SUMMARY

51-329 0 - 79 - 2

SUMMARY

INTRODUCTION

The Federal Government is the single most important determinant of this Nation's commitment to vaccine research, development, and use. Since 1902, Congress has enacted laws and Federal agencies have established regulations designed to ensure the availability of safe and effective vaccines. Public moneys have been used to support vaccine development and to purchase vaccines for public immunization programs.

For a number of reasons, various authorities have called for an assessment of the effects of Federal policies and regulations on the development, evaluation, supply, and use of vaccines in this country. [1] First, during the past 10 years, the number of vaccine manufacturers and licensed vaccine products has declined markedly. Some authorities fear that this decline may portend a decline in the commitment or capacity of the U.S. pharmaceutical industry to develop and supply vaccines needed to protect the American public.

Second, there are longstanding debates over both the adequacy of the procedures used by the Federal Government to help ensure vaccine safety and efficacy and the impact of Federal safety and efficacy regulations on the willingness of vaccine manufacturers to develop new products. Some industry representatives argue that Federal safety and efficacy requirements go beyond what is necessary to protect the public and add needlessly to manufacturers' production costs. Some, particularly consumer representatives, however, counter that to ensure the safety and efficacy of vaccine products in general use, the Federal Government should evaluate such products more comprehensively.

Third, in recent years, Government efforts to allocate limited public health resources more efficiently have intensified. Some attempts have been made, for example, to incorporate formal cost-effectiveness analysis (CEA) into the health program decisionmaking process regarding funding. The usefulness of this analytical tool as an aid in deciding how to allocate Federal health resources, however, remains a matter of speculation and considerable controversy.

Finally, in light of recent court cases broadening vaccine manufacturers' liability, there exists a great deal of uncertainty as to whom the courts will hold liable for rare serious injuries resulting from nondefective and properly administered vaccines. This uncertainty appears to be undermining congressional and vaccine manufacturers' support for large-scale public vaccination programs. Widespread publicity of the potential, though

[1] In March 1977, for example, the Department of Health, Education, and Welfare (HEW) published *Reports and Recommendations of the National Immunization Work Groups* (U.S. Ex. Br., DHEW, 1977). In this document, a number of problems related to vaccine development and use were delineated. Also presented were a number of alternatives to the Federal Government's existing vaccine policies. An HEW report to Congress made more recently, *Liability Arising Out of Immunization Programs* (U. S. Ex. Br., DHEW, 1978), focused on vaccine liability issues.

[2] In 1978, for example, Congress refused to fund a Russian flu immunization program as large as the one proposed by the Department of Health, Education, and Welfare (HEW).

statistically remote, dangers associated with nondefective vaccines may be eroding overall public confidence in the safety of vaccine products.

Problems, issues, and policy options in four areas of Federal vaccine-related policies are discussed below: 1) vaccine research, development, and production; 2) vaccine safety and efficacy; 3) cost-effectiveness of vaccination and implications for reimbursement; and 4) liability and compensation for vaccine-related injuries.

VACCINE RESEARCH, DEVELOPMENT, AND PRODUCTION

Federal vaccine policies in the civilian sector are established by at least three agencies within the Department of Health, Education, and Welfare (HEW): the National Institute of Allergy and Infectious Diseases (NIAID), the Bureau of Biologics (BOB), and the Center for Disease Control (CDC). (See figure 1.) These three agencies collaborate infor-

Figure 1.—Federal Establishments With Vaccine-Related Responsibilities

Two departments within the Federal Government have responsibilities related to vaccine research and development. The Department of Health, Education, and Welfare (HEW) facilitates the development and use of vaccines for civilian populations, and the Department of Defense (DOD) develops vaccines against pathogens that pose particular health hazards for military populations.[1] No Federal agency engages in vaccine production for commercial use.

Three agencies at HEW fund or supervise activities related to vaccines: 1) the National Institute of Allergy and Infectious Diseases (NIAID), 2) the Bureau of Biologics (BOB), and 3) the Center for Disease Control (CDC). For the most part, these executive branch agencies interact only on an informal basis in specific instances, when, for example, their respective jurisdictional responsibilities or scientific investigations overlap. There is no official mechanism for these agencies to coordinate their policies or activities. Hence, it is difficult for any one agency to assess the impact of its actions on either the action of other agencies or on the behavior of vaccine manufacturers.

The National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH), Public Health Service, funds vaccine research and development programs. Mostly, NIAID funds basic research and epidemiologic research, in which investigators attempt to assess the incidence, prevalence, morbidity and mortality of a disease. Such NIAID-sponsored research is often conducted by investigators in academic or government institutions. For some vaccines, such as pneumococcal, NIAID funds clinical testing. In FY 1976, NIAID spent a total of $68 million on vaccine-related research. Of this amount, approximately $45 million was spent on basic research and $23 million on applied research (Jordan, 1977).

The Bureau of Biologics (BOB) of the Food and Drug Administration (FDA), Public Health Service, is responsible for ensuring the safety and efficacy of vaccine products to be used either in clinical trials or by the American public. In FY 1977, BOB spent a total of $7.5 million. About $2.1 million of this amount was spent on product-related research, and the remaining $5.4 million was used to finance BOB's regulatory and product control activities (Jordan, 1977).

