national program or to modify existing vaccine schedules. These votes are recorded by the CDC and eventually made public. In most cases, a resolution takes effect after establishing a CDC contract for the purchase of that vaccine in the necessary amounts (Advisory Committee on Immunization Practices, 2008; Luman, *et al.*, 2008; Schmidt, *et al.*, 2004; United States Department of Health and Human Services, 2008, 13).

ACIP members are appointed by the Secretary of Health & Human Services. The ACIP normally contains an expert in each of the following fields: immunization practices and public health; use of vaccines and other immunobiologic agents in clinical practice or preventive medicine; clinical or laboratory vaccine research; assessment of vaccine efficacy and safety; and consumer perspectives and/or social and community aspects of immunization programs. At least one member must be an expert in this last category. In addition, the ACIP includes *ex-officio* members from federal agencies involved with vaccine issues, and non-voting liaison representatives from medical and professional societies and organizations (ACIP Home Page).

The dissertation seeks to understand how ACIP members make recommendations where a high degree of evidence exists (e.g., the primary age groups for which a new vaccine is needed and has been shown to be safe and effective) and where lesser (or no) evidence exists (e.g., interchangeability of vaccine brands) and poses questions about the bases of recommendations in these two circumstances. Presumably, where a high degree of technical consensus exists about the evidence and data, a decision generally will be made according to a clear decision rule. If a high degree of technical consensus does not exist, the decision probably will be based on a

variety of criteria, including readily available resources, decision-process constraints, and the available knowledge base, among other things. In short, where a reasonably clear, consensus-based decision-making process is in place and uncertainties are few, decision-makers generally follow a long-established decision rule. In the absence of a clear decision rule where uncertainties are high, decision-makers employ a variety of heuristic devices and techniques.

The ACIP presents an excellent case of for this research owing to the nature of research on vaccines. In the case of some vaccines—e.g., smallpox, polio, and measles—a high degree of technical consensus exists about the evidence and data. These vaccines have been shown to perform safely and effectively over time. Other vaccines—e.g., those involving HIV, autoimmune diseases, and certain types of prenatal infections—are controversial because evidence is divided over whether they are safe and effective when administered in certain dosages to certain populations (Blazek, 2008; Gentile, 2008; Gilca, *et al.*, 2008; La Torre, *et al.*, 2008; Ramsey, 2008; Szilagyi, *et al.*, 1994).

At the outset, it is important to recognize that a decision-maker may be called upon to “satisfice,” to borrow a well-known concept from Herbert Simon. Satisficing means that a decision-maker seldom makes decisions based on a purely rational process or with a complete, thoroughly reliable data set. He or she must search for a solution that can serve as a reasonably satisfactory decision rule based on the available information and resources, internal and external constraints (e.g., limited time, a small budget, and the press of other events and activities, among other things) and/or a limited knowledge base (Rehfuss, 1989, 45-49; Williams, 2002).

Using the ACIP as an example, this approach suggests that a physician who examines a vaccine to decide if it should be recommended to the CDC initially will try to find consensus in the available research record compiled by the FDA, the scientific literature, or among his peers

in the field. Is a vaccine safe, effective, and reliable based on clearly articulated, well-accepted medical standards? Does it meet certain widely recognized professional criteria used by ACIP members? If so, the decision rule is clear and the physician can, and probably will, recommend the dissemination and administration of the vaccine. If a consensus does not exist owing to scientific uncertainty—data are inconclusive or contradictory about the safety, effectiveness, and reliability of a vaccine—the physician still must make a recommendation. He or she can adopt a posture such as the precautionary principle—it is better to be safe than sorry so a particular vaccine should be rejected because its long-term effects are unknown—but the physician might decide that such a defensive principle will unduly hamper the development of new vaccines (Gollier and Treich, 2003). How, then, does the physician decide on a defensible recommendation? This dissertation explores that issue.

To gain access to a small group of decision-makers in the scientific arena—in this case, the health care field—I contacted M. Christine Cagle, Ph.D., Associate Director for Policy & Planning Divisions of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention, within the U. S. Centers for Disease Control and Prevention (CDC) and asked if she could identify appropriate decision-makers inside the agency. Dr. Cagle referred the matter to Jeanne M. Santoli, MD, MPH, Deputy Director, Immunization Services Division National Center for Immunization and Respiratory Diseases at the CDC. On Tuesday, February 12, 2008, Dr. Santoli spoke with me in a 30-minute telephone conversation and agreed to assist in arranging interviews with, and access to, members of the ACIP. Afterward, Dr. Santoli referred me to Jean Clare Smith, MD, Medical Officer, Assistant to the Director for Immunization Policy, Immunization Services Division, National Center for Immunization & Respiratory Diseases at the CDC. After I spoke with Dr. Smith, on Thursday, August 7, 2008, she forwarded a

memorandum to the ACIP executive secretariat asking that interviews with ACIP members be arranged. The text of the memorandum can be found in Appendix B. Thereafter, I contacted the ACIP members and arranged to interview them via telephone beginning in August 2008 and continuing until November 2008. Summaries of the interviews can be found in Chapter 4 and conclusions derived from the interviews can be found in Chapter 5.

CHAPTER 2  
THE LITERATURE ON SCIENTIFIC DECISION-MAKING  
UNDER CONDITIONS OF UNCERTAINTY

ACIP members are physicians engaged in the process of medical research, especially on the nature of infectious diseases and the efficacy, or lack thereof, of various vaccines.

Invariably, committee members are called upon to make decisions on vaccines when uncertainty exists, especially concerning new vaccines that have recently come to market. The FDA makes the initial determination of whether a particular vaccine should be allowed for use, so that agency is the critical gatekeeper for assuring the safe and effective performance of a specific drug.

Nonetheless, the ACIP plays a secondary role by reviewing data on the vaccine and making recommendations on the types of populations that should be served and the conditions under which they are served. If scientific uncertainty exists with respect to a specific vaccine—and in most cases so uncertainty exists regardless of the quality and quantity of clinical trials conducted by pharmaceutical companies—the ACIP sooner or later will be faced with uncertainty about the appropriate recommendation for a given vaccine. The key issue is how ACIP decision-makers handle scientific uncertainty and nonetheless reach a decision.

A rich literature on scientific uncertainty exists, although different schools of thought exist about how uncertainty should be approached. Some of the literature focuses on the inevitable epistemological problems that arise when researchers employ the scientific method (Bell and Lederman, 2003). Another strain of literature focuses on the nature of scientific decision-making in the public policy arena, with particular emphasis on the tensions between

scientists and non-scientists in the policy process (Whitney, 2003; Whyte, 1989). More to the point for the ACIP, another strain of literature is devoted specifically to medical decision-making and scientific uncertainty. This chapter will summarize the major tenets of each strain as a prelude to discussing ACIP decision-making in Chapters 4 and 5.

Because scientific decision-making, especially in a public agency, involves multiple actors working at different times under different constraints and relying on different sets of assumptions, the process is necessarily complex. Complex processes invariably involve uncertainty and risk (Driouchi, *et al.*, 2009; Jaffray and Wakker, 1993). As one group of researchers exploring the risk of devastating floods has observed, “Because all information about the future is uncertain, [researchers] must make decisions under uncertainty every day, in a complex, evolving social, institutional, and political environment. Given these conditions, and the limited information and time they have to address numerous demands, practitioners often deal with uncertainty by finding the best information they can quickly and easily obtain and interpret, making the decision required for the moment, and then moving on” (Morss, *et al.*, 2005, 1596).

Scientific decision-makers must be careful as they engage in decision-making “required for the moment” so they do not rely on fallacious reasoning. The reliance on heuristics and the prevalence of biases are not restricted to the citizenry. Experienced researchers also fall victim to a variety of biases when they think intuitively. The desire to predict the outcome that best represents the data with insufficient regard for prior probability and other nuances in the data has been observed in the intuitive judgments of individuals who have extensive training in statistics and extensive research experience. Although experienced researchers avoid elementary errors, their intuition is not free of bias or fallacious reasoning (Tversky and Kahneman, 1974, 1130).

What is unusual but not unprecedented is the failure of scientists to understand and apply well-known and relatively simple rules of research, such as the tendency of data to regress to the mean or the effect of sample size on sample variation. Seemingly elementary data collection and management techniques can be mistaken easily because most of the time when information is collected and analyzed it is not coded appropriately. Consequently, a researcher may have a large body of data and information on hand, but using the research materials appropriately becomes problematic, especially when uncertainties in the data make it difficult to recognize patterns that allow for convenient classification (Djulgovic, 2007; Bowker and Star, 1999).

The literature on scientific decision-making under conditions of uncertainty recognizes that all decision-making processes involve uncertainties, although the nature and extent of those uncertainties varies. Some uncertainties are treated as “suboptimal” owing to missing variables. This strain of the literature suggests that the iterative nature of scientific research and decision-making eventually will fill in gaps in the data. Given enough time and research, the missing variables will be identified and supplied (Lipshitz and Strauss, 1997). Other sources suggest that the concept of “uncertainty” is far more profound; it is not merely a question of missing information. Rather, some types of knowledge are missing because epistemology is necessarily imprecise. Scientific answers depend on how scientific questions are framed, and framing questions into researchable hypotheses is a human enterprise. Because human enterprises are subject to the imperfections of human beings, questions can be developed that cannot be answered or at least answered in a manner that is precise and free from bias (Tversky and Kahneman, 1974).

Researchers in psychology and sociology have identified a concept known as “cognitive dissonance,” which helps to explain why it can be difficult to advance scientific knowledge free



from bias, especially when uncertainty exists. Individuals and groups exhibit a variety of responses when they are presented with new information. If the new information seems to confirm previously-held beliefs and opinions, the listener readily accepts the information because it reinforces what he or she already believes. If the new information is inconsistent with previous views—or, worse, it actually undermines and calls into question long-held, deeply-felt beliefs and opinions—the listener may refuse to accept the information. This “cognitive dissonance” may increase over time as opinions are formed and viewpoints solidify, which is one reason why people tend to defend their views more vehemently as they age. An older person has something invested in his or her opinions—often, the individual takes pride in “getting it right”—so that changing a strongly-held belief is psychologically difficult. When cognitive dissonance occurs, the listener either refuses to hear the new information or hears it with a great deal of bias and distortion (Bradshaw and Borchers, 2000).

A person who is in a state of cognitive dissonance is uncomfortable. Consequently, the sooner he or she can justify accepting or rejecting a new proposition (preferably the latter), the sooner the dissonance will end. When an individual who is predisposed to reject a new scientific hypothesis learns that the data supporting the hypothesis are uncertain, even if that uncertainty involves trivial matters that eventually will be clarified with additional research, the uncertainty can be seen as an additional reason for assailing or rejecting the hypothesis. The role for decision-makers who wish to minimize cognitive dissonance, even in the face of uncertainty, is to frame uncertainty as part of the decision-making process and to find ways of handling uncertainty that will not undermine the legitimacy of scientific results.

### Scientific Decision-making in General

At a basic level, certainty in any decision-making may be a chimera. Decisions are based on a variety of assumptions and presuppositions, some known and stated beforehand, others not known and not stated. Even when the assumptions and presuppositions can be accounted for and stated, decision-makers face numerous uncertainties (Fothergill, 2000; Oostenbrink, *et al.*, 2008; Sarin and Wakker, 1998; Tversky and Wakker, 1995). In fact, not all uncertainties are alike. Some uncertainties involve risk, which is an event which can be assigned a reasonably accurate probability value, and genuine uncertainty, which is an unknown event with an unknown probability (Beach, 1975; Bouyssou and Pirlot, 2008; Michael, 1979; Platt and Huettel, 2008; Reckhow, 1994; Volz, *et al.*, 2005).

Anyone who follows the news is inundated with stories about risks inherent in modern life. News stories in recent years have raised concerns about the global warming crisis, the rising cost of health care coverage, the possibility that various chemicals cause cancer, and plans for rescuing the ailing economy (Platt and Huettel, 2008). These issues are complicated and diverse, but they require decision-makers to act based on a great deal of data as well as varying levels of uncertainty. In the meantime, the public has heard a great deal about risks in recent years, and many of the nuanced discussions are lost on them (Ozonoff, 2005). Yet still the stories proliferate: concern over asbestos exposure; fears about cancer; worry over the worldwide spread of AIDS; alarm about the appearance of “mad cow” disease; and the omnipresent unease over environmental contamination (Delavande, 2008; Gollier and Treich, 2003).

The general public is often fearful of risks that receive enormous media coverage because there seems to be little the average person can do to avoid risk. One group of researchers refers to this desire to avoid large-scale risks as a fear of “surprises” (Kinzig, *et al.*, 2003, 332).

Because they are so alarmed at the possibility of scientific surprises, the public often pushes scientists to minimize uncertainty and surprises by avoiding action altogether because inaction is somehow safer than action. This reaction, while understandable, is not always possible or, for that matter, desirable:

How should scientists and policy-makers deal with the possibility of surprises?

Obviously, by their very nature surprises cannot be fully anticipated, yet they can have far-reaching consequences. One strategy for dealing with surprises would be *avoidance*; namely do whatever we can to minimize the occurrence of surprise.

But even if desirable, this strategy would have the fatal flaw of being non-operational. Since we can never know for sure what will trigger a surprise, we cannot know what strategies minimize the trigger (Kinzig, *et al.*, 2003, 332).

Two well-known approaches to making decisions under scientific uncertainty in a manner that minimizes or at least seemingly manages scientific surprises can be labeled the “precautionary principle” and the “polluter pays” principle. The former is a strategy for avoiding surprises and the latter is an attempt to reallocate the financial risk that accompanies a surprise (O’Riordan and Jordan, 1995). Generally, the burden falls on regulators or consumers to demonstrate why a product of chemical is *not* safe, but the precautionary principle places the burden on manufacturers and importers to demonstrate why a chemical *is* safe before a product or chemical can be manufactured or sold (Basili, *et al.*, 2008; Costanza and Cornwell, 1992). The difficulty for decision-makers is that the precautionary principle presumes that uncertainty can be substantially reduced or eliminated altogether, and this assumption may be fundamentally flawed (Foster, *et al.*, 2000). A proponent of the principle might call for testing of a certain drug or chemical to ensure its safety, which certainly sounds reasonable, but at what point should the

drug or chemical be pronounced “safe”? The precautionary principle can serve as the basis for opponents to push for additional testing *ad infinitum* (Genter, 2006; Maguire and Ellis, 2005). Yes, a thousand tests suggest that the product is safe, but what about the potentially negative results from the one thousand-and-first test? We need to be safe rather than sorry—we need to wipe out uncertainty before we proceed—so researchers should perform another test followed by another and another (Basili, *et al.*, 2008; Ozonoff, 2005; Tallacchini, 2005).

The “polluter pays” principle is a cousin of the precautionary principle. It requires a company that proposes to manufacture or ship a potentially “dangerous” product to post a deposit or purchase a bond to cover any damages and cleanup that may occur during handling and shipment. Again, this may be a reasonable approach to handling risk, but the amount of the deposit or bond and the recipient(s) can be controversial, especially when quantifying a largely unknown risk to arrive at a figure for the deposit or bond. Moreover, if all the risk of damage is placed on the entrepreneur, the risk may serve as a disincentive to innovation (Gollier and Treich, 2003). What initially sounds reasonable becomes a means of encouraging decision paralysis in the face of risk and uncertainty (O’Connor, 1997; Pearce and Turner, 1992).

Scientists know that risk and uncertainty are givens, an unavoidable characteristic of all information and advancements in civilization (Tversky and Wakker, 1995). Despite the best efforts of scientists to remove or reduce risk and uncertainty, often their efforts resolve some previously unknown questions but, in the process, raise other questions (Clarke, 2006; Maas, 2007; Ruseva and Hang, 2007). The lay public seems to believe that uncertainty can be eliminated in the quest for scientific results and is frustrated and disappointed when scientists continue to cite uncertainty in announcing scientific results and conclusions (Bouyssou and Pirlot, 2008; Fothergill, 2000; Hayward, 2006; Sarin and Wakker, 1998). Global warming is a

prime example. The public is asking for precision about the nature and extent of the issue, and science thus far is at a loss to define the problem and identify its parameters. So many variables and unknowns exist when researchers examine a macro issue such as global climate change that it is enormously challenging to provide concrete data, much less effective political solutions, to this complex, difficult problem (Basson and Petrie, 2007; Graham, 2001).

Because so many scientific issues have become salient in recent years, interest in decision-making under uncertainty has been on the rise (Clarke, 2006; Fisher, 2003; Jensen, 2008). For example, in 1999, the University of California at Berkeley initiated work with Markov decision processes and probabilistic graphical models to assist in preparing risk analyses and decision matrices. The Berkeley work is exhaustively discussed on the university's website at: <http://www.cs.berkeley.edu/~jordan/muri/>. Unlike that effort, this research project is qualitative and does not seek to contribute to the mathematically-based quantitative decision analysis performed by the Berkeley researchers. Instead of focusing on probable outcomes of future events based on statistical probabilities, this research seeks to probe in depth as to how and why certain researchers made past decisions when faced with uncertainty. In other words, the dissertation seeks not to examine the likelihood that a certain action will be undertaken in the future; it seeks to probe why a certain action was taken in the past.

Ironically, scientific uncertainty in the health care field has grown even as knowledge about the human body and the mechanics of caring for the human body has grown. Each new discovery leads to the development of new diagnostic tools, new machinery, and new medicines. With each new innovation, however, come a host of new questions about procedures and treatment options, which are compounded by gaps in knowledge (Lipworth, 2007; Meyer and Meyer, 2005; Williams, 2008). As researchers Paul E. Plsek and Trisha Greenhalgh have

observed, “Not so long ago public health was the science of controlling infectious diseases by identifying the ‘cause’ (an alien organism) and taking steps to remove or contain it. Today’s epidemics have fuzzier boundaries (one is even known as ‘syndrome X’): They are the result of the interplay of genetic predisposition, environmental context, and lifestyle choices” (Plsek and Greenhalgh, 200, 625-626).

The so-called “crucial experiment” (an *experimentum crucis*) model became one of the popular myths of twentieth century science. According to this thinking, as scientific researchers, especially in medical science, investigate natural phenomena and offer hypotheses as to causes and effects, invariably they find competing hypotheses that contradict their work (Clarke, 2006; Jensen, 2008; Lipworth, 2007; Williams, 2008). Scientific schools of thought arise, each offering its own interpretation of the data and defending its position against all comers. This is a natural extension of the Hegelian understanding of a thesis followed by an antithesis. Eventually, one or more researchers conducts a breakthrough experiment—the “crucial experiment”—that allows for a synthesis of the heretofore competing, contradictory hypotheses. The crucial experiment is a culmination of the logical positivists’ work, suggesting that science is a series of “Eureka” moments that lurch toward understanding and eventually practical applications to the research (Green and Glasgow, 2006; Michaels, 2005; Pope, *et al.*, 2000). In the words of one researcher, however, “it is very rare to find determinative experiments in environmental health sciences. A single, well-constructed experiment almost never resolves a critical issue on the cause of disease...” (Krimsky, 2005, S129).

Some scientific decisions are made using mechanical systems, which have boundaries that are well-defined and fixed (Maas, 2007). An engineering problem, for example, involves mechanical processes that are reasonably well known. As long as the relevant variables are

considered and accounted for, an engineering problem usually can be resolved satisfactorily. By contrast, a complex adaptive system involves multiple parts and a collection of individual actors and processes (Sarin and Wakker, 1998). As a result, the outcome is not always predictable apart from computing probabilities, and even then the calculation requires researchers to build assumptions and contingencies into their models (Bouyssou and Pirlot, 2008; Clarke, 2006; Tversky and Wakker, 1995).

When making decisions in complex adaptive systems, decision-makers use rule sets to drive their actions. In a biochemical system, “rules” governing the behavior of the system are a series of chemical reactions triggered in accordance with fundamental principles of chemical interactions (Volz, *et al.*, 2005). Insofar as human reactions are concerned, rules can be thought of as the instincts and mental constructs influencing human behavior. In the health care field, different physicians make decisions based on different sets of mental models and approaches to practicing medicine (Lipworth, 2007; Platt and Huettel, 2008; Williams, 2008).

Complex adaptive systems interact with other complex adaptive systems, and these interactions lead to tensions and paradoxes that probably can never be resolved. In fact, the interactions are non-linear, leading to what some scientists refer to as “sensitive dependence on initial conditions.” Thus, “[b]ecause the elements are changeable, the relationships non-linear, and the behavior emergent and sensitive to small changes, the detailed behavior of any complex system is fundamentally unpredictable over time” (Plsek and Greenhalgh, 2001, 626).

The difficulty, of course, is that many models of scientific behavior assume linearity. The “end-to-end” approach first proposed by Vannevar Bush in the 1940s modeled scientific research as a “reservoir of knowledge” that could be tapped by society and used in practical applications. As scientific knowledge increased, the applications would have to be adjusted to

account for advances and more intricate, sophisticated processes. The Bush model presupposes that scientists will work together in an atmosphere of mutual collaboration, resulting in a kind of dialogue among and between scientific communities. As Morss, *et al.*, wrote, “Because natural and societal components of systems interact in complex ways, research that addresses only scientific aspects of a situation often fails to achieve the desired societal results.” For an end-to-end approach to work, decision-makers must emphasize integrated research into multiple systems. “End-to-end research, therefore involves multiple iterations to help information production and use adapt as science and society evolves. In situations with multiple interconnected decision makers, we learned to start by iterating from end to end with one (carefully selected) individual or group that is central to the decision, has flexibility to adopt new information...” (Morss, *et al.*, 2005, 1599).

Much of the literature on scientific decision-making under conditions of uncertainty, especially in the health care field, suggests that decisions are made incrementally, over time, through an iterative process involving complex adaptive systems (Blumenthal, 2004; Bridges, 2004; Lipworth, 2007; Williams, 2008). This summary of scientific decision-making is abstract and general with little explanatory power; therefore, to provide concrete data on the issue, it is instructive to select a group of decision-makers that addresses scientific and/or highly technical issues and examine their decision-making process (Volz, *et al.*, 2005). By studying the group and the decision-making approach employed by its individual members, the factors influencing decision-making can be understood and a theory of decision-making can be developed (Basson and Petrie, 2007; Hayward, 2006). Ideally, the same group of decision-makers will be involved in making decisions on a variety of issues so that if biases and an incomplete knowledge base exist for one decision, the same factors will influence a second decision (Maas, 2007; Meyer and



Meyer, 2005; Platt and Huettel, 2008). In Chapters 4 and 5 of this dissertation, the ACIP will serve as the group of scientific decision-makers under consideration.

### Scientific Decision-making and Public Policy

The scientific decision-making process seeks to advance knowledge by building on knowledge acquired previously, despite the problems associated with data accumulation discussed above; therefore, precision in data collection and analysis is an integral feature of research. Ideally, researchers seek to minimize ambiguity so they can communicate the results of their research as clearly and precisely as possible with other researchers. The level of confidence in a result or series of results increases within the scientific community as confirmation occurs; that is, as scientific activities are reported in the literature, ideally the results cumulatively support a research hypothesis or undermine the hypothesis. In any case, the objective is to discover results that can be measured and communicated precisely. The “success” of a research effort is judged in no small measure with how well the results can be replicated in the case of experimentation or how well the results fit with existing theories and data in the case of a quasi-experimental design (Wynne, 1992).

The policy process, however, is designed to address a societal problem or an issue of concern to a substantial number of citizens. The precision and nuances that frequently occupy scientific researchers are often absent from the policy arena. Policy-makers are not necessarily less concerned with discerning an “objective resolution” to a problem, however it might be defined, but they recognize that time often is of the essence, resources frequently are limited, and the political ramifications of policy choices may preclude selection of an optimal choice. “Satisficing” is the order of the day since it is seldom possible (and perhaps not even desirable) to accumulate all the information necessary to make a fully informed decision. Moreover,

sometimes policy-makers deliberately obscure the reasons for their policy choices or they build in ambiguities so the policy can attract political support that might not be available if the intricacies of a policy were known beforehand. It is entirely possible, and often likely, that a legislative body will enact a statute or a regulatory body will promulgate a rule that lacks even rudimentary specificity. What the policy lacks during the formulation phase can be supplied during the implementation phase (Kinzig, *et al.*, 2003, 330).

Complicating matters is the politicization of science policy as administrative agencies attempt to carve out a domain. Political concerns are never far from the forefront when public bureaucracies compete in the policy-making arena to establish and maintain a policy domain (Bourdeaux, 2008). Researcher D. D. Riley has contended that public administrators must be politicians, at least in part, not merely policy specialists or technocrats. “If bureaucrats are going to enter the political arena they will need to bring some coin of the realm—that is, they will need power,” he wrote. “Knowledge provides some, but not enough, so bureaucrats must find an expressly political base of power” (Riley, 1987, 60). Thus, public organizations are staffed by personnel who seek to establish a domain, distinguish the agency from its competition, and develop effective political strategies for maintaining—and perhaps strengthening—the agency’s domain. Aside from working with congressional committees and subcommittees in the political realm, public administrators cater to clientele groups concomitant with establishing a domain. These groups appeal to the agency to respond to the groups’ interests and, in turn, they provide knowledge and information to public servants (Riley, 1987, 60-63). Ideology and political consciousness are never absent from an agency’s agenda (Nathanson, 1999).

A public health agency faces an especially difficult challenge because it must rely on scientific knowledge that often is complex, highly technical, fiercely contested, incomplete, open

to interpretation, and poorly understood by the public and other third parties. According to one report, “public health agencies are having difficulty striking a balance between political responsiveness and professional values. Some endeavor to insulate themselves from politics; others are buffeted by political firestorms. Too frequently, public health professionals view politics as a contaminant rather than as a central attribute of democratic governance” (National Academy of Sciences, 1998, 154). Successful administrative agencies must learn to overcome this antipathy toward “playing politics,” but at the same time agencies must not be seen as overtly political. It is a fine line, but they must walk that line if they hope to exercise continued influence in the policy process (Bourdeaux, 2008; Davies, *et al.*, 2007).

It is axiomatic that the role and influence of administrative agencies in developing and directing public policy has increased substantially during the twentieth century (Longino, 1990). One reason for this growing influence is that executive branch agencies are able to “exercise strategic influence over policy-making because of their ability to identify issues, plan and administer programs to cope with emerging problems, and generate public support for policies they regard as desirable” (Rourke 1972, ix). Many models exist for describing how agencies compete in the policy realm. Models such as pluralism, public choice, and critical theory, among others, focus on the substantive activities undertaken by bureaucracies (Babidge, *et al.*, 2007; Schneider and Ingram, 1997). Other models, including the political model, the interactive model, and the tactical model, and focus on the process in lieu of the substance of bureaucratic activities (Adams, 2004). Of all these models, whether substantive or process-oriented, perhaps the knowledge-driven model comes the closest to offering a richly persuasive explanation of how an administrative agency—especially a public health agency that claims to rely on scientific research—can influence policy debates (Graham and Dickinson, 2007; Nutbeam, 2001).

