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The swine flu program was the Government's first attempt at immunizing the entire U.S. population. Findings/Conclusions: The Department of Health, Education and Welfare (HEW) lost its gamble in this episode of preventive medicine, but much can be learned from the program that should be useful in planning future immunization programs and related public health efforts. Legal liability continues to be a problem in immunization programs. All vaccine released for use utimately met Food and Drug Administration potency and safety standards. Potential protection provided by the vaccine is difficult to estimate. Not enough vaccine was produced or produced on time to immunize everyone in the United States had there been a swine flu outbreak. State readiness and implementation was never fully tested. Costs may far exceed the $135 million appropriated. Recommendations: HEW should establish key points in the program process for formal program reevaluation; improve informed consent procedures; improve potency testing; secure alternate procurement if manufacturers lag behind schedules; and consider all problems that arose in planning and implementing the program. Congress should establish a national liability policy before another mass immunization is needed. (DJM)

REPORT TO THE CONGRESS

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

The Swine Flu Program: An Unprecedented Venture In Preventive Medicine

Department of Health, Education, and Welfare

The swine flu program was, in the Department of Health, Education, and Welfare's view, a decision to practice preventive medicine, which has an inherent element of risk. In a sense, HEW lost its gamble. No swine flu outbreak occurred during the 1976-77 flu season. Nevertheless, much can be learned from the swine flu program that should be useful when planning future immunization programs and related public health efforts.

HRD-77-115

JUNE 27, 1977

COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

B-164031(5)

To the President of the Senate and the
Speaker of the House of Representatives

This report describes issues developed during our review of the National Influenza Immunization (Swine Flu) Program. It discusses considerations for future programs with respect to program justification and cost, Federal liability implications, vaccine production and testing, and program planning and implementation.

Although we expanded the scope of the review at the specific request of several House committees, we are issuing the report to the Congress because of the widespread interest in the program. As requested by the committees, we are issuing it now without written comments from the Department of Health, Education, and Welfare because of the need for timely consideration of the issues.

We made our review pursuant to the Budget and Accounting Act, 1921 (31 U.S.C. 53), and the Accounting and Auditing Act of 1950 (31 U.S.C. 67).

We are sending copies of this report to the Director, Office of Management and Budget, and the Secretary of Health, Education, and Welfare.

Comptroller General
of the United States

COMPTROLLER GENERAL'S
REPORT TO THE CONGRESS

THE SWINE FLU PROGRAM: AN UNPRECEDENTED VENTURE IN PREVENTIVE MEDICINE
Department of Health, Education, and Welfare

D I G E S T

The swine flu program was the Government's first attempt at immunization of the entire U.S. population. Faced with the possibility of an epidemic that could cost many lives and billions of dollars and offered a chance to prevent it, the Department of Health, Education, and Welfare planned, and the Congress approved, the $135 million swine flu program.

The decision to proceed with the program was based primarily on scientific evidence that an epidemic could scourge the Nation and that the health care system could carryout the mass immunizations. However, no known outbreaks of swine flu occurred during the 1976-77 season. (See pp. 11-15.)

SOME QUESTIONS ABOUT FLU NEED TO BE ANSWERED

For any future immunization effort as large or concentrated as the swine flu program, the many preventive health care questions that arose would likely have to be broadly considered again by all parties involved. The solutions devised for the swine flu program were not intended as a pattern for future efforts. (See pp. 15 and 16.)

In any event, when decisions must be based on very limited scientific data, HEW should establish key points at which the program should be formally reevaluated.

LIABILITY CONTINUES TO BE A PROBLEM

Although effective in getting the swine flu program started, legislation designed to solve program liability problems

--may result in profit to the insurance companies of nearly the entire $8.65 million premium paid by vaccine manufacturers for liability insurance (see pp. 19-21);

--leaves unresolved insurance company concerns about nonmeritorious claim risks (see pp. 21 and 22); and

--may result in indeterminable costs to the Government for litigation, awards, and settlements because of potential weaknesses in the form and procedures used to obtain "informed consent" from persons immunized (see pp. 22-29).

Insurance executives stated that the Government should be responsible for both the liability and the costs of litigation, since the Government will control all key aspects of any public immunization program. HEW's Assistant Secretary for Health stated that a national policy concerning compensation will have to be developed for any future mass immunization program. So that resolution of the liability issue does not delay or adversely affect public acceptance of future programs, GAO recommends that the Congress establish a national liability policy before another mass immunization program is needed. (See p. 29.)

GAO describes two ways the Government can assume liability at less cost than for the swine flu program. First, if experience gained from the swine flu program shows that considerable money can be saved and if HEW intends to continue rigorously testing and approving every vaccine lot, then total Federal assumption of the liability coverage for vaccine production should be considered. Second, the insurance industry could make manufacturers' premiums adjustable retrospectively based on claims experience. (See pp. 29 and 30.)

To evaluate the effect of Federal responsibility and liability for informed consent will take years. HEW should monitor this process as it occurs, for possible future program applications. (See p. 30.)

VACCINE TESTING MORE EXTENSIVE THAN IN 1975

All vaccine released for use in the swine flu program that GAO reviewed ultimately met Food and Drug Administration potency and safety standards. Almost 30 percent of the vaccine was considered subpotent, and the agency did not permit its release to the public until the minimum potency requirement was met. (See pp. 31-34.)

Tests showed that some of the trial vaccine did not meet specified potency levels, and trial participants were not given the same protection as the general public. The potency test does not accurately indicate the protection provided by the vaccine. (See pp. 33-36.)

Because of the deficient potency test and the continual differences in manufacturer and Food and Drug Administration test results, the agency should continue its own potency tests on all lots of flu vaccine until manufacturers' test results can be relied on. In addition, the agency should speed up its work to

--identify and resolve potency test variances with the manufacturers and

--develop and put into practice an improved method to measure potency and relate it to the level of protection provided by the vaccine.

To improve the accuracy of trial data and the protection of trial participants, the agency should test flu vaccine intended for trial use as it would be tested for public use.

POTENTIAL PROTECTION PROVIDED BY SWINE FLU VACCINE

HEW officials estimated, based on past experience and trials, that the swine flu vaccine would adequately protect 70 to 90 percent of those vaccinated. However, protection is difficult to estimate based solely on previous experience. (See pp. 38-41.)

Further, estimating protection based on trial results was complicated by problems in getting adequate antibody responses in younger people and by the inactivity of one vaccine component. (See pp. 41-45.)

The duration of protection provided by the vaccine is uncertain. (See pp. 46 and 47.)

NOT ENOUGH VACCINE PRODUCED OR PRODUCED IN TIME

HEW estimated in late March 1976 that manufacturers could produce and deliver 200 million doses of vaccine by the end of November. Primarily because of unresolved liability questions, the first delivery was delayed--from July to October.

Vaccine available then could immunize only about 12 percent of the population. Although three of the four manufacturers said they continued to produce at full capacity during the delay and the fourth had met its original estimate, vaccine production fell short of the original estimates by about 43 million doses and required over 2 months longer to produce. (See pp. 49-54.)

For future programs, HEW must determine in a timely fashion how the vaccine will be formulated and packaged and the delivery specifications, if vaccine is to be delivered on schedule. If manufacturers still cannot produce enough vaccine in time to meet the needs, alternative methods should be sought.

STATE READINESS AND IMPLEMENTATION

Each swine flu grant project offered immunization to anyone medically able to take the vaccine. However, because the epidemic never materialized and demand for vaccine was less than expected, the Nation's system for mass immunization was not fully tested. Some problems in planning and implementing swine flu immunizations at the local level should be considered for any future mass immunization programs.

State and local immunization projects were not ready to begin the program in July as planned. They were limited by

--less than full commitment by some project directors (see pp. 57 and 58);

--complex, incomplete, and late vaccine recommendations (see pp. 58-60);

--limited quantities and delayed delivery of vaccine (see pp. 60-65);

--less-than-expected participation by private doctors, volunteers, and others (see pp. 65-68);

--weaknesses in project operations (see pp. 68-73); and

--lack of State liability insurance (see pp. 73-75).

Project readiness and implementation were limited by biological and liability problems beyond the projects' control. Consequently, GAO could not determine whether State or local projects could be ready for future mass immunization programs. (See p. 75.)

In addition, State and local agencies will need better guidance and assistance from HEW in managing projects and will in turn have to make consistent firm commitments to HEW if any future mass immunization program is to succeed. The Secretary, HEW, should request the Department of Defense to revise its policy so that both military personnel and equipment can be quickly mobilized and effectively used in civilian immunization projects.

GAO recommends that the Congress consider the effect which inadequate liability protection might have on State participation in future immunization programs. The Government could (1) assume total liability for the program, (2) assume no liability for program participants, or (3) assume limited liability

similar to that provided under the swine flu program. (See pp. 76-77.)

PROGRAM COSTS

Total costs for the swine flu program cannot yet be accurately determined. In some instances, accounting data is too limited to identify precise costs; and, in others, not all costs have been incurred or determined. The total costs may far exceed the $135 million appropriated. (See pp. 78-85.)

AGENCY COMMENTS

Because of the need for timely consideration of the issues, GAO was asked not to obtain written comments. However, HEW, Department of Justice, and State officials were apprised of the matters discussed in this report. Their comments have been considered.

Contents

ABBREVIATIONS

CCA	chicken cell agglutination
CDC	Center for Disease Control
FDA	Food and Drug Administration
GAO	General Accounting Office
HEW	Department of Health, Education, and Welfare

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CHAPTER 1

INTRODUCTION

In early February 1976 a New Jersey public health laboratory sent four unusual isolates of influenza (flu) virus obtained from Fort Dix military recruits to the World Health Organization Collaborating Center for Influenza at the Center for Disease Control (CDC) in Atlanta, Georgia. By February 12, 1976, tests had shown that the isolates were a new flu strain closely related to swine flu viruses.

Isolating a new flu strain at the end of one flu season presented a unique opportunity to test the ability of the Nation's health system to organize itself in time to prevent a flu outbreak or an epidemic during the next flu season. By April 12, 1976, the House of Representatives and the Senate had passed a joint resolution (Public Law 94-266) providing over $135 million for a comprehensive, nationwide flu immunization program. The President approved the resolution on April 15, 1976.

Although popularly referred to as the swine flu program, the national flu immunization program was directed at both the swine flu and another flu strain known as Victoria flu. Victoria flu occurred in the United States during January 1976 and reached epidemic proportions during February. It was expected to be a prevalent strain during the coming flu season. Following normal practices, Victoria flu vaccine had already been produced in adequate quantities to immunize all individuals for whom flu was considered a high health risk.

Emphasis was placed on swine flu because it represented a new strain, to which the bulk of the population had no immunity. High-risk individuals would be greatly threatened by either Victoria or swine flu. Therefore, existing Victoria flu vaccine was combined with subsequently produced swine flu vaccine to form a "bivalent" vaccine for these individuals. For the general population, only a "monovalent" swine flu vaccine was provided.

THE OBJECTIVE AND GOALS OF THE SWINE FLU PROGRAM

The objective of the program was to establish an integrated, comprehensive immunization system capable of making swine flu vaccine (or bivalent vaccine, as appropriate) available to every person for whom it was not

contraindicated. Goals called for using both the public and the private health care delivery systems to immunize the entire population by the end of November 1976. This deadline was considered critical because, if an outbreak occurred, the disease could spread so rapidly that further immunization would have little controlling effect.

The season of intense flu transmission in the United States is generally considered to be September through March. The national strategy, therefore, called for vaccinating high-risk groups during July and August and the general population during September through November 1976.

The swine flu program represented a departure from the normal flu prevention and control policy in the United States. In previous years immunization of those groups particularly susceptible to the effects of flu infection was emphasized. During the pandemics of 1957 and 1968, limited mass immunization was attempted. (See pp. 39 and 40.)

Widespread vaccination of the general population had generally not been an objective because:

--Normally, foreknowledge of a coming flu virus is insufficient to permit development of an entirely appropriate vaccine.

--The attack rate of flu nationally between pandemics is usually low.

--Healthy individuals normally have a low frequency of serious complications from flu.

CHARACTERISTICS OF THE FLU VIRUS

Every flu virus has two surface antigens (proteins)--hemagglutinin and neuraminidase--that allow the virus to penetrate body cells and to spread throughout the respiratory tract. Hemagglutinin allows the virus to attach itself to a cell where it can penetrate and reproduce. Neuraminidase is believed to facilitate virus spread by helping release it from an infected cell so it can attach itself to other cells.

One unique characteristic of the flu virus is that hemagglutinin and neuraminidase change. Minor changes occur frequently and are referred to as antigenic drifts. At longer intervals, major changes, referred to as antigenic shifts, occur in hemagglutinin and neuraminidase.

Flu pandemics have been associated with major antigenic shifts. Pandemics are major epidemics due to a single virus strain which sweep around the world in a short time and cause marked increases in morbidity and mortality. Populations with no previous exposure to newly appearing antigens have no immunity against these new strains.

The rapidity with which flu may spread is unique among infectious diseases. In the well-studied Asian and Hong Kong flu pandemics of 1957 and 1968, the time from the initial isolation of a new flu strain to the spread of the disease to all major areas of the world was less than 6 months.