The Center for Disease Control (CDC), Public Health Service, in Atlanta, Ga., has a number of vaccine-related responsibilities. In addition to surveying and reporting the incidence, prevalence, morbidity, and mortality rates associated with selected infectious diseases, CDC coordinates the distribution of Federal funds to State and local health departments participating in federally sponsored immunization programs. It also operates a voluntary adverse reaction reporting system through which it receives voluntarily submitted case reports concerning adverse reactions to vaccines. Such case reports are submitted by health professionals who administer vaccines in public immunization programs and by some vaccine manufacturers.

[1] In addition, executive branch departments other than HEW and DOD sometimes help work on specific problems associated with Federal vaccine programs. The Justice Department, for example, is working at present on liability cases associated with the 1976 swine flu program.

really when the need arises, but for the most part, they establish policies independently for their respective areas of responsibility.

The Federal Government shares with the pharmaceutical industry the responsibility for researching and developing new and improved vaccines. Most often, the Government either finances or conducts basic and epidemiologic research on vaccines and target diseases, while pharmaceutical companies concentrate mostly on product development and clinical testing.

The Federal Government is totally dependent on pharmaceutical manufacturers for production and supply of vaccines used in public immunization programs. This dependence has created concern among some vaccine authorities, particularly in Government, because during the past few decades, the number of American pharmaceutical companies producing vaccines has declined substantially.

During the past 12 years alone, the number of licensed vaccine manufacturers active in this country has dropped from 37 to 18, a 50-percent decrease. During the same period, the number of licensed vaccine products has plummeted from about 380 to about 150, a 60-percent decrease. Only eight American pharmaceutical companies actually produce vaccines, and these companies hold about 70 percent of the approximately 150 current vaccine product licenses.

The exact reasons for the decline in the number of commercial vaccine manufacturers are unknown, although a number of possible contributing factors can be identified. Relative to the markets for other prescription items, the $98 million **vaccine** market is small. This limited sales market may not support a large number of competitive producers. Further, low profits, high capital investment requirements, extensive Federal regulations, and unpredictable vaccine liability risks may be contributing to the decline in number of vaccine manufacturers.

So far, there has been no major production or supply problem with any commonly used vaccine in this country, but there are some indications that potential problems may arise. There are no active manufacturers, for example, of 11 of the 51 currently licensed types of vaccines, including Rocky Mountain Spotted Fever (RMSF) vaccine. Further, the United States is dependent on a single American pharmaceutical company for each of 19 vaccine products, including poliovirus vaccine. The supply of a vaccine with only one licensed manufacturer easily could be interrupted or terminated because of technical production problems or changes in a firm's marketing plans.

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

Federal policies affect virtually every aspect of vaccine activity in the private sector. The collective short- and long-range effects of Federal Government policies on the behavior of vaccine manufacturers, however, is not known. Some Federal policies, such as those regarding financing of vaccine research and development, may stimulate vaccine manufacturers to develop and market new products. NIAID financing, for example, appears to have been a major factor in the development of pneumococcal vaccine. Other policies, such as the use of Federal standards for vaccine safety and efficacy, when combined with low profit margins and high liability risks, though, may discourage **vaccine** manufacturers. Further, the Federal Government purchases for public immunization programs approximately so percent of the doses of vaccines distributed in the United States.

For certain vaccines, therefore, Federal purchases determine both market size and selling price. Lastly, the Federal Government now contractually assumes legal responsibility for warning potential vaccine recipients in public immunization programs about the unavoidable risks of vaccinations. The legal and economic implications of the Federal Government's assumption of this responsibility are undetermined.

The Federal Government is committed to encouraging vaccine research, development, evaluation, and use. The absence of any formal mechanism for NIAID, BOB, and CDC to work in close collaboration, however, may contribute to a less than unified Federal effort to promote vaccine development and use. If Congress decides that available evidence regarding the decline in American pharmaceutical manufacturers commitment to vaccine research, development, and production warrants immediate action it could pursue at least one of three major options.

OPTION A-1:

Establish a permanent interagency body within HEW to:

- **Develop priorities for facilitating and coordinating vaccine research, development, and evaluation in the public sector;**
- **Monitor vaccine research, development, and production in the private sector; and**
- **Report to Congress periodically.**

Such a body could be composed of representatives from the Government establishments primarily responsible for vaccine research, development, evaluation, purchase, distribution, and promotion. Consumers and representatives from the vaccine research communities in academe and the pharmaceutical industry also could be included.

If given adequate resources and authority, an interagency body could help to establish comprehensive and unified Government policies regarding the allocation of public funds for vaccine research, development, evaluation, and use. Otherwise, it might merely add an unnecessary layer of bureaucracy.

OPTION A-2:

Establish either a small- or large-scale Federal vaccine production program.

The establishment of a Federal vaccine production program, either small or large, could decrease the Federal Government's total dependence on the pharmaceutical industry for vaccine production and supply and increase its control over the availability of vaccines.