The knowledge-driven model suggests that personnel working within an administrative agency will attempt to use their superior knowledge to justify their domain in a given policy arena (Hunt and Shackley, 1999). By contending that no other agency or political entity can bring the same high quality research and professional personnel to bear on a problem, an agency head seeks to convince all competitors within the federal government that they are less qualified than the agency in question to establish and maintain a domain in this policy area (Davies, *et al.*, 2007; Evermann, 2005; Graham and Dickinson, 2007). Moreover, because this is an issue that requires federal government intervention—e.g., a market failure situation, in the interest of the “public good,” or a similar policy argument—private entities such as corporations and interest groups cannot or will not provide the necessary and goods and services because non-governmental entities lack the combination of public legitimacy and specialized knowledge (Nutbeam, 2001).

An administrative agency must be careful to show that in using its superior knowledge in the policy arena it does not champion one set of ideological beliefs over others (Weiss, 1979). This is not to say that an agency must somehow be “objective,” for absolute objectivity in scientific study may be impossible (Funtowicz and Ravetz, 1993; Hunt and Shackley, 1999). Nonetheless, the agency must take pains to assure all constituencies that the knowledge used to influence public policy does not advance certain political ideals based on subjective preferences. In the words of one commentator, “If scientific inquiry is to provide knowledge, rather than a random collection of opinions, there must be some way of minimizing the influence of subjective preferences and controlling the role of background assumptions” (Longino 1990, 216). If an agency hopes to influence public policy by using expert knowledge based on scientific methodologies and data without being corrupted in the process, it must rely on the norms and

values generally recognized as legitimate within the scientific community, although even this endeavor potentially is fraught with controversy (Kitcher, 1993, 81-84; Laudan, 1977).

The difficulty, of course, lies in the fact that the knowledge-driven model invariably contains gaps in the data. No matter how much researchers attempt to gather data, perform testing, and interpret results, unanswered questions exist. Even the most knowledgeable agencies employing the most knowledgeable researchers will stumble upon incomplete data, contradictions, anomalies, and scientific uncertainties. Gaps in knowledge are especially pronounced in the area of scientific research (Funtowicz and Ravetz, 1993). Consequently, decision-makers often are forced to make decisions where substantial uncertainty exists. It is the phenomenon of decision-making under conditions of scientific uncertainty to which this dissertation is directed (Oostenbrink, *et al.*, 2008; Weiss, 1979).

In some cases, uncertainty can increase bureaucratic power because only an agency “expert” has the knowledge and resources necessary to understand an issue and resolve a problem. Elected representatives are generalists and lack the specialists’ background education and training; therefore, legislators require assistance from experts who can navigate through the jargon and confusing concepts to make sense of a complex, highly technical issue. Despite the arguably beneficial nature of some degree of uncertainty, at least insofar as the agency is concerned, large gaps in the data and enormous uncertainties beyond the tolerance of agency experts sometimes can present problems for decision-making (Funtowicz and Ravetz, 1993).

In light of the differences between the scientific decision-making process and the policy process, tension exists between the need for a scientifically sound decision with as few uncertainties as possible and a policy decision that meets the needs of a broad constituency. Science and policy rely on different levels of evidence deemed persuasive to their respective

audiences, so it is little wonder that they deal with uncertainty differently. Scientists reply on high evidentiary standards—requiring small a probability of at most five percent, and sometimes less than one percent, that an error has occurred—while policy-makers can reply on far less exacting standards as long as they can rhetorically persuade their constituents to support their conclusions (Gollier and Treich, 2003).

At least four difficulties arise from these different standards. First, the failure to recognize the differences can lead to miscommunication and frustration as policy-makers and the public believe that science has failed to meet their needs. Second, because scientists sometimes focus their research on questions that may represent esoteric value but are not necessarily transferable into practical applications in a short time frame, policy-makers and the public occasionally decide that science does not produce useful knowledge. In short, scientists' understanding of utility may differ markedly from the public's understanding of utility. Third, when scientists find it difficult to quantify uncertainty they may decide to focus on smaller problems or incremental parts of a problem even as policy-makers demand broad, large-scale answers in the face of uncertainty. Finally, the supposedly neutral language of scientific evidence and data may disguise a fundamental difference in understanding about what constitutes "knowledge." Scientific decision-makers may seek knowledge in and of itself, a purely abstract conception of data collection and analysis, while policy-makers and members of the public desire knowledge for its practical application (Kinzig, *et al.*, 2003, 330-331).

Table 2.1, below, summarizes the differences between science as it is generally understood by scientific researchers (the "Science" category) and as it is understood by non-science-based policy-makers (the "Policy" category). At the risk of over-generalizing and thereby perpetuating a facile dichotomy between science and policy, the table illustrates the

different uses and expectations that scientific decision-makers and public policy-makers bring to their respective roles. Any scientific researcher that works in a public agency must be cognizant that his or her work likely will be used to effect changes in public policy even if the results are imperfectly understood. The difference between the results as they are understood and reported by scientific researchers and the results as they are understood and reported in a public arena is sometimes referred to as the “science-policy gap.” As one might imagine, inaccurate translations of scientific research into policy decisions often are correlated to scientific uncertainty. The gap between science and policy can be bridged, to some extent, through effective communications. This exercise requires that scientific researchers perfect their communications skills while policy-makers concomitantly immerse themselves, to some extent, in the details of scientific debate (Bradshaw and Borchers, 2000).

Table 2.1: The Science-Policy Gap

<b>SCIENCE</b>	<b>POLICY</b>
Uncertainty and probability accepted	Certainty desired
Unequal access to information is a fact	Equal access to information is desired
Long-term	Short-term (often the election cycle)
Flexibility in research parameters	Rigid, specific need for quick information
Problem-oriented	Service-oriented
Discovery-oriented	Mission-oriented
Failure and risk accepted	Failure and risk intolerable
Innovation is prized	Innovation is suspect
Replication is essential for credibility	Beliefs are situational
Clientele diffuse, diverse, or absent	Clientele is specific, immediate, and insistent

These differences raise the question of how scientists should present information to policy-makers and the public when substantial uncertainties exist as to what is known and, for that matter, knowable. One method for effectively communicating information is called “expected utility theory,” which states that for any action that someone might take the actor must first identify each possible outcome it might engender and determine the relative likelihood, to

the extent possible, of that outcome. Scientists need to present the various scenarios that might result from a particular action and explain how and why such probabilities exist. This kind of “decision-tree” analysis may not be intuitively obvious to the non-scientist, but a persuasive case can be made if the various probabilities and outcomes can be clearly explained (Kinzing, *et al.*, 2003, 331).

Complicating the gulf between scientists and policy-makers is the over-generalization that occurs when individuals are classified using broad categories. “Scientists” do not comprise a single group of people that shares the same values and perspectives. Indeed, scientists who work inside public agencies may have different attitudes and ideas about scientific uncertainty when compared with academic researchers. Whereas the latter may profess allegiance to “pure science,” the former may be interested in advancing science as a means of achieving an agency’s objectives. Similarly, “policy-makers” is a larger category that does not account for the divergent perspectives among individuals who fall within the category. A legislator, duly elected and accountable to the voters, probably views his or her role differently than a career civil servant who gained employment through a competitive process and will never have to answer to the electorate, yet both legislators and unelected civil servants are policy-makers (Kinzig, *et al.*, 2003).

Despite the recognition that “scientists” and “policy-makers” are broad generalizations that contain numerous sub-categories, a dichotomy frequently exists between the expectations of decision-makers in each broad class. One reason for the differing expectations is that in many cases each group views members of the other group with suspicion. Scientists often express concern when they see the nuances and qualifications in their work ignored or misrepresented in the policy process owing to policy-makers’ desire to express qualified data and conclusions in



absolute, easily understood terms. For their part, policy-makers have been known to view scientists with disdain because the qualifications and nuances in scientific data, far from being a necessary component of the scientific process, can be seen as hedging. In addition, the professional jargon that scientists employ to communicate with other scientists can be misinterpreted by non-scientists as simply a means of deliberately excluding non-scientists from “the club,” and nothing more (Bradshaw and Borchers, 2000).

This second point bears further discussion. When policy-makers mistrust the very scientists they look to for information and data to support their policy decisions, the way policy-makers view scientific uncertainty is negatively affected (Dunn, *et al.*, 2008). Indeed, the uncertainty or lack of confidence in the efficacy of scientific results perceived by policy-makers can be classified in one of two categories. First, there is uncertainty about the uncertainty (Halpern, *et al.*, 2006). Many members of the public are confused when researchers within the scientific community argue and debate about the meaning of research findings. Honest divisions and debates within the scientific community—no doubt the result of the many sub-categories within the broad conception of a “scientific community,” as mentioned previously—can increase the sense of frustration that non-scientists feel when they seek to find “the answer” to a perplexing technical problem. Thus, in the debate over global climate change, some scientists contend that immediate action must be taken or the consequences will be dire. Other scientists prefer a “wait-and-see” approach, arguing that not enough data exist to predict with any reasonable degree of confidence the possible outcomes from global warming. To policy-makers and the general public, most of whom are not schooled in the intricacies of climatology and natural science, it is difficult to identify an appropriate response because each school of thought seems to have its credentialed adherents with supposed scientific credibility. To make matters

worse, the data are so complicated that a layperson cannot begin to fathom the subtleties and richness of the data (Lankshear, *et al.*, 2005; Pullin, *et al.*, 2003).

In addition, uncertainties associated with the scientific method do not seem to translate well into everyday life. As an example, consider the idea of significance. To a researcher trained in the use of statistical tools, to say something possesses “statistical significance” means that the occurrence probably is attributable to something than happenstance or random error. Some sort of relationship exists in the data. At the same time, statistical significance is not necessarily tantamount to practical significance. The existence of a statistical relationship does not mean that a practical, observable change is present (Ghosh, 2008; Michael, 1979).

It is easy to dismiss policy-makers and the public, however imprecise these designations may be, as seriously deficient in their sophistication or their understanding of science and uncertainty in decision-making. Such dismissals, while perhaps regrettable, are a luxury that some academic scientists may enjoy, freed as they are from the need to show practical significance in their research. For scientists working in public agencies—especially agencies where their decisions can affect a large part of the populace—the need to handle and communicate about uncertainty is pronounced. Perhaps nowhere is the need to come to terms with scientific uncertainty as crucial as in public agencies that grapple with medical decisions. Non-scientists may be willing to accept uncertainties when the results do not touch on their health, but when medical decisions are involved the demand for precision and uncertainty increases precipitously.

This idea that science and policy are fundamentally at odds with each other because science is fact-based and policy is opinion-based has been assailed, especially in recent years (Bradshaw and Borchers, 2000). A strain of the literature on recognizes that the idea of the

scientific method as a rigorous search for truth is exaggerated (Lipshitz and Strauss, 1997). Geographer Marvin Waterstone of the University of Arizona has warned against those who “cling to a nostalgic view that the ‘fundamental standards of scientific rigor’ are somehow given, rather than constructed” because they don’t want to embrace nihilism or the loss of absolute standards. In Waterstone’s view, it is not nihilistic to “recognize the thoroughly politicized and political nature of science as it now exists (and always has).” Instead, it is realistic to acknowledge “that science is a human activity, engaged in by embodied and contextualized individuals, and as such inescapably connected to other spheres of social life.” Scientific standards seek to provide a replicable, rigorous framework for understanding phenomena, but “there is nothing sacrosanct about those standards, and they have no special ontological status as pre-given or immutable” (Waterstone, 1998, 297).

If the bifurcation between science and policy is exaggerated, this realization means that scientists, especially those employed in public agencies that make decisions affecting public policy, must always be cognizant of the policy implications of their research and their decisions. The popular notion of the lone scientist in a desperate quest for “the truth” as he or she fends off political hacks cynically interested only in advancing their own careers, while it may occasionally bear a slight resemblance to reality, generally is an urban myth. Instead, scientific decision-makers must admit that science and policy are intertwined. Nowhere is this observation as obvious as in the area of scientific research on medical issues.

#### Medical Decision-making and Uncertainty

Medical researchers, especially those engaged in clinical research, typically use their background knowledge and expertise to sort through available treatment options and make a decision on the preferred course of action to pursue. They recognize that uncertainties exist, but

a decision must be made, nonetheless. Medical researchers generally formulate uncertainty in terms of: (1) the frequency (probability) of an event; (2) assessments of credibility intervals around the estimates of probability; and (3) entropy, which refers to the uncertainty associated with one treatment option versus another (Djulbegovic, 2007, 82).

According to information theory entropy, when the probability of various choices is equal it leads to a decision-making stalemate because a clear decision rule is absent. Maximum uncertainty exists because expected utility theory, which dictates that decision-makers act based on the probability that a desirable outcome can be achieved, cannot resolve doubt when probabilities are equal or risks are unquantifiable. If all desirable outcomes are more or less equal or unknown, something more is needed if a decision is to be made. This lack of information about the probability of desired outcomes is captured in the term “equipoise,” which refers to “equal beliefs, or equally distributed uncertainty about the relative effects of competing treatment alternatives” (Djulbegovic, 2007, 82). Equipoise does not necessarily indicate that a precise quantitative distribution of treatment effects can never be observed. Instead, the term has a looser meaning; it expresses the difficulty in decision-making that occurs when no one treatment option appears superior to others and there exists a possibility that the doubt will never be resolved satisfactorily. In other words, as medical researchers confront a novel problem, their educated guesses and elegant research hypotheses cannot suggest a preferred course of treatment. No clear decision rule exists or is likely to exist in the foreseeable future.

For many physicians, the choice of scientific methodology and analytic technique is tailored to the uncertainty about treatment effects; that is, they seek to maximize the benefits of a treatment option and minimize the risk of side effects. Thus, whichever drug or course of treatment that has the largest benefit for the smallest set of side effects is the preferred option. In

an effort to resolve the uncertainty associated with treatment effects in cases where no treatment option is immediately preferred, medical researchers often rely on an experimental protocol called “randomized controlled trials,” or RCTs. RCTs require patients to be enrolled in an experiment whereby one group of patients is administered a drug while another group is administered a placebo. Afterward, the differences between the patients’ health before and after the administration of the drug are calculated for each group and the results are compared between the two groups ((Djulbegovic, 2007).

When the estimated uncertainties about the cause and effect of competing treatments are high, it is difficult to know whether the observed effects were the result of the treatment(s) or owing to other factors such as patient selection, pre-existing conditions, unknown biases, or even random error. In situations where uncertainties are high, additional RCTs are the most efficacious means of resolving uncertainties. Presumably, trials will yield useful results because the RCTs will provide clear data on the performance of one alternative treatment when compared with a competing alternative treatment. Clinical trials work well when equipoise exists; that is, RCT is designed to be a “tie breaker” in cases where competing treatment options cannot be evaluated effectively through intuition or heuristic devices. Some researchers call the choice between seemingly equivalent alternatives “Alternative Futures,” or the choice between discrete alternatives where the outcome cannot be predicted with a reasonable degree of reliability beforehand (Djulbegovic, 2007).

When the treatment effects are dramatic or immediately recognizable—such as in the case of blood transfusions, insulin, or penicillin—RCTs are not necessary. The relationship between administration of the drug or treatment and the effect is reasonably clear. Mistakes can, and sometimes do, occur, but generally the uncertainties can be resolved with a reasonable

degree of clarity. A clear decision rule exists. Unfortunately, treatment effects are not always immediately recognizable no matter how many RCTs are used (Bornstein and Emler, 2001, 98-99).

Another level of uncertainty exists in medical research, and that involves a “Range of Futures,” or the possibility that no discrete alternatives exist or, in any case, the alternatives have yet to be identified. A good example of this problem is when a new drug is introduced into the marketplace. Despite the clinical trials conducted by pharmaceutical companies, invariably the time needed to determine whether long-term, negative side effects will occur—decades, in many instances—has not elapsed. Because data are limited, it is possible that the range of potential side effects is greater than one might predict even when reviewing the side effects associated with similar drugs from the same family of chemical substances (Bornstein and Emler, 2001; Lankshear, *et al.*, 2005, 375-375). Making comparisons and calculating risks when a Range of Futures is present is far more difficult than when Alternative Futures are involved because the former lacks precision in its data collection and analysis. Nonetheless, there is a high probability that given enough time and data, discrete categories can be developed and eventually the RCT method may allow researchers to discriminate among and between treatment options (Djulbegovic, 2007).

The worst case scenario in medical uncertainty can be called “True Ambiguity.” In these cases, the situation is so novel and knowledge about alternative treatments is so incomplete that researchers cannot begin to calculate the quantity or quality of discrete choices. Unlike a situation with a Range of Futures, it is impossible to determine whether enough information will be collected and analyzed to improve the decision-making process. One might label this scenario an “epistemological crisis.” The difficulty with True Ambiguity is not simply that data

are missing; a method of understanding data even if they were to be identified and collected is absent. Perhaps the method will never be found, or at least never found in a meaningful timeframe. A researcher faced with True Ambiguity should not despair that certainty is impossible and therefore become paralyzed with indecision, but he or she should recognize the travails associated with research when uncertainties outweigh certainties (Djulgovic, 2007, 83).

As an example, consider the dread disease smallpox. There was a time when treatment for this disease amounted to True Ambiguity. Prior to the 1790s, this “prowling spotted beast,” a virus that began with an infection of the mucous lining of the nose and throat, was poorly understood. The medical field was so primitive and the understanding of viruses and infections was so rudimentary that no amount of data collection could solve the dilemma of how to prevent infection and treat the disease. For medical researchers of the seventeenth and eighteenth centuries, the paucity of information that was known about smallpox did little more than describe what happened to the body. True Ambiguity existed because the description itself did not suggest a means for mitigating its effects.

When the disease invaded the human body, it initially produced flu-like symptoms: nausea, vomiting, headache, backache, and a fever as high as 104 degrees Fahrenheit. Severe abdominal pain and disorientation often set in, followed by the appearance of a distinctive pattern of symptoms, notably a series of small red spots on the tongue and in the mouth. The spots developed into sores, broke open, and spread the virus throughout the mouth and throat, causing the infected person to become contagious. About the time that the sores broke open in the mouth, a rash appeared on the skin and eventually erupted into large bumps filled with an opaque fluid. These pus-filled bumps, a clear sign of smallpox, were known as pustules, sharply

raised, round, and firm to the touch, reminding some observers of BB pellets embedded under a person's skin. If the victim survived the high fever, the pustules formed a crust and then a scab. By the end of the second week, all the sores had scabbed over and the scabs eventually fell off the skin, leaving a series of distinctive, pitted scars that signified a smallpox survivor. Smallpox was transferred through the air in tiny droplets expelled orally from an infected person, especially through coughing and sneezing, although talking could transmit the disease as well. Sometimes it was spread from person to person through blankets, linens, and clothing. With a relatively long incubation period—full-blown symptoms generally did not appear until 12 to 14 days after the first exposure—the virus had ample time to spread without detection. Moreover, it could survive in the open air for up to 24 hours, even in winter conditions (Creehan, 2001).

Smallpox infection at close quarters—for example, in army units, hospitals, schools, or prisons—often was a death sentence. During the eighteenth century, the mortality rate was commonly thought to be about 30 percent, but much depended on the age and general health of the victim. The virulent “sledgehammer” form of the disease may have claimed the lives of 60-80 percent of the infected population. For children, the elderly or the previously infirm, who seldom enjoyed good health to begin with, any form of smallpox was a cause for great anxiety.

Despite the great deal of information and data that eighteenth century physicians amassed, it wasn't until medical researchers all over the world eventually realized the causes and consequences of infections that a treatment for smallpox was in the offing. In 1796, a British physician, Edward Jenner, developed an effective vaccine after he read up on the known data on infections and conducted a series of experiments. The publication of his paper “The Inquiry” two years later was extremely controversial, causing some critics to characterize Jenner's vaccine as worse than the disease (Lewis-Jones and Baxby, 2001). The nature of infections and



the development of other kinds of vaccines were a long time coming, but Jenner and his progeny, in effect, transferred the problem from “True Ambiguity” into a “Range of Futures” issue. As the decades passed and more tests were conducted, the Range of Futures for smallpox became Alternative Futures. With Alternative Futures, the RCT method becomes an especially effective means of advancing medical research and reducing scientific uncertainty.

Despite its importance, equipoise is not the only important uncertainty principle in medical research. Ever since medical researchers began employing clinical trials to test the relative merits of alternative treatments, the justification for enrolling patients into the trials has been the need to resolve uncertainty among treatment options. The question naturally arises, however, as to whose uncertainty is morally relevant. Equipoise, which describes uncertainty among individual physicians, is different from uncertainty among the community of scientists and medical researchers. In the former case, a physician may be uncertain as to the relative benefits associated with a menu of potential treatments, but the physician has the option of reading the relevant medical literature, consulting with more experienced practitioners, or referring the patient to an appropriate specialist in the field. In a situation where the individual is uncertain but a higher degree of certainty may be available if the physician undertakes a reasonably diligent effort to discover the necessary information, enrollment in a clinical trial is not warranted.

The broader uncertainty principle that applies to the community of medical researchers presents a separate set of problems and issues. As researchers Lilford and Djulbegovic have observed, the crucial question is this: “How much uncertainty can we accept before entering a patient into a trial and by whom (patients, physicians, and community?)” (Lilford and Djulbegovic, 2001). Although the debate continues, generally if the individual physician finds a

genuine lack of consensus among scientists and physicians about an appropriate course of treatment, the appropriate step is to enroll the patient into a clinical trial as an efficacious means of resolving the dilemma.

Assuming *arguendo* that the enrollment of a patient in a clinical trial is seen as an acceptable method of resolving doubt as to treatment options, a difficulty can arise when the goals of the trial and the goals of the individual patient are different, as is sometimes the case. The study parameters may be strictly controlled and may require a regimen that is not ideally suited for an individual patient. When a single physician was treating a single patient, the patient's health and welfare were the paramount objectives in the physician-patient relationship. When the patient enrolls in a clinical trial, however, the interests of the researchers in ensuring to integrity of the research project became a factor in treatment decisions. This observation does not mean that physicians can knowingly compromise a patient's health in the interests of a higher good, but it does mean that making exceptions for a particular patient presents problems that may not necessarily be resolved in the context of a clinical trial (Bornstein and Emler, 2001).

Researchers have recognized the potential conflict of interest that exists between the researcher who must protect the integrity of the clinical trial and an individual patient who may need something that is not provided for in the trial. One way to resolve the conflict is through the use of game theory. According to this view, the "players" are the patient and the researcher. The solution to the game is to find an equilibrium point at which each player's game strategy is optimal when compared with other players' game strategy. In the context of an RCT, equilibrium is reached when the probability of random allocation at which both the patient and the researcher will most likely achieve their goals occurs. If one treatment is obviously superior to competing treatments, neither patient nor researcher is well-served by randomization. If the

results cannot be predicted in advance and if there are no clear guidelines for determining which treatment to superior to the alternatives, both the patient's and the researcher's most rational course of action is to randomize.

Statistical tools can be employed to investigate alternative treatments and their probable rates of success. In fact, some researchers have found a typical bell-shaped curve in testing new treatments, suggesting that such treatments used in RCTs are, on average, as likely to be inferior as they are to be superior to standard treatments. In other words, because there is no clear standard for differentiating among and between experimental treatments, randomization is the preferred course of action for resolving uncertainty in RCTs (Djulbegovic, 2007).

Resolving uncertainty through RCTs remains a crucial endeavor for scientists, but one medical researcher cautions against extending the effort too far:

As inevitable and unpleasant as many uncertainties are, one can argue that patients (and their doctors) should not even strive to completely eliminate uncertainties. Although the role of scientific method is to reduce uncertainties, a total elimination of uncertainty would be undesirable, since, it has been argued, it would lead to deterministic life—meaning that all events would be known in advance, in turn implying no hope, no ethics, no freedom of choice (Djulbegovic, 2007, 95).

In any case, desirable or not, eliminating uncertainty is not a realistic objective. Instead, researchers and practitioners alike must focus on managing uncertainty. This task involves determining when uncertainty exists, the cause of the uncertainty, and the likely consequences of uncertainty. Even if uncertainty cannot, and should not, be banished from the realm of science, it

can be managed. Ultimately, managing uncertainty in a responsible manner is the goal of ACIP members, as will be discussed in Chapters 4 and 5

As for the dissertation, the goal is to understand how ACIP members manage scientific uncertainty. Clearly, the group makes periodic recommendations to the CDC despite the ubiquity of scientific uncertainty, and the CDC publicizes those recommendations. ACIP meetings are open to the public; their recommendations are available online and in published reports, as discussed in Chapter 1. Consequently, the nature of ACIP recommendations is reasonably transparent and accessible. To understand the group's process for making recommendations, however, it is necessary to go "behind the recommendations" and delve into the factors that influence members' decisions. As discussed in Chapter 3, Grounded Theory is an appropriate method to achieve this goal.

## CHAPTER 3

### METHODS

The initial question that arises in embarking on this, or any, research project is the question of how data and information will be collected and analyzed. In this case, grounded theory (GT) serves as the principal research method for investigating decision-making within the ACIP. One of the early proponents of this qualitative method, Barney G. Glaser, defined GT as “a general methodology of analysis linked with data collection that uses a systematically applied set of methods to generate an inductive theory about a substantive area” (Glaser, 1992, 16). While the definition is a useful starting point for understanding GT, it is relatively vague.

GT is a useful approach in this endeavor because it is a loosely-structured research design. It allows a researcher to develop orienting ideas and concepts going into the project, but it recognizes that information uncovered during a literature review and in the course of conducting semi-structured interviews will influence the theory that is generated by the field work. As new data are collected and assessed, a researcher makes adjustments to the resultant theory (Corbin and Strauss, 1990; Holton, 2008). This process differs considerably from the traditional hypothesis generation and testing procedure usually found in a quantitative study.

In quantitative research, typically the hypothesis is developed well before testing and adjustments are not made afterward. The data either support the null hypothesis (that is, no correlation exists between the independent and dependent variables) or they fail to support the null hypothesis, which means that some kind of correlation exists. GT, by contrast, is a fluid research design that eschews traditional hypothesis testing. In the words of two well-known

researchers, Matthew B. Miles and A. Michael Huberman, grounded theory allows the research theory to “emerge from the field in the course of the study” (Miles and Huberman, 1994, 17).

GT is an acceptable research design for exploring qualitative data because it is well-suited for explicating rich narrative details. The question of the adequacy of a research design really is the question of whether the research tests for the problem that the researcher seeks to understand. A research design is a plan for answering the research question in a persuasive manner. Thus, the researcher needs to be able to determine with a reasonable degree of certainty or authority that the question under consideration is answered or not answered at the conclusion of the research (Holton, 2008; Sousa and Hendriks, 2006).

Unlike a strictly narrative structure, which provides details on how people acted and how events took place, GT is designed to understand the steps and thinking that led actors to take steps and resolve problems in certain ways. Thus, field research is a key component of grounded theory in that researchers make contact with participants to ask questions and explain why they behaved the way they did. Getting inside the participants’ view of reality allows researchers to develop a richly textured, nuanced description of the data (Corbin and Strauss, 1990; Key, 2004, 53-57; Martin and Turner, 1986; Strauss and Corbin, 1990).