The reasons for the rapid spread of flu are only partly understood. The short incubation period (24 to 48 hours), the large populations susceptible to infection, and the ease with which the disease is transmitted (fluids in the nose and mouth are expelled into the air when a person sneezes, coughs, or talks) play important roles. Because epidemics and pandemics occur most often in the winter, meterological conditions may also be important. Widespread simultaneous outbreaks often occur after a period of sporadic cases. This indicates that the virus is seeded throughout susceptible populations even by mildly ill individuals.

EFFECT OF FLU PANDEMICS

The effect of flu pandemics has been measured since the early 1800s by the number of deaths occurring in excess of the number of deaths expected. Excess deaths due to flu and resultant complications, such as pneumonia, are especially evident. Mortality is usually highest in the aged and in persons with chronic illnesses, such as pulmonary and cardiovascular diseases.

The worst flu pandemic on record occurred in 1918 and caused an estimated 20 million deaths worldwide and approximately half a million deaths in the United States. A unique feature of this pandemic was the unusually high mortality in persons 20 to 40 years old. The 1918 virus was similar in structure to the swine-flu-like virus isolated at Fort Dix in February 1976. Excess mortality in the United States during the Asian flu pandemic of 1957-58 was estimated at 69,800 deaths. During the Hong Kong flu pandemic of 1968-69, an estimated 27,500 excess deaths occurred.

According to CDC, the total costs of flu pandemics cannot be accurately determined. But for the 1968-69 pandemic, the cost of physicians' visits, hospitalizations, prescriptions, and losses of earnings in the United States was estimated at $3.9 billion.

FLU VIRUS VACCINES

If a human population has hemagglutinin and neuraminidase antibodies of a flu virus strain, the antigens of that strain can be neutralized and infection prevented or modified. Current flu vaccines, which contain antigens of killed viruses, stimulate the production of protective antibodies in a person without causing infection. Also, recently improved purification processes have allowed for increasing the vaccine antigenic content or potency without accompanying increases in serious adverse reactions.

Because of the ability of flu virus surface antigens to change, the appropriate antigenic composition of a vaccine is of major importance. Continuous surveillance of current flu viruses for evidence of antigenic change and the incorporation of the new antigens into the vaccine are essential.

In past epidemics, the time between a new virus isolation and peak disease incidence did not allow for appropriate vaccine preparation and mass distribution. The swine flu virus was detected at the end of a flu season. Consequently the necessary leadtime was available to prepare and distribute a new vaccine before the next flu season.

Vaccine production

In the United States six manufacturers are licensed to produce flu vaccine, and four are producing vaccine. Each manufacturer produces killed virus vaccine that has an expiration date permitting use within 18 months. The date may be extended, however, based on certain laboratory tests. The 18-month period is used because of antigenic drifts in flu viruses. Past vaccine production volume has usually been about 20 million doses annually.

Two manufacturers produce a "whole" virus vaccine from the entire killed virus, while the other two produce a "split" virus vaccine by chemically disintegrating the virus. In the swine flu program, both whole and split virus vaccines were produced in bivalent and monovalent formulations.

RESPONSIBILITIES OF PROGRAM PARTICIPANTS

For the swine flu program, the Department of Health, Education, and Welfare (HEW) planned to purchase 200 million doses of vaccine, which were to be made available at no cost to State and local health agencies. The agencies were to distribute the vaccine through public health, volunteer, and private sector channels, so that every person for whom the vaccine was not contraindicated could be immunized. Responsibilities for the HEW agencies involved and State and local health agencies follow.

The Center for Disease Control

CDC was the focal point for the mass immunization program. CDC was primarily responsible for:

--Purchasing and distributing about 200 million doses of vaccine.

--Instituting intensive epidemiologic and laboratory surveillance of the population to

1. Measure the extent and severity of flu on a national basis.

2. Evaluate the effectiveness of the vaccine and the vaccine delivery systems.

3. Investigate and control outbreaks.

--Providing financial and technical assistance and guidance to State and local health agencies in organizing and carrying out intensive mass immunization programs; capitalizing on organized settings, such as schools, governmental offices, and large private employers; as well as sponsoring special clinics and community programs.

--Organizing national interest groups and organizations to carry out public awareness campaigns at the national level and, through their local chapters or affiliates, to support State and local immunization programs.

--Serving as the focal point for diagnostic activities in support of State and local public health laboratory facilities.

The Food and Drug Administration

The Bureau of Biologics in the Food and Drug Administration (FDA) was responsible for testing vaccine before its release. These tests included laboratory analysis and clinical trials to ascertain the appropriate dose of vaccine and to document vaccine potency, safety, purity, and effectiveness.

The National Institute of Allergy and Infectious Diseases

The Institute was to greatly expand the scope and extent of existing intramural and extramural activities to carry out research, beginning in the summer of 1976 and continuing until another antigenic shift in the flu virus occurs. The following were to be included in such research:

--Intensive study of flu viruses circulating in the swine population and of changes in these viruses as related to increased transmissibility to man.

--The determinants of swine-to-man transmission and of later dissemination in man.

--Studies of the production of antibodies and of adverse reactions to the vaccines that were to be produced, to provide the data needed for determining dosage and usage.

--Determination of the efficacy of amantadine, the only drug licensed in the United States for treating viral respiratory disease, in preventing the spread of swine-flu-type viruses.

--Determination of the protection provided by swine flu vaccine in population groups, if outbreaks occur.

--Studies to test the technology for producing and using live flu vaccine during pandemics and to obtain data for comparing the efficacy of live virus vaccines and of killed virus vaccines made of whole viruses, split viruses, or surface antigens of the virus.

State and local health agencies

These agencies were relied upon to organize and coordinate immunization activities. HEW provided 63 project grants to 50 States and 13 cities and territories to help

pay additional expenses of mass immunization. The funds supported limited temporary employment and permitted the purchase of supplies (other than vaccine) and equipment.

The projects were to try to obtain commitments from major health care providers or potential providers, such as industries, schools, hospitals, nursing homes, and governmental agencies to immunize their employees, students, and patients. In addition, special clinics and community programs were to be provided to reach persons not vaccinated in other organized settings.

Special programs were to be directed toward providing the elderly with bivalent vaccine. Public awareness campaigns were to be carried out to maximize public acceptance of the need for flu vaccination. Heavy reliance was to be placed on voluntary assistance.

CHAPTER 2

PROGRAM JUSTIFICATION: PREVENTIVE MEDICINE

The decision to vaccinate the entire U.S. population against swine flu was, in HEW's view, a decision to practice preventive medicine, which has an inherent element of gamble. Faced with the possibility of an epidemic that could cost many lives and billions of dollars--and offered a chance to prevent it--HEW planned, and the Congress approved, a $135 million mass immunization program.

This decision was the result of scientific judgments about the possibility of a swine flu epidemic and assumptions about the capabilities of vaccine manufacturers and the Nation's health delivery system to counter it. Even though the decision was a gamble, the officials said that gambling with money would be better than doing nothing and gambling with lives.

In a sense, HEW lost its gamble with money. No swine flu outbreaks or epidemics had occurred by March 31, 1977--the end of the normal flu season. In addition, some persons suffered serious adverse reactions to immunization, although they represent a very small percent of the total immunized. On the other hand, much has been or can be learned from the program that should foster more informed decisionmaking by the Federal Government and by other participants in future immunization programs and related public health efforts.

EVENTS LEADING TO MASS IMMUNIZATION

In early February 1976, a New Jersey public health laboratory sent four unusual isolates of flu virus obtained from Fort Dix, New Jersey, to CDC. By February 12, 1976, CDC had shown that the virus was of a flu strain closely related to swine flu viruses. A special meeting of representatives from the Army, the State of New Jersey, and several health agencies of HEW was held at CDC on February 14. At this meeting plans were discussed to confirm the authenticity of the isolates and to evaluate the extent of the outbreak at Fort Dix.

By February 19, CDC had confirmed the outbreak and had distributed reports of the Fort Dix findings to all State epidemiologists; laboratory directors; and the World Health Organization in Geneva, Switzerland. Isolates from the outbreak were sent also to London's World Health Organization

Collaborating Centre for Influenza and National Institute for Biological Standards and Control. On February 20, isolates from Fort Dix were provided to all vaccine manufacturers and investigators for further study and for development of material suitable for vaccine production.

On March 10, 1976, HEW's Advisory Committee on Immunization Practices--a panel of Government and private experts in immunology which normally makes recommendations for using flu vaccines--met at CDC with representatives of HEW, the Army, and others. The Army advised the Committee of the following results of its studies at Fort Dix:

--Five swine-flu-like viruses had been isolated, including one from a recruit who died.

--Eight persons (later revised to six) hospitalized with flu had shown an increase in swine flu antibody levels through blood tests, a strong indication of swine flu.

--Several hundred recruits had been identified through blood tests as having swine flu antibodies.

--The outbreak had been observed during the first week in January, and the last case had appeared during early February.

Also CDC advised the Committee that other investigations around the country had revealed no significant evidence of swine-flu-like virus activity outside Fort Dix.

On the basis of this information, the Committee concluded that:

--Human-to-human transmission of swine-flu-like virus had occurred at Fort Dix.

--Other outbreaks might be in process or might be in the future.

--Vaccine must be produced and a plan for vaccine administration should be developed.

The Committee did not state whether persons should actually be immunized.

A March 13, 1976, memorandum from the Director of CDC to the Assistant Secretary for Health analyzed the

advantages and disadvantages of (1) no Federal action, (2) a limited Federal role with primary reliance on existing delivery systems and on spontaneous, nongovernmental action, (3) a national immunization program under virtually total Government responsibility, and (4) a combined public and private sector program. The memorandum recommended the last approach, as offering the best chance of immunizing the entire population.

Under the recommended plan, the Federal Government would advise manufacturers to produce, and would contract through HEW for, 200 million doses of vaccine. This vaccine would be made available at no cost to State health agencies which would plan for its distribution through public health, volunteer, and private sector channels. Federal cost for this program was estimated at $134 million.

After the CDC memorandum had been forwarded to HEW's Assistant Secretary for Health, the CDC Director conducted a telephone poll of Advisory Committee members concerning the recommendation. He reported that most of the members favored the mass immunization program.

The recommendation was approved virtually intact through HEW, the Office of Management and Budget, and the President's Domestic Council. On March 24, 1976, before endorsing the program, the President met with HEW officials, flu experts, and other scientific advisors. Immediately afterwards he announced the national swine flu program to the press. By April 12, the House and Senate had passed the joint resolution which provided about $135 million for a comprehensive, nationwide immunization program. The President approved the resolution on April 15.

Between April and July 1976, HEW initiated and completed initial clinical trials of the vaccine and awarded project grants to help States and territories implement the program. Meanwhile, no additional swine flu outbreaks had been detected anywhere in the world, despite increased surveillance.

As HEW began negotiations with vaccine manufacturers, however, a serious problem jeopardized initial program implementation--the question of liability insurance for vaccine manufacturers and other participants. In July the manufacturers threatened to halt production and to withhold existing supplies of vaccine unless the problem could be solved. At this time, HEW and the manufacturers generally concluded that legislation would be required

to solve the problem. (See ch. 3.) On August 10, 1976, the Congress, spurred by HEW and an urgent Presidential request and possibly reacting to mysterious deaths in Pennsylvania (although attributed to a cause other than swine flu--Legionnaires' Disease) approved the stalled swine flu program by authorizing the National Swine Flu Immunization Program of 1976 (Public Law 94-380, 42 U.S.C. 247b). Projects began immunizations on October 1.

JUSTIFICATION BASED ON SCIENTIFIC JUDGMENTS AND ASSUMPTIONS ABOUT HEALTH CARE NEEDS AND SYSTEM CAPABILITIES

Many of the limited facts available were used to both support and condemn the program. The validity of either position could be tested only over time. The decision to vaccinate everyone in the United States was based primarily on scientific judgments that a swine flu pandemic could occur at any time, regardless of whether additional outbreaks were detected in the interim. Underlying this decision were several assumptions, including (1) vaccine manufacturers could produce enough acceptable vaccine and (2) the public and private health care system could deliver the vaccine promptly to the entire population. Criticism of this decision was also based on judgments and assumptions.

Because less than one-fourth of the total U.S. population has been vaccinated, assumptions of health system delivery capabilities were never fully tested. (See ch. 7.) The manufacturers did not produce the quantities of vaccine needed to immunize the entire population. (See ch. 6.)

Conflicting opinions about the need to vaccinate

In April 1976 consultants from 15 countries attended a World Health Organization meeting to discuss the implications of the Fort Dix outbreak. One recommendation from the meeting urged countries producing flu vaccines to continue producing Victoria flu and Hong Kong flu 1/ vaccines and to initiate production of a killed virus vaccine made from the new swine-flu-like virus. Three possible strategies proposed for using the swine flu vaccine were (1)

1/This flu strain is of a different type and is much milder than the one which caused the 1968-69 Hong Kong flu pandemic.

stockpiling it as an emergency measure, (2) combining it with the currently recommended vaccines, or (3) administering it as an individual vaccine. Each country was to decide which course was most appropriate for its resources and needs.

A CDC official stated that several countries in addition to the United States planned swine flu programs. Only the United States decided to administer the vaccine in a mass immunization program.

Between the announcement of the national program in March and the first vaccinations in October, no other swine flu outbreaks were detected. While HEW officials and Federal Government advisory groups supported the program during this time, criticism came from other scientists and physicians, public health officials, and public interest groups.