A small Government program, designed to produce only "orphan" and experimental vaccines, would help ensure the availability of special-purpose vaccines not produced by the private sector. A small program probably would not substantially affect industry's profits from large-scale production programs, because industry would continue to be the major producer of commonly used vaccines.

By establishing a large-scale vaccine production program, the Federal Government would substantially control the availability of most vaccines in this country. In theory, therefore, it could ensure the production of commonly used vaccines (e.g., poliovirus vaccine) that currently have only one commercial manufacturer. Possibly, though, a large-scale Government production program might erode manufacturers' vaccine profits,

leading to a reduction in the pharmaceutical industry's commitment to vaccines. This ultimately might lead to a situation in which the Federal Government would be the sole producer of common I y used vaccines.

OPTION A-3:

Subsidize vaccine production by private industry.

Instead of establishing its own production program to ensure the availability of vaccines, the Federal Government could subsidize the production of selected products by vaccine manufacturers. Federal subsidy could be provided to vaccine manufacturers either in the form of direct contracts for production or as a condition of Government vaccine purchases.

Acceptance of this option by both the Government and vaccine manufacturers would eliminate any need for the Government to establish its own vaccine production facilities. If no manufacturer accepted Government subsidy, however, some vaccines would still not be produced.

VACCINE SAFETY AND EFFICACY

The Federal Government has regulated the quality of vaccines in this country for 77 years. During this period, the standards, procedures, and criteria used to evaluate vaccine quality have become quite rigorous. Existing Federal laws and regulations require vaccine manufacturers to test their products for several characteristics, including purity, sterility, and potency.

During the past 20 years, the Federal Government has increasingly emphasized the evaluation of vaccines' clinical efficacy and safety. Since the early 1960's, the Federal Government has required vaccine manufacturers to test their experimental products in prelicensing clinical trials. In addition, in its evaluation of some vaccines, the Government has placed increased emphasis on the vaccines' ability to produce a desired level of antibodies.

Federal responsibility for licensing vaccines and other biological products has resided with the Food and Drug Administration's (FDA) Bureau of Biologics (BOB) since 1972. BOB imposes strict standards for the premarketing assessment of vaccine safety and efficacy. Premarketing evaluations, however, have at least three limitations. The premarketing evaluation of the safety and efficacy of pneumococcal polysaccharide vaccine illustrate these 1 imitations.

First, premarketing clinical trials have inherent limitations, particularly with respect to the evaluation of vaccine safety. For one thing, the number of subjects who receive a vaccine in a clinical trial is quite small relative to the number of persons who receive the vaccine once it is marketed. In the case of pneumococcal vaccine, the total number of vaccinees in premarketing clinical trials was 23,000. Further, in most clinical trials, subjects are observed for adverse reactions for only a short period of time. As a result of these inherent limitations, rare adverse reactions or reactions with insidious onsets seldom, if ever, are observable in premarketing vaccine clinical trials.

Second, the Federal requirement that a vaccine be tested in prelicensing clinical trials can lead American vaccine manufacturers to conduct their clinical trials among foreign populations. This situation arises when the incidence of a disease is so low in the United States that manufacturers cannot conduct affordable or acceptable domestic clinical

trials. The use of data from clinical trials conducted in foreign countries can be problematic. The validity of using findings from studies conducted among foreign subjects **as** the basis for projections concerning levels of vaccine safety and efficacy in the United States may be questioned. Without foreign clinical trial data, however, evaluations of the safety and efficacy of some experimental vaccines might not be possible,

Altogether, 70 percent of the vaccinees in clinical trials BOB used to evaluate the safety and efficacy of pneumococcal vaccine were foreign subjects. Several foreign trials of pneumococcal vaccine were conducted among South African gold miners and New Guinean potato farmers, because the high incidence rate of pneumococcal pneumonia among these two populations permitted a statistically significant assessment of the vaccine's ability to prevent this disease.

Third, in some cases, bioethical problems or economic constraints may limit clinical testing of vaccines among high risk groups. To conduct an acceptable clinical trial, investigators both must withhold an experimental, but potentially lifesaving, vaccine from high risk control subjects and must vaccinate high risk experimental subjects who may be more prone to develop or less able to tolerate severe adverse reactions. Furthermore, the cost of conducting a clinical trial among high risk persons with similar medical problems can be substantial; there is some difficulty in locating specialized populations and investigators may have to pay for subjects' medical care during a trial. For these reasons, a vaccine might never be tested in clinical trials among persons with medical problems that constitute official indications for the vaccine's use.

FDA-approved indications for use of pneumococcal vaccine, for example, include chronic heart, lung, or kidney disease, but prior to Iicensure, the safety and efficacy of this vaccine were not specifically evaluated in clinical trials among people with one or more of these medical problems. The FDA-approved indications statement was based on findings from at least two studies that demonstrated that bacteremic pneumococcal pneumonia patients with one or more of these chronic medical problems died more frequently than did those without such problems.

Certain limitations of premarketing vaccine safety and efficacy evaluations might be overcome if more comprehensive data were collected regarding adverse reactions to vaccine products in general use. BOB has proposed regulations that would establish its authority to require vaccine manufacturers to submit to FDA selected types of reports regarding adverse reactions. At the present time, vaccine manufacturers are not required to submit such reports to any Federal agency. Implementation of these regulations would likely increase the number of case reports of adverse reactions, but case reporting by itself would not permit comprehensive postmarketing evaluation of vaccine safety.