#### The Origins of Grounded Theory as a Research Method

Grounded Theory grew out of the field of sociology during the 1920s, especially at the University of Chicago School. Herbert Blumer, a student of the American Pragmatist George H. Mead, coined the term “symbolic interactionism” to refer to the idea that people act based on events that have meaning for them. Meanings are derived from social interactions and the interpretations that individuals assign to those interactions. For Blumer, therefore, a new

research methodology was necessary to help social scientists understand human behavior (Glaser and Strauss, 1967, 14).

The philosophy of Pragmatism was the key to understanding Blumer's perspective. Often called the "American philosophy," Pragmatism is an idea most closely associated with the late nineteenth and early twentieth-century thinkers Charles Sanders Peirce, William James, and John Dewey. This philosophy champions a practical approach to problems, the possibilities inherent in a democratic ethos, the promise of individualism, the efficacy of the scientific method, and optimism for the future. Pragmatism was widely heralded as a valuable addition to western philosophy during the latter half of the nineteenth century up through World War II. In the post-war years, Pragmatism was eclipsed by philosophical traditions such as logical empiricism, existentialism, and critical theory. Richard Rorty, a neo-Pragmatist, attempted to resurrect the Pragmatic paradigm late in the twentieth century (MacIntyre, 2008).

Pragmatism assumes that the individual is the important unit of analysis. This is not to say that community is unimportant; rather, community service is best realized by encouraging the development of the individual. Just as Friedrich Nietzsche argued that an individual's perspective is crucial toward understanding the potentiality of a human life, the Pragmatists contend that perspective is a key component of their philosophy. A person makes choices in life, and the sum of those choices, in large measure, determines whether the person will succeed or fail. Pragmatism is not a consistent ideology that requires adherence to supposedly immutable propositions that must be linked logically with similar syllogisms. It is an experimental approach to the world. If an individual tries a course of action and it proves to be ineffective, the individual is well-advised to try something else in its stead (Churchill, 2008).

Consider modern Pragmatism through Rorty's work. Building on the work of the nineteenth century Pragmatists, Rorty suggested that no difference exists between something that is true and something that works as a practical matter. In other words, he argued that it is nonsensical to think that objective, immutable standards exist separate and apart from the real world. Plato's Theory of Forms, for example, which posited an unseen world of eternal truth and omnipresent standards, is impractical and therefore of no consequence. Immutable standards that can never be verified or achieved do not figure into human life. An epistemology that depends on such an abstract, esoteric notion becomes irrelevant, akin to the cliché asking how many angels can dance on the head of a pin.

In Rorty's opinion, human beings do not have an "essence" apart from their ability to use language and the socialization they receive as they grow from infancy. The only standards that apply to people, therefore, are those reached discursively. People build their lives on a foundation constructed from their language use, the rules and mores of society, and their belief in what works and what does not. Human nature can be changed—Rorty labeled it "contingent"—depending on circumstances and the need to adapt to situations. This theory of human nature is based on two concepts. First, as a materialist, Rorty contended that human beings construct their world. They engage in "sentence-uttering" as a means of coping with the world, but he did not believe that human frailties, weaknesses, or shortcomings are rooted in any essential human condition (MacIntyre, 2008).

Rorty's philosophy is designed to be liberating to the individual. So much of philosophical and ethical thinking has been focused on discovering immutable principles that cannot be shown to exist. In Rorty's view, when individuals realize that no laws of God or nature are responsible for the structure or operation of human society and mores, they will



recognize that human community is the result of individual achievement. Human beings built these institutions; therefore, human beings can modify and improve institutions. Rather than undermine the human search for meaning in the world, Rorty contends that the realization that human institutions are not external to human beings will cast aside “metaphysical comfort” and imbue human beings with a desire to make sense of the world themselves (Churchill, 2008).

Blumer and the Chicago School of Sociology found Pragmatism compelling because it was a philosophy that encouraged flexibility. In a famous critique that Blumer offered of a monograph on the lives of Polish peasants, he found that the methodology used by many sociologists was essentially little more than collecting anecdotal data and trying to make sense of it based on theories previously developed. Rather than attempting to acquire data to fit a preconceived notion of how the data fit together, Blumer wanted to “theorize from data rather than from the armchair” (Glaser and Strauss, 1967, 14).

Although early sociologists such as Blumer called for an approved methodology in the 1920s and 1930s, it wasn't until decades later that GT emerged as a stand-alone research methodology. The formal theory was first articulated by Barney G. Glaser and Anselm L. Strauss in their landmark 1967 book, *The Discovery of Grounded Theory: Strategies for Qualitative Research*. Glaser and Strauss as well as their intellectual progeny were disturbed by the debate between proponents of quantitative data analysis and proponents of qualitative data analysis because the dispute seemed to be artificial and unproductive. Before the advent of GT, theory generation was viewed by many researchers as a qualitative enterprise while theory verification was seen as the province of quantitative research. For Glaser and Strauss, this division was tantamount to a distinction without a difference. They contended that generating and verifying a theory should be a seamless web, an ongoing iterative process. As long as one

set of researchers generated theory and another tested it, there was a breakdown of communication. Often the qualitative data were “used in a nonsystematic and nonrigorous way,” which complicated quantitative measures and frustrated attempts to verify the theory. These complications and frustrations further exacerbated the divide between qualitative and quantitative schools of thought (Glaser and Strauss, 1967, 15). As Glaser and Strauss observed in their seminal work, the push toward verifying theory in lieu of generating theory “which has been linked with the growth of rigorous quantitative research, has had the unfortunate consequence of discrediting the generation of theory.” Indeed, qualitative theory generation “generally is labeled ‘unsystematic,’ ‘impressionistic,’ or ‘exploratory,’ and the flexible quantitative research ‘sloppy’ or unsophisticated.” In their view, such generalizations are unwarranted, and represent a fundamental misunderstanding of the importance of theory generation. “These critics, in their zeal for careful verification and for a degree of accuracy they never achieve, have forgotten both the generation of theory and the need for carefully appraising the different degrees of plausibility...” (Glaser and Strauss, 1967, 223).

According to Glaser and Strauss, GT improves on the old ways of thinking because it allows researchers to collect data and analyze that data iteratively. Since the results of the research are not clear beforehand—otherwise, there would be no point in undertaking the research project—a carefully constructed theory or a thorough research hypothesis can contain fundamental flaws that retard the research effort and often lead to inconsistent, uninteresting, or insignificant results. A method that allows for subtle changes in the basic assumptions of the research based on iterative results can lead to improved results because patterns and relationships identified in the data lead to refinements and changes in the way fieldwork is conducted and in the generalizations that are formed. This approach differs from the typical research design

wherein a researcher develops an hypothesis and, using methods deigned to test the hypothesis, determines whether the relationships among and between the data uphold or undermine a null hypothesis (Glaser and Strauss, 1967, 2-5).

In GT research, when the researcher believes that enough information has been amassed to serve as a defensible basis for theory generation, he or she closes off the research and begins the formal process of making sense of the data. It is important for the researcher to review the collected data systematically, thereby ensuring, to the extent possible, that the theory will fit the data and not vice versa. It is a difficult psychological endeavor to remain open to the data as opposed to developing a theory and trying to make the data support the theory even in instances where the fit is unnatural, but this is a crucial step in the GT process.

In addition, it is important to realize that more than one interpretation of the data is possible, so the researcher must not become paralyzed by the possibility that he or she is “wrong.” The researcher has spent time and energy compiling data and making sense of the information. Presumably, no one else knows quite as much about this particular piece of the puzzle as the researcher. Therefore, he or she must set aside fears of inaccuracy and sift through the data to construct the best theory possible. Subsequent researchers may contend that another interpretation is possible given these data, but ultimately the iterative nature of theory generation and academic research is the goal of GT as well as many other methods.

A skeptic might contend that field work is little more than a sophisticated form of anecdotal data collection—narratives collected for the sake of narrative with little or no generalizability—but such a rejoinder misses the point. Anecdotes are vignettes about *what* happened, but they are not explanations of *why* it happened. GT explores the why of past events by overlaying theories and concepts on top of a traditional narrative structure. It remains an

inductive, *a posteriori* approach, as opposed to the *a priori*, deductive approach used by researchers employing traditional positivist, quantitative methods (Singleton and Straits, 1999, 349-50).

If the field work is performed well, the resultant theory generated by the data, i.e., the *a posteriori* approach, will reflect the intricacies inherent in the field. Rather than constructing an hypothesis based on a “grand narrative” view of the world, a researcher using grounded theory delves into the specifics of a case or a series of cases without adopting a “variable perspective” where the cases are reduced to numerical representations of data points for purposes of quantitative comparisons such as regression analysis (Holton, 2008; Sousa and Hendriks, 2006; Dixon-Woods, *et al.*, 2004, 15-16).

Several caveats must be kept in mind. Because GT resembles other types of qualitative research methods and because it is counterintuitive to the traditional model of hypothesis development and quantitative testing, it is easy to mistake GT for other types of research methods or to blend methods. As one of the fathers of GT, Barney G. Glaser, has observed, the “intertwining of GT with preconceived conjecture, preconceptions, forced concepts and organization, logical connections and before-the-fact professional interest defaults GT to a remodeling of GT methodology to the status of a mixed methods qualitative data analysis methodology” (Glaser, 2004, 3).

Grounded theory is not designed to provide for an accurate description of observed phenomena the way that historiography, ethnography, or cases studies are designed. Glaser has written that “GT is not findings, not accurate facts and not description. It is just a straightforward conceptualization integrated into theory—a set of plausible, grounded

hypotheses. It is just that—no more—and it is readily modifiable as new data come from whatever source—literature, new data, collegial comments, etc.” (Glaser, 2004, 8).

### Using The Grounded Theory Method

GT theorists typically begin by discussing the temperament of the researcher. Initiating a research project when the theory or underlying objective is not always clear can be a daunting enterprise. The fear is that much time and energy potentially can be invested in the endeavor only to discover that little useful information and data are collected and the resultant insights do not lead to meaningful theoretical breakthroughs. Moreover, as a researcher becomes immersed in the details of a narrative, the tendency is strong to become sympathetic to the players, to in a sense be “captured” by the narrative. In such a case, a researcher may lose analytic distance and be transformed from a more-or-less neutral academic researcher into a polemicist for the cause. If one is to maintain what GT proponents refer to as “theoretical sensitivity,” it is crucial that a researcher eschew *a priori* hypotheses based on logical deduction. This is not to suggest that a researcher can or should abandon all conceptions about general propositions—in this instance, the notion that where a reasonably clear, consensus-based decision rule is in place, decision-makers generally follow the decision rule—but it does indicate that any preconceptions about the project and its utility, or lack thereof, should be avoided or, to the extent they cannot be avoided, acknowledged (Corbin and Strauss, 1990; Holton, 2008; Martin and Turner, 1986; Sousa and Hendriks, 2006; Turner, 1983).

GT analysis commences immediately with data collection. Again, this may seem counterintuitive to the general model of academic research where the initial phases of the project are devoted to hypothesis development and a literature review to determine who has tackled the problem previously. In those instances, the literature review is an integral feature in constructing

and refining a research hypothesis or theory that will be tested or explored in the research. Because GT is generated *after* the data are collected, the literature review serves only as another means of data collection, not as the basis for hypothesis formulation. This statement does not imply that a literature review is superfluous; rather, it treats literature as yet another source of data to be integrated into the comparative analysis process after conceptual development is underway (Corbin and Strauss, 1990; Martin and Turner, 1986; Sousa and Hendriks, 2006).

Data collection often consists of interviews with key participants. Although the researcher must direct the interview so as to stay on topic, it is important to allow subjects an opportunity to speak unencumbered by set boundaries. Accordingly, semi-structured interviews, as discussed previously, are a favored approach (Charmaz, 2003). As Glaser has written, “The mandate is to remain open to what is actually happening and not to start filtering data through preconceived hypotheses and biases to listen and observe and thereby *discover* the main concern of the participants in the field and how they resolve this concern” (Glaser, 2004, 8).

As data are collected, they are coded. Perhaps nothing is as abstract and difficult to fathom as the idea of coding in GT, but it can be understood by referring to data coding in quantitative research. Data coding for statistical purposes, for example, requires a researcher to assign variables to specific categories, which can then be used to collate data for subsequent comparisons such as regression analysis. The concept of assigning cases into categories is similar in GT except that the purpose is not to facilitate quantitative measurements. Instead, the researcher establishes theoretical classifications that allow him or her to understand apparently disparate phenomena by questioning their essential properties and assigning them to appropriate categories (Corbin and Strauss, 1990; Glaser and Holton, 2005; Holton, 2008).

While data are collected and coded, the researcher engages in a constant comparative method, which allows for systematic analysis. Incidents are compared with other discrete incidents to establish uniformity and provide insight for theory generation. The incidents form the basis for concept development. As more concepts are understood, they can be compared so the researcher can establish the best fit among the many concepts and choices available. Eventually, a core variable emerges to account for most of the variation concerning the problem or focus of the study.

One of the difficulties in any research project—but especially in a project such as GT where theoretical concepts and broad themes are developed while the data are collected—is the problem of knowing when to cease collecting data and write up the results. Some cases involve multiple actors and/or agencies, in which case it is difficult to know when a truly representative sampling of the population has been obtained (Corbin and Strauss, 1990; Sousa and Hendriks, 2006). Fortunately, in this project the number of ACIP members is finite—fifteen (allowing for some non-participation by current ACIP members as well as some participation by former ACIP members)—consequently, such issues do not arise. As will be apparent in subsequent chapters, data collection continued until all ACIP members who consented to an interview had been interviewed. Based on their responses to the interview questions as well as the literature on the ACIP and scientific uncertainty, GT was generated. Once theory was generated, it was written up and a model of ACIP decision-making was developed (Kennedy and Lingard, 2006). See Chapter 5 for more details on the conclusions of this study.

In GT, sorting occurs through the data collection process, but as the write-up proceeds, sorting continues and is refined. Beginning with the core variable—that is, the variable or factor that influences other variables and factors—the researcher must sort the categories and properties

that relate to the core variable (Corbin and Strauss, 1990; Turner, 1983). As patterns emerge, the researcher attempts to explain what happened and, more importantly, why it happened. In this case, the goal has been to understand scientific decision-making under uncertainty within the ACIP. The ACIP interviews provide data on the group's decision-making processes and the literature on scientific uncertainty provides data on how public servants make decisions in general.

Ultimately, after the interviews have been conducted, the purpose of grounded theory (GT) research is to compare cases and, based on the comparison, generate a theory that explains, at least to some extent, the similarities and differences in the data. Cases are compared and analyzed through a process of coding, which allows different interviews to be grouped according to their more prevalent characteristics. In short, coding is the process of "raising questions and giving provisional answers (hypotheses) about categories and their relations" (Strauss, 1987, 21-22).

Throughout the interview process, a researcher is constantly writing theoretical memoranda as a means of refining his or her thinking about the underlying theoretical concepts. Invariably, the researcher's thinking about the meaning of the interviews will evolve over time. In fact, one of the major virtues of performing GT research as opposed to traditional research where a theory or hypothesis is developed at the outset is that a researcher can take advantage of the evolution in his or her thought. A researcher develops theoretical presuppositions (i.e., research hypotheses) before most of the research has been performed. If the researcher discovers unexpected information or data during the research process, he or she has only limited use for such serendipitous results except insofar as he or she can adjust the hypotheses in the middle of the research. In fact, if the unexpected data undermines the original research hypotheses, the



findings can be unwelcome because it is problematic to adjust the original hypotheses after the research is underway. For researchers anxious to conclude the research process or secure funding or publication, unexpected findings can be a burden. More to the point, if the objective in performing social science research is to develop a model of how the world operates, unexpected results can greatly complicate model development (Draucker, *et al.*, 2007; Glaser and Strauss, 1967, 101-105).

By contrast, GT anticipates, indeed depends on, discovering unexpected results. That is the point of favoring a grounded theory methodology in the first place. By going into the research project with only a few expectations—it is impossible to set aside all preconceptions and expectations—and allowing the data to generate results that, in turn, lead to a theory, a researcher can take into account unexpected findings and freely adjust his or her thinking, as appropriate. The theoretical memoranda provide a researcher with insight into the evolution of the theory across time. At the conclusion of the project, the researcher can look back at memoranda from early in the project and compare them as more interviews were conducted, more data was generated, and more responses were coded (Draucker, *et al.*, 2007).

As more cases are coded, patterns begin to emerge which allow a researcher to develop categories. When no new categories can be developed based on the totality of the coded cases, the project is at an end and the researcher is ready to generate a theory about the meaning of the research. This process of ending the research and analysis is sometimes referred to as “theoretical saturation.” It is sometimes difficult to know when saturation occurs, and there is a natural tendency to “research an issue to death”; however, as the research progresses and the researcher acquires greater sensitivity to the subject matter, he or she should develop a sense of what information is appropriate and what is not (Glaser and Strauss, 1967, 111-113).

Presumably, the grounded theory that results from this exercise reflects meaning because it interprets the interviews and data in a way that makes sense of the phenomena being observed. Of course, because it is an interpretation, it need not be the only method of making sense of the phenomena. Reasonable minds can differ, and multiple interpretations often are possible. Having said that, the interpretation must be based on the data and must not extend beyond the findings discovered during the research. Once again, there is a natural human tendency to interpret the data so that the researcher sees what he or she wants or expects to see. The integrity of the GT requires a researcher to resist this impulse. If he or she is constantly reassessing the data with a critical eye and a sense of the limits of the data, the likelihood of self-deception should be minimized, although there are no guarantees that it can be completely eliminated (Glaser and Holton, 2005).

Because GT allows a theory to change as the data change, the likelihood that a weary researcher will be tempted to change the data to fit a rigid hypothesis diminishes. In traditional research, it is possible, although not necessarily commonplace, for a researcher to spend months or perhaps years on a research project only to discover fallacies in the hypothesis or some many missing variables in the data set that the research cannot be completed, or at least it cannot be completed with the resources currently available. This kind of disappointment can lead to frustration and perhaps, in egregious cases, to academic misconduct as the researcher seeks to salvage the work. Even if the researcher does not consciously falsify the data, there is enormous psychological pressure to find a way to rehabilitate the project. This kind of endeavor is not necessary with GT since the expectation exists that the theory will change as the data change.

Researchers sometimes find that as the months and years elapse, their thinking changes; they gain a deeper appreciation of the research problem as they immerse themselves in the

project. Because GT requires constant reassessment and comparisons, the sensitivities of the researcher should constantly evolve as his or her thinking about the case evolves. Glaser and Strauss, refer to the “constant comparative analysis of qualitative analysis.” By this, they are referring to coding cases for a category while simultaneously comparing a particular case with previous cases in the same category. In their view, “This constant comparison of the incidents very soon starts to generate theoretical properties of the category. The analyst starts thinking in terms of the full range of types or continua of the category, its dimensions, the conditions under which it is pronounced or minimized, its major consequences, its relation to other categories, and its other properties” (Glaser and Strauss, 1967, 106).

As a researcher begins the coding process, he or she will note that some categories naturally emerge from the data because multiple interview subjects mentioned the same or a similar answer which seemed to fit into a particular category. Other categories will be the result of a researcher’s particular predilections. This subjectivity is not to suggest that the categories are necessarily suspect—after all, a researcher brings certain background experiences, judgment, and education to the project—but it does suggest the need for a careful explanation of how and why categories were developed and the presuppositions that influenced the researcher’s thinking (Holton, 2008; Strauss and Corbin, 1990).

Depending on which sources are used to develop GT, several types of coding exist. Strauss and Corbin suggest three types of coding: (1) open; (2) axial; and (3) selective. A fourth category, theoretical coding, can be added to the list as well. Other GT theorists suggest slightly different coding, but these types are the most common found in the literature (Holton, 2008; Key, 2004; Lee, 2005; Martin and Turner, 1986).

The initial step, open coding, is developed using the theoretical memoranda. Open coding is an evolutionary process; the concept refers to naming and categorizing observed phenomena by examining data gathered through a literature search and/or through interviews. This ongoing process allows a researcher to form questions and refine lines of inquiry not only about specific observations, but about how the cases are linked to each other. Ideally, as the research continues and more data are collected, heretofore invisible connections and underlying patterns will become clear. The ongoing, iterative process of GT is conducive to identifying categories, their properties, and similarities among and between categories (Holton, 2008; Strauss and Corbin, 1990).

The next step, axial coding, involves an attempt to reassemble data so that connections between categories can be refined to show relationships. Whereas open coding is provisional and changes as data are collected, axial coding is performed later in the process. At or near the end of the research collection phase, when the literature search and the interviews are more or less completed, a researcher will begin to sift through the data and the theoretical memoranda to review the initial open coding process. As a researcher reviews his or her thinking, it becomes clear that certain relationships that appeared to be crucial in the early stages of the research may no longer appear to be crucial. Conversely, relationships that either were not visible or did not seem important at the outset will now appear to be far more significant (Strauss and Corbin, 1990).

Strauss and Corbin (1990) suggest several components of axial coding. First, causal conditions (CC) may emerge during this phase. In their words, CC involves “sets of events or happenings such as rules, regulations, beliefs, values, etc. that influence the phenomena” (Strauss and Corbin, 1990, 131). As any social science researcher realizes, however, demonstrating

cause-and-effect relationships is never easy, although initially it seems that it would be so. Generally speaking, to make a persuasive case for a causal association between one event (a) and a successive event (b), one would assume that if a pattern of changes in (b) varies in direct proportion to multiple changes in (a), we can conclude that (a) causes (b). Assuming that such direct and “clean correlation between (a) and (b) can be observed—which is a big assumption since few perfect associations exist in nature—there still may be intervening or spurious variables that influence causality. As Singleton and Straits write, though, “Associations, of course, are almost never perfect; and so a perfect association between variables is not a criterion of causality. In the social sciences, causal relationships often are implied from comparatively ‘weak’ associations” (Singleton and Straits, 1999, 79). As a component of axial coding, CC allows a researcher to make assumptions about cause and effect based on observations.

Contextual conditions (CN) are another important feature of axial coding. According to Strauss and Corbin, such conditions are the “specific sets of conditions (patterns of conditions) that intersect dimensionally at the time and place to create the set of circumstances or problems to which persons respond through actions/interactions” (Strauss and Corbin 1990, 132). Stated another way, the context of a situation or a series of cases can provide important clues as to what happened and why. The question of context is in a large measure the reason why some researchers favor qualitative research to quantitative research. The latter attempts to measure variation among and between variables by comparing measures of association at a fixed point in time. Implicit in such comparisons is that the variable labels are fixed at a specific point in time and do not change separate and apart from the variations found within the experiment or quasi-experiment. A researcher must control for all variables that can be identified as possibly affecting the outcome. The value of the results depends to a large degree on how well the

researcher identifies the variables and holds them constant. By contrast, qualitative research ideally provides insight into the rich nuances of the cases. In some instances, the nuances explored by researchers employing qualitative methods can assist subsequent researchers employing quantitative methods in identifying salient variables and thereby controlling for their effects in regression analyses (Singleton and Straits, 199, 248).

Axial coding also consists of Intervening Conditions (IC). ICs occur when something happens apart from what the researcher expected. In such cases, people employ unexpected strategies that do not appear to be related to the effect of causal conditions. In other words, an intervening cause—what some researchers label a “spurious variable”—has altered the relationship among and between cases. Because ICs can be present in any social science research, it is imperative to be vigilant for such conditions. As Strauss and Corbin observe, “Intervening conditions may be unexpected events or factors that result in certain behavior or action/interaction strategies associated with the phenomena. However, they also may promote the normal behavior associated with the phenomenon” (Strauss and Corbin 1990, 132).

Action/Interactive Strategies (AS) are “strategic or routine responses made by individuals or groups to issues, problems, happenings or events that arise under those conditions” (Strauss and Corbin 1990, 128). In other contexts, these might be called “coping mechanisms.” AS, therefore, refers to the concept that people respond to causal conditions, phenomena, contextual conditions, and intervening conditions by developing heuristic tools—rules of thumb—to assist them in responding appropriately (Glaser and Holton, 2005; Holton, 2008).

In the case of the ACIP, axial coding begins with the causal conditions that lead to consideration of a particular vaccine. The first causal connection is the development of the vaccine, followed by FDA approval. If these steps do not occur, the vaccine obviously never

comes to the ACIP for consideration in the first place. Next, the vaccine must be put on the ACIP agenda. This process occurs when a pharmaceutical company requests the group's attention or public or medical concern makes the issue imperative or the ACIP executive secretariat, for whatever reasons, decides that the vaccine should be added to the agenda.

Next in the axial coding process are the phenomena, i.e., the specific issues that are addressed in the study. Specifically, this study is devoted to exploring how the ACIP undertakes medical research on vaccines and makes decisions, especially in cases where a high degree of uncertainty exists. The decision-making process is discussed based on a review of the literature about the ACIP as well as interviews with current and former ACIP members.

The third step in axial coding involves contextual conditions, i.e., specific sets of conditions that create the set of circumstances pertaining to the phenomena. As discussed previously, a variety of contextual factors exist. First, the FDA approves the vaccine. The vaccine becomes salient among members of the public or the medical community. If a disease is especially worrisome—it is fatal, occurs frequently and is easily transmitted, or it causes a great deal of misery to patients or expense to the health care system—the disease burden is high and a vaccine recommendation is needed. In such cases, ACIP constituencies often pressure the group to add the vaccine to the agenda and make a decision on an appropriate dosage. In some cases, the executive secretariat may add the vaccine to the group's agenda for any, all, or none of these reasons.

Several intervening conditions can exist and might affect the phenomena in unexpected ways. For example, the FDA may modify or even withdraw its approval. The pharmaceutical company may decide to withdraw its vaccine from the market, as it did with the rotavirus drug

several years ago. Missing or conflicting data can cause the ACIP to forgo making a recommendation because there are too many unknowns (Carpenter, 2004; Rose, 2008).

The ACIP can delay making a recommendation, make a positive recommendation, make a negative recommendation or change a previous recommendation. The consequences of the committee's decisions depend on the content of the decision. If it is negative, dissemination of the vaccine will be limited. If it is positive, presumably the vaccine will be administered widely. Any decision probably will have budgetary consequences. In any case, the decision will be publicized by the CDC staff through various medical publications and outlets.

From axial coding, it is a short move to selective coding, which involves systematically using the findings from axial coding to develop a comprehensible, explanatory model. Selective coding requires the researcher to bring together what he or she has learned about the central phenomenon of the story. In other words, what narrative structure emerges from the data? If the researcher has been sensitive to the nuances and critical information gleaned from the interviews as well as the background information gathered during the literature review, a story should be visible from among all the data.