Canada, the only country to originally endorse the U.S. position, subsequently recommended selective rather than mass immunization. A CDC official reported that world opinion, though not openly critical of the U.S. decision, was to some degree, skeptical. However, an HEW official discounted most of the skepticism from other countries as mere rationalization. He stated that few, if any, other countries could readily produce enough vaccine for a mass program even if they wanted one. We did not evaluate other countries' vaccine production capabilities.

Critics' positions

As time passed without any detected cases of human-to-human spread of swine flu, critics argued that there was little probability of a pandemic. Further, because any immunization program carries a risk of adverse vaccine reactions, some critics urged that the vaccine be stockpiled until further evidence of virus spread became available. The critics' major contentions follow:

--A worldwide surveillance network had failed to detect any outbreak of swine flu since the outbreak at Fort Dix. Because previous pandemics have always been preceded by at least several outbreaks, the likelihood of a swine flu pandemic during the 1976-77 flu season became so remote that mass immunization was not justified.

--The evidence collected at Fort Dix and in a subsequent British study suggested that the new strain of swine flu was milder than other human flu viruses and that the single death attributed to the new strain could be disputed. The evidence suggested also that the new strain lacked the ability to compete successfully against other flu strains, especially Victoria, which was more likely to be the predominant strain during the 1976-77 flu season.

--The severity of the 1918-19 pandemic was due to conditions peculiar to the time. Overcrowding in military camps and widespread troop movements provided ideal conditions for propagating the disease around the world, and no antibiotics were available to combat secondary infections, such as pneumonia.

--The effectiveness of vaccines in protecting against flu is questionable.

--A mass immunization program would drain public health resources and result in lost opportunity costs to other programs.

HEW's position

HEW officials recognized that the swine flu virus might not result in a pandemic. However, they stated that major antigenic shifts in flu viruses had always led to pandemics. They pointed out that killed-virus flu vaccines had rarely been associated with severe adverse reactions or permanent disability. Such vaccines were considered medically safe and quite suitable for widescale community use.

HEW officials opposed stockpiling. They estimated that, even under ideal conditions, 3 to 3-1/2 months would would be required to distribute and administer the vaccine and allow it time to attain maximum effect. In previous epidemics, the average time from isolation of a new virus to major outbreaks in the United States was less than 6 months. They said that stockpiling could result in planning and organizing a mass immunization program, only to have an epidemic occur because they failed to stay ahead of the virus. They considered such action generally contrary to the concept of preventive medicine.

HEW positions on other criticisms follow:

--Although the Fort Dix outbreak was short lived, it was extensive. Similar small outbreaks elsewhere may have occurred, but gone undetected. These outbreaks may be "seeding" the population with the swine flu virus before exploding into a pandemic.

--The swine flu virus at Fort Dix was similar in structure to the 1918-19 virus. However, there was no data to justify an assumption that the Fort Dix virus would be as strong as the earlier virus. The strength of a flu virus cannot be determined before its epidemic occurrence in large numbers of people. The decision to vaccinate had to rest solely on the recognition that most of the population was susceptible to the new virus.

--The Hong Kong pandemic of 1968-69 resulted in over 27,000 excess deaths and cost an estimated $3.9 billion in medical care, industrial and school absenteeism, and future earnings of those who died. It is better to gamble with unnecessary health expenditures than with unnecessary death and illness.

--Although past immunization efforts against the Asian flu in 1957 and the Hong Kong flu of 1968-69 had failed to have any perceptible effect, it was because too little vaccine was administered too late. Isolating a new flu strain at the end of one flu season, as was done with the new swine flu virus, presented a unique opportunity for the Nation's health system to organize itself in time to prevent a flu outbreak or an epidemic during the next flu season.

--Lost opportunity costs to other programs were unpredictable and were not considered significant enough to halt the program.

Questionable assumptions about health system capability

HEW officials assumed that (1) manufacturers would be willing and able to produce enough acceptable vaccine in a short time and (2) State and local public health officials and private physicians would be willing and able to plan, organize, and execute the mass immunization program. The testing of these assumptions surfaced substantial problems regarding:

--The issues of professional and product liability, heightened by the prospect of a mass immunization program. (See ch. 3.)

--The combined ability of manufacturers and the Federal Government to produce, test, and make available sufficient quantities of acceptable vaccines for the entire population. (See chs. 4, 5, and 6.)

--The capability and willingness of State and local governments and private health care providers to effectively participate. (See ch. 7.)

--The direct and indirect costs of the program. (See ch. 8.)

HEW confronted these significant problems as they arose and at the same time recognized that, as time passed without an outbreak of swine flu, the probability of an epidemic decreased.

HEW never considered the continued absence of a reported outbreak of swine flu as sufficient evidence that a swine flu epidemic would not occur. Therefore, HEW never formally re-evaluated the decision to continue the program. Consequently, the program, although delayed and hampered by the problems which plagued it, was continued until December 1976. It was stopped at this time because of several reported instances of Guillain-Barre syndrome potentially related to the vaccine. A limited program using bivalent vaccine was restarted in February 1977, so that high-risk individuals would be immunized against Victoria flu.

CONSIDERATIONS AND RECOMMENDATION FOR FUTURE IMMUNIZATION PROGRAMS

Although detecting and preparing for swine flu was unique, the planned mass immunization program encountered some problems that will likely recur with any future mass immunization. At least some of the problems may--or already do--affect other public or private health care efforts.

Some questions that will have to be answered are:

--Was the Fort Dix outbreak an isolated incident that might have gone undetected in previous years?

--Must there be more than one outbreak, such as the one at Fort Dix, before an epidemic can be reasonably predicted?

--Must an epidemic be scientifically predictable--rather than just possible--before mass immunization is justified?

--When more than one flu virus is present, how can determinations best be made as to what vaccine or combination of vaccines is needed most by different segments of the population?

--How can the disease surveillance system be improved to better identify and trace virus spread?

--How can the availability of sufficient quantities of safe and effective vaccines best be assured?

--What will be the Federal role in covering professional and product liability claims?

--How can effective participation of State and local government and private health care providers be assured?

--How will the costs and benefits of any mass immunization program be determined or be related to potential alternate uses of public health resources?

For any immunization program as large or as concentrated as the swine flu program, the questions would likely have to be broadly considered again by all parties involved. The solutions devised for the swine flu program were not intended as a pattern for future efforts.

In any event, where program decisions must be made based on very limited scientific data, we recommend that the Secretary, HEW, establish key points in the program process for formal program reevaluation.

CHAPTER 3

SWINE FLU PROGRAM LIABILITY

IMPLICATIONS FOR THE FEDERAL GOVERNMENT

Liability problems threatened to end the national swine flu program before vaccinations could begin. Therefore, the Congress passed Public Law 94-380 providing for an exclusive remedy against the United States for personal injury or death arising out of the program. Although effective at getting the program started, this solution

- --may result in a profit to the insurance companies of nearly the entire $8.65 million premium for vaccine manufacturer swine flu liability insurance;
- --leaves unresolved insurance company concerns about nonmeritorious claim risks; and
- --may result in indeterminable additional costs to the Government for litigation, awards, and settlements because of potential weaknesses in both the informed consent form and procedures.

As of March 31, 1977, claims and suits against the Federal Government for damages from the swine flu program totaled over $300 million. The total amount of claims and suits ultimately filed against the Federal Government may exceed $1 billion. (See p. 83.)

Liability will continue to be a problem for future federally run or sponsored mass immunization programs. Therefore, permanent solutions to the problems surfaced by the swine flu program should be sought.

LEGISLATIVE SOLUTION TO LIABILITY CONCERNS

Liability became an issue in the swine flu program because several participants, including manufacturers and some States, could not obtain total liability coverage for the program. The manufacturers threatened to halt swine flu vaccine production and to withhold vaccine already produced if their liability concerns were not resolved. In several States lack of liability insurance could have inhibited program implementation. (See pp. 73-75.)

Insurance company concerns

Insurance officials pointed out that, in the proposed immunization program, public exposure and visibility of manufacturers would be magnified many times. They said that this exposure, coupled with the current legal climate, which rewards rather than reimburses claimants, could subject the manufacturers to an incalculable number of claims, and particularly to nonmeritorious claims alleging injury from immunization. One insurance official estimated that even if none of the swine flu claims were meritorious, potential defense costs alone could range from $9.5 billion to $25 billion. The result would be substantial losses for both insurance companies and the manufacturers, regardless of negligence in producing or distributing vaccine. Consequently, because of what the insurance companies' considered unmeasureable, and thus uninsurable, financial risks, they excluded the swine flu vaccine from the manufacturers' normal product liability coverage.

Manufacturers' concerns

Because of their experience with flu vaccine, the manufacturers did not expect the Government to indemnify them for their own negligence in producing or handling the vaccine. Their standard product liability policies normally include a substantial deductible portion. Between 1970 and 1975, over 70 million doses of flu vaccine were produced and distributed with fewer than 20 claims for damages. At least five of these claims were found to be nonmeritorious, and the maximum settlement for the others was $26,000. All costs to litigate, defend, and settle these claims were paid by the manufacturers under their deductibles.

The manufacturers' liability concerns stemmed from recent court decisions holding the manufacturers liable for injury or adverse reactions where no negligence in producing or handling vaccine was shown. The courts held the manufacturers strictly liable unless they communicated warnings of any hazards to the users of their products. In two cases, Reyes v. Wyeth Laboratories, Inc., 498 F. 2d 1264 (5th Cir. 1974), and Davis v. Wyeth Laboratories, Inc., 399 F. 2d 121 (9th Cir. 1968), the manufacturers of Sabin live polio vaccine were held liable to plaintiffs vaccinated in public clinics who were not properly warned of the hazards.

The manufacturers believed that the courts might apply the same strict liability standards in any litigation arising out of the swine flu immunization program. The vaccine would frequently be administered on a mass basis in public clinics

without the physician-patient relationship that generally accompanies the administration of prescription drugs. Consequently, the manufacturers sought protection against claims attributable to the swine flu immunization program other than those claims attributed to their own negligence.

The solution: legislation

HEW attempted to meet the concerns of the manufacturers by offering to include provisions in the vaccine contracts which would make it clear that the Government would assume the usual responsibilities of the manufacturers for (1) investigating and determining the risks of vaccination, (2) developing a statement of the benefits and risks of vaccination, and (3) taking reasonable steps to assure that all persons vaccinated would be notified of those risks and benefits. The Anti-Deficiency Act (31 U.S.C. 665 (a)) precluded HEW from including indemnification provisions in the contracts because such provisions might create obligations in excess of HEW's appropriation. Consequently, HEW could not assure the manufacturers that they would be protected from liability by a Government-developed information statement on the benefits and risks of vaccination.

In enacting the National Swine Flu Immunization Program of 1976, the Congress provided for an exclusive remedy against the Federal Government for personal injury or death arising out of the manufacture, distribution, or administration of the swine flu vaccine. It also made the Federal Government responsible for developing and implementing a written informed consent form and procedures for assuring that the risks and benefits of the vaccine were fully explained to each individual immunized.

Under the act, all claims for injury or death resulting from the program must be filed against the Federal Government and decided through procedures of the Federal Tort Claims Act (28 U.S.C. 2671 et seq.), as amended for purposes of the swine flu program. The Government has the right to recover costs to defend and settle these claims if negligent conduct or failure to carry out any contractual obligation or responsibility by participants is found. As a result of the act, the manufacturers agreed to continue producing and to distribute vaccine.

LIABILITY INSURERS' PROFITS FROM MANUFACTURERS' SWINE FLU INSURANCE MAY NEARLY EQUAL PREMIUMS

To insure against the Federal Government's right to recover, the four vaccine manufacturers obtained a total of

$230 million of liability insurance. The first $10 million of the $230 million is self-insured by the manufacturers. The remaining $220 million was purchased from more than 60 foreign and domestic insurance companies for an $8.65 million premium. Because this cost is considered a vaccine production cost, the Federal Government will fund both the $10 million self-insurance and the $8.65 million premium, or a total of $18.65 million.

Potential insurance company costs for manufacturer negligence are limited under the program. Under swine flu legislation, the Federal Government assumed the financial risks of nonmeritorious claims. Also the manufacturers' liability policies expand the definition of loss to include costs of litigation and payments for expenses incurred in investigating, negotiating, settling, or defending any right-to-recover suit by the Federal Government. According to an insurance industry representative, general liability policy limits normally apply only to costs incurred for claims and suits that result in a settlement or an award.

In addition, the premiums will not be retrospectively adjusted to reflect actual claims experience. Therefore, no portion of the premium will be refundable to the manufacturers, and hence the Government, even if a less-than-expected amount of claims are experienced.

Because of these insurance policy limitations, the liability legislation, and Federal funding of both the self-insurance and liability insurance premium, all recoveries by the Federal Government from manufacturers for litigation and settlement costs, up to $18.65 million, will be a recovery of Federal funds, the first $10 million of which will come from the manufacturers' self-insurance fund.

The insurance companies will defend the manufacturers in suits initiated by the Government. All costs to defend the manufacturers will be charged against the $10 million self-insurance fund. If the manufacturers are found negligent, litigation costs and settlements originally incurred by the Government will also be charged against the $10 million self-insurance until it is exhausted. Only then will costs be assumed by the insurance companies. The unexhausted balance of the manufacturers' self-insurance fund, plus interest, is returnable to the Federal Government. If the self-insurance fund is never exhausted, no expenses for litigation and settlement of claims will be charged against insurance company funds. Consequently, according to an insurance industry representative, the $8.65 million premium, less brokers commission and anticipated administrative expenses, could be total profit.