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 does have authority to remove a vaccine product from the U.S. market if available evidence suggests that the product is either unsafe or inefficacious. What BOB ap-

pears to lack, however, is any mechanism to collect comprehensive data on which to base its evaluations or with which to calculate the incidence of adverse reactions. Currently, BOB's postmarketing evaluations of licensed vaccines must be based largely on case reports that are voluntarily submitted by physicians to medical journals, to manufacturers, or to Federal agencies such as CDC or FDA.

To permit the collection of more comprehensive data regarding the safety of licensed vaccine products, CDC established last year a vaccine adverse reaction surveillance system. Reports concerning adverse reactions to vaccines administered under public immunization programs are voluntarily submitted, primarily by State and local health departments, to CDC. This system is very new, so it cannot yet be evaluated. Because it relies on voluntarily submitted case reports, though, CDC's system will not generate data needed to calculate the incidence of serious adverse reactions to particular vaccines.

Congress could await assessment of CDC's new voluntary case reporting system and take no action to strengthen the Federal Government's postmarketing vaccine surveillance mechanism. Alternatively, to permit the collection of data that could be used to evaluate selected vaccines more comprehensively, it could choose one or both of the following options.

OPTION B-1:

Authorize FDA to require vaccine manufacturers to conduct postmarketing surveillance of adverse reactions to specific vaccines and intensify Federal efforts to encourage voluntary reporting of such reactions by private sector physicians and clinics.

If given appropriate authority, FDA could require vaccine manufacturers to use their sales representatives, as well as practicing physicians, pharmacists, and nurses, to collect reports of adverse reactions to their licensed vaccine products. Further, FDA could require manufacturers systematically to report data collected concerning adverse reactions to either BOB or CDC. Such data then could be analyzed and used as a basis for BOB's evaluation of the safety of selected vaccines on the market.

Requiring manufacturers to file these reports, however, might diminish pharmaceutical manufacturers' commitment to vaccine research, development, and production. Some manufacturers might perceive such a requirement as an unacceptable economic and regulatory burden. Furthermore, the Federal Government at present has no effective means by which to compel private sector physicians to report the number and types of vaccinations they administer, let alone the number of adverse reactions to these vaccinations.

OPTION B-2:

Convert CDC's passive, voluntary case reporting system to an active, mandatory postmarketing vaccine surveillance system to monitor reactions to vaccines used in public immunization programs.

Congress could authorize HEW to undertake active postmarketing surveillance of selected vaccines administered under federally sponsored immunization programs. CDC could require State and local health departments participating in public vaccination programs to maintain records of the number of doses of vaccines administered and to solicit information regarding adverse reactions.

A system of active and mandatory postmarketing surveillance of vaccines administered in federally sponsored immunization programs would permit the collection of more comprehensive data regarding the safety and efficacy of licensed vaccines than will be collected under CDC's passive, voluntary case reporting system or under a PMS system as described in Option B-1. An active and mandatory postmarketing vaccine surveillance system coordinated by CDC, however, probably would require more resources than CDC's voluntary, case reporting system. Mandatory PMS activities also might be a disincentive for local and State public health clinics to participate in federally sponsored public immunization programs.

COST-EFFECTIVENESS ANALYSIS OF VACCINATION PROGRAMS

At present, the Federal Government promotes the use of at least eight immunizing agents. Seven of these agents are used to prevent common childhood diseases: measles, mumps, rubella, diphtheria, tetanus, polio, and pertussis. The remaining agent is used to prevent influenza primarily in adults or children with certain medical problems.

Every 1 to 2 years, Congress is asked to continue its financial commitment to federally financed immunization programs. Congress can base its funding decisions regarding these programs on a variety of criteria, including a general belief in the need for Government intervention to promote vaccine use, the effectiveness of prior and existing immunization programs, and the costs of continuing these programs.

One criterion that Congress has not often used to make its funding decisions is the cost-effectiveness of a given type of vaccination. Cost-effectiveness analysis (CEA) is an economic analytical tool that provides a systematic framework for comparing the economic efficiencies of two or more programs or procedures in achieving a given goal.

OTA conducted a CEA in which it calculated the net changes in costs and effects that would result from vaccination against pneumococcal pneumonia instead of continuing the present situation in which pneumonia is treated if it occurs. More than just an economic assessment of pneumococcal vaccination, OTA's investigation was designed to help illustrate the potential utility and limitations of using CEA to help allocate funds for Federal health programs in general and vaccination programs in particular.

In OTA's analysis, the net health effects and net medical care costs associated with a one-time pneumococcal vaccination program conducted in 1978 were assessed. Vaccination proved to be more cost-effective among the elderly than among any other age group. The results also showed that while vaccination would be slightly more expensive than treatment of pneumococcal pneumonia, vaccination would yield health benefits that could not be derived from treatment.