As is the case with any good story, one category will be the core while other categories will be subsidiaries. To use an analogy, in literary works invariably the protagonist will emerge from among supporting characters. Supporting characters undoubtedly influence the plot as well as the movement in the story, but the crucial storyline will focus on the central character. The job of the researcher in GT is to determine by sifting through the data which category is the most important and which categories are subsidiary.

The researcher will need to understand and explicate relationships among and between categories. To validate the relationships, the researcher will need to examine the interview



responses and other data to understand the nature and extent of the relationships. In some cases, gaps will exist and the researcher must determine which categories need further refinement or development (Holton, 2008). See Appendix D for the categories and subcategories of ACIP decision-making.

For some GT researchers, theoretical coding is a part of selective coding. Other researchers choose to separate the two processes. In any case, the goal of theoretical coding is to place the narrative that has emerged from the selective coding into a larger context. Ideally, a hypothesis will result to explain why the participants acted as they did. The difficulty with more traditional research (with the hypothesis developed at the outset) is that the hypothesis is based on an educated guess that may not accurately reflect the conditions under study. In GT, with the hypothesis developed at the end of the research process, the hypothesis should be more accurate because presumably the data collection will allow the researcher to formulate a more nuanced understanding of the salient issue(s). At the same time, the researcher must be careful to allow the hypothesis to be suggested by the data rather than force it (Glaser and Holton, 2005).

Throughout the coding process, the researcher's goal is to capture the emerging ideas and categorize them in the form of memoranda. Sorting of the memoranda is essential; it puts the fragmented data back together in a way that allows the researcher to construct a narrative and thereby provide meaning to the data that have been collected. The outline for constructing a narrative is determined by the concepts and themes that emerged from the interviews and data collection process.

It is important to wait until all the interviews have been conducted before constructing the narratives. If the major benefit of GT is the development of an "after-the-fact" hypothesis, all the facts must be in hand before then analysis begins. It is crucial that the researcher refrain

from developing a preconceived theoretical outline during the interview process. Any research project evolves, especially as the researcher collects more data. Consequently, the researcher's thinking may evolve until he or she finds that the project at its conclusion bears only a passing resemblance to the project at its outset. A virtue of GT is that the researcher is analyzing the data, absent preconceptions about the results, when all the data has been collected and the evolutionary process has ended.

## CHAPTER 4

### ACIP INTERVIEWS

Dr. Jon S. Abramson: Interviewed on Monday, September 8, 2008

Dr. Jon Abramson explained that the U.S. Food & Drug Administration (FDA) is the first line of defense in determining whether to offer a specific vaccine in the U.S. market. The ACIP never makes a recommendation until the FDA first decides that a vaccine can be sold in the country. Despite this safeguard, a FDA approval is not necessarily tantamount to a guarantee of safety. Because data are to some extent always incomplete and/or inconclusive, it is still possible that an FDA-approved vaccine is not safe and effective in certain doses or with certain populations. Thus, while the FDA serves as an important check on vaccines, it is not the sole arbiter of safety.

One of the beneficial aspects of the FDA approval process is generally the quantity (and, presumably, the quality) of the collected data. Of course, with regards to safety, “we are never absolutely sure,” but the fairly large efficacy trials necessary for pharmaceutical companies to secure FDA approval usually provide a rich body of data that will assist researchers and decision-makers in understanding the risks and potential benefits associated with a particular vaccine. In most instances, “we are pretty dang comfortable” about safety in light of the available data.

As an example, consider the human papillomavirus virus (HPV), the most common sexually transmitted infection in the United States, with approximately 6.2 million cases diagnosed each year. HPV is generally thought to cause cervical dysplasia, which can lead to the

development of cervical cancer. The HPV vaccine currently available on the market has been tested extensively; approximately 60,000 women have been studied. The difficulty in undertaking cancer studies, however, is that cancer often has a long latency period, so it literally can take decades before sufficient data is available to demonstrate that the vaccine effectively retards cancer growth (Contrera *et al.*, 2003). In the interim, however, researchers can search for signs of cervical dysplasia. Because cervical dysplasia is a precursor to cervical cancer, presumably the presence of dysplasia indicates a strong likelihood that cancer will occur and, conversely, the absence of dysplasia suggests that cancer probably will not occur. Although these assumptions are not necessarily accurate in 100 percent of cases, the causal link between dysplasia and cancer is sufficiently strong and persuasive that researchers feel confident they can rely on this relationship to make decisions about the HPV vaccine (Southall, 2008).

Despite the fact that the bar is pretty high for FDA approval and pharmaceutical companies must provide a wealth of data, this does not mean that the data are sufficient in every instance. The lack of high-quality, consistently reliable data is always a problem in medical research, although obviously it is a worse problem in some cases than in others. If the ACIP believes that the data are so incomplete that the committee members cannot make a decision, they will defer a recommendation unless and until more complete data are available. The working groups can communicate their concerns to the CDC, which in turn can investigate the means for acquiring the appropriate quality and quantity of data.

As an example of a problem with lack of data, Dr. Abramson cited the case of lyme disease, also known as borreliosis, an infectious disease caused by at least three species of bacteria borne by ticks. When the ACIP first considered a vaccine to fight lyme disease, the committee believed that the data were so incomplete and geographically limited that the

members could not offer a recommendation. The company offering the vaccine for marketing could have undertaken additional studies to generate sufficient data. Instead of investing so heavily in research, however, the company eventually withdrew the vaccine.

According to Dr. Abramson, another difficulty in making recommendations about vaccines is that doses and the timing of vaccine administration are often unknown, especially for new vaccines. Is a vaccine going to last for five years or ten years or for some other period of time? Should one dose, two doses, or more doses be administered? Typically, in the face of such unknowns, medical researchers will adopt a conservative approach. Consider a rotavirus as an example. The ACIP might review the available data and recommend that one dose be administered. Over time, after assessing new data, the committee could modify its recommendation so that two doses are administered. The period between the recommendations will provide an opportunity to see how the initial doses worked. Perhaps rare side effects will be observed. In approximately 95 percent of the cases, no known side effects occur, but perhaps in five percent of cases the rotavirus vaccine triggers severe diarrhea. In about 1 out of 10,000 infants, serious complications may occur. If the side effects and complications are so severe that the vaccine may endanger human life, the ACIP may withdraw the recommendation. That decision will depend on how committee members assess the potential risks and rewards of the vaccines (Brunell, 2008; Damlo, 2007; Meadows, 2007).

Risks and rewards, or costs and benefits, are always part of the ACIP's work. The committee has been instructed not to consider whether its recommendations will take money from government coffers because the CDC and other government officials do not want the ACIP to become, in essence, a board of accountants or economists. Nonetheless, costs—whether measured in dollars and cents or risks and rewards—always factor into ACIP decisions to some

extent. The crucial consideration is effectiveness versus efficiency. In the latter case, the decision on whether to recommend a vaccine would depend on whether the vaccine was effective in light of the cases; in other words, is there a “big bang for the buck.” In the former case, the question is whether the vaccine accomplishes its intended purpose. The vaccine might be extraordinarily expensive, but nonetheless extremely expensive. In such cases, the ACIP may recommend that the vaccine be administered in certain doses to certain populations and leave it to others to wrestle with the direct cost implications.

Dr. Lance Chilton: Interviewed on Friday, August 29, 2008

Dr. Lance Chilton began his interview by focusing on the importance of “looking for data where we can find it.” In his opinion, the data must address three factors: the efficacy of a vaccine, the safety of a vaccine, and the costs associated with the vaccine. Data can come from a variety of sources. A search of the medical literature obviously is crucial for increasing a decision-maker’s knowledge base, although it is by no means the only source of good, high-quality data. Expert opinion can be a source of data. Unpublished information developed by pharmaceutical companies can be valuable as well, although sometimes access to the data can be limited owing to concerns about proprietary information. In addition, because pharmaceutical companies have a vested interest in the outcome of ACIP deliberations, care must be taken to evaluate their data with a critical eye.

Collecting and evaluating data is an iterative process, which means that there is almost always some data available for making a decision, although the data are seldom complete and uncontested. In fact, ACIP decision-making is itself an iterative process. Typically, the meetings last two days and, except for a two-hour administrative session, are open to the public. Committee members talk through issues in a public forum, although “the suspense is out of it”

because much of the work is performed by sub-groups that meet, usually via conference call between full ACIP sessions, to discuss the specifics in the data. Sub-groups then report to the full ACIP during committee meetings and answer questions as they arise. The sub-groups, i.e., the working groups, are responsible for investigating the specific questions that will be addressed during the full ACIP sessions, and so they are especially important to the ACIP deliberative process.

Some ACIP members have suggested that safety, while an important issue, has been addressed effectively by the U.S. Food & Drug Administration (FDA); therefore, efficacy is a more crucial issue for the ACIP. Dr. Chilton takes issue with this perspective. He recognizes that the FDA performs a useful role in determining the safety of vaccines that are marketed in the United States, but Dr. Chilton believes that questions of vaccine safety must be considered anew by the ACIP regardless of the FDA's role. Because safety is not necessarily and either/or issue—either a vaccine is safe or it is not safe—these questions underlie all ACIP decision-making. A vaccine that is deemed “safe” when administered in certain doses or to certain populations may or may not be safe when administered in other doses or to vulnerable populations. The permutations and combinations must be factored into any analysis. The likelihood that an unsafe vaccine somehow slipped past FDA scrutiny is minimal, to be sure, but decision-makers must not be complacent and adopt assumptions unwarranted by the data.

In short, medical decision-making entails a large measure of uncertainty. The ultimate issue is whether decision-makers can live with a given level of uncertainty. To decide what an appropriate level of uncertainty is, ACIP meetings involve much discussion. Although the ACIP talks through issues and sometimes they debate points where consensus is absent, little politicking goes on behind the scenes, in Dr. Chilton's opinion. The discussions tend to focus on

medical issues, although costs obviously play a part as well. Cost is seldom a determining factor in a final recommendation, but it cannot be ignored or minimized. Divided votes sometimes occur, although consensus is not unprecedented. In any case, decision-makers do not feel the need to achieve unanimity in decision-making simply for the sake of unanimity.

Dr. Paul R. Cieslak: Interviewed on Tuesday, August 26, 2008

When I spoke with Dr. Paul R. Cieslak, he cautioned that any physician must live up to the Hippocratic Oath: Do no harm. In any decision-making process, he has to be convinced that the decision will not lead to deleterious consequences. This observation does not mean that Dr. Cieslak supports the precautionary principle. In fact, he is careful to distinguish his position from the precautionary principle, which suggests that it is preferable to be safe rather than sorry. In his opinion, decision-makers cannot become paralyzed by the thought that they might reach an incorrect decision, nor should they move forward hastily to make decisions when no data exists or when data are so contradictory their interpretation is unclear. A middle ground is desirable.

The concern about not doing harm is obviated somewhat by the U.S. Food & Drug Administration (FDA), which determines which vaccines are safe to use. Obviously, the FDA is not flawless in its analyses, but the ACIP generally can rely on the agency to screen out vaccines that are not safe, which means that Dr. Cieslak and his colleagues can be confident that a safety threshold has been met and the vaccine is not worse than the disease. The ACIP members' job, therefore, is to focus on the effectiveness, of lack thereof, of vaccines for specific populations. If safety issues arise, the group certainly will study and discuss the issue, but vaccines that have survived FDA scrutiny generally are safe. Questions about their effectiveness, however, may be in dispute.



The ACIP is not designed to be a consensus body, although often consensus is reached during the discussions that accompany group meetings. Typically, sub-groups comprised of specialists in a particular area will meet apart from the larger group and then present their findings when the ACIP reconvenes. In clear cases, the larger group will accept the sub-group's findings and the decision rule is reasonably clear. In other cases, however, members will discuss the findings and work through the issues. Depending on the circumstances, delving into the medical literature will provide useful guidance. In cases where the vaccine is not adequately discussed in the literature or gaps appear in the data, it is desirable to consider similar vaccines and analogize from those situations. Sometimes a specialist in a certain field or area of immunology sits on the ACIP, and he or she can provide useful insights into an issue. In those cases, the specialist may provide clues to the missing data, which in turn assists in arriving at a final decision.

Although different ACIP members obviously will emphasize different factors and variables in their decision-making, Dr. Cieslak believes that costs must be taken into consideration. The CDC employs economists to assist in making cost-benefit decisions. If this decision sounds callous—after all, we are all children of God and theoretically every human life has value—it is a realistic approach to decision-making. As an example, consider a person who wakes up to find a bat in his or her house. Prudence might suggest that the person undertake a rabies post-exposure prophylaxis to be safe. Yet when a cost-benefit analysis is performed, this seemingly reasonable approach seems far less reasonable. If there is an extremely low risk of infection—something like two cases out of tens of thousands—and the cost of treatment (approximately \$3,000) is high, the cost-benefit analysis suggests that the treatment should not

occur. No one has yet established a threshold for a quality-adjusted life year, but perhaps such a calculation would be helpful in medical-science decision-making (Bridges, 2004).

Dr. Janet A. Englund: Interviewed on Monday, October 6, 2008

At the beginning of our conversation, Dr. Janet A. Englund outlined the general ACIP decision-making process. Issues are placed on the agenda through a number of means, according to Dr. Englund. The CDC liaison can decide to discuss a particular vaccine or the chairperson can ask for a particular issue to be discussed after the ACIP working groups request its inclusion. In some cases, a vaccine will receive a great deal of discussion or it will be an important issue for many decision-makers because of its salience to a larger audience—policy-makers or the general public, for example; as a consequence, it naturally becomes a topic of discussion for the ACIP. Vaccines involving significant public health issues naturally are well-suited for ACIP consideration.

After a topic is placed on the agenda, typically the ACIP working groups investigate the issue in detail. The investigation may involve a literature review and/or it may rely on the appropriate experts, depending on the issue. During the regular ACIP meetings, the working groups present information to the full committee, although it is not uncommon for outside speakers to address the group if their expertise pertains to the issue under discussion. Throughout the deliberative process, the full committee will discuss the issue, ask questions, and debate. The meetings are open to all interested parties and a matter of public record, although discussions are limited to ACIP members and invited guests.

In terms of the factors that influence decision-making apart from discussions among the full ACIP membership, Dr. Englund pointed out that, just as other committee members have mentioned during their interviews, the FDA has primary responsibility for considering the safety

of specific vaccines. This recognition does not mean that the ACIP refuses to consider safety data in its deliberations, but it does mean that the FDA serves as a first line of defense. Because it is the regulatory body that sifts through the appropriate safety data and determines whether sufficient clinical trials have been conducted to satisfy the agency that a drug is safe, the ACIP has a high level of confidence that a vaccine licensed for marketing in the United States will be safe. With the FDA serving as the primary agency examining safety, the ACIP's role is to make recommendations on the administration of vaccines.

Considering all the data supplied by the CDC, the working groups, and other appropriate sources, committee members vote on whether to make a recommendation and, if so, what the recommendation should be. In some instances, a recommendation may not be ripe because some bit of data or information is missing, so the decision can be pushed onto the agenda at the next ACIP meeting. In other cases, the discussions and deliberations are so lengthy that a decision cannot be reached because the group has yet to complete its analysis of the important issues involved with recommending a vaccine. In those cases as well, the ACIP will delay the decision-making process until the committee is prepared to vote on a recommendation.

Although committee members prefer to reach a consensus decision, it is not always possible. Some members abstain from voting if they have corporate ties or if they believe they have a conflict of interest. In cases where the vote is close, some members choose to issue a minority opinion explaining why they disagree with the groups' vaccine recommendation. In rare instances, the group may issue a recommendation and later modify their decision if more data or studies suggest that such a revision is warranted. As an example, Dr. Englund mentioned the rotavirus vaccine. The ACIP has recommended the drug, but later the company pulled it

from the market and the FDA withdrew its license. Consequently, the ACIP withdrew its recommendation (Brunell, 2008; Damlo, 2007; Meadows, 2007, 26-27).

Dr. Englund indicated that costs are a consideration in decision-making, but it is not the primary issue. “Cost effectiveness is a better way to look at it,” she said. Risks and rewards are inherent in any medical decision-making, and so it is with vaccines. The crucial concern is whether the costs, taken broadly, are reasonably related to the effects. There is always a tradeoff that must be considered. On one hand there may be a vaccine that is expensive but effectively treats a disease that is common and serious among a large part of the population versus a vaccine that is inexpensive but is effective for a disease that is exceedingly rare. Other scenarios can be envisioned: A vaccine that is expensive but the disease it treats is relatively mild and common versus a vaccine that is expensive but it treats a rare fatal disease. There is no reliable way to assign exact numbers to these variables to judge their importance. It is left to ACIP members to debate which factors are important and why (Bridges, 2004; Dempsey, *et al.*, 2008).

At the conclusion of her interview, Dr. Englund stressed that the decision-making process is not linear. “‘It depends’ is the answer,” she said when asked what guides her decision-making philosophy. Because the variables involved in any situation are fluid and no two situations are exactly alike, she was reluctant to identify an overarching or guiding philosophical principle for making decisions in hard cases. Hard cases are difficult to generalize about because each case presents its own set of challenges. In addition, different committee members have different sensibilities because their backgrounds and professional experiences are different. Different outlooks are valuable and help to explain why the ACIP is an effective decision-making body; it allows for diverse perspectives to be taken into account as decisions are made. When I told her I

was searching for commonality among decision-makers who must make scientific decisions under conditions of uncertainty, she laughed. “Good luck with that,” she said.

Dr. Reginald Finger: Interviewed on Tuesday, August 26, 2008

A former ACIP member, Dr. Finger remains actively involved in public health and epidemiology. He indicated that all scientific decision-making entails risk, which is hardly surprising. It is how decision-makers approach risk that determines the quality, or lack thereof, of their final decisions.

The initial question for any decision-maker is how the magnitude of the potential benefit is weighed against the costs. This risk analysis is complicated by the time issue. Some studies require years, perhaps decades, before all of the costs and benefits are known and can be evaluated. In the meantime, inaction can lead to widespread disease proliferation in the absence of a vaccine. Thus, in some instances, an interim decision must be made even if the quantity and quality of the data are not ideal. Dr. Finger pointed out that he would never recommend a vaccine based on no data, but he recognizes that in some cases a recommendation must be made before all the data are collected and analyzed. In these situations, he would have no problem in making a provisional recommendation and asking for a reevaluation of the data in the future.

The CDC issues a *Morbidity Mortality Weekly Report (MMWR)*, which circulates data on specific diseases as state and territorial health departments report them. Moreover, the *MMWR* reports on infectious and chronic diseases, environmental hazards, natural or human-generated disasters, occupational diseases and injuries, and intentional and unintentional injuries. Because it is designed as a weekly update on crucial health issues for medical professionals, the *MMWR* discusses gaps in the data, areas where future research is needed, and provides a context on issues of interest to the public health community. In Dr. Finger’s opinion, this would be an ideal

place to place the vaccine decision in context and explain the need for additional long-term data collection and assessment.

Echoing many of his colleagues, Dr. Finger suggested that decision-makers perform a literature review as a first step to any vaccine decision. The ACIP employs sub-groups to serve as principal investigators, so often the sub-group members will perform a literature review to determine what additional data is required for the full ACIP membership to consider. In some cases, expert opinion can be used to flesh out the literature review.

Despite researchers' best efforts, gaps in the data sometimes exist. Dr. Finger indicated that it would be useful in these situations to recommend a permissive decision. In other words, the recommendation would highlight the fluid nature of the data and suggest that recipients can choose whether or not to take the vaccine as opposed to a stronger recommendation urging that the vaccine be administered to specific populations. The basis for the permissive recommendation, of course, presupposes that the population that will receive the vaccine understands the known costs and benefits. Informed consent is a crucial component to vaccine recommendations, as it is for any treatment decision.

Dr. Finger cited the concept of beneficence that underscores, or ought to underscore, health-care decision-making. Sometimes labeled the "first principle" of morality, the adage "do good and avoid evil" is a key component to understanding beneficence because it is the first step toward a "middle principle" of beneficence. Beneficence, or non-malevolence, is partially dependent for its content on how one defines "goodness," thus it is not a specific moral rule and cannot determine what constitutes the good. Nonetheless, some key features in a health-care context include: (1) never deliberately taking a human life; (2) never directly intending harm; (3) seeking a patient's good; (4) acting out of a sense of charity and justice; (5) respecting a patient's

religious beliefs; (6) always seeking the higher good; (7) never knowingly committing of approving of an evil action; (8) never treating others paternalistically; (9) using wisdom and prudence in seeking the common good. If decision-makers are guided by these concepts, their decisions, while never perfect, probably will be greatly improved (Carrel and Rennie, 2008; Sawicki, 2008).

Dr. Harry F. Hull: Interviewed on Tuesday, October 21, 2008

Dr. Harry F. Hull told me he has enjoyed a long career in epidemiology, especially working with state agencies. Accordingly, he was recruited for ACIP membership because the executive secretariat believed that the group needed expertise from an epidemiologist and, moreover, state epidemiologists were underrepresented on the ACIP. As of 2008, Dr. Hull has rotated off of the committee. Although he no longer attends group meetings or participates formally, he remains actively involved in vaccine research and public health issues through his consulting firm H. F. Hull Associates.

Dr. Hull began the interview by discussing how issues come before the ACIP. In some instances, a new vaccine is about to be marketed; therefore, pharmaceutical companies call attention to the drug so that the FDA can begin the licensing process and the ACIP can place the issue on the agenda. Generally, the FDA will reach a determination on whether the drug can be marketed before the ACIP makes a recommendation. (There is no point in making recommendations on a specific vaccine if the FDA will not allow the drug to be licensed and marketed in the United States.)

The executive secretariat, working in conjunction with the ACIP and working group chairs, finalizes the agenda for each ACIP meeting. Sometimes a new vaccine is so prominent that it is an obvious choice for ACIP consideration. In other cases, the CDC or the medical

community has raised questions about the efficacy of a vaccine and the issue comes to the ACIP's attention. If an issue is urgent, committee members occasionally meet via conference call to discuss how the issue should be addressed and whether it should be added to the agenda for the next meeting of the full committee.

Much of the investigative work takes place between full ACIP meetings as the working group delves into the specific features of a vaccine. The working groups are comprised of a subset of ACIP members, although third parties that do not serve on the full ACIP may become working group members. The overriding consideration is to assemble a team of health care professionals well-versed in the issues being discussed. This means that the working groups must have flexibility to determine the appropriate makeup of the group. All ACIP members participate on at least one working group, and their participation depends on expertise, the number of current working group members, and the need for additional persons who can perform the work.

“Now, there is always a lot of information available,” Dr. Hull reported. “These vaccines are licensed.” Thus, the pharmaceutical companies as well as the FDA and the CDC will supply data and background information to the ACIP and the working groups. By the time the issue is put before the ACIP, the group has access to all available information on the subject. That is not to say that all questions are answered or no uncertainties exist, but to the extent that anyone can answer questions, the ACIP can answer them because members have access to the best information available to anyone making a decision on the vaccine in question.

Despite the group's best efforts to make thoughtful recommendations, however, some vaccines appear safe and effective but subsequent studies suggest that the vaccine does not perform as expected. As many of his colleagues also reported, Dr. Hull referenced the rotavirus



vaccine. It was marketed as safe and effective; therefore, the ACIP issued recommendations on appropriate applications. Later, the manufacturer removed the drug from the market (Brunell, 2008; Damlo, 2007; Meadows, 2007). Another example is Menactra, a tetravalent conjugated meningococcal vaccine. Over 5.4 million doses of the vaccine were distributed in the United States beginning in 2005, when the vaccine was first introduced, through September 2006. During this time, 17 reported cases of Guillain-Barré Syndrome (GBS) occurred among vaccinated persons. Analysis of the data suggested that a small increased risk of GBS probably was associated with vaccination (Gardner, 2006; “Notice to Readers,” 2008; Schonberger *et al.* 1979).

Dr. Hull indicated that cost is always a part of the decision-making process, but it is only one among a series of variables that should be considered. The burden of the disease and safety issues figure into the calculations as well. When pressed to explain how much weight each variable should be assigned, Dr. Hull countered that weighing the risks and benefits of making a particular recommendation on vaccine use and dosage is not a straightforward, linear process. It is an iterative decision-making process. Much depends on the quality as well as the quantity of information. The interaction among and between working group members as well as the full ACIP often determines the nature and extent of the recommendations.

Dr. Franklin Judson: Interviewed on Friday, September 26, 2008

According to Dr. Franklin Judson, many of the issues related to decision-making under conditions of scientific uncertainty at the ACIP are obviated by the FDA decision-making process. Because the FDA is the first line of defense against the sale and marketing of vaccines—it offers “a high degree of confidence”—this agency, far more than the ACIP, must consider safety data before deciding to allow a vaccine to be offered to patients in the United States. For

this reason, the ACIP “may not be the best institution to study” in determining questions about the safety of vaccines. In Dr. Judson’s considered opinion, ACIP’s role involves “a more conservative process” than the process employed by the FDA.

In some cases, however, even after the FDA has approved a vaccine for sale and the ACIP has offered recommendations based on the best available data, additional studies may require both entities to reconsider their original decisions. The difficulty with medical and other scientific data is the iterative nature of research. Even after thousands or tens of thousands of cases have been considered and the best data has been generated and analyzed, subsequent studies may reveal rare side effects or features of the vaccine that were not known in earlier years. In such situations, the FDA may decide to pull a vaccine off the market. Alternatively, the FDA may decide to allow the vaccine to be offered, but the ACIP may revisit its recommendations in light of the new data. It may be appropriate to revise the recommendation, offer additional details on the dosage or administration of the vaccine, or it may withdraw its recommendations altogether. The rotavirus vaccine is a good example of a situation where the ACIP later revisited its initial recommendation (Brunell, 2008; Damlo, 2007; Meadows, 2007).

Another difficulty in decision-making with respect to vaccines is determining whether observed effects are “causal or associative.” In the former instance, a researcher can conclude with a reasonable degree of certainty that changes in a particular independent variable or group of variables led to changes in one or more dependent variables without intervening causes. In the latter case, changes in the independent variable may initially appear to trigger changes in a dependent variable, but the changes may be coincidental or imperfectly correlated. The distinction between causal and associative effects remain problematic for ACIP decision-makers,

indeed for decision-makers in virtually every situation where linearity is not easily discerned and patterns may not be readily apparent.

Unlike some former and current ACIP members, Dr. Judson remarked that he believed cost-benefit analysis is integral to the work of the ACIP. In a world of scarcity where recommendations on the use of certain vaccines means that other vaccines will not be available owing to the costs involved, ACIP members must be cognizant of cost-benefit analysis. “Efficacy is not the only appropriate issue here,” Dr. Judson remarked. This focus on costs is not to say that ACIP members must act as government accountants; instead, they must recognize that their decisions will hold repercussions on the quality and quantity of other vaccines that can be recommended in the future.

On the issue of costs, Dr. Judson cited as an example the Vaccines for Children Program (VFC), which supplies federally purchased free vaccines for immunizing eligible children in public and private practices at no cost to participating private health care providers. Government estimates suggest that approximately 60 percent of children in the United States may be expected to benefit from the VFC Program. Patients up to and including age 18 are eligible if they are enrolled in Medicaid or a state-mandated low-income health plan, are uninsured, or classified as American Indian or Alaskan Native.