It is too soon to determine how much of the $8.65 million premium the insurance companies will realize as profit. But, if the Congressional Budget Office estimate is accurate, nearly the entire premium will be profit.

Before the program began, the Congressional Budget Office projected that only $2.58 million in liability payments and litigation costs will be recovered from all third party program participants. Besides the vaccine manufacturers, this projection included all participating public or private agencies and medical or other health personnel providing vaccination without charge in accordance with informed consent procedures. Even if all recoveries are from the vaccine manufacturers, the $2.58 million would be paid out of the $10 million self-insurance funds. The insurance companies would, therefore, still make about an $8.65 million profit.

The accuracy of the Congressional Budget Office's projections will be proved only by experience. However, (1) between 1970 and 1975, the insurance companies paid no claims for negligence in the manufacture of flu vaccine and (2) FDA officials reported that, in addition to reviewing manufacturer test results, FDA had performed tests for safety, potency, and sterility on every lot of vaccine before release to the public. (See ch. 4.) Although the drug manufacturers are not relieved of their production liability, HEW's approval of every lot may significantly reduce the likelihood that the Government could recover for damages awarded or paid based on manufacturers' negligence.

UNRESOLVED INSURANCE INDUSTRY CONCERNS

The swine flu program legislation removed the insurance companies' concern about the financial risks of nonmeritorious claims by providing an exclusive remedy against the Federal Government under procedures of the Federal Tort Claims Act. This act, with certain exceptions, eliminates trial by jury, restricts liability for punitive damages, and limits attorney fees to a maximum of 25 percent of any judgment or settlement. Also a Department of Justice official said the Department's costs to litigate a claim or suit are substantially less than the costs of a private law firm. As a result, the number of nonmeritorious and frivolous claims and the costs to defend against them may be reduced. Additionally, the number of claims initially anticipated could be reduced because less than 25 percent of the population was vaccinated. As a result, the swine flu program will provide little experience for the insurance companies to predict nonmeritorious claim risks for future programs, especially ones that provide for remedy under any procedure other than the Tort

Claims Act. Consequently, the insurance companies' concern which caused them to withdraw coverage of the manufacturers for the swine flu program will continue to exist.

LIABILITY IMPLICATIONS OF FEDERAL RESPONSIBILITY FOR INFORMED CONSENT

Potential weaknesses in the consent forms used in the swine flu program and in the Federal Government's procedures to assure that every person immunized was informed of the vaccine's benefits and risks may result in excessive costs to the Government for litigation, defense, and settlement of claims.

If through Federal tort claims procedures and subsequent litigation, either (1) the informed consent form is judged insufficient to warn of the risks or (2) consent was not given or is judged inadequate because procedures used to communicate a warning in a particular case were deficient, the Federal Government may be held liable for damages caused by both severe and mild adverse reactions.

Although the Davis court case (see p. 18) defined the parameters of informed consent and provided a standard to determine when a warning is necessary, it did not specify how this duty was to be satisfied. A study performed for CDC indicates that there is wide divergence of opinion among the courts concerning the standard to be applied in determining whether the consent given is actually informed.

It will take several years to evaluate the effects of (1) decisions through Federal tort claims procedures about liability for the swine flu informed consent form and for the procedures used to communicate the warning in each case and (2) whether the Federal Government can or will recover costs of litigation and settlement from program participants negligent in informed consent procedures. In the interim, the Government can take additional steps to promote informed participation by prospective vaccinees in future immunization programs.

Potential weaknesses in consent form

There are no specific criteria for drafting informed consent forms. The adequacy of the language is defined only after being tested through legal procedures. However, the Davis court case set forth as one parameter that potential vaccinees must receive full disclosure of the existence and extent of the risk.

The informed consent form used for the swine flu program between October 1 and December 16, 1976, contained (1) no

specific warning of possible neurologic disorders, (2) a controversial statement concerning potential vaccine effects on pregnant women, and (3) no specific warning of the probability of getting the flu despite receiving the recommended vaccine. Information available before the swine flu immunizations began (1) identified neurologic disorders as a possible severe reaction associated by time with flu immunization in general, (2) questioned the accuracy and clarity of the statement concerning potential vaccine effects on pregnant women, and (3) estimated the risk of contracting the flu despite vaccination. As a result, the Federal Government's position with regard to claims resulting from any of these reactions may be weakened.

Informal procedures used to develop consent forms

Without criteria or formal procedures for developing informed consent forms, HEW's chances of making potentially expensive errors of omission were increased.

Before the passage of Public Law 94-380, in August 1976, HEW had drafted, printed, and distributed to the projects a one-page informed consent form. (See apps. I and II.) The form was entitled, "Important Information About Swine Influenza (Flu) Vaccine" and was produced in two nearly identical versions, one for persons who would receive monovalent vaccine and one for persons who would receive bivalent vaccine. At the bottom of the two versions was a section to sign and tear off, entitled "Registration Form."

The form was drafted primarily by CDC with the advice of an HEW attorney. CDC officials said that the risk and benefit statements on the form had been drafted based on flu and vaccine information provided by CDC personnel and on consideration of recent court decisions on manufacturers' informed consent liability. The form was then reviewed by personnel in each of the 63 grant projects, the Advisory Committee on Immunization Practices, and other CDC personnel. Their feedback was incorporated where appropriate.

Public Law 94-380 required HEW to consult with the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) on the content of the consent form. Formal approval was not required. The form was reviewed by the National Commission at a meeting with CDC officials on August 17, 1976. During the meeting, Commission members expressed concern over several issues. At least two members thought a new form should be drafted. The National Commission did not prepare a formal list of mutually agreeable recommendations at this meeting.

CDC officials at the meeting drafted a second page "Introduction" to the form (see app. III) in response to the National Commission's concerns. In addition, the "Introduction" included a statement to assure that individuals are advised with respect to their rights and remedies relating to any adverse effects of vaccine administration. A CDC official said that the Director of CDC had obtained oral approval of this "Introduction" from the National Commission Chairman. By August 31, 1976, over 83 million "Registration" forms and 39 million "Introductions" had been printed and shipped to CDC; the States; and to other Federal agencies, such as the Veterans Administration and the Bureau of Prisons. Also several States had printed both forms.

On September 20, 1976, the Chairman of the National Commission sent a letter to the Director of CDC recognizing CDC's "good faith" effort to incorporate the Commission's concerns, but expressing continuing concern about (1) contradictory statements on the two pages concerning vaccine safety during pregnancy, (2) possible confusion concerning the purpose of the "Introduction," and (3) incomplete information on whom individuals were to contact in cases of adverse reactions. No changes in the form were made with regard to these comments until after the program had been halted in December 1976. A new consent form was subsequently developed.

CDC drafted the new form during January because of concerns expressed by the Assistant Secretary for Health, the Advisory Committee on Immunization Practices, and others that a warning should be included about the risks of Guillain-Barre syndrome. The new one-page form, entitled "Voluntary Consent Form" (see app. IV), had a tear-off section entitled "Consent." It also incorporated new language to resolve the continuing concerns of the National Commission and others about the adequacy of the first two-page form. The Assistant Secretary requested a new form for the potential restart of the immunization program.

CDC's draft was to be reviewed by the National Commission at its next meeting scheduled for February 15, 1977. However, on February 7, 1977, the Secretary of HEW convened an open meeting of distinguished medical, scientific, and other experts to consider restarting the program. After the meeting, the Secretary announced a partial resumption of the immunization program for high-risk individuals to begin on February 8, 1977. CDC's draft of the new consent form was revised by the Secretary, with verbal input from the National Commission and congressional committee staff. However, the National Commission did not make official comments or give formal approval.

CDC officials said that the new form is not a balanced risk/benefit statement, only a risk statement. They believe the form will discourage some people from being vaccinated because it disproportionately portrays the risks. Although the new form states that 3 of every 4 persons vaccinated will probably not get the flu, in reality the probability is closer to 9 of 10, according to some CDC officials. Without a widespread epidemic of flu, the extent to which the consent form influences individuals to be or not to be vaccinated is indeterminable.

No specific warning on neurologic disorders

Vaccine recommendations made by the Advisory Committee on Immunization Practices in July 1976 warned of three possible types of adverse reactions to flu vaccinations:

--Fever, malaise (discomfort), myalgia (muscle pain), and so forth.

--Allergic reactions.

--Neurologic disorders.

Each of these warnings was specified in CDC's Morbidity and Mortality Weekly Report on July 23, 1976, and on circulars packaged with the vaccine for distribution. The first two were specified on the original "Registration" form. No specific warning on neurologic disorders was included.

The Advisory Committee's recommendation stated that a survey of medical literature since the early 1950s had revealed only about a dozen reports of neurologic disorders, including three fatalities, involving persons receiving flu vaccine. Two of the fatalities displayed clinical characteristics or had antecedents which strongly suggested causes other than flu vaccine. Evidence suggested that the third could have been caused by another viral disease. However, the association in time may be significant enough to warrant a warning.

CDC officials stated that reactions such as neurologic disorders were satisfactorily covered on the "Registration" form by the statement under "Special Precautions," which combined severe and allergic reactions stating that

> "As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated

with severe or fatal reactions. In some instances people receiving the vaccine have had allergic reactions."

In reviewing this form and the Advisory Committee's supplemental recommendation, the National Commission had no comments on the lack of a specific neurologic disorders warning.

Because of the incidences of encephalitis and Guillain-Barre syndrome and resultant claims for damages the adequacy of this statement is important in terms of protecting the Government. A study of liability in preventive medicine performed for CDC concludes that it is likely the courts will hold that there is a duty to warn even when the risk is statistically insignificant. Consequently, by generalizing the Advisory Committee's specific statement on neurologic disorders, HEW increased its risks of adverse decisions through the Federal tort claims process, which could significantly increase Federal costs of litigation and settlement. Because the Federal Government is solely responsible for the content of the informed consent form, it is unlikely that any of these increased costs would be recoverable because of other program participants' negligence.

The new consent form, issued in February 1977, has a specific statement on the risks of Guillain-Barre syndrome, but does not contain the neurologic disorders warning included in the Advisory Committee's July 1976 recommendations.

Controversial informed consent statements for pregnant women

The initial "Registration" form stated simply that "flu vaccine can be taken safely during pregnancy." The Advisory Committee on Immunization Practices' July 1976 supplemental recommendations concluded that

"* * * there are no data specifically to contraindicate vaccination with the available killed virus vaccine in pregnancy. Women who are pregnant should be considered as having essentially the same balance of benefits and risks regarding influenza vaccination and influenza as the general population."

During its review of the "Registration" form, the National Commission discussed these two statements with HEW officials. Some Commission members concluded that the positive statement on the "Registration" form read like a warranty and should be replaced by a statement similar to the conclusion made by the Advisory Committee. The Commission did not endorse the

wording of the Advisory Committee's conclusion, however, because it could not be easily understood by the public.

The second page "Introduction" form prepared in response to the National Commission's concerns included the exact wording of the Advisory Committee's statement on pregnancy. In a September 20, 1976, letter to the Director of CDC, the National Commission Chairman expressed additional concern over the issuance of another pregnancy statement on the second page "Introduction" rather than issuance of a single page revised form. The Commission was concerned that the statement on the "Introduction" was not necessarily consistent with the statement on the "Registration" form and may complicate understanding with respect to the advisability of vaccination during pregnancy. Also neither statement resolved the Commission's earlier concerns that (1) the clinical trials had not determined either the safety or efficacy of the vaccine with regard to pregnant women and (2) the Advisory Committee's conclusion had been based on experience rather than on conclusive studies showing benefits and risks.

Others also expressed concern about the statements on pregnancy. In congressional testimony on September 13, 1976, an attorney from a public interest law firm stated that "* * * the lack of data specifically contraindicating vaccination during pregnancy is due to the lack of any studies which show either the indications or contraindications during pregnancy." The attorneys also noted that (1) the Advisory Committee's conclusion was not written in lay terms and could not be easily understood by the public, (2) the conclusion gave no information concerning the risks to the fetus, (3) the assertion that the swine flu vaccine can be taken safely during pregnancy had not been deleted from the "Registration" form, and (4) the two statements appearing on two separate pages might be difficult to follow or synthesize. The attorney suggested that the two-page informed consent form be rewritten to be clear, straightforward, and correct.

The attorney also indicated that because of the problems with both the "Introduction" and "Registration" forms, the Federal Government could be subjected to large monetary settlements or awards for injuries to pregnant women or their offspring regardless of defects in the vaccine or negligence in its administration.

The new consent form uses neither statement on pregnancy from the original forms. Instead, it states simply for pregnant women:

"There is not now any specific data on whether the risks are the same or different from what they are for the general population. For this reason a pregnant woman should be advised by a doctor on the benefits and risks for her or her offspring."

A CDC official said that this change had been made in response to the concern of the National Commission and others.