General Applications of CEA

ISSUE C:

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

As illustrated by OTA's analysis of pneumococcal vaccination, CEA might be useful to Congress and the executive branch in allocating funds for vaccine-related programs ranging from research and development programs to public immunization programs. CEA also might be used to help guide reimbursement decisions. Potential users of this

type of analysis include the National Institute of Allergy and Infectious Diseases (NIAID), the Center for Disease Control (CDC), the Health Care Financing Administration (HCFA), the Advisory Committee on Immunization Practices (ACIP), and health planning agencies.

Despite its potential utility, this type of formal economic analysis has major limitations. It does not necessarily or easily take into account social values, moral judgments, legal implications, or political realities; it does not easily or commonly address issues of equity and distribution. Furthermore, the use of this type of analysis may serve to narrow the range of options considered to those that are most easily quantified.

If the present situation relative to the use of CEA in Federal vaccination and other health programs continues, the use of this technique will remain informal and voluntary, and in some cases, prohibited. Selection of the following option would likely increase the Federal Government's use of CEA.

OPTION C-1:

Federal agencies could include formal CEA in the process of allocating funds for vaccination and other health programs.

In theory, the judicious use of CEA could lead to better selection of economically efficient programs to reduce health care costs or improve health status. No reasonable estimate, however, can be made of the potential reduction in overall health care costs that might result from such use. One of the potential dangers of greater application of CEA, is that it might lead to use of this technique when, in fact, such use is unnecessary or inappropriate. To minimize this danger, it would be important for policy makers to keep in mind CEA's limitations.

At present, the utility of CEA in allocating health care resources has not been fully assessed. Mandating the use of CEA at this time probably is premature and might lead to misallocation of funds. OTA is currently conducting an assessment of CEA as a method of evaluating medical technologies and will publish a report entitled The Cost-Effectiveness *of Medical Technologies* in the summer of 1980.

CEA and Its Relationship to Reimbursement for Vaccinations

ISSUE D:

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

Only two preventive vaccines are currently marketed for general use by persons over the age of 65: influenza vaccine and pneumococca] vaccine. In 1976 and 1978, Congress appropriated funds for influenza vaccination programs; it has not funded pneumococcal vaccination programs. Traditionally, the Federal Government chooses for its public immunization programs vaccines that help prevent selected childhood diseases, most of which are communicable.

Under existing law, Medicare is authorized to pay for the treatment of influenza and pneumococcal pneumonia, but not for vaccinations to help prevent these diseases. In a cost-benefit analysis of influenza vaccination, health benefits and potential cost-savings were demonstrated. In OTA's analysis, vaccination against pneumococcal pneumonia was shown to be most cost-effective among the elderly. To allow Medicare to pay for preventive vaccinations, Congress must amend the Medicare law.

OPTION D-1:

Amend the Medicare law to permit reimbursement for preventive vaccinations.

Congress could amend the 1965 Amendments to the Social Security Act to permit Medicare to pay for preventive immunizations. At the same time, it could establish or allow HEW to establish criteria for determining which specific immunizing agents should be included in the Medicare benefit package, e.g., agents that help prevent diseases that particularly affect the elderly, agents that have been proved both safe and efficacious, agents that have been shown to be cost-effective.

Both influenza and pneumococcal vaccines would likely meet all three of these criteria. If an additional criterion were that an agent not be included in publicly financed immunization programs, however, influenza vaccine would not be included in the package.

The impact of Medicare reimbursement on the elderly's demand for vaccination has not been determined. If the price of vaccination is a barrier to demand, then reimbursement by itself might increase such demand. It is possible, however, that Medicare reimbursement would need to be supplemented with other Federal efforts, such as a consumer health information program, to increase demand for vaccinations. Regardless of its effect on demand, Medicare reimbursement would shift the cost of vaccination from elderly vaccinees to the Federal Government. The net cost of providing vaccinations through public immunization programs, however, might be lower than that of providing vaccinations through reimbursement to private sector physicians.

CEA Methodology and Data

ISSUE E:

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

There are a number of generic difficulties associated with CEA methodology. One is that the models used to relate costs to outcomes vary from one study to another. This limits the comparability of the results of such studies. Another problem is that there is no widely agreed upon health status index that can be used to measure the health effects of medical interventions. In OTA's analysis of pneumococcal vaccination, the health status index used to measure the effects of vaccination on morbidity and mortality was quality-adjusted life years (QALYs). While the use in OTA's analysis of weights based on the results of surveys may represent a methodological advance, a great deal of work in improving health status indexes used in CEAs still remains to be done.

In the course of conducting its analysis of pneumococcal vaccination, OTA found that securing appropriate data for the analysis was a significant problem. Clearly, the time required to conduct CEAs and the rigor of the results of such analyses depend heavily on the availability of certain types of data. Exploration and resolution of key data problems, therefore, would seem to be prerequisites for any routine Government use of CEA.

OPTION E-1:

Federal agencies, including HEW, could begin to develop standardized and refined CEA methodology and basic data sets for CEAs.

The legislation creating the National Center for Health Care Technology (NCHCT) permits the Center to conduct CEAs and to develop general methodology. To force analysts to confront some of the methodological weaknesses or areas of disagreement in CEA, NCHCT could conduct pilot evaluations of certain medical technologies. Data problems could be addressed jointly by NCHCT, the National Center for Health Services Research (NCHSR), and the National Center for Health Statistics (NCHS).

