6.

FINDINGS AND ISSUES

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VACCINE RESEARCH, DEVELOPMENT, AND PRODUCTION

FINDINGS (See chapter 2.)

- By financing a $6 million pneumococcal vaccine research and development program, the Federal Government successfully stimulated at least one U.S. pharmaceutical company to spend an equal amount of its own money to develop, obtain licensure for, and market a pneumococcal vaccine.
- In 1976, in spite of receiving Federal funds, another pharmaceutical company, which had been an active vaccine developer and producer since 1915, abandoned its pneumococcal and most of its other vaccine research, development, and production programs; this company cited the cost of complying with certain Government regulations as one reason for its withdrawal.

ISSUE A:

The extent and nature of Federal Government intervention needed to ensure sufficient levels of vaccine research, development, and production

Vaccines are an important cornerstone to the prevention of certain infectious diseases in this country. Therefore, maintenance of the capacity of the U.S. pharmaceutical industry to research, develop, and produce vaccines is of vital concern to the Federal Government. To date, in spite of a continuing decline in the number of vaccine manufacturers and products since around 1950, the industry has continued to supply this country with most of the important vaccines for which there is public demand. In recent years, however, the capacity and willingness of the industry to continue innovative vaccine development and production has been seriously questioned.

Federal policies may be affecting manufacturers' decisions to withdraw from the vaccine business. The major unanswered question, however, is this: When viewed in combination with general economic factors, what impact do selected Federal Government policies have on the overall commitment of U.S. pharmaceutical manufacturers to vaccine research, development, and production? Specific areas of concern are described below. Policy options related to these areas of concern are presented in chapter 7.

Federal Financing of Vaccine Research and Development

The appropriateness of the Federal Government's role in financing basic and epidemiologic research on infectious diseases is generally not in dispute (Hilleman, 1976; Jordan, 1977). Most federally supported research is conducted outside the pharmaceutical industry in academic and governmental research settings. Some companies undertake federally financed research, as did Lilly in the case of pneumococcal vaccine, and a few companies, such as Merck and Lederle, fund basic research themselves. For the most part, though, basic and epidemiologic research is conducted outside the industry.

The appropriateness of Federal financing of vaccine product development is a matter of considerable controversy. Traditionally, the primary source of financing for actual vaccine product development has been individual pharmaceutical companies hoping to develop a marketable product. In the case of pneumococcal vaccine, however, funding for product development also was provided by the National Institute of Allergy and Infectious Diseases (NIAID), a Federal agency.

Federal financing for vaccine product development provides a classic illustration of the more general controversy regarding the Federal Government's role vis-a-vis private industry in financing product development. One view is that Government has a public responsibility to finance the development of vaccines with documented or potential value for the public, especially in the absence of private sector initiative to do so. From this perspective, the Federal Government's provision of funds to industry for vaccine product development is analogous to its purchases from industry of vaccines to be used in public immunization programs. Further, Federal provision of funding to private industry for vaccine product development may be more efficient than either of the two infrequently used alternatives of: 1) establishing Government facilities to develop vaccines, or 2) using non-governmental vaccine development facilities in academic institutions or other not-for-profit settings.

An opposing view of Federal Government financing of vaccine product development, is that it not only is unnecessary, but actually may impede privatd sector research efforts. Some pharmaceutical companies do not want to accept Federal research funds, because once they do, their research findings become public record and can be used by competing firms to develop similar products. Other firms believe that by accepting Government contracts, they lose flexibility in their ability to allocate company resources —both facilities and personnel.

Federal Vaccine Safety and Efficacy Requirements

A vaccine manufacturer's ability and willingness to comply with Government regulations concerning vaccine safety and efficacy are other factors that may influence a company's decision either to bring a new vaccine to the market or to continue producing a licensed product.

The standards and procedures used by the Food and Drug Administration's (FDA) Bureau of Biologics (BOB) to assess the safety and efficacy of vaccines are discussed in chapter 3 and in appendixes 3.1 through 3.4. Because vaccines contain either attenuated (weakened) live organisms, or materials extracted from micro-organisms such as viruses or bacteria, BOB requires manufacturers' products to meet certain standards for purity, sterility, safety, and effectiveness. To assess the safety and efficacy of new vaccines, for example, BOB requires manufacturers to generate data from premarketing clinical trials. Further, once a product is marketed, not only must manufacturers test their vaccine products themselves, but they must submit to BOB samples of vaccines for verification of the results.

The pharmaceutical industry often complains that the costs of complying with existing premarketing safety and efficacy regulations have become so exorbitant, and the process so time-consuming, that the marginal value of developing or producing a new product is often too low to warrant manufacturers' efforts (Johnson, 1978). Some researchers believe that Federal regulations, promulgated by FDA for all prescription drug products, both increase the cost and delay the introduction of new products, and that the latter effect may be more detrimental to people's health than potential adverse reactions to less thoroughly tested drugs (Warden, 1978). FDA contends that current Federal reg-

ulations have not kept any new important therapeutic or biological products off the U.S. market (Kennedy, 1978).

FDA at present has little ability to monitor the use of drugs or collect comprehensive data about adverse reactions to marketed products. Currently, it is attempting to obtain statutory authority to conduct postmarketing surveillance of selected prescription drugs. As discussed further in this chapter beginning on page 107 and in chapter 7, such authority could include surveillance of vaccines.

Federal Government Vaccine Purchasing Policies

The Federal Government is the largest single purchaser of vaccines produced in this country. Federal vaccine purchasing policies, therefore, can affect pharmaceutical manufacturers' profits from vaccine sales. Some pharmaceutical manufacturers cite inadequate profits from vaccine sales as a deterrent to vaccine research, development, and production (Schmeck, 1978). Some companies, though, apparently do earn profits on the vaccines they produce and also reinvest a portion of these profits in vaccine research and development (Schmeck, **1978).**

Government purchasing policies can influence two factors that determine a vaccine manufacturer's profits from a particular vaccine product: 1) size of the market for the product, and 2) the product's selling price. Federal Government purchasing of measles vaccines for its childhood immunization programs, for example, has been a major determinant of the size of the measles vaccine market. In 1965, Congress included measles vaccine in the Community Health Service Extension amendments, which authorized provision of this vaccine through community immunization programs; as a result, in 1966, about 7.9 million doses of measles vaccine were distributed throughout the country (Sencer, 1973). In 1969 and 1970, Congress authorized no funds for community immunization programs, and in those years, the total number of doses of measles vaccine distributed dropped to 4.9 million and 4.5 million, respectively. When funding was resumed in 1971, about 8.1 million doses of measles vaccine were distributed. (See appendix 4.2.)