On one hand, he suggested, the VFC program is admirable because it attempts to provide vaccines for children who desperately need them but probably would not receive them owing to costs. On the other hand, however, the program is tantamount to an unfunded mandate because the federal government is forced to finance vaccines in cases where no other funding source can be found. Thus, an FDA-approved vaccine that is recommended by the ACIP may require federal funding of the vaccine, which could run into the billions of dollars. The use of the funds

in and of itself may not be a problem, but what happens if the ACIP recommends a vaccine that requires a large expenditure to treat a common but relatively mild disease and then later another vaccine comes before the group and it will offer relief for a far more virulent disease but federal funding is unavailable owing to the VFC-mandated purchases of the first vaccine? The ACIP is not charged with considering costs, but Dr. Judson contended that such considerations invariably factor into the decision-making process (Dempsey, *et al.*, 2008).

Dr. Tracy Lieu: Interviewed on Monday, September 29, 2008

Dr. Tracy Lieu formally ended her term as an ACIP member shortly before she spoke with me, although she remained a member of an ACIP working group. In her view, the ACIP is greatly assisted by the FDA because the latter serves as a first line of defense in ensuring the safety of any vaccines marketed in the United States. Nonetheless, just because the FDA has determined that a particular vaccine can be safely administered, this conclusion does not mean that the vaccine ought to be recommended. “We [ACIP members] need to be convinced that a vaccine is a reasonable value in terms of cost effectiveness,” she said.

Dr. Lieu indicated that the ACIP agenda is set by Dr. Larry Pickering, the group’s executive secretariat, as well as the committee chair. They receive input on appropriate topics and issued from various sources, including the CDC. ACIP members have little direct influence over the vaccines that will be considered by the committee or the working groups.

After a vaccine is brought before the group, costs can never be removed from the ACIP’s work because every comparison of a vaccine’s effectiveness always involves tradeoffs. She cited several examples to illustrate the point. The first case occurred early in 2004 as she was beginning her tenure as an ACIP member. At the time, the committee was reviewing data on a meningococcal vaccine to protect against meningitis. The vaccine was undoubtedly effective,

but the cost—on the order of \$90,000 to \$160,000 per life year saved—was extremely high given the relative rarity of meningitis. Outside social and political factors complicated the decision-making process. “Meningococcal causes panic,” Dr. Lieu observed. The public becomes disproportionately alarmed when stories of meningitis outbreaks occur, especially because such outbreaks often involve young people in high school and college. Public alarm “is a large factor” in ACIP deliberations when vaccine decisions are well-known to the public. Dr. Lieu was quick to point out that social and political factors rarely play a decisive role in ACIP decision-making; even when these factors are present, they only tangentially affect the outcome. In the case of meningitis, the committee will recommend that the vaccine be used even though the price per life year saved is exorbitantly high and probably would force the ACIP to reach a different conclusion if the disease were not as high-profile (Dempsey *et. al*, 2008).

The second example occurred late in 2005 and involved the varicella vaccine. Varicella, or chicken pox, is rarely a fatal disease, but it still elicits concern among people with young children. Typically, medical professionals administer a single dose of the vaccine. In some cases, however, patients who receive a single dose still contract chicken pox, although the disease is considerably milder than it would have been if the dose had not been administered. In any event, the CDC asked the ACIP to recommend a second dose to increase the probability that the disease would not occur. A chair of one of ACIP’s working groups argued in favor of administering a second dose but no one else on the committee was convinced. For perhaps the only time in ACIP history, the chair’s vote was not seconded and the committee refused to recommend a second dose, much to the CDC’s (and, presumably, the working group chair’s) chagrin.

While the deliberations were ongoing, the ACIP learned that a leading drug manufacturer, Merck, was going to release a new combination measles, mumps, rubella, and varicella (MMRV) vaccine for children 12 months to 12 years of age. The MMRV vaccine was developed to reduce the number of injections required in the routine childhood immunization schedule and increase the percentage of children immunized against varicella within the first two years of life. Similar to other combination vaccine products, medical researchers promoting the new vaccine anticipated that the MMRV vaccine would reduce patient discomfort and increase clinic efficiency. For many young children, receiving injections can cause discomfort and may even be traumatic; therefore, reducing the number of vaccines and administrations generally is seen as beneficial.

A difficulty occurred because research suggested that the MMRV combination was more likely to trigger febrile seizures, which are convulsions brought on by a fever in small children or infants. In fact, the seizures seemed to more than double when the MMRV vaccine was administered as opposed to the MMR vaccine alone. A febrile seizure can cause a child to lose consciousness and shake uncontrollably. Sometimes a child will become rigid or twitch in a portion of the body. In most instances, febrile seizures last a minute or two, but the seizures can be as brief as a few seconds or as long as 15 minutes. Febrile seizures generally occur in children between the ages of six months and five years, especially in toddlers.

The dilemma was therefore easy to state but difficult to resolve: Febrile seizures are rare, but there is a risk, however slight, that they can occur when the MMRV vaccine is administered. If the MMRV vaccine is administered, however, approximately 2,000 children are saved from undergoing additional shots for every one child who suffers the seizures. Moreover, febrile seizures may still occur with the MMR vaccine, so “maybe seizure risk is there but you front-

loaded” the risk with the MMRV vaccine. “Is this an acceptable risk?” Dr. Lieu asked. “I would like to see public opinion research on the risk.” Again, the ACIP will recommend vaccinations based on the scientific data, but it would be helpful to know what the public thinks about such a tradeoff (Kerr, 2003).

Dr. S. Michael Marcy: Interviewed on Tuesday, August 19, 2008

Dr. S. Michael Marcy readily agreed that decision-making about vaccines involves instances when a clear decision rule exists and instances when the decision rule is muddled owing to incomplete, inconsistent, or contradictory data. In all cases, though, the decision-making process is the same, or it ought to be.

The first consideration in making recommendations on vaccines is to determine the size of the population that will be vaccinated followed by an inquiry about the disease burden. A vulnerable or high-risk population must be identified—e.g., Native Americans, Intuits, persons with compromised immune systems, sickle-cell anemia, and so forth—because recommendations will vary depending on demographics. A large, healthy, ethnically homogenous population versus an at-risk population directly affects vaccine types and dosages. In addition, the responsiveness of the population to a given vaccine can affect the recommendation. If the population that receives a vaccine produces antibodies, which in turn prevents the spread of a disease to other people, especially other at-risk groups within the population, this beneficial result will influence the recommendation.

Dr. Marcy pointed out the need for data, although he recognized that the quality and quantity of data are never perfect. When he discovered that the paramount issue involved scientific decision-making under conditions of uncertainty, his initial response was playful and ironic. “Decisions made under conditions of uncertainty? I didn’t know there were any other

kinds. Lewis Thomas, the great medical essayist once said (and I am paraphrasing): ‘Science moves from truth to truth as new facts are discovered, rejecting old truths as new ones appear. We are, thus, fundamentally, always in error.’”

He summarized ACIP decision-making—indeed, any kind of medical decision-making—as occurring across a spectrum of responses in a bell-shaped curve. At one end of the spectrum, some decision-makers simply will not make a decision absent an overwhelming mountain of data even though such voluminous, precise, persuasive data seldom, if ever exist. These people are so worried about the possibility of error they may suffer from “analysis paralysis.” This is a kind of precautionary principle in action. It is better to be safe than sorry: Since any decision-making or action necessarily must be undertaken under conditions of uncertainty, and uncertainty means risk is involved, it is simply preferable to take no action than to risk the unknown. The problem with such behavior, however, is that no action is in itself an action—a tacit embrace of the status quo ante. The status quo ante may seem to be the safest, most desirable choice among a menu of choices owing to its familiarity, but it is not risk-free. Especially in times of crisis or rapid change, accepting the status quo risks obsolescence and may actually exacerbate problems because no forward movement to fix problems allows them to fester.

At the other end of the spectrum are decision-makers who willingly make decisions in the absence of high-quality data because they believe that movement is needed. These decision-makers recall Carl Sandburg’s wry observation, “I’m an idealist. I don’t know where I’m going, but I’m on my way.” Decision-makers who accept cutting-edge theories and practices because they are cutting-edge and they hold the promise of innovative approaches to medicine risk being fool-hardy or, worse, dangerous. Fortunately, such decision-makers generally are in a minority, at least on the ACIP.



Dr. Marcy said he was in the third category, i.e., among those decision-makers who recognize that some data are necessary, but perfect data or data that is complete and thoroughly consistent is not possible in most instances. In his experience, most ACIP members and other medical professionals fall into this category. ACIP meetings typically operate on a consensus system whereby the group seeks to reach agreement before the entire body offers a recommendation on a vaccine. Participants generally recognize that a decision must be made even if some questions about the vaccine remain unanswered. To that end, the meetings often revolve around whether data exist on the effectiveness and the efficacy of a particular vaccine. In the former case, a vaccine is effective if its successful use for an intended purpose can be demonstrated in the world. By contrast, a vaccine can be shown to be efficacious if its successful use for an intended purpose can be demonstrated in a laboratory under experimental conditions. Sometimes effectiveness and efficacy overlap, but not always. If the two overlap, the decision rule is relatively clear—the data, imperfect though they might be, strongly suggest that the vaccine should be used. If effectiveness can be shown but not efficacy or vice versa, ACIP members must debate the point until an agreement is reached.

Although data ought to be considered objective measures of performance, in cases where there is no clear decision rule—that is, when effectiveness and efficacy fail to overlap—subjective measures become important. Often a senior person will speak up and share his or her experiences. A Harvard-educated, board-certified expert in a particular area of medicine or an acknowledged expert in a certain vaccine or type of disease can do much to sway the rest of the ACIP membership, especially younger members who are on the fence about a particular decision. In these cases, the decision is based on personality factors, which are far more

subjective than the supposedly objective data generated through clinical trials and real-world applications of a vaccine.

Cost is a factor that influences vaccine recommendations, although for many people this may seem out of place. How much is a human life worth? If this question is anathema, it nonetheless is an important consideration in a world of scarce resources. Is it preferable to spend millions of dollars on a vaccine that prevents or retards only one potentially fatal disease in a narrow population or should the funds be used to treat diseases that affect many more people but which may not be as dangerous to a larger cohort? In other words, is it better to plan for events that seldom occur or, when they occur, affect only a few people, but they affect the population deeply or is it better to plan for events that occur frequently but affect a larger number of people.

Wrestling with costs raises a broader question, namely a concern about the utility cost-benefit calculation that invariably is required in public-policy decision-making. Policy-makers face such tough, difficult choices all the time. One group desires A, another desires B, and still another desires C, but choices A, B, and C are mutually exclusive. Assuming the policy-maker is not already philosophically predisposed or required by law, policy or regulation to select one alternative from among the others, making a defensible choice is daunting. A decision-maker must engage in a cost-benefit calculation weighing the advantages of each choice against its disadvantages while taking into consideration the number of people affected. A policy-maker will choose a course of action that provides the greatest good for the greatest number, although the basis for making this determination can be subjected to interpretation.

The calculations can become hopelessly confused. How does a policy-maker weigh the depths of preferences? A large percentage of the population may be against providing millions of dollars for, say, medical research into AIDS, but their opinions are not deeply held. By contrast,

a small percentage of the population may strongly believe that millions of dollars are required for AIDS research, but their preferences are in a distinct minority. Should the policy-maker strictly adhere to the desires of the larger percentage, many of whom are only marginally interested in the issue, at the expense of the smaller group that desperately seeks the funding for important medical research? A strict utilitarian calculation does little to provide an equitable resolution to a significant, and by no means merely hypothetical, policy problem (Dempsey *et. al*, 2008).

In any case, Dr. Marcy concluded his interview with an admonition that “we can’t wait for certainty” in decision-making. ACIP members argue about the quality and quantity of the data, but in the end they realize they need to reach defensible conclusions about which vaccines should be used. Decision-makers who allow themselves to become frozen in indecision are doing a disservice to their patients and their profession.

Dr. Julie Morita: Interviewed on Thursday, September 18, 2008

As was the case with several of the medical professionals that I interviewed, Dr. Julie Morita was ending her ACIP service in 2008, although she planned to continue attending meetings and participating, to the extent possible, in the committee’s deliberations. Dr. Morita said she was unique, or at least rare, among ACIP members because her background and professional experience have been at the local level in the public health arena. Accordingly, she has worked “in the trenches” in a way that many committee members have not. This experience on the front lines means that she often must focus on practicalities that other ACIP members don’t necessarily focus on in their decision-making. Consider costs as an example. The ACIP charge is not to consider costs; however, as a practical matter costs figure into virtually every decision, including decisions on medical treatment and vaccine development. The admonition not to consider costs is designed to remove committee members’ focus from serving as *de facto*

accountants and free them to discuss and make recommendations on the most efficacious vaccines available.

Nonetheless, despite the desire to deemphasize costs, Dr. Morita suggested that as someone who has served in public health on a local level, she has to remember that in a state such as Illinois, where she lives, does not provide universal health coverage. ACIP recommendations on vaccines for children do not include cost as a criterion, but it is an issue in other contexts whether explicitly stated or not (Bridges, 2004; Dempsey *et. al*, 2008).

In response to questions about the factors she considers when making vaccine recommendations, Dr. Morita explained how the ACIP makes decisions. The full committee meets only three times a year. In between full committee meetings, ACIP working groups, which consist of a smaller subset of committee members, meet on the telephone and in person to wrestle with the salient issues. The working groups are where much of the work is performed. Working group members begin by asking the CDC staff to provide them with data on the specific vaccine(s) under consideration. The CDC staff researches the medical literature and also identifies experts in the field.

In some cases, the literature search provides clear-cut information on the state of the science about a vaccine. Moreover, some working group members may possess enough information even without reviewing the medical literature to provide data and information necessary for the working group to prepare a recommendation for the full ACIP to discuss. In other words, a clear decision rule exists and the relatively stable, uncontested state of the data make decision-making relatively simple.

In cases where the data are contested or gaps in the data are large, the working group may direct the CDC staff to contact the experts and ask them to appear and discuss the state of

knowledge about a particular vaccine or disease. Owing to the prestige of the CDC and the ACIP, in most cases the experts will agree to come and share their expertise. The working group meetings featuring experts consist of a presentation followed by a vigorous question-and-answer period. Assuming the working group believes it can make a recommendation based on expert opinion after the session has ended, the matter is concluded until the next full ACIP meeting. At the full ACIP meeting, the working group presents the recommendation and the reasoning behind the recommendation for comment. Sometimes the full ACIP engages in discussion and debate. In other cases, the recommendation is accepted with very little discussion, especially when the data suggest that only one reasonable conclusion is warranted.

The committee sometimes has to weigh costs and benefits among different vaccines for the same disease. Dr. Morita cited the as a prime example, as did other interviewees. At one time, there were two products available on the market. One vaccine had been available for over a year and the data on its performance was reasonably complete. A second vaccine was relatively new and not nearly as much was known about it. Medical professionals, including ACIP members, face enormous pressure to make schedules consistent and uniform so that the potential for mistakes is reduced. The problem is that not all products are alike. One vaccine may require three doses while another requires only two. Generally, the fewer the number of doses, the more desirable the product is because it subjects the patient to fewer hassles, less pain and inconvenience, and sometimes lower cost. In some instances, however, the product requiring more doses may be superior because it generates fewer side effects or it is more effective in ameliorating the symptoms (Brunell, 2008).

Instances when multiple vaccines are involved require the ACIP to weigh the pros and cons of doses and, to the extent practicable, standardize the recommendations. If uniformity and

consistency are not possible, committee members must provide information on their reasoning and the details of their recommendation. They do this as much as they can by looking at data that is already available as well at similar models. Thus, if there is a vaccine already in use and it is similar to the one under consideration, the ACIP, probably at the working group level, will examine the evidence about the similar model and apply it to the instant case.

Although the full ACIP struggles to reach consensus, ultimately the committee is not a consensus-seeking body. A vote must be taken and a recommendation must be made. At the end of the full committee meeting, several options are available. First, the committee can decide that it does not have enough information and must seek greater expert input or the working group needs to keep compiling information. In such a case, no recommendation is made because the issue is not ripe for a decision. Alternatively, the committee can make a provisional recommendation that will stand until such time as new information or study results are available. In other cases, the ACIP will make a recommendation because the data are reasonably complete and the decision can be made with confidence. Even a final decision made with confidence is subject to change as future circumstances warrant. No matter how complete or good the data, the nature of scientific decision-making is such that there is always room for error or improvement.

Dr. Kathy Neuzil: Interviewed on Thursday, October 30, 2008

When I spoke with Dr. Kathy Neuzil, she acknowledged that no decision-making process is without gaps in the data, conflicting information, and unanswered questions. By its very nature, decision-making involves uncertainty and risk. Moreover, every decision-maker has his or her own biases, preconceptions, and peculiar way of approaching a problem.

In Dr. Neuzil's view, all decision-makers have to grapple with the same set of issues. "When there is less evidence, you have to weigh how bad the disease is and whether there are

other options,” she said. A disease with a high mortality rate and few options apart from a particular vaccine should be treated differently than a less virulent disease or a disease where other vaccines or treatment options are available. In the former case, ACIP members probably will be more likely to reach a positive recommendation on a vaccine even if conflicting data or gaps in the data exist simply because the need is great. Decision-making is not made in a vacuum; it must be undertaken with a realization of the urgency, or lack thereof, of the issue.

Consider the case of Pertussis, or whooping cough, an extremely contagious disease caused by the bacterium *Bordella pertussis*. Whooping cough is characterized by a severe hacking cough accompanied by an intake of breath that sounds similar to a “whoop.” Perhaps as many of 50 million cases of whooping cough are diagnosed each year, and some 300,000 people die, making it a leading cause of death among vaccine-treatable diseases. According to Dr. Neuzil, as a vaccine was being developed, reasonably complete data were available for patients up to 64 years of age, but limited data were available for patients 65 and older (Advisory Committee on Immunization Practices, 1997; Casey and Pichichero, 2005; Gustafsson, *et al.*, 1996). Although ACIP members would prefer to have more complete data, they had to make a recommendation on a specific Pertussis vaccine although they did not have access to the information they would like to have. If a decision-maker waits until complete data are available, a decision might be delayed or perhaps never made. For diseases that are serious and widespread, it is more important to reach a decision on a vaccine that can provide a reasonably effective treatment in the short term rather than wait and risk more deaths and misery.

Speaking of widespread diseases, the ACIP may be called upon to make recommendations on a vaccine to prevent a pandemic. The difficulty in making recommendations is that there are few instances where clinical data exist for pandemics.

Because particular pandemics are unprecedented, researchers have little experience in treating such widespread diseases or developing effective vaccines. Nonetheless, a decision-maker cannot afford to be paralyzed by indecision because few if any precedents exist. A recommendation must be made if the pandemic is to be controlled. “Pandemic data cannot be accurately collected, so you have to extrapolate,” she remarked.

In terms of the normal decision-making process for the ACIP, Dr. Neuzil explained that the working groups are responsible for meeting between regular meetings of the entire ACIP. Sometimes the working groups convene via conference calls, and sometimes they meet face-to-face. Depending on the issue under discussion, working group members may direct the CDC to provide them with data, conduct literature reviews and searches, or invite experts in the field to come and make formal presentations either to the working group or the full ACIP membership. When the working group believes the issue is ripe, its members present its findings to the full ACIP membership for discussion and a possible vote on the recommendations. The full ACIP tries to reach consensus, but sometimes a vote is necessary if there are substantial differences of opinion and consensus cannot be reached.

Although costs are not an integral part of the ACIP’s deliberations, Dr. Neuzil indicated that she and her colleagues recognize that costs cannot be completely ignored. Members “are highly sensitive to disease burden and cost.” If a disease is severe and few options exist, it makes sense to recommend a particular vaccine even if the costs are high. In contrast, if a disease is not especially serious and other, less expensive options exist, the costs may make use of the vaccine prohibitively expensive. In those cases, the cost issue may factor into the committee’s recommendations.



Ms. Patricia (Patsy) Stinchfield: Interviewed on Friday, August 29, 2008

Ms. Patricia (Patsy) Stinchfield had recently completed a four-year term as a voting ACIP member and was set to serve as a nurse-practitioner non-voting liaison representative when I spoke to her. In fact, Ms. Stinchfield was the first and only nurse ever to serve on the committee, although the ACIP probably will continue to appoint at least one nurse-practitioner in the future owing to the practical, “in-the-trenches” experience that a nurse brings to the committee, which is comprised of a large number of academics.

Ms. Stinchfield recognized that medical decision-making always carries a high degree of uncertainty, but a decision must still be made. As an example, she cited the Severe Acute Respiratory Syndrome (SARS), which originated in China in 2002 and spread to other countries thereafter. The flu-like symptoms and accompanying lethargy, followed by gastrointestinal problems, coughing and sore throat, made a diagnosis difficult because non-specific symptoms can indicate a variety of diseases. By the time SARS had been identified, it had spread throughout Asia and into other parts of the world. Some information filtered in from China and Canada, but U.S. health care providers were ultimately left to their own devices, at least in the early days of the outbreak, to determine an appropriate course of treatment.

In most instances when a new disease appears, medical researchers undertake a series of tests to determine the cause of the disease, to the extent possible, as well as the most efficacious course of treatment. The testing process can take years and, in the case of chronic animal studies, possibly decades. In the case of SARS, however, time was of the essence. Medical professionals had to rely on their past experiences and previous cases to treat the disease in the short term. Although they did not know what caused SARS, they realized it was infectious and required patients to be quarantined. Gradually, they determined that antibiotics designed to

treat respiratory tract infections could be modified to treat SARS. Although many unknown variables existed, and continue to exist, about SARS, decision-makers responded expeditiously because circumstances required a quick response (Holmes, 2003).

“I am the one who wants to know all the information,” Ms. Stinchfield remarked during the interview. If the information is unavailable or is contradictory, a decision must still be made. The first step in such a situation is to clarify the question. This action may sound obvious, but many times researchers do not have a clear understanding of the question under consideration. Is the purpose to treat the disease in the short or eradicate it in the long run? Is the goal to address all issues related to a particular vaccine, for example, or compare two vaccines side-by-side?

When vaccines are compared side-by-side, the decision-maker has to weigh factors that are not always clear. If two vaccines for rotaviruses manufactured by different pharmaceutical companies are compared and one has more data than the other because one is relatively new and the other is not, the comparison is difficult. In such situations, the decision-maker moves on to consider other variables. Take a vaccine that requires three doses as an effective course of treatment versus a vaccine that requires two doses. Occam’s razor might push a decision-maker to choose the vaccine that requires the fewer number of doses because it puts the patient through a lesser ordeal. On further analysis, it may be clear that the three doses are relatively painless and produce less discomfort for the patient than the two doses of a competing vaccine. A side-by-side comparison also requires a decision-maker to examine side effects and costs (Meadows, 2007, 26-27).

The question of costs is “one of the more frustrating things for us at the ACIP,” says Ms. Stinchfield. A cost-benefit analysis is not a straightforward calculation. “Cost and benefit compared to what?” she asks. This question goes back to her initial desire to clarify the question

about the ultimate goal in decision-making. Is the goal to reduce the number of deaths or to reduce the number of cases where an outbreak occurs? This concern is analogous to emergency response planners who must consider two scenarios—whether to plan for a low impact-high occurrence event (such as an automobile accident) or a high impact-low occurrence event (such as an airplane crash). Each scenario requires planning, but in an age of scarcity, how are these cases to be prioritized? Also implicit in this issue is the question of a depth of preferences. Should a vaccine that is desperately needed by a few people be accorded more or less value than a vaccine that is somewhat needed by a large group of people?

A strict economic analysis might focus on government accountability; does this recommendation consider the biggest bang for the dollars invested through federal programs such as Medicare or Medicaid? Although clearly ACIP members recognize that their recommendations have at least an indirect impact on fiscal policy, the committee does not have access to such economic data. In Ms. Stinchfield's view, the ACIP would not want to review these data even if they had access. The ACIP is "in a transition phase" where it is asking drug manufacturers to provide data on costs, the committee has avoided becoming too immersed in economic data because their primary responsibility is to consider the safety and efficacy of vaccines. Questions of costs, while important, are secondary to medical considerations (Dempsey *et. al*, 2008).

Dr. Jonathan Temte: Interviewed on Tuesday, November 25, 2008

During his long career, Dr. Jonathan Temte, an associate professor in the Department of Family Medicine at the University of Wisconsin School of Medicine and Public Health, has developed expertise in infectious diseases and immunizations. Consequently, he was interested in the work of the ACIP well before his tenure began as a committee member. In fact, he

formally began his association with the ACIP after serving as a liaison to the committee on behalf of the American Academy of Family Physicians.

At the outset, Dr. Temte indicated that his role as an ACIP member is to use “new and existing technologies and vaccines” in an attempt “to set policy to use resources wisely.” Because he has been integrally involved in clinical work and seeing patients throughout his career, he said he views his primary contribution to ACIP as “injecting the sensibilities of a working clinician.” Researchers who have not practiced medicine in a clinic in many years or who have spent their careers engaged in pure research may not fully appreciate the challenges faced by physicians who work day-in and day-out with patients suffering from a variety of infectious diseases.

As of November 2008, Dr. Temte chaired an ACIP working group; thus, he was well-suited to appreciate the means by which issues are added to the committee’s agenda. Issues come before the group through several avenues. He indicated that the ACIP steering committee sometimes solicits topics for discussion. The CDC often brings topics to the ACIP, and in other cases the topics are obvious because a new disease or vaccine is salient enough to warrant the committee’s time and attention. According to Dr. Temte, “the universe of potential topics is very large but is narrowed by what new vaccines have been licensed” as well as the diseases that arise and alarm the medical community. Occasionally, issues are brought before the committee because the public is so concerned about a disease that individuals contact the CDC or, alternatively, public fears receive media coverage, which unquestionably can influence the agenda. The ACIP may also revisit issues that have been discussed in the past if new information and data are available and a reexamination is in order.

After an issue is added to the agenda, the working groups are the venue where the “heavy lifting” is done because the groups explore the details involved in a disease or a particular vaccine. “A lot of trust is put in the working groups,” he observed. The full ACIP will debate the issue and ultimately vote on an appropriate recommendation, but the working groups must first compile a dossier on what is known and unknown about the state of the science.

Like all of the ACIP working groups, Dr. Temte’s group is on a tight schedule. It is easy to be overwhelmed by the large number of vaccines and diseases that must be scrutinized as well as the complexity of medical data. Typically, working group members wrestle with data synthesis at one meeting. In other words, the working group discusses what information they know from experts, consultants, a literature review, and their own expertise. At some point, they must “get a handle on the data” so they can present a narrative to the full ACIP and tell the story of the disease and the ways in which the vaccine will effectively treat that disease. Without data synthesis, a narrative is lacking and the data are little more than a mass of facts jumbled together. The working groups’ task, first and foremost, is to make sense of the universe of data.