No statement of probability of contracting swine flu after being vaccinated

The "Introduction" form states that a special swine flu vaccine was prepared and tested which should protect most people who receive it. The Director of CDC's Virology Division, Bureau of Laboratories, stated that the results of the clinical trials for swine flu vaccine show that (1) at least 70 percent of persons over 25 years of age who receive the vaccine will be fully protected and (2) up to 90 percent of the vaccinees will be protected from any serious infection which would cause confinement to bed or hospitalization. (See ch. 5.) Therefore, 3 of every 10 persons vaccinated could still contract swine flu.

An analysis of recent court decisions, performed for CDC before swine flu immunizations began, indicated that for the consent to be truly informed, the warning must specify the risks of contracting the disease from both the vaccine and the natural virus. Though there was no recognized risk of contracting flu from the swine flu vaccine, there was a quantifiable risk of contracting the flu after vaccination.

The lack of such a specific warning would become important only if persons who were vaccinated contracted swine flu and as a result made claims for damages. Then, through Federal tort claims procedures, a determination would have to be made as to whether the word "most" adequately conveyed the risk involved. The new consent form, although possibly oversimplified in its statement, does specify that "a single shot will protect approximately three out of four persons age 25 and over * * *."

Informed consent procedures: meeting HEW guidelines could not always be assured

Even if HEW's prescribed informed consent procedures are determined adequate, neither HEW officials nor project coordinators could visit every clinic to assure that the procedures were followed and that every person immunized was informed of

vaccine benefits and risks. This further adds to the prospect that, regardless of defects in the vaccine or negligence in its administration, the Federal Government can be held liable for damages caused by both severe and mild vaccine reactions. The extent of resultant litigation and settlement costs depends on the number of claims filed, extent of injury, and decisions on the adequacy of procedures used in each case. The methods used by HEW and the States to assure compliance with informed consent guidelines are discussed in more detail in chapter 7. (See pp. 69-71.)

CONSIDERATIONS AND RECOMMENDATIONS FOR FUTURE IMMUNIZATION PROGRAMS

Insurance executives stated that because the Federal Government will control all key aspects of any immunization program conducted as a matter of public policy, the Government should be responsible for both the liability and the costs of litigation. HEW's Assistant Secretary for Health stated that a national policy concerning compensation will have to be developed for any future mass immunization program.

So that resolution of the liability issue does not delay or adversely affect public acceptance of future programs, we recommend that the Congress establish a national liability policy before another mass immunization program is needed.

The Secretary of HEW is required by the liability legislation to study the scope and extent of liability for personal injury or death arising out of immunization programs and alternative approaches to providing protection against such liability. We recommend that this study focus on the most cost-effective approach to compensate vaccine injury victims which at the same time will promote the continual production of vaccines by the manufacturers.

Two alternatives to consider for manufacturer liability insurance

The liability legislation for the swine flu program makes participants responsible for their own negligence. As shown, this approach may result in profits for the insurance industry at Federal expense with respect to the vaccine manufacturers. However, because of the potential expense related to defending nonmeritorious claims, the insurers believe that the manufacturers will be uninsurable for future mass immunization programs at an acceptable premium, without some Federal assumption of liability. We recommend that the Secretary, HEW, consider

two alternatives for Federal assumption of liability at less cost than for the swine flu program as discussed below.

First, if experience gained from the swine flu program shows that considerable savings can be realized and if HEW intends to continue rigorous testing and approval of every vaccine lot, then the Secretary, HEW should consider total Federal assumption of the liability coverage for vaccine production. In effect, by giving the manufacturers $10 million for self-insurance and $8.65 million for the liability insurance premium, the Federal Government may already have relieved the manufacturers of their financial responsibility for negligence and may have assumed financial liability for vaccine production.

A second alternative would be for the insurance industry to make premiums for the manufacturers' liability insurance adjustable retrospectively based on claims experience. Consequently, if claims do not exceed the premium, the manufacturers, and hence the Government, could recover the unused premium minus insurance company costs. However, if costs to litigate and settle claims exceed the face value of the insurance coverage, the manufacturers, and hence the the Government, will incur costs in addition to the initial premium. Because of the limited profit potential of this approach, its success would depend on insurance company willingness to insure the manufacturers on such a basis.

Informed consent recommendation and considerations

To evaluate the effect of Federal responsibility and liability for informed consent will take years. We recommend that the Secretary, HEW, monitor this process as it occurs for possible future program implications. In the interim, steps such as the following should be considered:

--Develop criteria and standard procedures for drafting and reviewing informed consent forms. Such criteria and procedures should allow for the timely development of the form without time-pressured consideration of appropriate comments and opinions. Full disclosure of the benefits and risks of vaccination should be clearly stated.

--Develop a plan to systematically monitor and document that HEW's informed consent procedures and requirements are implemented at the projects and clinics. (See pp. 75 and 76.)

CHAPTER 4

REGULATION AND TESTING OF VACCINE USED FOR THE SWINE FLU PROGRAM

All vaccine released for public use in the swine flu program that we reviewed met FDA potency and safety standards. The vaccine underwent testing procedures more extensive than those used for flu vaccine released in 1975.

To insure that potency requirements were met and to verify potency test data submitted by manufacturers, FDA performed its own tests before releasing swine flu vaccine for public use. FDA potency test data for about 55.5 million doses indicated that about 15.5 million doses were subpotent. FDA did not permit this vaccine to be released to the public until it met the minimum potency requirements. FDA tests also showed that some vaccine used in the clinical trials did not meet specified potency levels. Further, the potency test has deficiencies as an indicator of protection provided by the vaccine.

Manufacturers and FDA routinely conducted safety and other tests on vaccine before it was released to the public. Similar tests were not always conducted on clinical trial vaccine lots by FDA until after the lots were made available for use in the trials. Consequently, the added protection provided to the general public by FDA verification testing of manufacturer test data was not afforded to all clinical trial participants.

FDA REGULATORY ROLE

Although flu vaccine has been licensed since the 1940s, the vaccine's composition is periodically changed to conform to the prevailing flu virus causing illness. When the composition is changed or other changes are made, such as those involving the manufacturing process, a license amendment is submitted. FDA officials stated that, based on the information submitted in the amendment, they determine whether the changes require clinical testing under investigational new drug regulations.

Because swine flu vaccine was to be made from a new flu virus strain, FDA had to approve a flu vaccine license amendment for each manufacturer to permit release of vaccine. FDA also establishes potency levels and certifies vaccine labels and package circulars proposed by the manufacturers.

Investigational new drug applications

When FDA determines that clinical studies are necessary, the sponsor of a new drug must test the drug under closely controlled circumstances. The evidence obtained from such studies is included in a license application submitted by persons seeking to market a biological product.

Under FDA procedures, the sponsor, after submitting an investigational new drug application, must wait 30 days before beginning clinical trials unless notified by FDA that trials may begin sooner. This delay enables FDA to review the application to make certain it contains necessary information and to insure that patients are not exposed to unwarranted risks. The sponsor may initiate clinical testing 30 days after FDA has received its application, unless in the meantime FDA has raised objections. FDA may waive the 30-day requirement if it believes such action is justified. The 30-day period was waived for the swine flu clinical trials because FDA decided that very little time was available before the trials had to begin. Also, according to HEW officials, the 30-day period was waived, in part, because of the extensive experience with flu vaccines.

FDA usually requires the sponsor to submit, as part of the application, a report on the results of preclinical animal tests from which the sponsor has concluded that clinical trials can be conducted with reasonable safety. FDA did not require preclinical animal investigations because, according to FDA officials, the swine flu vaccine was not a completely new product. FDA determined that existing data and experience on flu vaccine was applicable and adequate to satisfy preclinical requirements.

Requirements after approval of vaccine license amendment

After approval of all licensing requirements and before vaccine is released to the public, FDA may require manufacturers to submit samples of production lots and related test results. FDA reviews these and sometimes conducts tests within its own laboratories to verify the results obtained by the manufacturers. FDA may either release a lot or reject it when necessary to insure conformance with standards.

FDA is required to insure that manufacturers continue to meet standards for safety, purity, and potency after issuance of a license. FDA officials said that this legislative mandate is met when they review manufacturer test records and

inspect manufacturing facilities. According to FDA officials, FDA is not required by law to perform its own tests on flu vaccine for clinical use or for release to the public.

Manufacturers must show through the required tests that their product conforms to standards of safety, purity, and potency. Other tests are performed to verify amounts of ingredients specified on vaccine labels.

TESTING PROCEDURES FOR SWINE FLU PROGRAM VACCINE MORE EXTENSIVE THAN THOSE USED IN 1975

During 1975 FDA reviewed manufacturer test results and performed its own tests for potency, sterility, safety, and endotoxin (an undesirable flu vaccine contaminant) levels on every lot of flu vaccine before its release to the public. FDA performed the same tests on swine flu program vaccine lots covered by our review. FDA reported that these tests had been conducted on every lot of vaccine released. In addition, FDA's assays of various vaccine ingredients were expanded over 1975 levels because of increases in personnel and funding provided by the swine flu program.

WEAKNESSES OF POTENCY TEST

Since 1968 manufacturers have been required to determine the potency of flu vaccine by use of the chicken cell agglutination (CCA) test. The test assesses virus concentration by measuring the ability of the virus to clump chicken red blood cells. It expresses vaccine potency in terms of "CCA" units; the higher the CCA value, the greater the vaccine's potency.

FDA officials and others involved in vaccine regulation have stated that the CCA test is seriously limited as a method of determining the potency of flu vaccine. A potency test is designed to measure the ability of a product to produce a given result by laboratory tests or clinical trials. Preferably, the result measured relates directly to the product's protective value. However, swine flu clinical trials showed that increasing the vaccine's potency did not necessarily result in an increase in antibody response among volunteers.

FDA officials believe that the CCA test has certain deficiencies, which include variations in red blood cells due to different sources of supply and the opportunity for subjective test interpretations. FDA has been unable to correct these problems through workshops with manufacturers.

FDA has researched alternative potency tests since 1968 and obtained data on several experimental potency tests during the swine flu program vaccine clinical trials. FDA officials said that they anticipate having a more reliable and relevant potency indicator in the near future.

FDA AND MANUFACTURERS DIFFER IN POTENCY TEST RESULTS

Three of the four swine flu vaccine manufacturers consistently reported potency test results which were higher than FDA test results for the same lots of vaccine submitted to FDA under the swine flu program. For example, 1 manufacturer's test results on 49 vaccine lots submitted during 1976 showed that 47 had a higher potency value than that shown by FDA's tests, 1 had the same test results, and the remaining lot scored lower.

According to FDA officials, in assessing potency for flu vaccine released to the public, FDA tests every vaccine lot to insure that the manufacturer's vaccine is at least equal to a specified CCA value. In establishing the swine flu vaccine potency level, FDA officials consulted with CDC and National Institute of Allergy and Infectious Diseases officials. These groups agreed that based on clinical trial evidence, the potency requirement for swine flu vaccine should be 200 CCA units. The officials concluded that the clinical trials indicated that adequate antibody responses with acceptable levels of adverse reactions were generally obtained at this potency level.

We reviewed test results for about 55.5 million doses of vaccine that the manufacturers had tested and submitted to FDA for release to the public. Based on the results of its own potency tests, FDA advised the manufacturers that about 15.5 million of these doses were subpotent. In these cases the vaccine was not permitted to be released to the public. Every lot released to the public that we reviewed met FDA potency test requirements.

Potency testing on clinical trial vaccine

Potency problems encountered with vaccine lots submitted for release to the public also existed with lots used in clinical trials. One purpose of testing the vaccine in clinical trials was to establish an effective yet safe dosage level by determining antibody responses and adverse reactions to various potency values. HEW officials tested responses and adverse reactions to each manufacturer's vaccine generally

at potency levels of 200, 400, and 800 CCAs. Clinical trial instructions called for the manufacturers to supply vaccine at these levels. FDA also evaluated several vaccines with lower dosage levels for use in children, as well as another type of flu vaccine that was eventually recommended for high-risk groups.

Three of the 4 manufacturers' test results for 34 vaccine lots submitted for use in the trials showed that in every case manufacturers' potency values exceeded those determined through FDA tests. FDA tests also showed that 29 of the 34 lots were below the desired clinical trial values. For example, 1 manufacturer reported a potency value of 1,224 CCAs for a vaccine lot which, according to FDA tests, had a CCA value of 720; the lot was supposed to have a CCA value of 800. A vaccine lot designated in the clinical trials as a 220-CCA vaccine submitted by another manufacturer contained 228 CCAs based on the manufacturer's tests and only 132 CCAs based on FDA's test.

Appendix V compares manufacturer and FDA clinical trial potency test results for swine flu vaccines. None of the vaccine designated as 400 or 800 CCAs met these levels when FDA tested them. For the 400- or 800-CCA vaccines, the highest FDA potency test results were still lower than the lowest determination made by the manufacturers.

Although FDA tests on clinical trial vaccine indicated that the potency was generally lower than desired, FDA did not require manufacturers to increase the potency to the specified levels before using the vaccine in clinical trials. According to FDA officials, this would have delayed the clinical trials for almost 1 month.

FDA officials said that they had considered that the differences in potency values were to be expected as a result of test variations occurring under the conditions of testing experimental vaccines in a short time. They stated that three of the four manufacturers, based on preliminary CCA testing by the FDA, had in fact added additional antigen to these experimental vaccines. FDA officials said that a long time would be required to obtain vaccine material very close to the 200, 400, 800 estimates and this interval would have seriously delayed the clinical trials. The results of the first clinical trial with these vaccines indicated that they performed comparably over a very broad range of CCA values. They felt that the time required to obtain precise potency values with reformulated vaccines would have greatly delayed, but not changed, vaccine recommendations.