The Federal Government also dramatically altered the market for swine flu vaccine. In essence, by enacting the swine flu program of 1976, under which almost the entire U.S. adult population was to be immunized, Congress created a huge temporary market for swine flu vaccine. Actual production of this vaccine totaled about 157 million doses; by the time the program was terminated, about 45 million doses had been administered (U.S. Cong., GAO, 1977).

The size of the market for pneumococcal vaccine has not yet been affected by Government purchasing policies, because the Government does not directly purchase this vaccine. On the basis of the examples cited above, however, it is reasonable to expect that should the Federal Government purchase this vaccine for its public immunization programs, it would thereby increase the size of the pneumococcal vaccine market.

In addition to market size, Government purchasing policies can affect the selling price of vaccines. Manufacturers charge vaccine purchasers in the private sector generally higher prices than they charge the Federal Government. (See appendix 4.5.) In general, however, the cost of vaccines to the private sector has remained fairly low. For reasons that are *not* entirely clear, this apparently continues to be the case. In fact, for some vaccines, such **as** measles, the price has actually dropped (Risky, 1978).

Several factors may be contributing to low vaccine prices. First, it may be that American consumers are unwilling to pay higher prices. Often neither the societal value of an item nor the cost of producing it has much bearing on consumer perception of the

item's value. This may be true with regard to vaccines. Second, it might be that vaccine manufacturers are selling their products at low prices to maintain goodwill with the Government and to forestall further Government regulation. Various companies may produce vaccines for Government immunization programs as a public service. In the swine flu program, for example, manufacturers agreed to participate on a nonprofit basis. A third possibility is that low vaccine prices are affected by Government purchasing policies. These policies may allow certain manufacturers to minimize their risks by obtaining secure shares of the vaccine market. Large volume contracts also permit manufacturers to reduce product packaging costs, and eliminate or reduce their advertising costs.

To contain the cost of its immunization programs, the Federal Government purchases vaccines on a low-bid contractual basis. In theory, at least, Government contracts are awarded to those manufacturers best able to cut costs and expand vaccine production volume. In some cases, vaccines purchased by the Federal Government are produced by only one manufacturer. Theoretically, a manufacturer who essentially has a monopoly on the market for a particular vaccine product, such as poliovirus vaccine, is in a good position to negotiate a selling price to the Federal Government that will yield the company a reasonable profit. In general, however, this does not appear to be the case.

In comparison to the price of some similar products, such as influenza vaccine, the manufacturer's selling price for pneumococcal vaccine is relatively high—between $4 and $5 per dose. This price may reflect, in part, the high production costs associated with the manufacture of a product that is actually a combination of 14 different vaccines; it also may reflect an effort by Merck, the manufacturer, to recoup its investment in research and development of this vaccine, or to increase its rate of return on vaccines in general.

Unresolved Vaccine Liability Issues

To get the pharmaceutical industry's cooperation in producing swine flu vaccines for its public immunization program, in 1976, Congress enacted unprecedented legislation mandating Federal Government assumption of swine flu vaccine manufacturers' "duty to warn" liability. Unexpectedly, about **soo** of the approximately **40** million recipients of swine flu vaccine reportedly contracted Guillain-Barre Syndrome (GBS), a rarely reported paralytic syndrome. In the wake of many legal debates, the Department of Health, Education, and Welfare (HEW) is slowly settling some GBS liability claims.

The liability problems encountered with the swine flu program have heightened vaccine manufacturers' concern with vaccine liability issues. Citing liability as a major reason, one manufacturer, Merrell-National, has terminated its vaccine production by selling its vaccine business to another company, Connaught Laboratories, Inc. The effect of unresolved vaccine liability and compensation issues on the willingness of U.S. pharmaceutical companies to engage in vaccine research, development, and production, at the very least, would seem to warrant further investigation.

An analysis of vaccine liability and compensation problems was presented in chapter 5 of this report. General issues are discussed further in this chapter beginning on page 119, and possible options for congressional action are presented in chapter 7.

Federal Government Vaccine Production

No Federal agency produces vaccines for commercial use. So far, the American pharmaceutical industry has been able and willing to supply most vaccines needed by the American public. Some authorities, however, apparently believe that, because of industry's diminishing capacity or commitment to produce or supply certain vaccines, greater

Federal Government involvement in vaccine production may become necessary (Krugman, 1977).

An option for the Federal Government to undertake vaccine production and an option for it to subsidize production by private industry are presented in chapter 7.

VACCINE SAFETY AND EFFICACY

FINDINGS (See chapter 3.)

- The procedures used to evaluate the safety and efficacy of pneumococcal vaccine prior to licensure did not allow investigators to predict the incidence of rare or insidious-onset adverse reactions and included only limited testing of this vaccine in persons at high risk of dying from pneumococcal disease.
- The Food and Drug Administration's (FDA) Bureau of Biologics (BOB) has statutory authority to remove from the U.S. market licensed vaccines that it deems to be unsafe or inefficacious; however, neither BOB nor any other Federal agency currently collects data needed to conduct comprehensive postmarketing evaluations of the safety, efficacy, or conditions of use of licensed vaccines.

ISSUE B:

The value and potential implications of establishing an active, possibly mandatory, postmarketing surveillance (PMS) system to assess the safety, conditions of use, and possibly efficacy, of licensed vaccines

Perceptions of the need for strengthening postmarketing surveillance of adverse reactions to licensed vaccines depend, first, on one's perception of the adequacy of the current premarketing safety requirements, and second, on one's confidence in the Government's ability to develop an effective PMS system.

BOB is publicly responsible for evaluating the safety and efficacy of all vaccine products sold in the United States. Before BOB (technically, FDA) issues a manufacturer a license to market a new vaccine product, it requires the manufacturer to provide clinical documentation of the product's safety and efficacy. In terms of evaluating vaccine safety, premarketing clinical trials and studies probably do allow detection of most types of acute local and systemic adverse reactions. The limitations of basing evaluations of vaccine safety exclusively on data from premarketing clinical trials, however, appear to be these:

1. Premarketing clinical trials involve small numbers of people and short periods of observation, so investigators frequently are unable to detect rare or delayed-onset adverse reactions.
2. Because some preventable diseases have such a low incidence rate in the United States, premarketing clinical trials to evaluate vaccine efficacy and safety may have to be conducted in foreign countries; the data generated by foreign trials, however, may or may not be applicable to the U.S. population.
3. For reasons of bioethics and economics, clinical trials of new vaccines most often are conducted among healthy persons; hence, the safety and efficacy of certain vaccines may not be evaluated in clinical trials involving primarily high risk persons for whom vaccination may be most beneficial.