Depending on the quality and quantity of the data, a working group may have multiple meetings to determine whether they can make a recommendation in the absence of meaningful data. On some occasions, working group members have the data they need and they can construct a reasonably complete narrative. In this situation, members can devote their time to exploring the “evidence framework,” which means the working group will develop a list of policy options to present to the entire ACIP membership. The framework is more than just a narrative; it is a compelling analysis that offers a conclusion based on the data synthesis.

Dr. Temte recognized that in many instances data are missing. Echoing his colleagues’ comments, he said that when gaps exist, he falls back on past experiences, analogies to similar

situations and cases, and previous ACIP recommendations. “You do as much as you can with scientific information,” he remarked, “and then you have to use your own best judgment.”

Cost-benefit analysis always factors into the recommendations that the ACIP makes. Dr. Temte said he has taken a graduate-level course in analyzing cost-effectiveness, so he probably has more formal training in this area than most physicians have. Every decision that a group such as the ACIP makes involves costs and risks; the nature of decision-making, especially in the medical field, requires a balance between the two. Pharmaceutical companies that develop vaccines include data on costs and benefits as part of the package of information they present because they must make a persuasive case for the use of a specific vaccine. As an example, he cited the human papillomavirus virus (HPV), which has a great deal of cost-efficacy data available. As a result of available, high-quality data, making a decision on HPV is relatively straightforward compared with a decision regarding a rare disease such as Anthrax. Yet Anthrax can be a significant public health problem under the right conditions. The uncertainties inherent in decision-making for Anthrax do not obviate the need for making a decision, but they do alter the risk-reward calculation that must be undertaken (Contrera, *et al.*, 2003; Southall, 2008).

Decision-making will never be a linear exercise. A decision-maker is forced to consider each case on its own merits. Some cases will be relatively clear because the disease and/or the vaccine are well-known and have been exhaustively studied. “A structure exists,” Dr. Temte said. “The [decision-making] process is thought through very well and provides consistency and quality.” In other cases, the process is riddled with missing variables and inconsistencies, but decision-makers still must act despite uncertainties. Lack of data or missing information does not relieve the decision-maker from responsibility for ultimately making a recommendation.

## CHAPTER 5

### CONCLUSIONS

The paramount objective in this study was to interview as many of the 15 current and 11 former ACIP members as possible from a list provided by the ACIP executive secretariat. Ultimately, I contacted all 26 people on the list via e-mail and/or the telephone and interviewed half of them. Eight of the people on the list never responded to e-mail and telephone call invitations and the others indicated their willingness to be interviewed, but they had to reschedule repeatedly and simply never were able to participate. Because the research consisted of a literature review and interviews and did not involve experimentation, prior approval from the university's institutional review board was deemed to be unnecessary.

#### The Interview Process

Interviews were conducted between August and November 2008 via telephone. Because committee members were located throughout the country and seldom had more than a few minutes to speak, no effort was made to meet in person. ACIP meetings are held three times a year in Atlanta, but the agenda typically is so crowded that committee members have little time or inclination to be interviewed. Thus, telephone interviews were the most efficacious method for discussing the ACIP decision-making process. Occasionally, an interviewee agreed to provide additional information after the interview, such as background data, a curriculum vitae, or a link to their website so I could report information on their education, medical training, and professional experiences.

The same broad, semi-structured interview questions were used for all participants, although I sometimes asked them in a different order depending on how the conversation proceeded and the way interviewees steered the discussion. A copy of the interview questions can be found in Appendix A. A few interviewees were so anxious to talk and pontificate on their experiences that I did not need to prompt them very much. Others were more taciturn and had to be prompted constantly. One interviewee expressed reluctance to participate because, in her view, the questions were too open-ended and she didn't know how the data would be used. I sought to assuage her concerns by providing more detail on the nature and purposes of the dissertation research. Eventually, she felt better about participating and the interview proceeded. In every case, interviewees agreed that I could use their names in the dissertation and I did not have to provide them with a copy of my interview summaries or the dissertation text prior to publication. Two interviewees requested copies of the final dissertation, and I agreed to make such copies available.

The participants received little or no notice before the interview process apart from an e-mail and a short introductory note sent by Dr. Jean Clare Smith, Medical Officer, Assistant to the Director for Immunization Policy, Immunization Services Division, National Center for Immunization & Respiratory Diseases at the CDC, and a follow-up e-mail from me. As a CDC representative to the ACIP, Dr. Smith's participation was crucial. She provided me with a list of current and former ACIP members. Moreover, because she contacted the physicians to tell them that I would contact them soon and thereby graced me with the imprimatur of the CDC, my research possessed a degree of legitimacy it would not have had without Dr. Smith's assistance. I doubt I would have had the same level of participation from ACIP members had the CDC not



agreed to provide access to the committee. The text of Dr. Smith's message can be found in Appendix B.

Typically, I exchanged e-mails with the ACIP member and/or his or her assistant to find a mutually convenient time to talk. When the time was selected, I usually called the interviewee, although in three cases the interviewee preferred to call me. Whenever possible, I opted to initiate the call so I could exercise at least a modicum of control over the interview. I learned the importance of initiating the call myself when a potential interviewee said he would call me and failed to follow through. The following day, I tried to call him, but I was never able to make contact. Even my e-mails were unsuccessful. Perhaps the gentleman simply forgot to call me and was embarrassed about it afterward. Perhaps he experienced an emergency and I was far from his mind. In any case, I never discovered the reason he failed to call and the interview never occurred. At least when I initiated the call, I could aggressively follow up without having to wait for my subject to try and contact me.

The interviews lasted between 10 minutes and 30 minutes each. Although the interviews were not tape-recorded, copious notes were taken and theoretical memoranda were written immediately following the interviews. The memoranda formed the basis for the summaries found in the preceding chapter.

### Grounded Theory and the ACIP

After all the interviews had been completed and the theoretical memoranda were written, individual participant categories were coded according to emerging themes. Constant comparative coding comparing all categories from participant to participant was performed. Theoretical coding allowed me to identify relationships among the core categories and their sub-categories. These coding efforts were used to integrate ideas and determine focal concepts that

emerged from the study. Interviews were conducted until potential participants no longer responded to my entreaties. Theory generation focused on one or more core categories that emerged during the post-interview process.

The first step involved data coding, which commenced during the first week of November using the theoretical memoranda and interview notes as a guide. After reading through the memoranda several times, several themes emerged, and I began to developing the core categories. The next step involved open coding. I initially developed 10 separate categories, but by the time I finished sifting through the interview data, I collapsed the original categories into four core categories. I narrowed and combined the categories so that I would not have too many categories to work with or categories where more than one case could fit. Concepts were built from comparisons among and between categories.

In my view, the four categories that emerged from the open coding process involved, first, the organizational structure of the ACIP. Understanding how and why the committee exists is crucial to understanding how the ACIP collects data and engages in its decision-making process. In addition, it is necessary to appreciate the various constituencies that the ACIP deals with throughout its decision-making because the committee's meetings and debates are aimed at producing usable data in the form of vaccine recommendations, so group members must understand their constituencies. Use of the word "constituencies" is not to suggest that committee members believe they must subordinate their preferences to the preferences of the groups with which they interact. Rather, the relationship between the ACIP and its constituencies is more fluid. ACIP members depend on other groups to supply them with information and data. In turn, the ACIP attempts to analyze that information and data and supply recommendations based on the group's expertise. The third category was how the group

chooses to consider uncertainties in the data. Is disease burden the crucial issue, i.e., should the group make a recommendation even though data are missing because the disease is so terrible the potential benefits far outweigh the potential risks of doing nothing or delaying a decision?

Table 5.1: Summary of Open Coding Results

Code	Concept	Frequency
<b>Organizational Structure</b>	• Agenda setting	4
	• CDC-Interface	3
	• Working groups	6
	• Full ACIP meetings	6
<b>Constituencies</b>	• Pharmaceuticals	4
	• The CDC	5
	• Medical community	3
	• The general public	4
<b>Uncertainty vs. Certainty</b>	• Missing Data	6
	• Conflicting Data	3
	• Disease Burden/safety	5
	• Costs	8
<b>Consensus vs. Voting</b>	• The need to decide	4
	• Nature of the issue	2
	• Individual assessments	5

How should costs be addressed, i.e., if we recommend that millions be spent for this vaccine does that take money away from the development and distribution of promising vaccines for even more virulent diseases? Finally, the category of consensus versus voting is a necessary part of open coding. If the ACIP speaks with one voice in a consensus process that can be more impressive than if the group members are divided and feel the need to vote and issue multiple opinions on an issue. See Table 5.1 on the preceding page for a summary of the open coding categories and the frequency of interviewee responses in each category.

Step three involved axial coding. This is a process that deconstructs the sequence of events leading from the causal conditions giving rise to the ACIP decision-making to the

phenomena of decision-making through the contextual conditions, intervening conditions, the act of decision-making itself, and the consequences of the decision-making process. See Table 5.2 for a summary of the axial coding results in this study.

Table 5.2: Summary of Axial Coding Results

<b>Causal Conditions</b> A set of events that influence the phenomena	<b>Phenomena</b> What is going on in this study?	<b>Contextual Conditions</b> Specific sets of conditions that create the set of circumstances pertaining to the phenomena	<b>Intervening Conditions</b> Circumstances that occur and may affect the phenomena in unexpected ways	<b>Action/Decision</b> The events or actions that are undertaken as a result of the deliberative process	<b>Consequences</b> Outcomes or actions that happen as a result of the events or actions undertaken
CC1: Vaccine development  CC2: FDA approval of the vaccine  CC3: Request from a pharmaceutical company to recommend a vaccine OR  CC4: Public or medical concern over the safety and effectiveness of a vaccine AND/OR  CC5: Decision of the ACIP executive secretariat to add an issue to the agenda	PH 1: exploring how the ACIP undertakes medical research under conditions of uncertainty  PH 2: Reviewing how the ACIP makes decisions through working group activities and ACIP committee meetings	CONTCOND1: FDA approval of the vaccine  CONTCOND2: Saliency of a specific vaccine  CONTCOND3: Disease burden  CONTCOND4: Pressure from constituencies for the ACIP to make a recommendation  CONTCOND5: Decision of the ACIP executive secretariat to add an issue to the agenda	IC1: The FDA decides to revisit or rescind approval for a vaccine  IC2: A pharmaceutical company removes the vaccine from the market  IC3: After a literature review or expert testimony, the ACIP decides to delay a recommendation until missing or conflicting data can be improved	A/D 1: The ACIP delays making a recommendation OR  A/D 2: The ACIP makes a recommendation OR  A/D 3: The ACIP changes a previous recommendation	CONSEQ 1: The recommendation is publicized by the CDC staff and through various medical publications  CONSEQ 2: If the recommendation is negative, the dissemination or treatment with the vaccine will be limited  CONSEQ 3: If the recommendation is positive, the vaccine will be administered to the target populations in accordance with the recommendation  CONSEQ 4: If the recommendation had budgetary consequences, public funds may have to be spent to ensure the vaccine is administered appropriately

In step four, theoretical coding identified relationships among the core categories and their sub-categories. The coding was used to integrate ideas and determine focal concepts emerging from the study. Theory generation focused on the core categories that I developed.

The core categories and subcategories, along with a discussion of each, follow. A summary of the core categories and subcategories can be found in Appendix C. A detailed discussion of this process follows.

First Core Category: A Description of the ACIP Decision-making Process

Every interviewee spoke about the ACIP decision-making process in some detail. Respondents discussed three key aspects. First, much of the actual data collection and analysis occurs in the working groups. Afterward, the working groups present the data and, in some cases, their recommendations to the full ACIP membership. Finally, the ACIP must decide whether to make a recommendation on a specific vaccine and, if so, what the recommendation will be. In some instances, the recommendation is made through a consensus process. In other instances, the members vote and the majority dictates the content of the final ACIP recommendation. Within each step of the process, however, respondents differed slightly on their descriptions of how decisions were made and uncertainties were addressed.

First Subcategory: Working Group Activities

The ACIP working groups are comprised of a subset of the full ACIP along with as many outside experts and medical researchers as the working group chair believes are necessary. Unlike administrative agencies that must be staffed according to fairly rigid employment guidelines, the ACIP is an advisory committee and therefore can select personnel on a fluid basis. Membership on a particular working group depends on a variety of factors such as whether there is an opening, the needs of the group, the expertise of the ACIP members, and the complexity of the issue being considered.

Some respondents viewed the working group as a coordinator of information, but the legwork and research is performed by CDC staffers that provide support to the ACIP. Other

respondents said that working group members can rely on CDC staffers for assistance in running down specific articles or contacting certain experts to participate in working group or ACIP meetings, but ultimately working group members must delve into the literature and data themselves. Still others reported that the character and activities of the working groups depended in no small measure on the chair and his or her predilections. Some chairs prefer to rely heavily on the CDC while others encourage working group members to become involved in every aspect of research and data evaluation.

The key insight in the ACIP working group process is the manner in which scientific uncertainties are addressed. Recall in Chapter 2 that some scientists are concerned that uncertainties are not known and, to some extent, not knowable. In other words, there is a fundamental epistemological problem, namely that some information will never be acquired because the source of the information cannot be adequately identified. For information to be acquired, a problem must be expressed as a researchable issue amenable to the scientific method. Even metaphysical problems that do not depend upon the collection and analysis of observable data can be fashioned into a problem presumably soluble through deductive means. But some scientists argue that a few issues are not amenable to deductive or inductive reasoning and therefore remain beyond the scope of human understanding.

While this fundamental dilemma over whether human can conceive of knowledge that is unknowable will continue to perplex philosophers of science, it does not perplex ACIP decision-makers. The unstated presumption is that data on vaccines and their potential side effects are for the most part known, and definitely knowable. When the ACIP deals with uncertainties, it is not seen as a core problem of the uncertainties inherent in some epistemological problems. Rather, it is seen as a problem of missing data.

### Second Subcategory: Full ACIP Activities

If the working groups are where the work of compiling data and sifting through the intricacies of the data occurs, the full ACIP is where science meets policy. The entire ACIP membership meets in Atlanta periodically, typically three times a year. The purpose is to make recommendations on whether certain vaccines should be administered to certain populations. All interviewees agreed that the role of the entire ACIP was to consider data on vaccines and evaluate their effectiveness and efficiency. At first blush, evaluating public policy would appear to be relatively simple and straightforward, but not everyone can agree on the appropriate ACIP procedures. In some cases, interviewees reported that determining how a vaccine was added to the agenda was not clear. Sometimes the executive secretariat informed ACIP members that an issue was ripe for discussion. In other cases, the CDC or another health-related agency would ask that a topic be added for discussion. Occasionally a pharmaceutical company marketing a specific vaccine would ask for ACIP buy-in.

After an issue is placed on the agenda, ACIP members review the data on clinical trials and other relevant information to compare the results with expected outcomes. This kind of evaluation is not as straightforward as it initially appears. The data and information necessary to reach a definitive conclusion or a defensible decision may not be available, or, if it is available, it may be ambiguous or contradictory. Unintended consequences or intervening acts may occur, which require a reevaluation of the vaccine or even a delay in making a recommendation. On some occasions after the ACIP has made a recommendation, the group revisits the recommendation later and changes it as new data and medical research becomes available.

During their meetings, ACIP members employ a range of tools to evaluate programs. Assuming that scientific studies are available of a sufficient quality and quantity, members sift

through the conclusion to determine whether a scientific consensus exists. Often, the working groups have provided summaries of the studies before the full ACIP meets. Probably the most prevalent and intuitive evaluative techniques involve before-versus-after studies; consequently, these data are especially valuable. As the name suggests, when these data are available, committee members examine a problem before the program was implemented and compare it with the period after implementation. This type of evaluation works well when only a few personnel are involved, the time period is short, and the program is well defined and narrow in scope. As the number of people grows, the time expands, and the program becomes larger and less well defined, it becomes difficult to determine whether changes occurred owing to the program or because of other factors or intervening variables. Fortunately, in many scientific studies, the before-versus-after methodology is employed.

Other studies include time-trend projection research. In these studies, researchers rely on preprogram data to project likely results after a particular program is implemented. Afterward, they implement a program and compare the actual results with the projected results. If the actual results are not in line with projections, researchers can then trace the deviations in an attempt to isolate and correct problem areas. As was the case with before-versus-after studies, however, it is not always a simple matter to determine which factors contributed to the actual results. Many scientific studies rely on time-trend projection research as well.

ACIP meetings typically last two or three days. Although the executive secretariat has developed a fixed agenda, it is not written in stone. If committee members believe, based on their discussions and deliberations, that more time is needed to sift through the available scientific studies or if they need to hear from experts who are not available at the current meeting, they can ask for more time, table the issue, delay their recommendations until a later



meeting, or simply ask that the issue be removed from the agenda permanently. In other words, ACIP members do not feel compelled to reach a decision simply for the sake of reaching a decision. They are to be guided by the quantity and quality of the data as well as their own perceptions about an appropriate course of action.

Having said that, most ACIP interviewees mentioned the realization that in most cases a decision must be made even if complete and incontrovertible data are not always available. The nature of scientific decision-making is necessarily iterative and uncertain. If the data are unavailable or so incomplete as to raise more questions than they answer, a decision must be delayed until some later time. In a majority of cases, however, by the time it gets to the ACIP the issue has been vetted fairly well—especially considering the FDA’s approval process, which requires vaccine manufacturers to provide a plethora of data and scientific information—so it is unlikely that insufficient data exists. In short, ACIP members do make a decision when a vaccine is considered by the group.

Whether they expressly mentioned it or not during the interviews, it was clear that ACIP members recognized the policy implications of their decision-making. Most of the committee members have enjoyed extensive careers working in the public health arena. Many have worked in government service. They are not scientists working on “pure research” in isolated laboratories, but they are making recommendations on appropriate vaccines for appropriate populations. Consequently, they recognize that their decisions will have policy ramifications.

In fact, because the ACIP is comprised of health care professionals that advise government policy-makers and are not engaged in medical practice while serving on the ACIP, the committee is a deliberative, policy-making body. By virtue of their participation in ACIP activities, the professionals who serve on the committee are responsible for policies that will

filter out through other government agencies. To the extent that a science-policy gap exists, ACIP members are charged with developing policies that will bridge the gap. They are medical practitioners charged with making policy decisions.

#### Third Subcategory: Consensus vs. Voting

Interestingly, some interviewees responded that the ACIP is more or less a consensus-making body. In other words, decisions are reached by the full committee after the working groups and invited experts have presented the information to the ACIP. Committee members discuss the salient issues and try to assuage concerns about missing data or possible problems associated with the administration of the vaccine. According to some interviewees, the discussions can last anywhere from a few minutes to a few hours to a few days, although if the discussions last more than a few hours often the issue is tabled until it can be considered in greater detail at a more opportune time. The final outcome depends in no small measure on how confident the ACIP members are in the quality and quantity of data they have at their disposal.

Ideally, the entire committee can reach consensus on the recommendation. In many cases, they do exactly that. In other cases, however, the data are not universally regarded as persuasive or gaps in the data compel some members to vote against a vaccine or perhaps abstain from making a decision without more information. If the questions and concerns are pervasive, the committee may choose to delay a decision until such time as more expertise can be brought to bear or until new studies are available for consideration. If the disease burden is high or time is of the essence, the committee may not enjoy of the luxury of waiting on a decision. Therefore, a vote is taken and the majority determines the nature of the recommendation. ACIP members who are in the minority and believe that the majority has erred certainly have the right to make

their views known, orally or in writing, as they deem appropriate. An advantage to the advisory committee structure is its flexibility in decision-making.

Second Core Category: The “Certainty” Aspects of the ACIP Decision-making Process

All interviewees agreed that decision-making is undertaken with a degree of uncertainty. Dr. S. Michael Marcy was the most articulate respondent on the issue of uncertainty. Recall that he said, “Decisions made under conditions of uncertainty? I didn’t know there were any other kinds. Lewis Thomas, the great medical essayist once said (and I am paraphrasing): ‘Science moves from truth to truth as new facts are discovered, rejecting old truths as new ones appear. We are, thus, fundamentally, always in error.’” Even the less philosophically inclined agreed that uncertainty always exists. Although the interviewees could not or would not provide a specific explanation of how they reach decisions—most respondents said they consider a variety of issues and not necessarily in a linear fashion—they all agreed that uncertainty is a problem and must be a part of their decision-making. Nonetheless, virtually every interviewee pointed to factors that helped to resolve uncertainty.

The fact that the interviewees believe that uncertainty can be resolved—that is, the gaps in the data can be filled in—means that they have implicitly rejected the idea that uncertainty is an epistemological black hole. Uncertainty exists, but it need not paralyze the decision-making process. They also recognize that even if gaps exist, a decision has to be made. Fortunately, the FDA handles most of the data collection and analysis, which means that the ACIP has the far easier task of assessing the available data rather than attempting to serve as a frontline agency for compiling data and initially assessing its efficacy, or lack thereof. The ACIP’s role is to make recommendations on vaccines after many of the most crucial health and safety issues already have been vetted by the FDA, but committee members can ask for more data, defer a decision,

make a decision even when substantial data gaps exist, subsequently change a recommendation, or rescind a recommendation altogether. In short, many options exist; consequently, committee members have a wide range of options that aid in decision-making.

#### First Subcategory: FDA Approval

The FDA must act before a drug can be marketed in the United States. As a result, this agency is the first line of defense to ensure that safe and effective vaccines are offered to patients. The FDA requires pharmaceutical companies to provide extensive evidence and numerous clinical studies before the drug is approved. Many interviewees explained that a vaccine is never brought before the ACIP for consideration until after the FDA has completed its review. Generally, the same data that is provided to the FDA is provided to the ACIP.

At the same time, interviewees recognized that the ACIP does not simply rubberstamp the FDA. Although the FDA is the first line of defense, it is not the only line of defense. Moreover, because the ACIP is considering whether to offer a vaccine to vulnerable populations or in particular doses, the questions it considers differ, to some extent, from the FDA review. Just because the FDA determined that a vaccine met a threshold requirement for sale in the United States, this does not mean that all questions regarding the safe and effective use of the vaccine have been resolved (Carpenter, 2004; “The FDA Is No Place for Politics”; “Politics Trumps Science at FDA,” 2005; Rose, 2008).

#### Second Subcategory: Scientific & Medical Literature

A review of the relevant scientific and medical literature is another means for resolving uncertainty in ACIP decision-making. Typically, after a vaccine is placed on the agenda and assigned to a working group, the group will ask the CDC staffers who provide administrative, technical, and logistical support to perform a literature review. In some cases, especially when a

disease has been researched exhaustively, voluminous information exists. In other cases, the scientific record is thin and the literature review reveals very little new information. In those instances where questions linger, the working group members may ask the CDC to search for experts in the field who can provide additional data.

ACIP members realize that a review of the scientific literature can provide valuable background information for their decision-making process, but in some cases the literature raises almost as many questions as it answers. The iterative nature of scientific research means that occasionally one strain of literature reports on study results that reach conclusions contravening previously published studies. In these situations, the CDC staffers and ACIP working group members will explore the different features of each study to determine why the differences exist and how they might be reconciled. Sometimes the uncertainty can be resolved when the differences in the published studies are accounted for, but in other cases the uncertainty only deepens because the anomalies cannot be easily explained.

Even if the vaccine under review is new and the published literature is sparse and not exactly on point, it can be helpful to review the information that is available. Knowing what data are available and what are not can be useful as ACIP members determine how much time and attention they need to devote to reviewing a vaccine. If the vaccine is part of a well-known family of drugs with a great deal of research data supporting its safe and effective use, the review will differ markedly from their review of a vaccine where little background data are available. Presumably, the ACIP will spend appreciably more time asking questions and sifting through FDA data on the lesser-known vaccine.

### Third Subcategory: Expert Knowledge

The ACIP occasionally seeks out experts to attend a working group session or full ACIP meeting and discuss a particular disease or vaccine under review. In some instances, the expert may be invited to join the working group and thereby share his or her views over the course of multiple meetings. Although an expert does not necessarily have all the answers to outstanding questions and concerns, at least he or she can frame the issue and steer committee members toward an appropriate course of action.

Although the ACIP has responsibility for recommending policies affecting the nation's health, to some extent, committee members generally function outside of the public eye. Moreover, because ACIP members are among the elite of the medical profession, they do not share the public's occasional disdain for, and mistrust of, expert knowledge. Indeed, the ACIP is a bastion of expert knowledge. The purpose of the ACIP in the first place is to ensure that the CDC has a second layer of experts in immunology and infectious diseases to advise government scientists on the appropriate vaccines that are needed to ensure the health and safety of the citizenry, especially vulnerable populations such as children, persons with compromised immune systems, and the elderly.

Expert knowledge obviously is not infallible, but in the absence of other data or when the information at hand is confusing and inconclusive, experts often possess the background education and professional experience to sift through the morass and provide clear direction on an appropriate outcome to a seemingly insoluble dilemma. This is one reason why ACIP members occasionally ask recognized experts in the field to address working group sessions. Faith in medical experts can be taken too far, but on the whole the ACIP benefits from the advice of recognized experts in the field.

#### Fourth Subcategory: The Effect of Similar and Previous Decisions

The ACIP is not bound by its precedents; that is, the group is free to consider each vaccine that comes before it based on whatever factors the current committee members deem to be important. Nonetheless, in some instances it may be instructive to look back at previous ACIP decisions, especially when those decisions involve a similar vaccine, and discern whether the previous decision can assist in discussing the instant case. As mentioned previously, decision-making is not necessarily a linear process, and each vaccine can be evaluated based on the predilections of ACIP members, but seeing guidance from past decisions is a reasonable method of reaching decisions.

In the law, precedent is afforded great weight. Except in exceptional cases, precedents should be adhered to because they provide continuity with the past. In the medical field, precedents serve a different purpose. Medical professionals are not attempting to develop a seamless web of logically consistent, more-or-less rationally defensible positions. Rather, they are focused on finding clues to the likely effects of a specific vaccine. The kinds of questions they ask are: Will this vaccine effectively treat the disease it is designed to treat? In treating the disease, will the vaccine trigger any negative side effects? If the vaccine triggers negative side effects, are those side effects so severe that the treatment becomes, in effect, worse than the disease? What are the costs—socially, medically, economically—to treating the disease versus not treating the disease?

Sometimes these questions can be answered fairly accurately and completely. In other instances, the data simply are unavailable or they are unclear to make a sound decision. When the data are unavailable and other means of resolving uncertainty are ineffectual, looking to previous decisions can provide at least a small measure of certainty. If a vaccine under

consideration has similar characteristics to a vaccine that was previously recommended, there may be clear, defensible grounds to recommend the new vaccine. Looking to similar cases is not an ideal decision-making posture in the medical field—it would be preferable to consider this particular vaccine without worrying about similar vaccines—but in tough cases looking at previous decisions may be an effective means of resolving uncertainty in the absence of other means.