FDA SAFETY TESTS NOT PERFORMED ON ALL VACCINE BEFORE THE CLINICAL TRIALS

Safety tests performed on the swine flu vaccines included (1) a general safety test of the vaccine in animals, (2) tests for sterility and endotoxin levels, and (3) random tests to assay various vaccine ingredients or additives. Our review of selected lots of vaccine showed that FDA had routinely verified manufacturer safety test results before vaccine lots were released to the public. However, according to FDA officials, FDA did not routinely verify manufacturer test data on clinical trial vaccine before it was made available for use in trials. Our review of manufacturer test data for clinical trial vaccine lots and of lots for which FDA safety test results were available disclosed no indication of safety hazards. Still, the added protection provided to the general public by FDA verification testing of manufacturer test data was not afforded to all clinical trial participants.

General safety test

The general safety test in animals is designed to identify extraneous toxic contaminants that may have been introduced into the vaccine through the manufacturing process. The test is time-consuming, requiring a minimum of 7 days. During the test, vaccine is administered to two guinea pigs and two mice. For the vaccine to meet safety requirements, all test animals must survive, show no unexpected or irregular symptoms, and weigh no less at the end of the test period than at the beginning. If these requirements are not met in the initial test, up to two retests are allowed on the species which failed. FDA officials said that retests are allowed because failures may be caused by factors peculiar to the test animal rather than to the product.

We reviewed FDA and manufacturer general safety test results for 52 lots of swine flu vaccine intended for release to the public. Although some retesting was done, all lots ultimately passed both tests.

Other tests

FDA and manufacturer data showed that test results for sterility and endotoxin on every vaccine lot that we reviewed were satisfactory. Also random tests of some ingredients and additives did not indicate any problems.

RECOMMENDATION FOR FUTURE IMMUNIZATION PROGRAMS

Because of the weaknesses in the CCA test for potency and the continual differences in manufacturer and FDA test results, FDA should continue to perform potency tests on all lots of flu vaccine until manufacturer test results can be relied on. In addition, the Secretary, HEW, should require the Administrator, FDA, to accelerate efforts to

--identify and resolve sources of potency test variances with the manufacturers and

--develop and implement an improved method to measure potency and to relate it to the level of protection provided by the vaccine.

Also, to enhance both the accuracy of clinical trial data and the protection afforded to clinical trial participants, we recommend that the Secretary require that flu vaccine intended for clinical trial use be tested on a basis consistent with tests of vaccine intended for public use.

CHAPTER 5

POTENTIAL PROTECTION PROVIDED BY SWINE FLU VACCINE

HEW officials estimated that the swine flu vaccine would adequately protect 70 to 90 percent of those vaccinated. Potential protection was estimated based on HEW observations of the effectiveness of past vaccines and on the results of swine flu clinical trials.

The changing nature of flu viruses and problems of achieving optimal composition and timely distribution of the vaccine have made it difficult to effectively immunize against flu in the past. Previous efforts to combat pandemic flu have not been successful. The swine flu program differed from past vaccination efforts because the swine virus was isolated earlier and because the high-priority Federal mass vaccine delivery program was the first of its kind. Consequently, the potential protection provided by the swine flu vaccine is difficult to estimate based solely on previous experience.

The swine flu clinical trials measured antibody responses in individuals vaccinated. The trials did not demonstrate how well an antibody level protects against a flu attack. They did measure what percentage of individuals vaccinated would achieve an antibody level which HEW officials said would provide adequate protection. Estimating the protection provided by swine flu vaccine based on the results of these trials was complicated by problems in achieving adequate antibody responses in younger age groups and uncertainty regarding the role of one vaccine component which was inactive in the vaccine. In addition, the length of protection provided by the vaccine is uncertain.

QUESTIONABLE PROTECTION PROVIDED BY PREVIOUS FLU VACCINES

HEW officials reported that estimates of potential protection provided by swine flu vaccine were based on previous experience with flu vaccines in the United States and other countries. They stated that the effectiveness of flu vaccines against the most virulent flu virus types over the past 25 years had ranged between 67 and 90 percent protection. They added that there was no reason to assume that the swine flu vaccine would be any less effective.

Scientific literature shows considerable disagreement as to the specific degree of effectiveness of past flu virus vaccines. Although experts believe that prior flu vaccines provided some protection, estimates of effectiveness ranged from 20 to 90 percent. The degree of effectiveness of the swine flu vaccine has been questioned by some immunization program critics because of the failure of past flu vaccines to appreciably affect the course of epidemics.

Flu viruses usually undergo minor but continuous changes from year to year. The virus is unique among agents which infect man in that it can change its identity to such an extent that the specific immunity established in response to a previous infection may give little protection against a new flu virus. This change is a significant consideration because the protective value of a flu vaccine is probably related to its similarity with the invading virus. Occasionally, perhaps every 10 to 15 years, a flu virus changes significantly, rendering existing vaccine, as well as the body's defense mechanisms, virtually worthless. Flu differs from polio, smallpox, measles, and other viral diseases because the infecting virus agents for these diseases do not change.

Because of the leadtime needed for the flu vaccine manufacturing process, decisions as to vaccine composition have usually been made months before the flu season began. When the virus characteristics change after the vaccine has been manufactured, the vaccine's protective value is less than optimal by the time it is used. Even during previous pandemics, when major virus changes were detected in other parts of the world before the virus spread to the United States, vaccine production and use could not keep pace with the spread of the virus.

The Asian flu pandemic of 1957 and the Hong Kong flu pandemic of 1968-69 demonstrate the effect of major virus changes and of problems in administering vaccine in time to impede spread of the disease. Outbreaks of Asian flu were reported in China in April 1957. The pandemic circled the globe in less than a year. It peaked in the United States in November 1957. In a 1969 article 1/ addressing both the Asian flu and Hong Kong flu pandemics, the Director of the Division of

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1/R. Murray, "Production and Testing in the USA of Influenza Virus Vaccine Made from the Hong Kong Variant in 1968-69," Bulletin of the World Health Organization, vol. 41, 1969, 495 and 496.

Biologics Standards 1/ stated that, in November 1957, 49 million doses of Asian flu vaccine had been released, but because of distribution and other delays, the amount used before the peak of the Asian flu pandemic had been much less. He noted that, considering the time required to build up protection against the disease, the number of people effectively immunized was small. In the United States an estimated 69,800 deaths resulted from this pandemic.

Similarly, the Hong Kong flu pandemic was first recognized in August 1968. The pandemic peaked in the United States during the first week of January 1969, less than 4 months after the virus material necessary to produce vaccine was made available to manufacturers. At this time only 15 million doses had been released. An estimated 27,500 deaths in the United States were attributed to this virus.

The Director of the Division of Biologics Standards questioned whether the use of flu vaccine had any detectable effect on the 1957 or 1968 pandemics. He stressed that priority be given to research into the problem of making sufficient vaccine available in time to counter a threatened flu epidemic.

A group of Government virologists who reviewed experience with flu between 1957 and 1972 concluded:

> "It is generally agreed that inactivated vaccines containing the appropriate antigenic concentration in suitable potency will provide a reasonable degree of immunity for a limited period of time. This statement simply means that on some occasions the vaccine has worked and on others it has not. * * * There is no doubt that properly constituted aqueous inactivated vaccines can provide some measure of protection. How much protection they afford is open to question. Protection rates are clearly influenced by many features peculiar to the vaccine, the virus, and the host--and by methods used by the investigators."

1/FDA's Bureau of Biologics was established on July 1, 1972, at which time the Secretary, HEW, transferred the Division of Biologics Standards from the National Institutes of Health to FDA. Before July 1972 the Division of Biologics Standards was responsible for biologics regulation.

The swine flu program was the first Federal attempt to immunize the entire population before a potential flu epidemic. HEW officials believed that the resultant opportunity for optimal vaccine composition and timely mass immunization would enhance the swine flu vaccine effectiveness. HEW officials reported that, because no further outbreaks of swine flu occurred, a direct observation of effectiveness in humans has not been possible.

DIFFICULTIES IN ESTIMATING PROTECTION PROVIDED BY SWINE FLU VACCINE

The potential effectiveness of any vaccine could best be determined by challenging (deliberately exposing) vaccinees to the disease and comparing the results to those in a control group of deliberately exposed nonvaccinated persons. However, HEW officials said scientists decided that tests involving a live virus challenge with a new viral strain such as the swine flu virus are very difficult to perform and could pose a potentially serious health hazard in the United States. According to HEW officials, "Over the past decade or so there has been a general scientific consensus that antibody studies * * * not challenge experiments would be sufficient as the indicator of vaccine efficacy."

The 1976 swine vaccine clinical trials, conducted by Government-sponsored investigators, measured participants' antibody levels before and after receiving the vaccine. Though the trials did not demonstrate how well an antibody level protects against a flu attack, they did measure what level of antibody a vaccine recipient should expect to attain. According to HEW officials, an antibody level of 40 or greater should provide sufficient protection. HEW officials estimated that, based on the clinical trials, approximately 70 to 90 percent of swine flu vaccine recipients would develop antibody levels of at least 40.

Adequate protective antibody levels were not achieved in persons age 24 and under in the first phase of clinical trials. A second phase was necessary. As a result, vaccine recommendations were made late in the program for some age groups of persons age 24 and under. Also the dosage recommended to provide protection for high-risk children under age 3 was based on very limited data.

Compounding the difficulty in determining the protection provided by swine flu vaccine is that one antigenic component,

neuraminidase, which is normally active in flu vaccines, is inactive in the swine flu vaccine. The importance of this component is uncertain. In addition, because no swine flu outbreak occurred during this flu season and because swine flu may still have pandemic potential, the length of protection provided by the vaccine may be important. However, the length of protection is also uncertain.

Recommendations made late in the program for some younger age groups

The results of the initial clinical trials were reported on June 21, 1976. While both vaccine types, split and whole product, performed acceptably in groups over 24 years of age, whole product vaccines produced better, but less than the desired, antibody responses in the 18-to-24 age group. Neither vaccine was acceptable for those under 18. For this latter group, improved antibody responses were obtained with more potent concentrations of whole virus vaccine; however, the incidence and severity of adverse reactions were considered unacceptable at these levels.

The initial trials included about 1,250 children, ages 3 to 18, and over 500 young adults ages 18 through 24. Children under 3 years of age were not studied in the initial trials because of their greater susceptibility to vaccine reactions and the resultant desire of investigators to test the vaccine in older children before proceeding with this group.

The Advisory Committee on Immunization Practices did not establish vaccine recommendations for persons under age 18 based on the results of the initial trials. The Committee recommended a single dose of whole virus vaccine for persons 18 through 24, but noted a possible need for a second dose if additional trials so indicated. Consequently, HEW officials began additional clinical trials with 3,300 participants age 24 and under to determine if a second dose would create a "booster" effect resulting in an adequate protective response, yet keeping reactions to a minimum. Children under 3 were included in these tests.

Based on preliminary data from the ongoing trials, on September 17, 1976, the Advisory Committee 1/ recommended

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1/These recommendations were developed for the Advisory Committee by the Committee on Infectious Diseases of the American Academy of Pediatrics.

that high-risk children 3 to 18 years of age receive 2 doses of 200-CCA, split virus bivalent vaccine, administered at least 4 weeks apart.

Additional recommendations for those under age 24 were not made until November 19, 1976. At that time the Advisory Committee recommended

--2 half-strength (100-CCA) doses of split virus bivalent vaccine for high-risk children 6 months to 3 years of age,

--2 full-strength (200-CCA) doses of split virus monovalent vaccine for normal children ages 3 to 18, and

--a second dose of monovalent vaccine for young adults ages 18 through 24.

If the first two groups received initial vaccination during the remaining days of November, they would not have had adequate antibody protection until early to mid-January, about 2 weeks after their second vaccination. Thus, they would not have the full recommended protection until the peak of the flu season. In addition, the supply of split virus vaccine available in November was inadequate to immunize all the normal children ages 3 to 18 years.

For the young adult group the recommendation for two vaccine doses was not made until 4 months after the first vaccine recommendation. Project officials told us that some of this group may not have been made aware that they needed a second dose.

Recommended dosage for high-risk children under 3 years of age based on limited trial data

Besides the problem of timeliness, bivalent vaccine was recommended for high-risk children 6 months to 3 years of age even though no children under 3 were tested with bivalent vaccine and very limited trial data was available for children 6 months to 3 years of age especially for antibody responses. Because of the limited data in this age group and the traditional difficulty of developing vaccine for very young children, one official of the National Institute of Allergy and Infectious Diseases believed that vaccine would not be recommended for children under 3 unless an outbreak of swine flu occurred.

A total of 88 children 6 months to 3 years of age were tested using 2 doses of monovalent swine flu vaccine. Vaccines from the four manufacturers were used--two manufacturers make split virus vaccines and the other two make whole virus vaccines. Vaccine recommendations for high-risk children 6 months to 3 years of age were based on results of ongoing trials as reported on October 22, 1976. At that time, results were available for only 21 children for antibody response and 43 for adverse reactions.

The data indicated that antibody levels were adequate for children 6 months to 3 years of age with only one manufacturer's split virus vaccine. However, antibody response data for this vaccine was available with respect to only five children. Vaccine of the other split virus vaccine manufacturer provided an acceptable antibody response in only two of the five children for which antibody responses were available. Adverse reactions were unacceptable for the whole virus vaccines.