As demonstrated in the swine flu immunization program, the limitations of premarketing evaluations of the safety of certain vaccines may lead to problems both for vaccinees and for Federal policy makers. In 1976, before the swine flu program was underway, there was a great deal of uncertainty regarding the extent, if any, to which neurological problems would occur as adverse reactions to swine flu vaccine. To avert what was believed by some at the time to be a potential swine flu pandemic, however, Congress approved a large-scale public immunization program. Subsequently, and quite unexpectedly, about 1 of every 100,000 swine flu vaccinees developed the neurological disorder, Guillain-Barre Syndrome (GBS). (See appendix 5.l.) A multitude of GBS-related health and legal problems from the swine flu immunization program consequently arose. Uncertainty regarding the types and expected incidence of rare adverse reactions to swine flu vaccine ultimately proved expensive—in terms of lives and money.

BOB appears to have substantial authority to ensure that a vaccine manufacturer complies with current regulatory standards for product quality. This Bureau also has authority to remove a product from commerce if: 1) a manufacturer fails to comply with standards, or 2) upon BOB's review, a product is found to be unsafe, ineffective, or misbranded. Mechanisms by which BOB (technically, FDA) can take products off the U.S. market include product recalls, injunctions, and seizures, as well as license suspension or revocation procedures. (See appendix 3.3.)

While BOB may have adequate authority to remove unsafe or ineffective products from commerce, however, it may not have adequate authority to collect comprehensive data on which to base its postmarketing evaluations. BOB has proposed regulations that would establish its authority to require vaccine manufacturers to submit to FDA all reports they receive regarding adverse reactions to their vaccine products. Some manufacturers, although they are not required by law or regulation to do so, do submit reports of adverse reactions to BOB voluntarily. Under current regulations, though, manufacturers are required only to maintain 5-year records of reports of adverse reactions and to provide access to these records to BOB inspectors. (See appendix 3.3.) BOB's evaluations of licensed vaccines, therefore, have to be based largely on voluntarily submitted case reports from physicians who administer these vaccines. Isolated case reports submitted to manufacturers, medical journals, or Federal agencies such as the Center for Disease Control (CDC) or FDA cannot be used to determine statistically significant incidence rates of adverse reactions to specific products.

To permit the collection of more comprehensive data regarding the safety of licensed vaccine products, at the end of last year, CDC established a passive vaccine surveillance system to collect—primarily from State and local health departments—voluntarily submitted case reports regarding adverse reactions to vaccines administered under public immunization programs. (See appendix 3.7.) CDC's system is very new, so its effectiveness cannot yet be evaluated.

Because it is both passive (i. e., CDC does not actively solicit reports of vaccine reactions) and voluntary (i.e., State and local health departments are not required to submit reports of adverse reactions), however, CDC's system at best will allow case reporting of rare adverse reactions not detected in premarketing clinical trials. Data collected under CDC's new system will not permit correlation of the number of reported adverse reactions with the total number of vaccine doses administered in a given period of time in a defined population. As currently planned, in other words, CDC's system will not generate the data needed to calculate statistically significant incidence rates of vaccine-induced adverse reactions.

The advisability of developing some type of active and mandatory postmarketing surveillance system to collect and analyze data regarding patients' reactions to drugs that have been released for marketing currently is being studied by the Joint Commission of Prescription Drug Use, as well as by groups within FDA. Furthermore, the proposed Drug Regulation Reform Act of 1979 (S. I075) contains a provision that would permit FDA to conduct postmarketing surveillance of selected products released for general use. Inclusion of this provision was intended, not to reduce premarketing safety evaluation requirements, but to add a postmarketing requirement for testing of new products representing important therapeutic breakthroughs, whose potential toxic capabilities could not be precisely determined in premarketing tests.

The Federal Government spends far more money on vaccine research and development than it does on evaluation of vaccine safety and efficacy. In 1976, the National Institutes of Health (NIH) spent at least $68 million on basic and applied vaccine research, while the Bureau of Biologics (BOB) spent $7. s million to assess the safety and efficacy of experimental and licensed biological products, including vaccines (Jordan, 1977). In these two agencies alone, the Federal Government spent approximately nine times as much money on the search for new vaccines as it did on assessing safety and efficacy of existing vaccines. To complete the comparison between Federal expenditures on vaccine research and development and Federal expenditures on the evaluation of vaccine safety and efficacy, one should include the amount spent for these purposes by other Federal agencies, such as CDC and the Department of Defense (DOD). Relative to annual Federal expenditures for vaccine research and development, purchases, and distribution (and possibly liability claims made under the swine flu immunization program), however, Federal expenditures for the evaluation of vaccine safety and efficacy are even less.

The potential implications of an increased Federal commitment to evaluate more comprehensively the safety and efficacy of the products it helps develop, licenses, and purchases for use in public immunization programs are discussed in chapter 7.

COST-EFFECTIVENESS ANALYSIS OF VACCINATION PROGRAMS

The findings and issues relating to the use of cost-effectiveness analysis (CEA) are categorized into three topics of concern: 1) general applications, 2) specific use in reimbursement decisions, and 3) methodological and data problems. While to some extent, concerns in these areas overlap, each area has particular issues that deserve individualized discussion.

General Applications of CEA

FINDINGS (See chapter 4.)

- OTA's cost-effectiveness analysis of vaccination against pneumococcal pneumonia could be used to assess the relative economic efficiency of vaccinating different age-specific segments of the population.
- OTA's analysis also could be used to identify factors, some of which are subject to control, that substantially influence the cost-effectiveness of vaccination against pneumococcal pneumonia.

ISSUE C:
The degree to which CEA could be useful in allocating Federal funds for vaccination and other health programs

Potential Uses

Most decisions to allocate public funds for vaccine-related programs at present are based on considerations of social values, biomedical research findings, clinical perceptions, political implications, and legalities. The potential utility of CEA in decisions regarding funding of either vaccination or other publicly financed health programs has not been thoroughly investigated. OTA is currently studying the potential uses and limitations of CEA as a tool for evaluating various types of medical technologies. (An OTA report entitled *Assessing the Cost-Effectiveness of Medical Technologies* is due to be released in the summer of 1980.)