### Third Core Category: The “Uncertainty” Aspects of the ACIP Decision-making Process

All interviewees expressed their realization that decision-making necessarily involves a great deal of uncertainty. The crucial requirement for effective decision-making is to manage uncertainty appropriately, i.e., adopting a decision-making process that does not avoid making a decision owing to the uncertainty, makes a hasty decision that fails to account for the uncertainty, or makes a decision that accounts for the uncertainty but avoids its implications. Uncertainty exists owing to three related factors, as will be discussed in the subcategories below.

Notice that ACIP members do not view uncertainty the way that the general public views uncertainty. As discussed in Chapter 2, many members of the public are fearful of uncertainty. They press scientists and technical policy-makers to eliminate uncertainty. For much of the public, uncertainty is always a case of missing data, a problem to be solved if scientists will just “get the lead out” or “put their noses to the grindstone.” For the public, a scientific problem is akin to an algebraic equation. If the scientific community will simply solve for  $x$ , the problem eventually will be solved because the answers ultimately are knowable. The fact that scientists claim they don’t know certain things means either they are not trying hard enough or they are hiding something in a misguided effort to protect themselves and their fellow scientific elites.



### First Subcategory: The Non-linearity of Scientific Decision-making

ACIP members recognize that science is far more iterative and far less certain than the public generally realizes. Scientific decision-making is not necessarily linear, although decision-makers usually try to approach the process as a rational enterprise that can be fit into a more or less linear decision-making model. (The ACIP decision-making model will be discussed momentarily.) Because scientific decision-making frequently involves multiple variables and a great deal of missing data, it proceeds in fits and starts. In some cases, one group of researchers will solve a piece of a larger puzzle, which then will serve as the foundation for research performed by others working in distant laboratories. Occasionally, decision-makers will stumble upon a discovery through serendipity or they will realize that their initial approach was misguided and they need to begin again if they hope to produce useful data and research conclusions.

Consider the ACIP and the decision on whether to recommend the administration of a particular vaccine. ACIP working group members generally ask the CDC staff to provide the groups with information and data. In cases where the data are incomplete or conflicting, the ACIP may ask that experts address the appropriate working group to augment existing information with expert opinion. The available studies and expert testimony may reveal that a vaccine produces harmful side effects or may exacerbate other illnesses not associated with the disease being treated by the vaccine. In other instances, the available data could suggest that a vaccine is safe and effective but, with the benefit of subsequent studies, it becomes clear that the vaccine produce unintended consequences. In those cases, the working groups and the full ACIP may revisit the original decision and modify the recommendation, as appropriate.

### Second Subcategory: The Iterative Nature of Medical Research

Medical research and decision-making is famously iterative. New drugs and vaccines that are promising today may be found later to be ineffective or they may be effective but are supplanted by more effective vaccines in the future. Breakthroughs in medical research can occur at a plodding, slow pace, or they may be accelerated by simultaneous breakthroughs in dozens of laboratories and clinics around the world. An issue that is uncertain today may be resolved tomorrow, only to raise a series of additional questions that must be addressed through future research. Such is the nature of scientific and medical research that it is never-ending (McCaffrey, *et al.*, 2007).

The myth of the lonely scientist laboring away on the crucial experiment, as discussed in Chapter 2, has captured the public imagination. It is little wonder that the public views science in this manner. A large part of the American mythology is that the individual can pull himself up by his bootstraps and make whatever he will of his life, despite potentially dire circumstances and seemingly insurmountable obstacles. This “high noon” ideal of success heralds the worth of the individual without appreciating the differences between a single person’s decision-making and the decision-making process that guides the scientific community. In addition, simply because a particular model of success applies to an individual—setting aside the possibility that even individuals need something beyond grit and determination to succeed in a world where numerous forces influence the outcome of a situation—this observation does not necessarily carry over to a group decision-making process.

Pharmaceutical company researchers conduct experiments long before the company brings a vaccine to market. After the drug is up for review, FDA scientists require a variety of data and experimental results before they sign off on a vaccine. Even after all of this

experimentation and review, the ACIP goes through a thorough process of data collection and analysis to ensure that committee members are persuaded that the vaccine is safe and effective. At each step, some questions are answered and others are raised. When new questions are raised, new data may be required or the questions, depending on their nature and extent, may be tabled for another time. Seldom is there a full, accurate, thorough dossier that addresses all questions about a vaccine in a manner that satisfies every constituency. The hope is that over time more and more questions will be answered, and probably they will be, but the iterative nature of science is ongoing, never-ending.

Third Subcategory: Limitation of the Knowledge-Driven Model and Gaps in the Data

Any government agency or advisory committee depends to some extent on the knowledge-driven model as a legitimizing principle. If the entity could not lay a reasonable claim to possessing a measure of specialized knowledge necessary to assist in making important public policy decisions, the entity would be hard-pressed to justify its existence. Thus, the knowledge-driven model is an important method by which agencies assure their constituencies that they are a necessary part of the policy-making apparatus.

A major difficulty occurs, of course, because the knowledge-driven model has its limitations. Owing to uncertainties of scientific knowledge—not to mention the epistemological problems in producing scientific research in the first place—the knowledge-driven model is not complete. It is a necessary but insufficient model for understanding how scientific decisions are made. All the current and former ACIP members interviewed for this dissertation recognized the uncertainties in their knowledge base, and they were troubled by those cases where they are called upon to make recommendations on vaccines when the data are far from complete. At the

same time, however, they all recognized that uncertainties are part of the decision-making process. For some ACIP members, such as Dr. Lance Chilton, it is important for decision-makers to always be “looking for data where we can find it” because the quality of the decision depends on the quality and quantity of the data.

Not everyone believed that incomplete or conflicting data were especially problematic. Commenting on FDA’s exhaustive data-gathering procedures, Dr. Harry Hull observed that “there is always a lot of information available. These vaccines are licensed.” Dr. Jon Abramson agreed. Because of the FDA’s work, “we are pretty dang comfortable” about safety when the ACIP makes recommendations. Because the FDA requires so much data to be submitted before it will approve a drug, generally the information that is sent to the ACIP is as thorough and complete as possible. Consequently, many ACIP members have a high degree of confidence in the quality and quantity of the data.

Having said that, no data set is absolutely complete. More studies can always be performed and additional research is almost always needed. By its nature, the knowledge-driven model depends on large amounts of data. Medical research requires large numbers of cases and time can present a problem owing to long latency periods necessary to gauge the full impact of side effects. Despite the relative confidence supplied by the FDA approval process, some data is absent, ambiguous, vague, or conflicting.

Moreover, care must be taken to distinguish between uncertainties owing to gaps in data and uncertainties because the nature of the question presents epistemological challenges. This distinction is crucial because it will determine how a researcher handles the uncertainty. In the former case, the information is knowable, but not known. Thus, more research and a refinement of the research questions and/or analytical processes eventually may lead to answers. By

contrast, when a question is large and perhaps imprecise—or when it raises value questions that underlie the scientific enterprise—no amount of research will resolve the uncertainty satisfactorily. A question such as the relationship between multiple vaccines administered over time in varying doses to a person as he or she grows from a child through puberty and into adulthood may be enormously complicated and it may be exceedingly difficult to answer, but the scientific problem can be broken into smaller pieces that, if enough time and resources are allocated, can be addressed. Asking whether it is ethical to recommend that experimental vaccine be administered to adolescents whose hormones may interact with the drug in unknown ways is a different issue requiring a different answer. The knowledge-driven model provides little guidance on resolution of this problem.

#### Fourth Core Category: The Role of Cost-Benefit Analysis in ACIP Decision-making

The question of costs was one of the most important and contentious issues facing ACIP decision-makers. Seven of the 12 interviewees specifically mentioned costs and benefits without verbal probing from me. For the general public, discussing costs in conjunction with medical research is unseemly—human life is precious and should not be calculated on a balance sheet—but decision-makers in the medical field recognize that costs and benefits must be considered.

The cost of medical care has always been a controversial issue, and no wonder. If human life is worth something more than a mere commodity, as most people steeped in the Judeo-Christian tradition believe, placing a price tag on the steps necessary to protect and perhaps prolong human life seems distasteful. At the same time, in an age of scarcity where resources are limited and where not everyone has access to quality, affordable health care, costs cannot be ignored.

### First Subcategory: Costs are not a Part of the ACIP Mandate

As part of its mandate, the ACIP is charged with responsibility for making vaccine recommendations irrespective of costs because the group is not supposed to worry about federal budgetary issues. The CDC, which staffs the ACIP, does not want the medical professions who work with the ACIP and the working groups to serve as *de facto* budget officials. The reason the ACIP was established in the first place was to allow experts in infectious diseases, pediatrics, and public health issues to deliberate on vaccines and their efficacy and provide their best advice on the dissemination and administration of the drug. They are not experts on cost-benefit analysis; accordingly, decisions on costs are supposed to be made by others in the administrative process.

### Second Subcategory: Costs as an Integral Feature in All Decision-making

Despite the admonition that costs are not part of the ACIP mission, they also are never removed from decision-making. As many of the interviewees mentioned, a tradeoff always exists. If the ACIP recommends the administration of an expensive vaccine, that recommendation, assuming it is followed by the CDC and other health agencies, may cost many millions of dollars. In an age of scarcity when resources are finite, the millions spent to distribute and administer a particular vaccine are not available for the distribution and administration of other vaccines. Therefore, it is important that ACIP decision-makers consider the disease burden when they make recommendations. They are more likely to recommend that a costly vaccine be widely distributed if the disease is fatal and widespread. Obviously, the utility calculation changes if the disease is not fatal and if it is rare. Some ACIP members stated immediately that they would consider costs up-front while others indicated that they leave the cost issue to others.

### A Model of ACIP Decision-making Under Conditions of Uncertainty

A model is a simplified view of how the world operates. Because it allows researchers to isolate key factors that explain how the case works and how similar cases might work, it is helpful in understanding the information in this, or any, study. Indeed, based on the coding discussed above, a model of ACIP decision-making under conditions of uncertainty can be developed. The model explains how an issue, e.g., consideration of a vaccine, moves through the process from the time it is placed on the ACIP agenda until the committee makes a formal recommendation. A graphic depiction of the decision-making process is found in Figure 5.1.

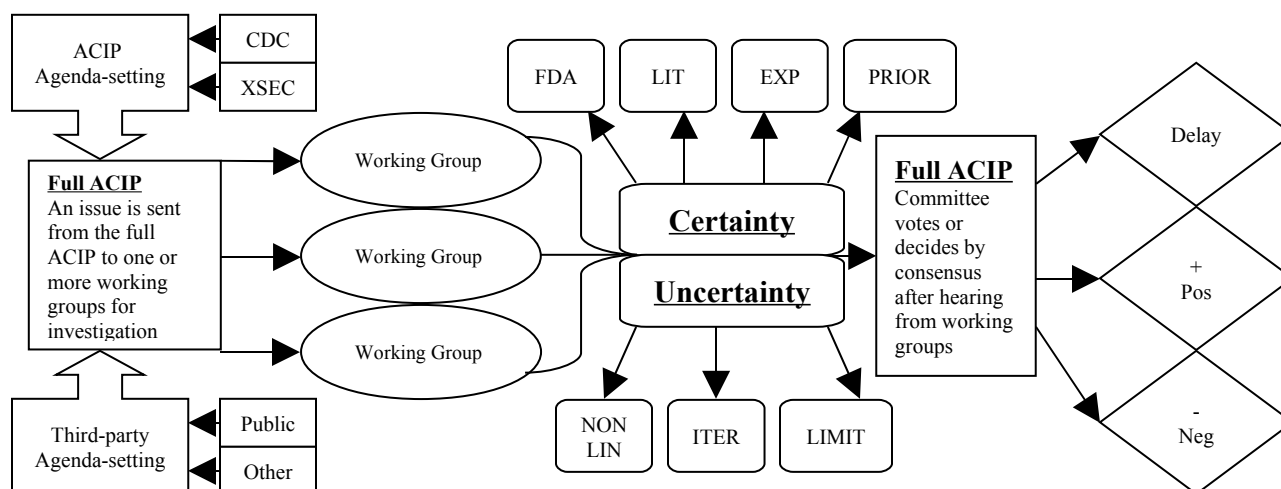


Figure 5.1: A Model of ACIP Decision-making Under Conditions of Uncertainty

The decision-making process commences when an issue is placed on the ACIP agenda either from ACIP-affiliated entities such as the CDC or the executive secretariat or via a third party such as other medical research agencies or entities or the general public. In most cases, the CDC or the executive secretariat will set the agenda, but third parties can add issues to the agenda, although normally they do not. A disease that sweeps through the world and garners considerable media attention or a highly-touted, promising new vaccine that is heavily promoted

by the pharmaceutical industry may be ripe for ACIP attention as well. Sometimes the ACIP seeks out issues for consideration and sometimes the issues cry out for attention.

The ACIP is not a well-known committee. Consequently, in most cases the issues that wind up on the group's agenda does not originate from the general public. To the extent that public pressure concerning vaccines exists, the CDC or the FDA will serve as the first line of defense. In fact, the advisory nature of the ACIP ensures that this group, although it considers scientific data and makes expert recommendations, generally does not receive public scrutiny the way that more high-profile government entities do.

After an issue is placed on the agenda, the entire ACIP assigns it to the appropriate working group. The issue can be assigned to an existing working group or a new working group can be established, as appropriate. Because the ACIP is an advisory group and does not function as part of the rigid hierarchy found in most federal administrative agencies, considerable flexibility exists as to the structure and operation of working groups. The number of members, their work regimen, the issues they will address, and their methods of operation are determined by the working group chair in conjunction with the CDC as well as the interests and needs of the working group members. ACIP members are professionals who have donated their time and talents to the committee and the working groups. Unlike many federal administrative agencies, where much of the work is related to managing, motivating, punishing or rewarding career employees, the ACIP and its working groups are able to focus on the issue at hand with minimal distractions.

The majority of the research and investigation of a vaccine occurs within the framework of the working groups. The working group immediately begins researching the issue by defining the parameters of what they know, what they do not know, and what they need to know.



Some tried-and-true sources of information are the FDA's files and records used to approve the vaccine for sale in the United States. A literature search also can provide data and published information on studies affecting the safety and effectiveness of the vaccine. Expert knowledge can be a valuable source of information as well, which explains why the ACIP occasionally asks medical experts to weigh in on vaccines, especially when the FDA file leaves some questions unanswered and the literature review provides little information or data.

The interviewees for this study stated that they did not view ACIP decision-making as formulaic. By this, they meant that the working group and full ACIP meetings proceed in accordance with the needs of the members, which depend in no small measure on the particular issue under consideration. If an issue is relatively straightforward and a large quantity of high-quality data already exists, such a case does not require prolonged consideration. By the same token, an issue where great uncertainty exists must be addressed carefully. Deliberations may stretch across multiple meetings and, in extreme case, a final decision may be postponed until more data or information can be compiled. The committee's actions depend not on rote requirements or specific timetables established ahead of time. The committee moves as quickly or slowly as the issue warrants. If the disease burden is high and a vaccine is desperately needed to stem the rising tide of a pandemic, the committee will act with greater dispatch than if the disease burden is low and the need for the vaccine is far less pressing.

Prior ACIP decisions in similar instances can shed light on the appropriate course of action. As with virtually any deliberative body, the ACIP affords great weight to its past decisions. When other avenues of decision-making are foreclosed or have produced few useful results, determining how the group decided similar past issues will help to guide decision-making in the instant case.

ACIP members recognize that uncertainties exist owing to a variety of factors—the non-linearity of scientific decision-making, the iterative nature of scientific research, and the limitation of the knowledge-driven model. As the interviewees mentioned repeatedly, these uncertainties always exist, no matter how much data or information is available. Uncertainties are especially pronounced in medical research because so many variables influence the decision-making process and side effects of a vaccine may not be known for many years after the drug is marketed owing to long latency times (Contrera *et al.*, 2003).

After the working group wrestles with uncertainties, it reports back to the full ACIP in advance of a full ACIP meeting. When the full ACIP meets to discuss the vaccine, the working groups present information and their conclusions. At that point, the ACIP must reach a decision on whether it should recommend that dissemination and administration of the vaccine. The decision can be the result of consensus or, in cases where the group cannot reach consensus, a vote can be taken. In any case, the decision can be one of three choices: (1) Delay making a decision pending new data; (2) a positive recommendation that suggests that the vaccine be administered in a particular way; or (3) a negative recommendation indicating that the vaccine should not be administered, or at least not administered to a certain population in a certain manner.

Uncertainties occasionally will require the ACIP to slow down the decision-making process while the group searches for new data or new data sources. Implicit in this decision-making process is the understanding that uncertainty always exists and must be handled. No serious thought is given to the idea that the issues are so imprecise and the data so incomplete that a decision can never be made. ACIP members realize that they may need to revisit a recommendation at a subsequent time if new information comes to light or that data gaps will

require future refinement. Thus, a decision, once reached, is not irrevocable. The iterative nature of the decision-making process and ongoing vaccine research mean that uncertainty need not paralyze the ACIP's efforts.

Like most modern scientific researchers, ACIP members do not subscribe to the “crucial experiment” school of thought. Recall from Chapter 2 that the public often believes that a lone, heroic scientist working in a laboratory will experience a “Eureka” moment, or a series of moments, after which all becomes clear and science can solve a problem. Most scientific researchers understand that such moments are rare. Instead, data are accumulated by multiple researchers over time and, in many cases, the effects of the data are unknown. Later researchers working with those data may find an application that was previously unknown or they may interpret the data in new ways that provide insight into other research, perhaps filling in the gaps in data sets along the way. In short, the ACIP realizes that the decision-making process can be made linear, but the data generation process is more iterative and piece-meal owing to the nature of the scientific method.

The virtues of this model of ACIP decision-making are that it simplifies what can be a complex and difficult decision-making process and makes it easy to understand how the ACIP works from the time an issue is placed on the agenda until the time a recommendation is made. Although scientific decision-making can be messy, inefficient, and sometimes unproductive, the model captures the rational way in which decisions are made even if exceptions exist and some decisions are reached in a less straightforward manner. Because the ACIP and the working groups follow a loose, non-rigid series of steps that eschews a rigid, vertical hierarchy, the movement of activities from left to right in the model accurately displays the ACIP decision-making process.

As with any model, however, it has limitations. Because each vaccine is different and the quality and quantity of the data that comes before the ACIP is different, the focus will vary from one case to the next. In the case of a vaccine where a great deal of information and consensus exists, the certainties outweigh the uncertainties. For a new vaccine, the data may be incomplete because the lead time necessary to evaluate the effects may mean that studies cannot effectively evaluate potential side effects. Such uncertainties, however, may be acceptable if the disease treated by the vaccine is virulent and the need for treatment is urgent. In those cases, the ACIP members interviewed for this dissertation indicated that they would accept the risks inherent in making a positive recommendation because the probable benefits were so high. If they turned out to have been mistaken in their recommendation, they could revisit the decision at a subsequent ACIP meeting (Crout, *et al.*, 2009; Lave and March, 1993, 19-34).

#### Understanding Scientific Decision-making Under Conditions of Uncertainty

Although the ACIP represents a small, relatively homogenous body of medical researchers, some generalizations can be drawn from studying the ACIP decision-making model. Care must be taken not to over-generalize, of course; as long as the presuppositions are clearly stated and the biases are known, the generalizations can help to explain how scientists and medical researchers deal with uncertainty.

Each of the respondents interviewed for this study explicitly or implicitly rejected the precautionary principle as a basis for reaching scientific decisions. At first blush, this principle seems prudent. If the physician's first responsibility is to honor the Hippocratic Oath and do no harm, is it not better to be safe than sorry? The concern is that ACIP members might rush to judgment and make recommendations on vaccines that have lingering uncertainties. In a worst case scenario, the possibility exists that a few years or decades after the recommendation is made

a case emerges showing a long-term negative consequence to the application of the vaccine. The quintessential example is the drug thalidomide, which was administered to pregnant women during the 1960s as treatment for morning sickness. Later research indicated that the drug caused birth defects. Thousands of infants were born with deformed limbs as a direct consequence of thalidomide usage (Yang, *et al.*, 1997).

Thalidomide is the exception that proves the rule. Although it is true that some high-profile cases exist where more time and research was needed to assess the results of clinical trials before a drug was administered, in thousands of other cases waiting on answers to questions where data may not exist or where the uncertainties are so great that it may be years or decades before conclusive results are known is detrimental to patients. This is especially true in cases where disease mortality is high and few other treatment options exist. Moreover, the risk of side effects often is relatively small whereas the risk of no treatment is extremely high. In such situations, rejecting a drug because a small risk of side effects exists without weighing that risk against the large benefits is not justified.

Risk is a part of life. Every physician recognizes this when he or she makes a patient diagnosis. The question is whether the risk can be managed effectively. Because the idea of “better safe than sorry” assumes that decision-making can be made with a reasonable degree of certainty, it is an unrealistic method of resolving cases where uncertainty is great, data are missing or conflicting, or doubt exists as to the outcome of a decision. As some of the interviewees remarked, the purpose of a scientific research body is to make the best decisions possible based on sound science and the state of the data. If scientific decision-makers wait for complete information, they will suffer from what one ACIP member called “analysis paralysis.” A certain amount of credible data is necessary for a decision to be made, but good scientists

know when more data is needed and when the necessity of an immediate decision is the paramount concern. It is always a balancing act, but experience in the field and an appreciation of the urgency of a decision—this is what several ACIP members referred to as the “disease burden”—can help decision-makers know when further study is needed and when a decision is required (Fisher, 2003).

For some members of the public, the “polluter pays” principle also is an axiom that hardly needs to be explained or defended. This principle suggests that the entire burden of bringing a particular product to market must be borne by the manufacturer. In the normal course of business—for example, when a chemical is marketed and it has a high degree of risk but also a high degree of financial reward for the manufacturer—the marketplace may easily absorb the cost and the company will be willing to accept the burden for any potential damage that may be occasioned by the company’s product. Even if a pharmaceutical company invests a great deal of time and money in drug trials that do not produce a marketable product, the company can absorb the costs because it still earns a large return on investment through the marketing of its successful drugs. In the case of a successful vaccine, the costs can be passed on to the customer (in this case, the patient and/or the patient’s health care provider). An expensive new drug that initially is funded by a pharmaceutical company and eventually is financed through the health care system—thereby allowing the drug maker to recoup the investment as well as earn a profit—is a prime example of a well-functioning health care system (Ghosh, 2008).

In market failure situations, however, government may need to step in to ensure that the burden is not too daunting for the private sector, especially under conditions of uncertainty. For vaccines, where risks and uncertainties abound, the pharmaceutical companies bear the burden of a vaccine’s success or failure. If the market for a new drug is small, but the needs are high—for

instance, if a new AIDS vaccine is developed, few people need it, the costs are high, but the people who need it must have it soon or they might die—a pharmaceutical company may be unwilling to market the drug. There is an opportunity cost in offering a drug that few people will use when the company could be offering a drug that would help a larger number of people. As a matter of public policy, however, government may decide that it is in the best interests of everyone in the polity to ensure that the number of terminal AIDS cases declines. In this kind of “market failure” situation, a government policy has been developed to meet a perceived need, but the marketplace in the normal course of business is unwilling to bear the burden of the “polluter pays” principle. If government desires the drug to be available, it will have to assume the risk by assuring the private sector that the risks will not fall entirely (if at all) on an individual pharmaceutical company (Gollier and Treich, 2003; O’Connor, 1997; Pearce and Turner, 1992).

ACIP decision-makers recognize that their recommendations and the repercussions can determine whether drug manufacturers continue to conduct research into vaccines and offer them for sale in the United States. Although the group is not charged with responsibility for determining whether the pharmaceutical company will bear the costs and risks of developing a new vaccine or whether a third party, including government, will pay, the reality is that any decision-making body, especially one that is making recommendations with a substantial impact on the public, cannot avoid at least considering costs tangentially. Every dollar that is used to develop, market, and administer a particular vaccine is a dollar that is not available to develop, market, and administer another vaccine. Broadly speaking, therefore, costs are always a factor in decision-making because public policy decisions are not made in a vacuum.

Aside from the cost issue, problems sometimes arise when regulators and the general public ask scientific researchers for answers to unanswerable questions. The law may require

that regulations be established for all known side effects of a drug when little or no information is available on the long-term effects. When trying to enforce regulations after they are developed, regulators and government decision-makers stumble over insoluble problems and insurmountable regulatory hurdles because the legal burdens set forth under the applicable laws and regulations are unworkable.

Third parties often ask for certainty in scientific decision-making because they do not fully understand the nature of scientific decision-making and sometimes they ask because they have a political agenda. As discussed in Chapter 2, science can, of course, be politicized. This conclusion is hard to avoid when one examines federal environmental regulations in the United States and their demands for certainty in their standards and criteria (Costanza and Cornwell, 1992; O’Riordan and Jordan, 1995). Public organizations are hardly bastions of objective, neutral information and scientists are not always seekers of truth, however (Carpenter, 2004; “The FDA Is No Place for Politics”; Intemann and De Melo-Martin, 2008; Pielke, 2008). They, too, have a vested interest in the outcome of scientific studies as these organizations attempt to establish and maintain a domain, compete for scarce resources, and play the games of bureaucratic politics (“Politics Manipulating Scientific Decisions, Recent Report Shows,” 2004; “Politics Trumps Science at FDA,” 2005; Rose, 2008; Van Der Wal, *et al.*, 2008; Whitford, 2007; Wise, 2006).

Part of the clash between science and politics—the “science-policy gap” referenced in Chapter 2—is the result differences emphases in the disciplines. There is no small irony here: The language of politics often suggests that standards can be set with absolute certainty and precision, but in reality policy-makers are willing to accept ambiguity, vagueness, and biases in order to garner sufficient political support so they can enact a statute, adopt a regulation, or



otherwise paper over points of contention, thereby leaving it for another time and place to hash out specifics in the policy. By contrast, the language of science is filled with caveats, qualifications, and statements about the uncertainty of data and the conditions necessary to ensure that a study can be replicated. Yet in many cases the outcome of studies can be quite precise and accurate—subject, of course, to the caveats originally stated. Thus, politics pretends to be absolute, and it is far from that, while science claims to be relative and it comes far closer to absolute knowledge than does the political realm (Butos and McQuade, 2006; Costanza and Cornwell, 1992).

ACIP members are trained as medical professionals, but they all recognize that they exercise policy-making influence. In fact, that is the purpose of organizing the committee in the first place. Similarly, any governmental entity that is charged with addressing scientific issues ultimately will feed its decisions into the policy-making process. Otherwise, there is no point in government organizing such a committee. When science professionals make policy decisions, in one sense they close the science-policy gap because they must use their knowledge and expertise to reach sound decisions that are both scientifically accurate, to the extent possible, and defensible within the public policy realm.

Aside from the politics, good scientists assume that uncertainty is a feature of all information and data and must be confronted without illusion. Although researchers in the scientific community can live with doubt and ambiguity in their research, the lay public often clamors for absolute precision. It is therefore incumbent upon scientific researchers to communicate the idea that boundaries exist for human knowledge and invariably limitations exist. This is far easier said than done because the public often does not understand the intricacies of the scientific method and the limitations in the data.