The vaccine recommendations for high-risk children 6 months to 3 years of age were made by the Advisory Committee although the advice of the Committee on Infectious Diseases of the American Academy of Pediatrics was obtained. With regard to the recommendations for this age group, the Chairperson of the Committee on Infectious Diseases stated that:

--The extreme risk to this age group if a flu outbreak occurred outweighed the potential adverse reactions from the vaccine.

--Even though children under 3 had not been tested with bivalent vaccines, the Committee believed that if the children could tolerate monovalent vaccine, they could also tolerate bivalent.

--The Committee believed most children would receive the split virus bivalent vaccine which produced the best antibody response. 1/

The importance of neuraminidase is uncertain

In an effective vaccine, antigens stimulate the production of antibodies which can neutralize or inhibit the spread

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1/The manufacturer of this vaccine produced about 27 million doses as opposed to about 6.8 million for the other split virus vaccine manufacturer.

of a virus. Many experts believe that an ideal flu vaccine should contain both hemagglutinin and neuraminidase antigens so that the body might build antibodies against both. Although the role of neuraminidase is not well defined, hemagglutinin is considered more important.

Hemagglutinin works to help prevent the contraction of flu infection. Experts believe that neuraminidase probably helps prevent the spread of infection and reduce the severity of any infection that occurs.

Unlike previous flu vaccines, the swine flu vaccine has a relatively inactive neuraminidase component. A CDC official said that the seed virus, which cultivates the primary ingredient of flu vaccine, used by each of the manufacturers had readily detectable levels of neuraminidase before production. However, he did not believe that a manufacturing deficiency caused the inactivity of the neuraminidase component. He believed that the neuraminidase antigen of the swine virus is unstable and loses its activity during the vaccine production process.

Flu vaccine experts would prefer to have a vaccine with an active neuraminidase component; however, an HEW official pointed out that the hemagglutinin component is more important and might provide adequate protection by itself.

Several laboratory and animal studies support this observation. These studies show that hemagglutinin antibodies directly neutralize the flu virus. Vaccine containing only hemagglutinin was given to animals and produced almost 100-percent protection. When vaccine containing only neuraminidase was given to animals, protection was significant but less than that with hemagglutinin.

We could not identify any studies isolating the hemagglutinin effect in man. One study that attempted to isolate the effect of neuraminidase in man disclosed that it produced about 50-percent protection.

FDA and CDC officials said that they have no plans to increase the neuraminidase activity in the swine flu vaccine. Consequently, the role of neuraminidase and the question of whether it will be added to the swine flu vaccine should the vaccine be used again next year are uncertain.

Uncertain duration of protection provided by swine flu vaccine

Opinions vary on how long the flu vaccine might provide protection. A manual of diagnosis and therapy, published by one of the flu vaccine manufacturers, states that immunity provided by vaccination lasts only 1 year.

An official of the National Institute of Allergy and Infectious Diseases said that the usual figure given for length of protection is 1 year. However, he referred to studies which showed results ranging from little protection after the first year to good protection after 2 or 3 years. The official noted that although antibody levels of 20 or 40 are generally associated with resistance based on past experience, it is very difficult to define a protective antibody level.

A CDC official stated that the length of time an antibody response of 40 would provide protection depends on the previous priming or exposure of those vaccinated. He said that children would not have continued protection; whereas, older population groups that had previous exposure should have longer protection--at least through the next year. However, this official noted that certain studies indicate that a substantial number of persons would have some protection after as many as 3 years.

In February 1977 CDC reported that:

> "Some decline in antibody titers [measures of antibody response] resulting from swine flu vaccination is expected, but is not expected to be large.
>
> "Recent laboratory tests on sera drawn from volunteers 7 months after participation in the National Influenza Immunization Program vaccine trials in April 1976 have shown an anticipated slow decline in swine influenza virus antibody titers. A subsample of 30 individuals in the 25-34 year age group revealed that the percentage with titers of ≥ 40 ('equal to or greater than 40') decreased from 90 percent to 67 percent. Percentage of persons in the 35-51 age group with titers of ≥ 40 declined from 97 percent to 73 percent. Titers of ≥ 20 were virtually unchanged.

"While many infections are thought to be prevented by a titer of at least 20, a titer of $\geq$40 is thought to represent a more acceptable degree of protection. Based on previous findings, swine antibody titers of vaccinated persons should level off after an initial decline. A larger study is planned later in the spring to determine the levels of antibody remaining in the volunteer population 1 year after immunization. Substantial antibody titers lasting for several years are anticipated."

Other past pronouncements and scientific literature offer little support for expecting the vaccine to provide adequate protection beyond 1 year.

The length of protection may lose importance if the swine virus changes substantially or if the Fort Dix swine flu outbreak turns out to be an isolated occurrence. If a swine flu outbreak occurs but with a substantially changed virus, a new vaccine will be needed.

CHAPTER 6

VACCINE PRODUCTION

HEW estimated in late March 1976 that vaccine manufacturers could produce and deliver 200 million doses by the end of November. However, between June and August after production had begun, there were serious concerns as to whether vaccine would be available to start the program at all. Manufacturers had been unable to satisfy needs for liability insurance and had threatened to stop production and withhold existing supplies of vaccine.

The liability issue was resolved for the swine flu program with the passage of legislation on August 12, 1976. (See p. 18.) Only one manufacturer had stopped production, and then only for a short time. However, total production, about 157 million doses, fell short of the original estimates by about 43 million doses. The one manufacturer that had stopped production was the only one that produced more vaccine than originally estimated.

The total period of vaccine production required about 2 months longer than estimated. Delivery of the initial supplies of vaccine to immunization projects was delayed from July to October.

Only about 25 million doses were available for distribution by October 1. By December 1 fewer than 112 million doses had been shipped to the States and other projects. Thus, if swine flu outbreaks followed by an epidemic had occurred, vaccine was available to immunize about 12 percent of the population by October 1 and only about 53 percent by December 1. As in the case of previous pandemics, too little vaccine would have been available too late, but for different reasons. (See pp. 39 and 40.)

ESTIMATED QUANTITIES OF VACCINE NEEDED

HEW's initial cumulative vaccine production and distribution target dates called for:

--8 million doses by July 9.

--120 million doses by September 3.

--200 million doses by October 29.

The schedules were revised slightly when HEW issued a request for vaccine production proposals on May 27. The request asked for proposals to supply vaccine at a maximum of 160 million doses of monovalent swine flu vaccine and a maximum of 40 million doses of bivalent swine and Victoria flu vaccine. The request included schedules providing for delivering vaccine in 100,000-dose increments beginning in July, with both monovalent and bivalent to be produced and shipped concurrently. Thereafter, bivalent was to be delivered as soon as possible but no later than September 1. Seventy-five percent of the minimum guaranteed amount of monovalent vaccine was to be delivered by September 1; complete deliveries were to be made on or before November 15.

QUANTITIES OF VACCINE PRODUCED DID NOT MEET PROGRAM GOALS

The first indication that manufacturers would not be able to produce the desired quantities occurred in June. At that time the manufacturers submitted their first formal proposals for vaccine production and delivery. The proposals included estimates showing that only about 80 million doses could be produced by October 1, with delivery starting in July, and that 146.7 million doses could be available by December 1.

Revised proposals were submitted in August and September, but estimated quantities of vaccine to be available decreased rather than increased.

The August proposals showed that only 20 million doses could be available by October 1 and that only about 113 million doses could be available by December 1. These estimates reduced the June estimates by almost 75 percent for the amount of vaccine expected by October 1 and by almost 25 percent for the amount expected to be produced for the entire program. The estimates were also about 43 percent lower than the estimated 200 million doses needed to immunize the entire population.

HEW officials noted that the supply proposed in August was clearly insufficient to meet the target date for immunizing the entire population by mid-November. Therefore the Secretary of HEW urged manufacturers to increase the supply as soon as possible. HEW agreed to support any level of effort by the manufacturers necessary to increase the supply. HEW also agreed to extend the production period and to accept deliveries through January 15, 1977.

Vaccine availability estimates included in letter contracts signed as of September 22, 1976, showed a further decrease in the supply by mid-November. The estimates were lowered to 108.9 million doses by December 1; deliveries were to begin in October 1976. Even with production time extended to January 15, manufacturers again estimated that they could produce only 146.7 million doses, as estimated in the June proposal.

In September HEW lowered its estimate of need for vaccine from 200 million doses to 160 million. The reduction was largely based on public attitude surveys taken in August, which showed that only about 53 percent of the population over 18 years of age planned to be immunized.

During congressional testimony on September 13, three of the four vaccine manufacturers stated that their total production capabilities had been committed to producing swine flu vaccine. The fourth manufacturer had stopped production for a short time because its June production estimates had been met. As previously stated, however, this manufacturer subsequently produced additional vaccine and was the only company that exceeded its original June estimate.

The inability of manufacturers to produce the desired quantities was attributed principally to these intervening and unforeseen circumstances:

--A less-then-expected yield per egg.

--A mistake resulting in one manufacturer producing about 6 million doses of an incorrect vaccine.

Vaccine yield per egg was less than expected

Simply stated, production involves innoculating fertile eggs with seed virus. After several days, the virus-rich embryonic fluids are harvested. The virus is purified, concentrated, and inactivated. Finally, the inactivated virus concentrate is diluted so that the end product will be of a specified strength or will contain a specific amount of viral antigen per dose. Thus, the dose yield per egg depends not only on the biological process of virus developing in the embryo, but also on the strength specified. The production cycle of a particular batch of vaccine takes about 2 months.

The proper strength for a new type of flu virus vaccine is determined through clinical trials. These trials involve testing a range of strengths in volunteers to determine which strength gives the best antibody response with the least rate of adverse reactions. Although the initial clinical trials for the swine flu program were not completed until June 1976, in April HEW estimated a yield of about two doses per egg. This estimate was based largely on experience with production of flu vaccines and preliminary information about the swine flu vaccine.

At least one manufacturer attributed the vaccine production problem to a less-than-expected yield per egg. This manufacturer noted that the actual yield had averaged a maximum of only 1.3 doses per egg and that this had adversely affected the total amount of vaccine the company could produce within the HEW time frame. HEW's contracting officer said the other three manufacturers had also reported a lower yield per egg than the estimated two doses.

During congressional testimony in September 1976, the Assistant Secretary for Health stated that though HEW was aware of problems with yield per egg, which some manufactureres were experiencing from time to time, most of these had been reported as resolved satisfactorily.

Because of the biological nature of dosage yield per egg, we determined neither the validity of the factors which influenced dosage yield per egg nor its actual effect on the quantities of vaccine produced. (See ch. 4.)

One manufacturer produced about 6 million doses of an incorrect vaccine

One manufacturer mistakenly produced about 6 million doses of a different swine flu vaccine. The vaccine produced (called Shope strain) was developed from a 1931 swine flu virus strain which is related to, but different from, the swine flu virus isolated during the Fort Dix outbreak.

HEW concluded that the Shope virus vaccine could not be recommended for use in the swine flu program because it did not produce the same level of antibodies as did the swine flu vaccine. The Shope vaccine was not to be offered to the public except under extreme emergency conditions--in the event of an epidemic in which all the swine flu vaccine had been exhausted. If needed, this vaccine would have been used for persons over 35 years

of age. The production of 6 million doses of Shope vaccine by mistake delayed the availability and reduced the expected quantity of the manufacturer's swine flu vaccine.

AVAILABLE VACCINE WAS NOT RELEASED

To make immunization available to all Americans, swine flu program strategies and timetables called for vaccine to be delivered between July 9 and November 15, 1976. Although some vaccine had been produced, none was made available for use in July. As previously discussed, manufacturers were unwilling to furnish vaccine for the swine flu program without adequate liability protection. Also HEW did not provide manufacturers specific information pertaining to vaccine formulas, packaging inserts, and delivery specifications before the planned July starting date. Manufacturers claimed this had inhibited their ability to provide vaccine as planned.

Liability protection was provided by the Congress through Public Law 94-380 on August 12, 1976, and HEW provided contract and cost specifications to the manufacturers by early September. Vaccine was finally released by the manufacturers for use on October 1--about 3 months after the planned starting date for immunization phase of the swine flu program. The October 1 release date was used because Public Law 94-380 provided that liability claims could not be filed against the United States until after September 30, 1976.

Untimely decisions on vaccine formulas, packaging inserts, and delivery specifications

Three of the four manufacturers testified before the Subcommittee on Health and the Environment, House Committee on Interstate and Foreign Commerce, on September 13, 1976, that to meet vaccine quantity and delivery schedules proposed in June, HEW's decisions on vaccine formulas and packaging inserts should have been made available by mid-July 1976. The manufacturers pointed out that these decisions were essential before they could prepare, label, or deliver finished vaccine.

Because of the need to have the vaccine tested, manufactured, and delivered within a short time, HEW assumed many responsibilities for which manufacturers are normally responsible. These responsibilities included, but were not limited to:

--The investigation and determination of the safe and effective dosage and adequate directions for using vaccine.

--The investigation and determination of the risk and benefits of innoculation with the vacine and the development of an adequate statement on the risk and benefits.

--The content of the labeling of the vaccine, including its compliance with laws and regulations.