Cost-effectiveness analysis has several potential uses. First, CEA provides a systematic framework for comparing the economic efficiency of programs that produce similar, if not the same, results and that compete for limited funds. Thus, it might be used to compare the economic efficiency of a program designed to prevent a specific disease to the efficiency of a treatment program for that disease among specified populations. In OTA's analysis in chapter 4, for example, the efficiency of preventing pneumococcal pneumonia through vaccination was compared to the efficiency of continuing to rely solely on medical treatment of that disease (primarily through the use of antibiotics).

Second, theoretically, CEA could be used to compare the efficiency of medical programs aimed at eliminating different diseases. If standard CEA methodologies were to be developed and adopted, and program effects on health status could be measured in common terms, then comparisons among programs might be possible. In OTA's nalysis, net cost per quality-adjusted life year (QALY) gained through pneumococcal vaccination ranged from $1,000 to $82,100 for individuals aged 25-44. It is conceivable that the cost-effectiveness ratios for a pneumococcal vaccination program might be compared to ratios for other types of health programs. The potential feasibility and implications of making and using comparisons among programs will be discussed in OTA's upcoming report on CEA.

Third, CEA might be used to help identify target populations among which reduction of disease would be the most cost-effective. According to OTA's analysis, for example, if public policymakers wanted to increase the cost-effectiveness of a pneumococcal vaccination program, they might do so by encouraging vaccine use among the elderly. Efforts to encourage such use could include subsidizing the cost of administering the vaccine to elderly individuals within the private sector, or having public health clinics offer the vaccine to the elderly at no charge.

Fourth, CEA might be used to help identify particular factors that influence the efficiency of a preventive or treatment program. Such factors may include variations in the cost of services provided, the efficacy and safety of the technology involved, and the degree of disability produced by the target disease(s). Factors that would influence the cost-effectiveness of a pneumococcal vaccination program, for example, are discussed in chapter 4.

Potential Users

CEA potentially could be used by both Congress and the executive branch in decisions regarding the allocation of Federal funds for vaccine-related programs. The National Institute of Allergy and Infectious Diseases (NIAID), for example, might use this

type of economic analysis to help decide which types of vaccine research programs to fund. NIAID might use CEA to help identify diseases, the prevention of which would provide the largest economic gain. It also might use this type of analysis to select a particular type of research to fund, for example, basic research on an organism versus applied research on a vaccine.

FDA's Bureau of Biologics (BOB) might use CEA to help design formulations of certain types of vaccine products. Currently, for example, there are 83 known types of pneumococci, 14 of which are represented in the recently licensed pneumococcal vaccine. If epidemiologic research demonstrates the existence of geographical variations in the prevalence of the **83** types of pneumococci, then specialized pneumococcal vaccine products could be formulated to match the variations. CEA could be used to help calculate the marginal costs, risks, and benefits of adding or removing selected types of pneumococci from the basic vaccine formula. Cost-effectiveness calculations could be used to help determine the advantages and disadvantages of developing separate vaccines for specific categories of individuals at high risk of contracting pneumococcal pneumonia.

The Center for Disease Control (CDC) possibly could use CEA to help decide how to allocate its funds for public immunization programs. CDC has informally assessed the potential economic benefits derived from immunization programs that have already been implemented (Sencer, 1973), but at the present time, it does not routinely use formal CEA to assess prospectively the potential effects of planned immunization programs.

CEA also could be used by the Health Care Financing Administration (HCFA) to help select vaccines or other types of health technologies into the Medicare and Medicaid benefit packages. As illustrated in OTA's analysis, for example, by paying for pneumococcal vaccine, Medicare would help improve the health status of its beneficiaries at a relatively low cost. (See chapter 4 and discussion of "CEA and Its Relationship to Reimbursement for Vaccinations, " page 112.)

CEA also might prove useful to the Advisory Committee on Immunization Practices (ACIP), a private body of experts that advises CDC on the need for public vaccination programs. In recommending against a mass immunization program for the pneumococcal vaccine, ACIP relied on information on the vaccine's clinical efficacy and safety, the susceptibility of high risk groups to the disease, and degree of mortality caused by pneumococcal pneumonia and bacteremia among high risk groups. In making its recommendation, ACIP did not use cost-effectiveness analysis to determine the vaccine's usefulness for different ages or groups at high risk.

Limitations

Cost-effectiveness analysis is subject to certain limitations. First, it does not necessarily or easily take into account social values, moral judgments, legal implications, or political realities. At most levels of Government decisionmaking, these factors may limit the relevance of formal economic analysis. In the aftermath of the problems encountered with Guillain-Barre Syndrome (GBS) among vaccine recipients under the publicly funded swine flu program, for example, Federal legislators (in the absence of an apparent crisis) might be reluctant to embark on another mass public immunization program for other types of influenza—no matter how cost-effective. Further, if a cutoff is used in decisions about whether to fund programs or use technologies, and if the cutoff point is based on such considerations as how much it may cost to produce each extra quality-adjusted life year (QALY), then society will be using CEA to place an explicit dollar value on human life. Whether this situation would be morally or politically acceptable is not known at this time.

A second, and related, limitation of CEA is its strong focus on economic efficency. Issues of equity and distribution are not easily or commonly addressed by cost-effectiveness analysis. In general, CEA models are not designed to assess shifts in benefits and costs such as income redistribution.

Third, although cost-effectiveness analysis may be helpful in comparing alternative methods of attaining a goal, its use may serve to narrow the range of options considered to those most easy to quantify. For example, the analysis in chapter 4 concerned the changes in medical costs and health effects expected from pneumococcal vaccination. Whether better nutrition or better housing might be a more cost-effective approach to reducing the incidence of pneumococcal pneumonia was not considered.

A fourth limitation of CEA is its investment orientation. One premise of such analysis is that moneys spent on programs today may yield benefits and savings—some now and some in the future. In an era of scarce money and possibly balanced budget, the willingness of society to sacrifice present benefits for possible future ones cannot be predicted. At a minimum, a certain level of confidence in the yield of future benefits from present investments will be needed to permit the use of CEA calculations.

The matter of confidence, however, leads to another limitation of CEA. There are a number of generic difficulties associated with the methodology of cost-effectiveness analysis. Some are minor, others more serious. These methodological problems, along with problems of availability of data, are discussed in the "CEA Methodology and Data" section on page 115.