To the extent that these agencies are able to overcome methodological and data problems, the feasibility of conducting CEAs, and using the results might increase. Improvements and standardization of data sets, though, could be expensive. Further, there might be some difficulty in attempting to improve the state of the art of CEA, while at the same time standardizing major aspects of it. To help overcome this, considerable flexibility in setting and revising methodological standards would be necessary.

LEGAL LIABILITY AND COMPENSATION FOR VACCINE-RELATED INJURIES

All vaccines, even when properly manufactured and administered, may pose risks to vaccinees. Permanent disability or death from vaccination, however, occurs only rarely. In general, the societal benefits of vaccination greatly outweigh the risks. For a very small number of vaccinees, however, the risks of vaccination exceed the benefits.

Under the existing legal liability system, persons injured as a result of vaccination must go to court and establish fault for their injury in order to receive compensation. To establish fault, the plaintiff (injured person) generally sues one or more of the participants in the vaccination process, e.g., a party that manufactures, distributes, pays for, encourages the use of, or administers the vaccine.

The major vaccine liability issue at present does not involve injury caused by negligence on the part of vaccine manufacturers or physicians, i.e., defective vaccine products or improper vaccine administration. Rather, it involves the inherent, unavoidable, though statistically remote, risk of vaccine-induced severe injury or death. In legal terminology, vaccines, though socially useful, are “unavoidably dangerous” products. Parties involved in the vaccination process attempt to avoid liability for inevitable injury by warning potential vaccinees about the existence of unavoidable risks.

In three major cases in the past 11 years, plaintiffs have won large judgments against vaccine manufacturers for injuries caused by nondefective and properly administered vaccines. One court argued that compensation for injury should be borne by the vaccine manufacturer as a cost of doing business, with costs passed on to the general public in the form of price increases. In essence, this court ruled that because no other mechanism to compensate injured vaccinees existed in society, the vaccine manufacturer should pay. While adopting a more explicit insurance rationale for compensating injured vaccinees, Federal appellate courts in these cases have shown an increased tendency to develop some doctrinal basis for their decisions on where liability for injury should rest.

Current case law has placed ultimate liability for breach of the “duty to warn” vaccinees about the inherent risks of vaccines on vaccine manufacturers. At present, the

duty to warn is being contractually transferred by manufacturers to HEW, which in turn is attempting to transfer this responsibility to State and local health agencies participating in public immunization programs. It remains unclear whether transfer of the duty to warn can be accomplished to the satisfaction of a court. There is no definite way to predict whether a court will find HEW's informed consent statements and the way in which they are given to be adequate; nor is there any way to predict, in the event that a court finds the duty to warn has not, been discharged, whom the court will hold liable.

The duty to warn raises ethical issues in public immunization programs. On the one hand, warnings are supposed to provide information on vaccine risks and benefits so that informed individuals can decide whether to be vaccinated or not. On the other hand, the Federal Government is an active promoter of vaccination programs, and the overwhelming majority of States and other territorial jurisdictions have mandatory childhood vaccination laws. In at least some cases, therefore, the vaccinee's ability to give informed consent to vaccination is moot.

Furthermore, the uncertainty surrounding appropriate methods of discharging the duty to warn already appears to have had two major impacts on vaccination programs. First, some vaccine manufacturers' willingness to produce and supply vaccines has been affected by the uncertainty over the price and even availability of liability insurance. Second, the highlighting of severe adverse reactions and associated liability problems has shaken the American public's confidence in the general safety of vaccines.

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 individuals who are injured as a result of vaccination in public immunization programs can be based on two rationales: 1) that the Government has a social responsibility to compensate individuals harmed as a result of their participation in vaccination programs intended in many instances to benefit, not only the individual vaccinee, but society as a whole; and 2) that liability insurance problems are having an adverse effect on public immunization programs.

If the Federal Government takes the position that responsibility for compensating injured vaccinees will be determined by the courts, then it will be doing its best to avoid compensating the injured. Legal discharge of the duty to warn would mean that there would be no liability or compensation for injury.

If HEW successfully defends its current position that underlying responsibility for the duty to warn still rests with vaccine manufacturers, manufacturers' increased liability costs will be passed on to the Federal Government and other purchasers of vaccines in the form of higher vaccine prices. It is also conceivable that some manufacturers will stop participating in public immunization programs. Some, as one former major vaccine manufacturer did, might withdraw from vaccine production altogether.

HEW's assuming responsibility to develop an informed consent statement and its requirement that State and local health agencies use this statement probably will absolve the latter agencies of liability. This absolution likely will have a positive impact on State and local health agency participation, but probably will not have a significant impact on their actual liability. Because of the procedural problems in suing Government agencies and the "deep pockets" of manufacturers, injured vaccinees probably will continue to focus their lawsuits on vaccine manufacturers.

Because the Federal Government is heavily involved in all phases of vaccine development, quality assurance, promotion, and use, it could develop approaches for more easily compensating injured vaccinees that do not rely solely on the judicial process. A central element of each of the two options presented below is easier access to compensation for vaccine-related injury.