Because it does not operate within the public eye, the ACIP has avoided the controversy that sometimes swirls around high-profile public agencies. Nonetheless, committee members must communicate their recommendations to agencies such as the CDC and the FDA that do have public constituencies. The use of vaccines can be contentious, especially among citizens who mistrust government and medical elites and who believe, for example, that childhood vaccinations cause harm out of proportion to the benefits they provide. Thus, the ACIP could find itself under the glare of the public spotlight at any time. Whether or not its decisions will be known by the public, an agency or advisory committee is well-advised to act as though its decisions will be salient to the general public.

As discussed in Chapter 2, one reason that the lay public views scientific research as precise and more or less absolute is because the popular model of the scientific process sets forth a linear, orderly process. This model can be helpful because it suggests that science is a rational process that can be easily mastered and used to translate theoretical concepts and ideas into practical, workable applications. In some cases, this linear, step-by-step procedure works as intended, but often science is far more iterative and diverse than this model suggests (Morss, *et al.*, 2005, 1598-99).

Several interviewees suggested that studying the ACIP provides a false sense of the orderly nature of scientific decision-making because the committee is small, has a limited mandate, and has a specific focus—on whether to recommend the dissemination and use of FDA-approved vaccines—that is often missing from other scientific decision-making bodies. Studying a large issue such as the AIDS virus, for example, would provide a window into a difficult, constantly evolving, multiple-actor scenario that is not visible in a study of the ACIP.

The point is well-taken. At the same time, by studying the ACIP, it is possible to examine the ways in which a small group of dedicated professionals goes about placing issues on its agenda, organizing working groups, sifting through data, and making recommendations when great uncertainty exists. The decision on whether to recommend particular vaccines under various conditions may not be as complex or challenging as exploring global climate change, AIDS, and many other complex scientific issues, but the decision is important, nonetheless. Moreover, it is instructive to understand the ACIP decision-making process because it provides insight into how scientific decision-makers wrestle with conditions of uncertainty.

Uncertainty is ever present. As Benjamin S. Halpern and his colleagues wrote in 2006, “there are essentially two types of numerical uncertainty—one type can be removed with more data...and the other type cannot.” In their view, “[a]lthough the treatment of uncertainty can seem daunting...people have long accepted it in many aspects of their daily lives. We fly in aeroplanes, we drive across bridges, and we manufacture and use chemicals” (Halpern, *et al.*, 2006, 13).

These researchers raise an excellent point. The difficulty that most non-scientists have when they grapple with uncertainty is that they do not understand the context in which decisions are made. Scientific issues are so complex and usually require so much background information that the average person cannot make sense of the salient issues. If risk and reward can be placed into context, however, laypersons can understand comparative risk even if they do not always grasp the specific details of science policy. The task for policy-makers who make decisions in a highly technical, complex field is to help non-scientists understand the context.

As Halpern, *et al.*, suggest, flying in airplanes is a good example. If a policy-maker can demonstrate that flying in an airplane carries a specific risk, based on accident data in the

domestic commercial aviation industry, the risk of different types of harm using a specific vaccine can be compared with flying in an airplane. A layperson may not comprehend the numbers, but he or she at least can fathom the meaning of such a comparison. “Well,” the person might say, “I fly in airplanes all the time. Even though I know there is a risk that the airplane might crash, I believe the risk is low enough to tolerate. The benefit—I can get to my destination in a relatively short time compared with alternative modes of transportation—outweighs the risk of flying. I get that. Now, if you tell me that the risk of using a specific vaccine is ten times lower than the risk of being involved in a commercial airline crash, I now see that the vaccine, while not completely risk-free, is not very risky” (Trautmann, *et al.*, 2008).

A risk management professional might object to this type of comparison because it requires numerous assumptions in order to calculate risk data. Risk is not always a straightforward measurement; a variety of variables will influence how risk is calculated. Some risks may be incalculable simply because they, too, raise scientific uncertainties owing to missing data. In seeking to objectify risk, a person may inadvertently end up making apples-to-oranges comparisons. Risks associated with travel versus risks associated with a drug that will interact with biological processes in the human body are difficult to compare because the nature and consequences of each risk depend on many factors that in themselves may need to be isolated and compared. There is always a risk to taking qualified, limited scientific studies and translating them into language and concepts that non-scientists can understand. In egregious instances, the data can be misused to downplay a relatively high risk by making assumptions that may not be true in a real-world context.

Granted, these are good points to discuss, but the rejoinder is that all data and conclusions can be manipulated. For science professionals who seek to communicate as much accurate data

as possible, the chore is to find the most appropriate means of translating scientific information into easily understood messages that do not misrepresent the data or hide the uncertainties. The difficulty of the task does not obviate the need to complete the task. As Halpern, *et al.* write, “[t]here is no single best tool for dealing with uncertainty—the best choice will depend on the management context and the quality and quantity of data available” (Halpern, *et al.*, 2006, 13).

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APPENDICES



## APPENDIX A: INTERVIEW QUESTIONS

Protocol: A Grounded Theory method was used. The interview commenced with a broad question, then narrowed as the interview progressed. The interview questions focused on emerging themes. I posed questions and wrote copious notes, occasionally capturing an exact quotation. Afterward, I wrote theoretical memoranda and coded the interviews, as appropriate. Underlying themes and meanings were obtained from participants and drove the interview process.

- 1) Broad questions to begin the interview are listed below. All were telephone interviews and lasted between 10 and 30 minutes. The average time was approximately 20 minutes. In some cases, the subject raised these issues during the conversation so the questions did not have to be broached.
  - a.) Tell me about the ACIP and its role in medical decision-making in the United States.
  - b.) How did you come to join the ACIP?
  - c.) What is your role as an ACIP member?
- 2) What is the decision-making process at the ACIP? What is the role of the working groups?
- 3) If the subject does not raise the issue, ask about cost-benefit analysis in ACIP decision-making. If he or she raises the issue, explore the concept.

- 4) Can you think of instances when the ACIP has had to make a decision about a vaccine when there was uncertainty in the data or disagreement among ACIP members?
- 5) How does the ACIP resolve disagreements? Is it a consensus process?
- 6) What would you change about the ACIP decision-making process if you could?

## APPENDIX B: E-MAIL FROM DR. JEAN CLARE SMITH TO ACIP MEMBERS

Dear ACIP Members, current and recent:

I am sending this message on behalf of J. Michael Martinez, who is working toward a Ph.D. in public policy and public administration at the University of Georgia. He was referred to me by Jeanne Santoli (Deputy Director, Immunization Services Division), and has asked to interview those of you who are willing regarding his dissertation on scientific decision-making under uncertainty. He would like to conduct interviews between now and October, and write up the results over the following several months. He envisions that interviews would take ~10-15 minutes.

Following is a description of the project, provided by Mike:

Scientific Decision-making under Uncertainty: Project Purpose and Criteria

Mike Martinez

The purpose of this project is to understand scientific decision-making when uncertainty exists. Thus, the research will examine a discrete decision-making process where a high degree of technical consensus exists about the evidence and data and compare it with a discrete decision-making process where little technical consensus exists about the evidence and data. The hypothesis is that in the former case, the decision generally will be made according to a clear decision rule. If a high degree of technical consensus does not exist, the hypothesis is that the decision will be based on a variety of criteria apart from the decision rule, including readily available resources, decision-process constraints, and the available knowledge base, among other things. In short, where a reasonably clear, consensus-based decision rule is in place, decision-

makers generally follow the decision rule. When such a decision rule is absent, decision-makers must rely on factors outside of the issue context, which requires them to use discretion.

To undertake this project, it will be necessary to select a group of decision-makers that addresses scientific and/or highly technical issues and identify two separate, reasonably well-defined issues requiring discrete decision-making. Ideally, the same group of decision-makers will be involved in making decisions on each issue. In the case of vaccines, the project entails interviewing members of the Advisory Committee on Immunization Practices (ACIP) about the part(s) of a vaccine recommendation where a high degree of evidence exists (e.g., the primary age groups for which a new vaccine is needed, and has been shown to be safe and effective) and the part(s) of a recommendation where lessor (or no) evidence exists (e.g., interchangeability of vaccine brands) and posing questions about the bases of recommendation in these two circumstances. What factors influence the recommendations a committee member will make? What steps and thought processes are involved in decision-making in each case? Ultimately, how does a committee member reach a decision in the face of scientific uncertainty?

Mike will be in touch with each of you to discuss whether you are willing to participate in the interview, and to schedule a convenient time. Let me know if you have any questions.

Jean Clare Smith, MD, MPH

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## APPENDIX C: ACIP MEMBER BIOGRAPHIES

As of November 2008, the roster of 15 ACIP members included Dr. Carol J. Baker, a professor of pediatrics specializing in molecular virology and microbiology and head of the section on infectious diseases at the Baylor College of Medicine in Houston Texas. She also serves as president of the National Foundation for Infectious Diseases, a non-profit organization dedicated to educating the public and health care professionals about infectious diseases. With more than 300 original publications and book chapters to her credit, Dr. Baker is a well-known expert in pediatric infectious diseases.

Robert L. Beck, an attorney from Palmyra, Virginia, serves as the ACIP's consumer representative.

Dr. Lance Chilton is a professor of pediatrics at the University of New Mexico School of Medicine as well as a pediatrician with the Young Children's Health Center. A Johns Hopkins-educated physician, Dr. Chilton completed his residency at Children's Hospital of Pittsburgh in July 1974 after being board certified in pediatrics.

Dr. Paul R. Cieslak serves as medical director of the Immunization Program and program manager of the Acute & Communicable Disease Prevention Program within the Oregon Department of Human Services (DHS), Public Health Division Emergency Preparedness Program (PHEP), an initiative designed to anticipate, detect, assess, and understand the health risks and deleterious effects of an emergency. In 2004, Dr. Cieslak received the Charles C. Shepard Science Award for outstanding scientific contribution to public health.

Dr. Janet A. Englund is an associate professor of Pediatrics, Children's Hospital and Regional Medical Center at the University of Washington in Seattle as well as a clinical associate at the Fred Hutchinson Cancer Research Center. With a special interest in the diagnosis, prevention, and treatment of respiratory virus infections in diverse populations, including young infants, and pregnant women, Dr. Englund serves as a lecturer for the American Academy of Pediatrics, and an annual vaccine course sponsored by Foundation Merieux/World Health Organization. In addition, she is a member of the U.S. Food & Drug Administration (FDA) Antiviral Therapy Advisory Committee (2001-2004), and a council member of the Pediatric Infectious Disease Society (2003-2005).

Dr. Franklyn Judson is a Denver physician who specializes in infectious diseases. He currently serves as Chief of Infectious Diseases with the Denver Health Medical Center and has been a physician with the Department of Preventive Medicine and Biometrics at the University of Colorado since 1987. A graduate of the University of Pennsylvania Medical School, Dr. Judson has been active in a variety of medical groups and advisory committees throughout his long and distinguished career, including the Medical Advisory Boards of the Rocky Mountain Drug Consultation Center and Rocky Mountain Planned Parenthood. He was appointed to the Presidential Advisory Council on HIV/AIDS by President George W. Bush in 2003.

Dr. Susan Lett is the medical director, Immunization Program, Division of Epidemiology and Immunization, within the Massachusetts Department of Public Health in Jamaica Plain, Massachusetts. She also practices as a Preventive Medicine Specialist at New England Regional New Born in Chestnut Hill, Massachusetts. After graduating from the Medical College of Virginia School of Medicine in 1980, Dr. Lett has spent her professional career as a preventive medicine specialist.

Dr. Tracy Lieu is a professor and director of the Center for Child Health Care Studies, Department of Ambulatory Care and Prevention, Harvard Pilgrim Health Care and Harvard Medical School. Dr. Lieu also is the Children's Hospital Site Director of the Harvard Pediatric Health Services Research fellowship and practices as a part-time pediatrician with Harvard Vanguard Medical Associates. Her research involves primary care delivery, family-centered outcomes, and cost-effectiveness. Among her many current projects, Dr. Lieu is engaged in several CDC-supported projects in vaccine safety, delivery, and economics, and a National Institutes of Health-sponsored study of disparities in childhood asthma. Dr. Lieu has served on national policy-making committees including the U.S. Preventive Services Task Force and ACIP.

Dr. S. Michael Marcy attended Pomona College for undergraduate work and received his M.D. degree in 1961 from the University of Pennsylvania School of Medicine. He completed his pediatric postgraduate residencies at the Massachusetts General Hospital and Boston City Hospital. After serving in the army in Germany from 1964 to 1967, Dr. Marcy returned to Boston to complete a three-year fellowship in pediatric infectious disease. In 1970, he joined the Kaiser-Permanente Health Care Program and served for more than 35 years, first as a full- and then as a part-time primary-care pediatrician at their Panorama City, California facility. He is currently also an Adjunct Researcher with the Kaiser-Permanente program working as a part-time investigator with the UCLA Center for Vaccine Research and the CDC. Dr. Marcy also is a Clinical Professor of Pediatrics at the University of Southern California and University of California at Los Angeles Schools of Medicine. He has served on numerous local, national and international committees, including the American Academy of Pediatrics (AAP) Committee on Infectious Diseases (Red Book Committee), the AAP Committee on Continuing Medical

Education, and committees formed by the AAP, American Academy of Otolaryngology, and the National Committee on Quality Assurance to develop clinical guidelines for the treatment of pediatric upper respiratory infections.

Dr. Julia Morita is a board certified pediatrician who has been medical director of the Immunization Program at the Chicago Department of Public Health since 1999. Before that time, Dr. Morita practiced general pediatrics in Tucson, Arizona, and she also completed training at the Centers for Disease Control and Prevention in the Epidemic Intelligence Service Program.

Dr. Morita serves as a consultant to the Chicago Department of Public Health's Emergency Preparedness Program as they develop the Chicago Pandemic Influenza Plan. In addition to her work with ACIP, she is involved with the Chicago Area Immunization Campaign, the Illinois Immunization Advisory Committee, and the Illinois Chapter of American Academy of Pediatrics' Committee on Infectious Diseases. Dr. Morita has published several articles addressing racial and ethnic disparities in immunization coverage levels among children and adults.

Dr. Kathleen Neuzil is senior clinical advisor, PATH, and clinical associate professor of medicine at the University of Washington in Seattle. Her primary research interest is focused on vaccine-preventable diseases, and the scope of her work includes both epidemiologic studies and clinical trials. Studies of the impact of influenza, respiratory syncytial virus and pneumococcal disease on various populations using administrative databases are on-going. She also participates in clinical trials of new vaccine candidates with on-going studies assessing varicella, conjugate pneumococcal, RSV, and influenza vaccines in adults and children. Dr. Neuzil's work



has been published in prestigious academic journals, including the *New England Journal of Medicine*.

Dr. Mark H. Sawyer is professor of clinical pediatrics, Division of Pediatric Infectious Disease, at the University of California-San Diego Medical Center and Rady Children's Hospital in San Diego. He also serves as medical director of the San Diego Immunization Partnership, San Diego County Health & Human Service Agency (HHS), Immunization Branch. A graduate of the University of Chicago Medical School, Dr. Sawyer has devoted his career to practicing pediatric infectious disease medicine. He currently focuses his research activities in three major areas: (1) Immunization delivery through a contract with the San Diego County HHS Immunization Program; (2) Clinical trials of new vaccines; and (3) Application of molecular diagnostic testing of infectious disease in clinical practice.

Patricia (Patsy) Stinchfield has been a nurse in health care for almost 25 years. She is currently a pediatric nurse practitioner specializing in infectious disease and immunology at the Children's Hospitals and Clinics in St. Paul, Minnesota. She also serves as program director for the Children's Immunization Project, a collaborative effort in Minnesota designed to provide immunization information to parents, providers, and the community. Stinchfield serves as an adjunct clinical faculty member at the University of Minnesota's School of Nursing and sits on several committees, including the Minnesota Department of Health Immunization Advisory Committee and the Children's Hospitals and Clinics Safety Steering Committee. She is also a consultant on pediatric immunization issues for the American Nurses Association. A frequent presenter on immunization topics at local and national conferences, including the Centers for Disease Control and Prevention's National Immunization Conference, she is a graduate of Moorhead State University and the University of Utah School of Nursing.

Dr. Ciro Valent Sumaya is founding dean and holds the Cox Endowed Chair in Medicine at the School of Rural Public Health at the Texas A & M Health Science Center in College Station, Texas. Before moving to Texas A & M, Dr. Sumaya was a professor and researcher at the University of California-Los Angeles and also served as associate medical dean at the University of Texas Health Science Center at San Antonio. While he was in San Antonio, he established the South Texas Health Research Center. A 1966 graduate of the University of Texas Medical Branch in Galveston, Dr. Sumaya interned at the University of Southern California and served as a pediatric resident at St. Christopher's Hospital for Children in Philadelphia. He later studied children's infectious diseases as a postgraduate at Tulane University, where he also earned a master's degree in public health and tropical medicine. In 1993, he was appointed to the Presidential Task Force on National Health Care Reform.

Dr. Jonathan Temte is an associate professor in the Department of Family Medicine (DFM) at the University of Wisconsin School of Medicine and Public Health. He joined the DFM faculty in September 1993. He earned a bachelor's degree from Luther College, Decorah, Iowa, in 1980, an M.S. in biological oceanography from Oregon State University in 1986, and a Ph.D in zoology from the University of Wisconsin in 1993. Dr. Temte earned an M.D. from the University of Wisconsin-Madison Medical School in 1987. He has an extensive variety of research and teaching experience, and received the Resident Research Award in 1993 and the Baldwin Lloyd Clinical Teaching Award in 1996. Throughout his professional career, Dr. Temte has published widely in the area of marine mammal reproductive biology and specializes in birth timing of seals and sea lions. He currently serves as the director of the Wisconsin Research and Education Network (WREN) and sits on pandemic influenza and bioterrorism working groups for the state of Wisconsin. His current research interests include viral disease surveillance in

primary care, timing and cost-effectiveness of influenza treatments, management of febrile illnesses in children, and infectious disease aboard commercial airliners. In addition to his other works, Dr. Temte is the medical director of the Wingra Family Medical Center.

As of November 2008, the ACIP roster also includes ex officio members that represent affiliated organizations with an interest in vaccines and effective diseases. In addition, several former members remain actively involved in vaccine-related issues. All former ACIP participants remain active in medical research and practice.

As the former ACIP chairman and a well-known pediatrician specializing in infectious diseases, especially influenza, Dr. Jon S. Abramson remains actively involved with the committee. He currently serves as the Weston M. Kelsey Professor and Chair of the Department of Pediatrics at the Bowman Gray School of Medicine at Wake Forest University in Winston-Salem, North Carolina. In addition to chairing the ACIP, in the past Dr. Abramson has chaired the Committee on Infectious Diseases of the American Academy of Pediatrics. Early in his career, he held a fellowship at the University of Minnesota Medical School and completed his residency at the North Carolina Baptist Hospital.

Dr. Norman W. Baylor currently works as director of the Office of Vaccines Research and Review (OVRR) in the U.S. Food & Drug Administration's (FDA's) Center for Biologics Evaluation and Research (CBER). He previously served as deputy director of OVRR and associate director for Regulatory Policy. Dr. Baylor received his B.S. degree in medical microbiology from the University of Wisconsin, Madison, and his M.S. and Ph.D. degrees in microbial genetics and molecular microbiology, respectively, from the University of Kentucky. He spent three years as a postdoctoral fellow at the University of Virginia School of Medicine in the Department of Microbiology and Immunology, and three years with Program Resources Inc.

as a senior research scientist at the National Cancer Institute-Frederick Cancer Research Facility. Dr. Baylor also currently serves as FDA's liaison to ACIP, a member of the U.S. Department of Health and Human Services' National Vaccine Advisory Committee, and a member of the Advisory Commission for Childhood Vaccines. In addition to his other activities, he has served as an expert advisor to the World Health Organization on several global vaccine initiatives. As of this writing, he has been with the FDA for more than 16 years.

Col. Theodore (Ted) Cieslak, M.D., currently serves as the Defense Department liaison officer to the CDC as well as an ex officio ACIP member. A graduate of the Ohio State University College of Medicine, he served as a practicing pediatrician for five years before entering a fellowship in pediatric infectious diseases at Walter Reed Army Medical Center in Washington, D.C. Following a tour as the infectious disease consultant at Brooke Army Medical Center in San Antonio, Texas, he was appointed chief of field operations and then chief of the operational medicine division at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Maryland. Dr. Cieslak remains active in biowarfare and bioterrorism defense, and serves as consultant to the U.S. Surgeon General. He has lectured widely on biodefense and disaster response and has worked with the Department of Defense, the CIA, the FBI and various state health departments. He also has held clinical associate professorships at the Uniformed Services University and the University of Texas Health Science Center and also serves as a military flight surgeon.

Dr. Geoffrey S. Evans is the director of the Division of Vaccine Injury Compensation within the Health Resources and Services Administration (HRSA), an agency of the U.S. Department of Health & Human Services, the primary federal agency for improving access to health care services for people who are uninsured, isolated or medically vulnerable. Comprising

six bureaus and 12 offices, HRSA provides leadership and financial support to health care providers in every state and U.S. territory. HRSA grantees provide health care to uninsured people, people living with HIV/AIDS, and pregnant women, mothers and children. They train health professionals and improve systems of care in rural communities. Dr. Evans has published widely in the areas of infectious diseases, especially in children. A board-certified pediatrician, he graduated from the George Washington University School of Medicine and Health Sciences.

Dr. Reginald Finger, an ACIP member from 2003-2006, is a physician with more than 23 years of public health experience. He earned a B.A. in mathematics from Northwest Nazarene College, an M.D. degree from the University of Washington, and a Master of Public Health, Epidemiology, from the University of Washington. Dr. Finger completed an internship at Ball Memorial Hospital in Muncie, Indiana, and a preventive medicine residency at the University of Washington. During his long career, he has served as director of preventive medicine with the El Paso County Department of Health and Environment in Colorado Springs, Colorado, as well as a state epidemiologist with the Kentucky Department for Public Health. Since 2006, he has served as an independent medical researcher in Colorado Springs.

Lt. Col. Wayne Hachey is the director of preventive medicine and surveillance for the Office of the Assistant Secretary of Defense, Force Health Protection and Readiness. He earned a bachelor's degree and a master's degree in Pediatric Nursing. In addition, he earned a medical degree at Southeastern College of Osteopathic Medicine and an M.P.H. at Uniform Services University of Health Services (USUHS). Dr. Hachey is board certified in Neonatal-Perinatal Medicine and Preventive Medicine. He is currently serving as a subject matter expert in Pandemic/Avian influenza for the U.S. Department of Defense (DOD), where he has developed many of the DOD medical policies and guidance regarding Avian/Pandemic influenza.

Dr. Florence Houn works with Dr. Baylor in the Office of Vaccines Research Review in the Center for Biologics Evaluation and Research (CBER) with the U.S. Food & Drug Administration (FDA). CBER was created to protect and enhance the public health through the regulation of biological and related products including blood, vaccines, allergenics, tissues, and cellular and gene therapies. Biologics, in contrast to drugs that are chemically synthesized, are derived from living sources (such as humans, animals, and microorganisms), are not easily identified or characterized, and many are manufactured using biotechnology. These products often represent cutting-edge biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions that presently have few or no other treatment options. Dr. Houn currently works as deputy director of CBER. A graduate of the Albert Einstein College of Medicine of Yeshiva University with a M.D. degree, she has practiced internal medicine, public health and general preventive medicine for more than two decades.

Harry F. Hull, M.D. is a medical epidemiologist with more than 30 years of experience in infectious disease control. He was graduated from the Johns Hopkins University School of Medicine and is board certified in pediatrics. Dr. Hull also serves as a fellow of the American Academy of Pediatrics. Trained in epidemiology at the CDC, he is an adjunct professor of pediatric infectious diseases at the University of Minnesota School of Medicine and an adjunct professor of infectious disease epidemiology at the School of Public Health. Dr. Hull served as the state epidemiologist for New Mexico and Minnesota. In those positions, he controlled bubonic plague outbreaks, uncovered a national problem with contaminated body parts used for transplantation, and investigated numerous E. coli and Salmonella outbreaks from contaminated food. He guided Minnesota's efforts to prepare for bioterrorism and pandemic influenza as well. His international work includes eradicating smallpox in Bangladesh and building

immunization programs in Africa, where measles kills 15% of the children. In addition, Dr. Hull directed the Global Polio Eradication Initiative at the World Health Organization in Geneva, Switzerland. He is a past-president of the Council of State and Territorial Epidemiologists.

Dr. Rosemary Johann-Liang works as the chief medical officer for the National Vaccine Injury Compensation Program within the Health Resources and Services Administration (HRSA). Prior to joining the HRSA, she spent six and a half years working with the FDA, where she was deputy director of the agency's Division of Drug Risk Evaluation. She is a board-certified pediatrician with research interests in infectious diseases.

Linda Murphy is a senior health specialist with the Centers for Medicare and Medicaid Services (CMS). CMS is the federal agency that administers Medicare and Medicaid programs through 10 field offices organized according to subjects, such as Medicare health plans, Medicare financial management, Medicare fee for service operations, Medicaid and children's health, survey & certification and quality improvement.

Dr. Kristin Lee Nichol is chief of medicine at the Minneapolis VA Medical Center as well as a professor of medicine in the Department of Medicine at the University of Minnesota. She frequently serves as a spokesperson for the National Coalition for Adult Immunization and is the national VA representative to the Health and Human Services' Interagency Group for Pandemic Preparedness Planning. With research interests in preventive medicine and ambulatory care, Dr. Nichol has spent much of her career researching adult vaccines, especially influenza and pneumococcal vaccination. She earned medical and public health degrees from the University of Minnesota and conducted her internal medicine training at the University of California in San Francisco and the University of Minnesota.

## APPENDIX D: CATEGORIES AND SUBCATEGORIES OF ACIP DECISION-MAKING

First Core Category: A Description of the ACIP Decision-making Process

First Subcategory: Working Group Activities

Second Subcategory: Full ACIP activities

Third Subcategory: Consensus vs. Voting

Second Core Category: The “Certainty” Aspects of the ACIP Decision-making Process

First Subcategory: FDA Approval

Second Subcategory: Scientific & Medical Literature

Third Subcategory: Expert Knowledge

Fourth Subcategory: The Effect of Similar and Previous Decisions

Third Core Category: The “Uncertainty” Aspects of the ACIP Decision-making Process

First Subcategory: The Non-linearity of Scientific Decision-making

Second Subcategory: The Iterative Nature of Medical Research

Third Subcategory: Limitation of the Knowledge-Driven Model and Gaps in the Data

Fourth Core Category: The Role of Cost-Benefit Analysis in ACIP Decision-making

First Subcategory: Costs are not a Part of the ACIP Mandate

Second Subcategory: Costs as an Integral Feature in All Decision-making