Finally, another aspect of CEAs that needs to be taken into account are the resources required for their conduct. Just as there is a wide range of CEAs—in terms of complexity, alternatives considered, the amount of original data collection required, etc.—there is an enormous range of time and financial resources required to conduct such analysis. When existing data can be used and the analysts are familiar with the subject areas, a relatively formal CEA can be conducted for perhaps **$5,000** to $10,000. More commonly, however, a much larger effort will be needed. Hundreds of thousands of dollars can be spent, using many person-years of analyst and support personnel time. While this factor is not strictly a limitation of the technique, it could limit its use.

Potential implications of increasing the Federal Government's use of formal CEA in allocating funds for vaccination and other health programs is briefly discussed in chapter 7.

CEA and Its Relationship to Reimbursement for Vaccinations

FINDINGS (See chapter 4.)

- According to OTA's cost-effectiveness analysis, administration of pneumococcal vaccine to roughly 5 million people over the age of 65 might be expected to yield a net gain of about 22,000 quality-adjusted life years (QALYs) at a net societal cost of $23 million over the vaccinees' lifetimes.
- Several factors influence the cost-effectiveness of pneumococcal vaccination. Depending on the different assumptions made regarding these factors in OTA's analysis:
  —Vaccinating 5 million people over the age of 65 could cost society as much as $88 million and in turn yield 84,000 QALYs; or instead, it could save society as much as $18 million and yield about 22,000 QALYs.

—An additional QALY gained by a vaccinee over the age of 65 could cost society as much as $4, 000 or yield a net savings.

ISSUE D:

Whether the Medicare law should be amended to permit reimbursement for preventive vaccinations

The Medicare law specifically excludes preventive vaccinations from its list of reimbursable benefits. This exclusion may be incongruous with other major Federal policies related to vaccines. First, the Federal Government spent $6.5 million to help develop pneumococcal vaccine, and on the basis of clinical evidence, the Food and Drug Administration (FDA) approved the use of this vaccine for the high risk group of those over 65 years old. Thus, the Federal Government cannot pay for pneumococcal or other vaccinations among the elderly, even though at least one Federal agency has stated that the elderly would benefit from pneumococcal vaccination (U.S. Ex. Br., BOB, 1977).

Second, while the Medicare **law** does not permit payment for the prevention of pneumococcal pneumonia through vaccination, it does allow payment for the treatment of pneumococcal pneumonia. According to OTAs cost-effectiveness analysis in chapter 4, use of the new vaccine to help prevent pneumococcal pneumonia is a reasonably inexpensive method of saving a year of life for an elderly vaccinee. Further, this analysis shows that regardless of the size of its financial impact, the use of this vaccine would yield health benefits that cannot be derived from treatment.

The Social Security Act Amendments of 1965, which established Medicare and Medicaid, was modeled after private health insurance plans that specifically excluded payment for most preventive health services. Preventive immunizations, therefore, along with physical examinations, examinations for eyeglasses, and examinations for hearing aids, are not reimbursable under Medicare. (Note: Under Medicaid, vaccination coverage varies from State-to-State. The number of States that pay for this preventive service for adults under Medicaid was not assessed in this study.)

The regulations implementing the Medicare Act expressly forbid payment for vaccinations by Medicare unless a vaccination is used for treatment after injury or direct exposure to a disease. In addition, they specifically exclude payment for influenza vaccines, which, along with pneumococcal vaccine, are the only types of preventive vaccines available for extensive use among the elderly. The regulations read as follows;

> Immunizations.—Vaccinations or inoculations are excluded as "immunizations" unless they are directly related to the treatment of an injury or direct exposure to a disease or condition, such as antirabies treatment, tetanus antitoxin or booster vaccine, botulin antitoxin, antivenin sera, or immune globulin. In the absence of injury or direct exposure, preventive immunization (vaccination or inoculation) against such diseases as smallpox, polio, diphtheria, etc., is not covered. (Flu injections are administered as a preventive measure and are excluded from coverage without regard to a patient's particular susceptibility to influenza.) In cases where a vaccination or inoculation is excluded from coverage, the entire charge should be denied.
>
> (Medicare Carriers Manual, paragraph C, section 2050.5C, 2050 services and supplies, **205.5** drugs and biological.)

Legislation has been introduced in Congress to expand Medicare coverage to include selected preventive services, and some bills include payment for vaccinations, In March 1979, for example, Congressman Claude Pepper (D-Fla.) introduced H.R. 2560, which would provide payment for biologics under Part B of Medicare.

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The impact of reimbursement on the demand for vaccinations by Medicare beneficiaries cannot be projected on the basis of currently available data. Studies to date, however, have shown a general tendency toward increased utilization of preventive health services when the cost of such services is reduced or eliminated. (See appendix 4.1.) The results of these investigations are mixed, though, and no studies relate specifically to the demand for vaccines by older adults. On the one hand, reimbursement could have an important impact on the demand for pneumococcal vaccine. The cost of vaccination in the private sector is about $11. For many Americans 65 years and older, this cost alone might be a possible deterrent to the use of pneumococcal vaccine. On the other hand, if this cost is not a substantial determinant of use, reimbursement through Medicare would likely have little impact on demand.

How, if at all, the Federal Government's legal liability for vaccine-induced injury would be affected if it paid for a vaccine through Medicare rather than through a publicly financed immunization program is also unknown. At present, the Federal Government is not held legally liable for breach of the duty to warn beneficiaries about the inherent risk of other medical goods and services paid for through Medicare. Furthermore, harm produced through provider or manufacturer negligence is the legal responsibility of those parties, not an involved insurance carrier who serves only as a fiscal intermediary or insurance underwriter. Because of the current uncertainty surrounding the Federal Government's legal liability for vaccine-induced injury, however, projections about the impact of reimbursement on the Government's liability cannot be made. (See chapter 5.) Medicare would pay for the treatment of vaccine-related injuries among its beneficiaries.

The safety, efficacy, and cost-effectiveness of both influenza and pneumococcal vaccines may not yet have been comprehensively evaluated. The safety and efficacy of influenza vaccines are debated almost annually. In the case of pneumococcal vaccine, much of the data on which FDA's Bureau of Biologics (BOB) based its prelicensing evaluation was generated from studies in foreign populations, (See chapter 3.) Extrapolating foreign data to U.S. populations may not yield an accurate indication of the vaccine's safety and efficacy among persons residing in this country, particularly the elderly. Possibly, however, an evaluation of the safety and efficacy of pneumococcal vaccine among Medicare beneficiaries can be based on additional data that have been generated since the vaccine has been marketed. Further, this vaccine has not been widely evaluated in other types of Medicare beneficiaries, that is, those with end-stage renal disease or other chronic illnesses. NIAID has helped coordinate such research efforts, and results of some of these investigations should be available in the spring of 1980.