OPTION **F-1:**

Assume responsibility for defending all claims of vaccine-induced injury incurred in public immunization programs and maintain authority to sue negligent parties.

This model is analogous to that used in the swine flu program. Under this option, the Federal Government would become the primary defendant in legal actions involving claims of injury sustained as a result of participation in public vaccination programs. The Federal Government would assume liability for the duty to warn, but would retain the right to *sue other* parties for injuries caused by negligence. This approach would somewhat insulate manufacturers from the expense of defending lawsuits. Manufacturers' costs incurred in assisting the Government in the preparation and defense of lawsuits, however, would remain.

With the Federal Government as the primary focus of claims for compensation, flexibility in the Government's posture with regard to the kinds of proof that would be needed to obtain compensation would be possible. For example, although foreseeability is a fundamental concept in assigning legal liability, in the swine flu program, Guillain-Barre Syndrome (GBS) was not initially a foreseeable consequence of immunization. In its processing of swine flu-related injuries, the Federal Government apparently is relaxing this condition and relying more on finding causation between alleged injury and swine flu inoculation. If the Federal Government were to adopt a similar approach in the future, compensation would depend less on whether an adequate warning had been given than on whether significant injury had occurred as a result of immunization.

Immediate and direct costs to the Government would increase under this option because of the administrative expense of processing, evaluating, and defending claims, and because of the compensation costs for successful litigants. Long-term costs, however, might or might not increase, because liability insurance costs are handled as business costs and passed on to the purchasers of vaccines. Indirect "costs" such as decreased public participation in public immunization programs might be less, because this would represent a positive approach, or at least not a passive one, to the problem of injured vaccinees.

While this approach might be an improvement for the class of injured vaccinees in terms of their chance of receiving compensation, it might not be an improvement for the rare individual who successfully maneuvers the current litigation process and wins a large award. The tradeoff between more awards of less individual worth and high individual awards, though, is typical of the kinds of tradeoffs that would have to be made between continuing the current situation and developing a more compensation-oriented system.

OPTION F-2:

Establish a federally operated program to compensate vaccinees injured as a result of being vaccinated in public immunization programs.

A frank compensation approach could range from modification of the current legal liability system, to integration into existing social insurance programs, to melding with approaches that have similar bases for compensation, such as that for compensating persons injured in medical experimentation.

To establish a Federal compensation system, four principal issues would have to be addressed. First, criteria for the selection of vaccinees eligible for Federal compensation would have to be established. Compensation could be limited, for example, to persons whose injuries result from vaccines whose use the Government promotes to a substantial degree.

Second, the types and severity of injury qualifying a vaccinee for compensation would have to be established. Some test of causality and a cutoff point on the severity of injury that would be compensated would have to be established.

Third, limits to compensation would have to be established. Under a Federal compensation system, which is oriented away from the adversary process toward the assumption of societal responsibility for injury, some general standards or levels of compensation would have to be established. The system could be structured to pay for injured persons' needs as they occur.

Fourth, financing mechanisms would have to be created or selected. The limited number of injuries arising out of public immunization programs means that a free-standing compensation system probably would not be warranted. Any specific approach would need clarification, public debate, and compromise.

The advantages and disadvantages of establishing a federally operated compensation program would depend largely on the specific program adopted, but in many respects might parallel those cited in Option F-1. Court costs to the Federal Government probably would be less under this option than under Option F-1, but administrative costs probably would be higher. In addition, injured vaccinees might have easier access to compensation under this option.

SCOPE OF THE STUDY

This study adresses four areas of concern regarding Federal vaccine policies: 1) the impact of Federal policies on the commitment of American pharmaceutical manufacturers to conduct vaccine research and develop and supply vaccines, 2) the adequacy of Federal vaccine safety and efficacy requirements, 3) the potential utility and limitations of cost-effectiveness analysis (CEA) in decisions regarding the allocation of Federal funds for vaccination and other health programs, and 4) vaccine liability and compensation issues that have arisen in connection with nondefective, properly administered vaccines used in public immunization programs.

No attempt was made to address all areas of Federal vaccine and immunization policies. Thus, for example, the study did not include an in-depth analysis of the administration or effectiveness of federally sponsored immunization programs, and consequently, did not include an examination of the roles of State and local health departments participating in such programs.

Furthermore, the study was limited to an examination of vaccine policies for the civilian population. Concerns regarding the vaccine-related activities of the Department of Defense (DOD), therefore, were not addressed.

To illustrate salient issues in the first three policy areas cited above, case studies based on recent events and experience with polyvalent pneumococcal capsular polysaccharide vaccine were developed. This vaccine, which is the newest vaccine on the U.S. market, can be used to help prevent pneumococcal pneumonia. It is described in more detail in figure 2.

Vaccine liability and compensation problems have not arisen specifically in connection with pneurnococcal vaccine, in part, because its use has not been actively promoted by the Federal Government. To illustrate these issues, therefore, OTA reviewed recent vaccine liability case law, principles underlying the pricing of vaccine manufacturers' liability insurance, and experience with adverse reactions under the swine flu and other federally sponsored immunization programs.