According to OTA's analysis in chapter 4, the cost-effectiveness of vaccinating against pneumococcal pneumonia versus continuing reliance solely on treatment varies substantially depending on the age of the vaccinee and values assigned to selected variables, e.g., duration of immunity. In terms of cost-effectiveness, with the possible exception of end-stage renal dialysis, however, most benefits currently reimbursable under Medicare probably have not been as thoroughly evaluated through statistical analysis as has pneumococcal vaccine in OTA's cost-effectiveness analysis.

Possibly because our Nation's social policymakers have not viewed the elderly as a prime target for preventive services, Medicare currently pays for almost no preventive services for its beneficiaries. According to OTA's analysis, vaccination against pneumococcal disease would benefit the elderly. Kavet has demonstrated that vaccination against influenza also yields benefits for the elderly (Kavet, 1972).

In chapter 7, the potential implications of permitting Medicare to pay for preventive vaccinations are discussed.

CEA Methodology and Data

FINDINGS (See chapter 4.)

- The methodology of CEA as applied to vaccines and other preventive technologies is in a developmental stage.
- Standardized methodologies have not been used in CEAs of preventive technologies.
- Some of the basic data required or desired for OTA's cost-effectiveness analysis of pneumococcal vaccination were lacking or difficult to secure.

ISSUE E:

Whether the Federal Government should seek to overcome methodological problems of CEA and problems related to the availability of data for CEAs

Methodology

The methodology of CEA has certain generic difficulties. The problems discussed below relate to variations in models, measures of effectiveness, treatment of time, external i ties, and equity as well as distribution.

One problem is that the models used to relate costs to outcomes vary from one study to another. Two basic types of analyses that relate costs to outcomes can be used: cost-effectiveness analysis (CEA) and benefit-cost analysis (BCA). Both have been applied to vaccines (Schoenbaum, 1976; Sencer, 1973; Weisbrod, 1961). In BCA, effects of one program across the economy are considered, while in CEA, two alternatives to achieve a given goal are compared. In BCA, costs and effects (benefits) are valued in the same—invariably monetary—units. In CEA, however, while costs are valued in monetary terms, effects (e. g., improvement in health) are not necessarily quantified in dollar terms. BCA methodology facilitates comparisons across various sectors of resource allocation, but in health care, the gain in flexibility may be more than countered by methodological difficulties and offended sensibilities.

Consistency of models is a problem even when only CEAS are considered. In the CEA models applied to medical technologies to date, there have been many variations. For example, the Klarman and Guzick study of influenza valued health effects from influenza but not death (Klarman, 1976). Further, the value assigned to morbidity averted by vaccination was based on the expected gain in productivity from increased working time. Weinstein and Stason included in their model the costs of illness in the extended years of life that would result from receiving treatment for hypertension (Weinstein, 1976), but did not include the morbidity from such illnesses. The selection of costs and effects and the assignment of values to them are decisions made by each analyst based on the model he or she follows. A lack of consistency in cost-effectiveness models used for CEAs means that the results are less likely to be comparable across studies and that evaluating the usefulness of each analysis is a complex and difficult task.

Another methodological problem centers on the measurement of effects. There is no widely agreed upon health status index that can be used to value the health effects of medical technologies. Health is a complex, multidimensional concept. Measures of health can range from mortality rates to morbidity rates, to estimates of functioning capacity, and even to "feelings of well -being." To conduct a CEA of a preventive technology that

affects both death and illness, a health status index that incorporates both these effects is needed. In OTA's analysis, the index used was one developed to mitigate this methodological difficulty through the use of a multidimensional measure of health called quality-adjusted life years (QALYs), (See appendix 4.4). Further, the values for QALYs in OTA's analysis were based on previous surveys of weights to be assigned to various levels of morbidity or reduced functioning. Although use of such surveys may represent an advance over the usual practice of the analysts' using their own weighings (based on their own preferences in regard to disability, etc.), much broader surveys are needed to assess how various populations value levels of health.

Improved health status indexes will have to incorporate the degree to which various aspects of psychological, social, and physical functioning affect well-being. This will be necessary in order to assign weights to morbidity days. Does prolonging the life of a chronically ill patient result in a net gain or loss in well being? Under what circumstances? Research on health status indexes is currently taking place at the National Center for Health Services Research (NCHSR) and the National Center for Health Statistics (NCHS) (Wan, 1978).

A third methodological problem is uncertainty and inconsistency in ways of dealing with time. As mentioned in the pneumococcal vaccination case study, future costs and benefits are usually valued less highly than those occurring in the present, and therefore are discounted. Discounting of costs is generally recognized as a necessary principle. The question of what discount rate to apply, however, is unsettled. (See appendix 4.4). The Office of Management and Budget (OMB) believes that the rate should be 10 percent for Government projects, but the appropriateness of this value is a matter of judgment, not interpretation of data. Even more serious are the inconsistencies among studies. Further questions concerning discounting are whether it is appropriate to discount health effects, and if so, at what rate. For costs, financial discounting rates can be used as proxies, but where can we find proxies for the rate to be applied to health?

Additional methodological difficulties in CEA are whether and how to incorporate externalities. Should a CEA include, for example, any of the effects on people other than the patient, if the patient's death results in other people's becoming orphans or widows? How can these effects be identified and measured? The methodology of CEA has not progressed to the point where these questions can be answered consistently. There are many other examples of externalities whose inclusion in or exclusion from CEAs is not a settled matter. Should effects on other sectors of the economy be included? To what extent? A successful pneumococca] vaccination program, for example, might affect the productivity of workers by improving their health and possibly might affect the demand for other social services and housing for the elderly by prolonging vaccinees' lives. Other externalities might relate to other effects on the health care system. A successful pneumococcal vaccination program might result in a need for more chronic care facilities relative to these for acute care. Should those potential effects be taken into account by a CEA?

Another methodological problem of CEA is the difficulty of taking into account questions of distributional equity. Like other types of economic analysis, CEA primarily evaluates the efficiency of resource allocations. Aggregate measures of cost and benefits may neglect or disguise variations that are important for specific subgroups of the population. Even though aggregate cost-effectiveness measures might show that a program would result in an improvement in societal economic welfare, program beneficiaries and payers might not be the same. If Medicaid were to pay for vaccinations for nonworking, low income individuals, for example, then these individuals would derive the benefits of

vaccination, but the program would be financed by employed taxpayers who would not benefit directly from the program. Again, issues of distribution and equity largely involve differences in judgments and personal values rather than differences in empirical findings.

The above discussion does not exhaust the list of methodological shortcomings, but rather covers the major difficulties that are common to CEAS as a class of studies. These methodological problems should be viewed in perspective: Although some of the basic concepts of CEA and BCA are several years old (see appendix 4.3), the many current aspects of its methodology have been developed a great deal in a fairly short time. It was not until 1974, for example, that a serious call was made for testing the sensitivity of CEA results to changes in certain variables (Roberts, 1974). Quality-adjusted life years (QALYs) area recent development and are in need of much refinement. Also, CEA methodology still does not routinely include efficacy rates and side effects of technologies. These and other examples may not represent problems inherent to CEA methodology but perhaps are symptoms of a technique still in the process of maturing.

Data

A major difficulty in applying cost-effectiveness analysis to a medical technology is the lack of appropriate data. The pervasiveness of data problems was illustrated in OTA's study of pneumococcal vaccine. Pneumonia is the leading infectious cause of death and the fifth overall cause of death in the United States (U.S. Ex. Br., Census,]977). pneumonia is a *major* cause of hospitalization and restricted activity, and as a cause of death is exceeded only by heart disease, cancer, stroke, and accidents. Because of its importance, one would expect data on pneumonia to be more detailed than for most illnesses.

Klarman stressed that CEA required a clear link between cause and effect (Klarman, 1967). Many of the data needs in OTA's study pertained to that link. For example, the incidence rate of pneumococcal pneumonia is not known. Does it account for 10 or 35 percent of all pneumonia? The morbidity and mortality from pneumococcal pneumonia is equally difficult to assess. Without answers to epidemiologic questions, determining the pattern of the disease and the effect of the vaccine is difficult.

For data other than clinical data used in its analysis, OTA relied mostly on the National Center for Health Statistics (NCHS) in HEW. NCHS data have major limitations, which characterize data from other statistical sources, as well. One major 1imitation is the lack of population-based data. Health data in general are oriented to describing specific medical diseases or conditions, but cannot be aggregated to describe the population. The Health Interview Survey (HIS), for example, has collected data on certain chronic conditions, but not on the number of different people involved. Since a person may have more than one chronic condition, merely summing the number of different chronic conditions would produce a gross overestimation of the number of people afflicted. Such data problems hindered OTA's calculation of the cost-effectiveness of pneumococcal vaccination for people with certain chronic conditions who are considered at high risk of contracting or dying from pneumonia.

Although existing data are disease-centered, they do not convey a total sense of a specific disease. For example, of all 1976 hospital discharges with pneumonia listed as a diagnosis, 66 percent had pneumonia listed first, and 34 percent had it listed subsequently (U.S. Ex. Br., NCHS, HDS). Restricting consideration of pneumonia to first-listed diagnoses would understate the extent of the disease. Too little is known, however, about

how pneumonia interacts with other medical conditions to make a precise statement about the (at least) 34 percent of cases in which pneumonia occurred with another condition.

The failure to specify the full effect of a disease is even more serious with mortality data. Deaths are attributed to a certain cause in NCHS data only if it is considered the underlying cause of death, i.e., the cause that initiated the sequence resulting in death. Thus, for a terminal cancer patient with pneumonia who died, cancer would be reported as the cause of death. For an otherwise healthy person who contracted pneumonia and died, pneumonia would be listed as the cause of death. Limiting consideration of pneumonia as a cause of death to cases in which pneumonia was the underlying cause would understate pneumonia's role in causing death. Including all cases in which pneumonia was listed anywhere on the death certificate (pneumonia mentions) however, would overstate its role.

Because the mortality data reported by NCHS do not reflect certain subtleties, they minimize pneumonia's role in causing death. The problem, which also applies to other health data, is that the effect that one medical condition has on another is not taken into account. Identifying interactive effects and formulating a methodology to incorporate multiple causes into mortality data are at an early stage of development. The availability of mortality data concerning multiple causes is intertwined with methodological difficulties. NCHS is developing multiple cause data at the present time.

In addition to being hindered by the lack of population-based data and methodological problems, the use of data is handicapped by incompatible definitions and categories. NCHS collects data covering a wide range of health matters, but inconsistencies among the data sets inhibit merging these sets to describe the health and resource utilization of the population. The population base for death certificates, for example, differs from that for the Health Interview Survey (HIS). Mortality statistics are based on death certificates of the entire U.S. population, including the military and institutionalized populations; HIS though, surveys only the civilian, noninstitutionalized population.

Much the same problems that characterize incidence and utilization data also pertain to expenditure and price data. The Health Care Financing Administration (HCFA) in HEW publishes an annual series of health expenditures. Data on the prices of particular services and expenditures for certain diseases, however, are less readily available. Rice and her colleagues have complied expenditures by broad diagnostic groupings, such as infective and parasitic diseases, diseases of the respiratory system, and accidents, poisonings, and violence (Cooper, 1976; Rice, 1976). Medicare carriers and intermediaries, including many Blue Cross and Blue Shield plans, collect data on the prices of particular services in order to calculate customary and reasonable charges, the basis of their payment to physicians. Neither Medicare nor any other third-party payer, however, routinely constructs national estimates from these regional data. Periodic surveys of physician prices such as that by Schieber, et al., are another data source, but an irregular one (Schieber, 1976). The dearth of national cost **data is** illustrated by the widespread use of data complied by Scitovsky and McCall from the records of one practice in California (Scitovsky, 1977). Although the drawbacks of generalizing from such limited experience are well known, in the absence of acceptable alternatives, data from this practice are used for prices, utilization, and disease expenditures.

More than a litany of deficiencies, these data problems have implications for the feasibility of performing cost-effectiveness analyses as an ongoing activity. If cost-effectiveness analyses of technologies were performed with any regularity, special tabulations, such as were required for OTA's analysis, would tax the resources of NCHS. Since the

time required to conduct an analysis and the rigor of the results depend so heavily on the data available, exploration and resolution of key data problems are prerequisites for any routine Government program of cost-effectiveness analysis.