Most of the issues discussed in connection with pneumococcal vaccine are applicable to other types of vaccines. Some issues, however, may not have been comprehensively illustrated as a result of using only one vaccine in these case studies. Court cases involving liability for injury caused by nondefective poliovirus and swine flu vaccines most likely have implications for all vaccinations.

This report pertains on] y to vaccines for human use.

ORGANIZATION OF THE REPORT

This report has seven chapters. Following chapter 1, which is an introduction and summary to the entire report, case studies based on experiences with pneumococcal vaccine are presented in chapters 2, 3, and 4. In chapter 2, the impact of Federal financing on the research and development of this vaccine is discussed; chapter 3 contains a description and analysis of the procedures the Federal Government used to evaluate the safety and efficacy of this vaccine; and in chapter 4, OTA's cost-effectiveness analysis (CEA) of pneumococcal vaccination is presented. Chapter 5 contains a review of recent vaccine liability court cases, principles that underlie the pricing of liability insurance, and liability experience under the 1976 swine flu immunization program.

Findings from the case studies of pneumococcal vaccine and the review of liability topics are summarized in chapter 6. These findings are used to introduce more general discussions of selected issues in each of the four major policy areas addressed in this report.

Congressional or executive branch options to address the issues discussed in chapter 6 are presented in chapter 7. In some cases, the options are mutually exclusive, in others, they are not. The implications of maintaining the status quo, along with the pros and cons of each option, are discussed.

The history of pneurnococcal research and pneumococcal vaccine development prior to 1967 is described in appendix 1.1. Appendixes which follow this contain technical reference material for chapters 2, 3, 4, and 5.

51-329 0 - 79 - 3

[page omitted]

This page was originally printed on a dark gray background.
The scanned version of the page was almost entirely black and not usable.

Figure 2.—Pneumococcal Diseases and Polyvalent Pneumococcal Polysaccharide Vaccine—cont.

pneumococcal pneumonia permit physicians to treat many patients without hospitalization.

Unfortunately, two problems have arisen in connection with antibiotic treatment of pneumococcal diseases. First, in a substantial number of cases, the use of antibiotics fails to prevent death caused by bacteremic pneumococcal pneumonia. In spite of receiving appropriate antibiotic therapy, as many as 17 to 30 percent of patients with bacteremic pneumococcal pneumonia have been reported to die from their disease (Austrian, 1964).

Second, in some instances, certain types of pneumococci have become resistant to antibiotics. The development of resistant strains has been reported in South Africa (Jacobs, 1978), New Guinea (Hansman, 1971), and the United States (U.S. Ex. Br., CDC, 1977). So far, resistance to at least eight antibacterial agents has been demonstrated. The development of resistant strains of pneumococci reduces the overall effectiveness of available antibiotics in the treatment of pneumococcal diseases.

Polyvalent Pneumococcal Polysaccharide Vaccine

Recent efforts to develop a vaccine to help prevent pneumococcal pneumonia were stimulated in part by findings regarding the limitations of antibiotic therapy. These efforts, culminating nearly 70 years of basic and clinical research, proved successful. On November 21, 1977, the Food and Drug Administration (FDA) issued Merck Sharp and Dohme, an American pharmaceutical manufacturer, a license to market its 14-valent pneumococcal capsular polysaccharide vaccine (PNEUMOVAX). In August 1979, FDA issued Lederle Laboratories a license to market a similar product (PNU-IMUNE).

Pneumococcal vaccine, which appeared on the U.S. market in February of 1979 is composed of purified polysaccharides from the capsules of 14 different types of pneumococci. When injected into humans, these 14 capsular polysaccharides stimulate the formation of serum antibodies that provide immunity against 14 types of pneumococcal organisms. The duration of immunity conferred by the vaccine is unknown. Some researchers estimate that the period of protection lasts for at least 3 years; others claim that it may last a lifetime (Weibel, 1977).

In premarketing clinical tests, pneumococcal vaccine appeared to be relatively safe. While minor reactions such as pain or erythema (redness at the injection site) were fairly common, no deaths and few serious adverse reactions to the vaccine were reported. Since the vaccine has been on the market, however, a few cases of more severe transient adverse reactions have occurred (Broome, 1978; Uhl, 1978; Semel, 1979). Pneumococcal vaccine does not contain live organisms and therefore cannot itself cause pneumococcal infection.

The 14 types of pneumococci represented in the vaccine reportedly account for approximately 80 percent of pneumococcal infections in children and adults (Austrian, 1977). In premarketing clinical trials, pneumococcal vaccine produced an acceptable increase in serum antibody titers in at least 80 percent of the subjects tested. In some studies, at least an 80-percent reduction in the incidence of pneumococcal pneumonia occurred among vaccinees (Austrian, 1976; Smit, 1977). In other studies, however, the reduction of disease among vaccinees was less (Riley, 1977).

FDA-approved indications for use of the 14-valent vaccine specify prevention of pneumococcal pneumonia or bacteremia in individuals over 2 years of age who are at high risk of developing and dying from these pneumococcal infections. High risk individuals include those with chronic physical conditions (such as heart, lung, or kidney disease, diabetes, or cirrhosis of the liver); those in chronic care facilities; those convalescing from severe diseases; and those over 50 years old.