LEGAL LIABILITY AND COMPENSATION FOR VACCINE-RELATED INJURIES

FINDINGS (See chapter 5.)

- Ž At present, persons injured as a result of being vaccinated in a publicly financed immunization program must seek compensation through the legal liability system.
- In spite of contractual transfers of the "duty to warn" from vaccine manufacturers to the Federal Government, the legal assignment of this responsibility will be determined by future court cases and cannot be predicted at this time.

ISSUE F:

The extent, if any, to which the Federal Government should assume legal responsibility for compensating vaccinees injured in public immunization programs

Developing Federal mechanisms to compensate injured vaccinees can be based on two rationales: 1) social responsibility for those harmed by preventive medicine practices that often have public health goals in addition to benefits conferred on individuals, and 2) the consequences of liability insurance problems on vaccination policy per se.

The Federal Government is an active promoter of vaccination programs, and the overwhelming majority of States and U.S. territorial jurisdictions have mandatory childhood vaccination laws. Vaccination programs often have dual purposes: 1) to protect the general or specifically targeted segments of the population against particular infectious diseases, and 2) to protect the individual. If a high percentage of the target population is vaccinated, many unvaccinated individuals may gain protection from a disease through herd immunity. From the standpoint of society as a whole, as well as from the standpoint of most vaccinated individuals, the morbidity and mortality that vaccination helps prevent greatly exceed the morbidity and mortality that vaccination causes. For the statistically small number of individuals who experience rare severe adverse reactions, including permanent disability or death, however, this is not the case.

The kind of vaccine liability that has led to major concerns has not been liability for injuries that result from faulty behavior such **as** negligence in the manufacture or administration of a vaccine, but liability for injuries that are associated with inherent, and more or less predictable, vaccine risks. In classical negligence law, the element of fault is pronounced, and negligent behavior can be corrected to diminish the problem or injury in which it results. The problem of injury resulting from nondefective and properly administered vaccines, however, is essentially unavoidable. All vaccines have certain inherent risks, and because of this, will produce severe injury to a very small percentage of vaccinated individuals no matter what precautions are taken.

In their quest for an equitable solution, the courts have shown an increased tendency to find some doctrinal basis for compensating the injured. While the courts are turning toward the insurance concept of spreading the risk, though, they must continue to work within the legal framework of an adversary, faultfinding process. As the courts adopt a

more explicit insurance rationale for their decisions on where liability should rest, the adequacy and appropriateness of a judicial approach to compensation for vaccine-induced injury comes into question.

The duty to warn raises ethical issues in public immunization programs. The basic issue is the moral obligation of the Federal Government to compensate vaccinees for injury sustained under circumstances over which they were unable to exercise any control. Especially for mandatory vaccination programs, the duty to warn is not a legal doctrine designed to avoid injury; it is a doctrine designed to avoid or assign liability for injury. Warnings are supposed to provide potential vaccinees (or their parents or guardians) with information on the risks and benefits, so that the person informed can decide whether to be vaccinated or not. Children who are not vaccinated may be prohibited from entering school. When vaccination is mandatory, potential vaccinees have no options.

Concern over liability insurance has affected and may again affect vaccination programs. In the recent swine flu immunization program, manufacturers were denied liability insurance by the insurance industry until Congress enacted legislation (Public Law 94-380) providing that all tort suits had to be brought against the Federal Government through a modification of the Federal Tort Claims Act. The Government retained the right of subrogation only against manufacturers and program participants who were negligent.

The possible implications of another insurance availability crisis include the following:

Vaccine Manufacturers.—The production of vaccines is a private enterprise. Although the cost of liability insurance is a business expense that can be passed on to the purchasers of vaccines, evolving judicial theories of liability for vaccine-related injuries cause uncertainties in pricing liability insurance. The high cost, or even possible unavailability, of such insurance could cause vaccine manufacturers to withdraw or reduce their commitment to produce and supply vaccines.

Government.—The primary use of vaccines is to promote public health. The Federal Government has assumed major responsibility for ensuring the safety and efficacy of vaccines and for promoting their use through public immunization programs. Furthermore, the great majority of States and territorial jurisdictions have passed legislation requiring certain vaccinations prior to school entry. As of September 1976, 47 out of 54 jurisdictions (the 50 States plus the District of Columbia, Guam, Puerto Rico, and the Virgin Islands) required vaccinations before entry to school, 42 being mandatory, 5 permissive. At present, vaccine liability insurance is provided largely by private enterprise, and insurance regulation is a function of the States. With another vaccine liability insurance crisis, which might lead vaccine manufacturers to refuse to supply vaccines for public immunization programs, the Federal Government might have to produce vaccines itself and also could end up as insurer or insurance regulator.

Health Care Providers.—The threat of liability may reduce the private, voluntary promotion of, and participation in, vaccination programs by physicians and other health care providers. The crucial liability issue in vaccination programs is not traditional negligence, but the duty to warn of potential side effects, The legal theory of informed consent has been particularly disturbing to providers because of the difficulty in knowing prospectively (before an injury occurs) when that duty as been discharged or not.

The Public. —The individual's right to know of the risks and benefits accompanying a particular vaccine is of little substance if the right to refuse the vaccine is not available.

Mandatory vaccination laws work against this right, but voluntary programs will suffer if the information provided has the effect of raising fears of vaccine side effects. Insurance availability difficulties raise public fears that something is wrong with the vaccine under question or draw excessive attention to rare, though serious, side effects. The occasional large awards from litigation or even providing more certain compensation through the development of alternative approaches to litigation will not mitigate the negative impact of the liability problem on public participation in vaccination programs.

Liability for the rare, severe, and unavoidable adverse health effects of vaccines has had an effect on vaccination programs way out of proportion to the magnitude of the risk. Furthermore, in addition to the negative impacts on vaccination programs of liability problems discussed above, the cost of liability insurance is becoming a matter of greater concern to those who ultimately must pay for those costs—Federal, State, and local governments, and vaccinees. By raising overall program costs, higher liability insurance costs may limit the size and scope of certain types of public immunization programs. Higher liability insurance costs do not necessarily lead to increased amounts of compensation or to the provision of compensation to a larger number of injured vaccinees; nor do they lead to more timely compensation, since the dispensation mechanism is the legal system.

Two policy options for mitigating vaccine liability problems and for improving injured vaccinees' access to compensation are presented in chapter 7.