Accordingly, HEW was responsible for furnishing manufacturers specific requirements for vaccine formulas, labeling, packaging, and logistics of delivery. The CDC contracting officer said that normally this information would be provided in the request for vaccine production proposals. However, the request was issued on May 27, 1976, without some of the final specifications, and several amendments to the request were made after it was issued. For instance:

--The request did not contain specific vaccine formulas (i.e., CCA strength per dose), and this information was not available until late July, after the initial clinical trials had been completed and evaluated. Since the formulas were not available, the requests for proposals asked the manufacturers to submit proposals showing estimated vaccine volume and deliveries based on each of the three vaccine formulas (200, 400, and 800 CCAs) used in the clinical trials. (See pp. 34 and 35.) However, manufacturers could not prepare vaccine of appropriate strength for release without the formulas.

--Package inserts were not finalized and furnished to the manufacturers until September 1976. These inserts showed risk and benefits associated with the vaccine and could not be prepared until the clinical trials had been completed. Package inserts were required for each shipment of vaccine.

Some manufacturers also claimed that HEW's delay in providing final contract terms--including quantities--adversely affected vaccine availability. Though the technical terms of the contract--pertaining to packaging, labeling, and shipping--might have caused delays in release of vaccine, there is no indication that the absence of a contract adversely affected production of vaccine.

The manufacturers initiated production by late March 1976. Although they had no formal commitments from the Government on standards, quantities to be produced, or final terms of purchase contracts, they knew there would be no competitive bids for vaccine. They also knew that CDC planned to purchase all swine flu vaccine the manufacturers could produce and that vaccine would have to be procured within a very short time for it to reach the population before the coming flu season.

HEW initially planned to award contracts to the four manufacturers by May 28, 1976. However, because of liability problems, letter contracts providing for deliveries of vaccine and for payment on a provisional basis were finally signed in September 1976. Final contracts had not been signed as of June 16, 1977.

INSUFFICIENT QUANTITY OF VACCINE TO PROTECT ALL CHILDREN UNDER 18 YEARS OF AGE

Because of the limited quantity of vaccine suitable for immunizing normal (not high-risk) children 3 to 18 years of age, less than 10 percent could have been immunized. Consequently, no mass immunization of this age group was attempted.

Two full-strength (200-CCA units) doses of split virus monovalent vaccine were recommended for this group on November 19, 1976. The 2 manufacturers of split virus vaccine produced about 44.7 million doses, of which about 9.8 million doses were in monovalent form. Thus, the necessity for a 2-dose regimen to achieve the desired antibody response dictated that fewer than 5 million of the estimated 58 million normally healthy children ages 3 to 18 could be immunized.

RECOMMENDATION FOR FUTURE IMMUNIZATION PROGRAMS

HEW must determine vaccine formulation and packaging and delivery specifications in a timely fashion if vaccine delivery is to meet necessary schedules. If manufacturers still cannot produce enough vaccine in time to meet the delivery schedules, we recommend that the Secretary, HEW, seek alternative procurement methods. Such methods might include plans for (1) standby facilities at other drug-manufacturing plants and (2) standby Federal production facilities.

CHAPTER 7

PROJECT READINESS AND IMPLEMENTATION

Each swine flu grant project offered immunization to anyone for whom the vaccine was not contraindicated. However, due to the lack of swine flu activity and a less-than-expected demand for vaccine, the Nation's system for mass immunization was not fully tested. Some problems surfaced in planning and implementing swine flu immunizations at the project level which should be considered for any future mass immunization programs.

Immunization projects were not ready to begin in July as planned and were unable to fully implement program strategies. State and local public health structures demonstrated varying degrees of willingness to respond to the potential national health threat from swine flu. Project readiness and implementation were limited by:

--Less than full commitment by some project directors.

--Complex, incomplete, and late vaccine recommendations.

--Limited initial quantities and delayed delivery of vaccine.

--Less-than-expected participation by private medicine, other health care providers, and volunteers.

--Weaknesses in project operations.

--Lack of State liability insurance.

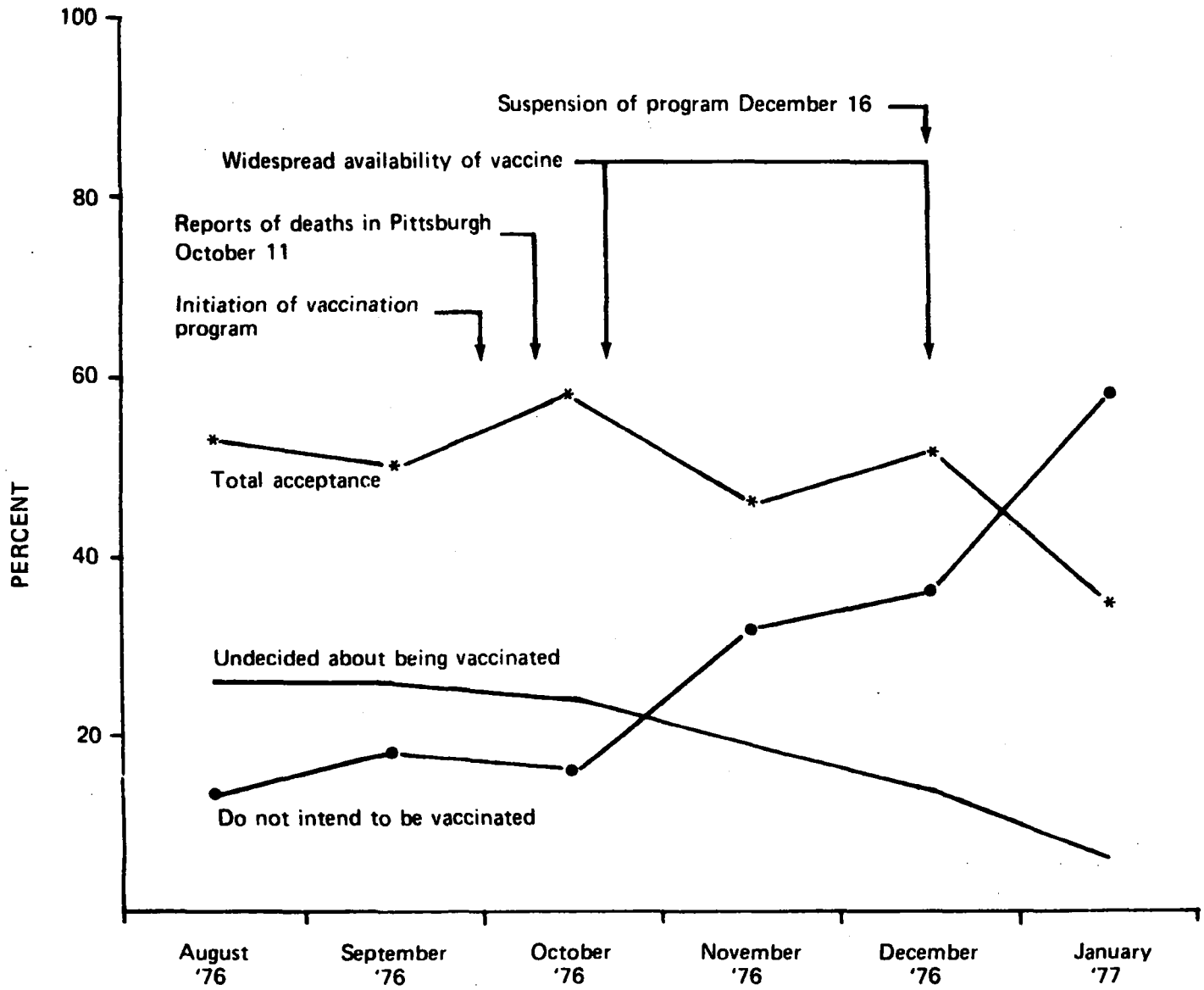
DEMAND FOR VACCINE WAS LESS THAN EXPECTED

The original intent of the swine flu program was to immunize every person in the United States for whom the vaccine was not contraindicated. However, when the program was suspended on December 16, 1976, only about 22 percent of the total population had been immunized. Even so, an HEW official noted that the 45 million immunizations was the greatest number ever given in a 2-1/2-month period.

Public opinion surveys taken monthly during the swine flu program showed that almost everyone was aware of the program. However, the surveys showed also that the number of people who did not intend to be vaccinated increased continuously and overall acceptance of the program declined after immunization began in October. The following chart developed for CDC summarizes the survey results.

Figure 1

PUBLIC ATTITUDES TOWARD VACCINATION AGAINST SWINE FLU
AUGUST 1976–JANUARY 1977
UNITED STATES



Source: Opinion Research Corporation national sample of adult population (18+ years) in the U.S. Interviews took place during the first 10-14 days of the months indicated.

Reasons frequently given during the surveys for non-acceptance of the program were that

--the vaccination was not necessary,

--there could be adverse effects,

--the vaccination would not prevent flu, or

--the vaccine could cause flu.

LESS THAN FULL COMMITMENT BY SOME PROJECT DIRECTORS

Commitment of project leadership was perceived essential to program success. The national strategy relied heavily on immunization projects for their experience in conducting immunization programs and as logical distribution centers for vaccine. Vaccination of the entire population by mid-November depended on full mobilization of all health delivery systems--both private and public--under the general leadership and direction of the project directors.

Although all project directors developed acceptable plans and obtained approved grants, some did not actively support the national program--particularly the decision to immunize the general population. Some openly criticized or questioned the need for a national program to the news media and to local community program directors.

CDC officials reported that, though many project plans were of excellent quality, some project directors clearly evidenced a lack of serious intent to conduct mass immunization programs.

At least three State project directors deemphasized the mass immunization program. Each director seemed to support the program for high-risk groups because the bivalent vaccine offered protection against the Victoria flu. Each director believed Victoria flu would be the prevalent strain in the 1976-77 flu season.

One of the three State projects received a grant for about $700,000 in June 1976. The grant was awarded based on plans to immunize about 1.5 million high-risk persons and 4.2 million other susceptibles. On July 7, 1976, the project director issued a news release stating that high-risk individuals should be immunized and that vaccine would be available for others who wanted it. Although the director

did not rule out the possibility of a swine flu epidemic, he said the evidence indicated that seeding for the swine flu virus had not occurred. The news release added that, based on present information, the likelihood of a swine flu epidemic during the 1976-77 flu season was low and that immunization would probably have to be repeated next year if the threat of swine flu still existed.

Another State project, after receiving an immunization grant of about $400,000, issued a statement that emphasis would be placed on immunizing only high-risk individuals. Remaining susceptibles would be immunized in regular clinics, at their request, with minimum effort to encourage them to do so. CDC officials who reviewed the flu program in this State reported that counties were not carrying out community-wide immunization programs. The Director of CDC, in a letter to the project director, expressed concerns about the project director's commitment to the national immunization effort and the appropriate use of Federal funds.

A third State project submitted plans for immunizing 75 to 90 percent of the State's population and received an immunization grant for about $500,000. Shortly after requesting the grant, the project director issued the following instructions to local health officers and district flu coordinators responsible for carrying out community programs.

> "* * * Let's not encourage people to get shots, [we] can't really say [the shots are] * * * absolutely necessary, and you don't need more work than CDC will generate for you. But, must push to inform [the] public that they will have reactions and may even get the flu in spite of [the] campaign (different kind of flu). * * *"

In a letter to the State nurses association--a prime source for volunteers--the project director said that the possibility of swine flu becoming epidemic during 1976 was not overwhelming.

COMPLEX, INCOMPLETE, AND LATE VACCINE RECOMMENDATIONS

Project directors were limited in their ability to develop strategies for immunizing population groups under 25 years of age. Throughout the planning stages of the program--April through September--there were no firm dosage recommendations for these groups. Dosage recommendations made in September and November were complex and difficult to

manage and were received too late to effectively protect these groups before the season of intense flu activity. (See pp. 42 and 43.)

The complicated and incomplete vaccine recommendations which existed throughout the program caused project directors difficulties in administering vaccine and in informing the public on proper dosage requirements. Contrary to experience in most years when vaccine recommendations were the same for everyone, the swine flu program had two formulations of vaccine (bivalent and monovalent), two types of each formulation (whole and split virus), and different dosage recommendations involving both formulations and types for specific age groups and doses for some age groups had to be administered over an extended period.

To further complicate matters, the Committee on Infectious Disease of the American Academy of Pediatrics had issued a precaution against using whole virus vaccine for high-risk children ages 3 to 18. The Committee stated in September 1976 that if whole virus vaccine were used, side effects would be greatly accentuated. However, the labeling on individual vials of vaccine shipped to immunization projects did not indicate whether the vaccine was whole or split.

The first of two clinical trials to determine vaccine dosage recommendations was completed in June 1976. The first trials did not produce dosage recommendations for the under-18 age groups and produced only partial recommendations for the 18-through-24 age groups. The second trials resulted in vaccine recommendations for virtually all age groups, but not until mid-November 1976--or almost 2 months after immunizations began. (See pp. 41 and 42.)

Although dosage recommendations were incomplete, CDC encouraged planning for immunizing all age groups. Thus, some project directors developed strategies for coordinating the swine flu program with back-to-school immunization and assessment programs. These plans were changed because a safe and effective dosage had not been determined for normal (not high-risk) children when immunizations began on October 1.

Further, based on the July recommendation, project directors had to develop procedures for informing and educating the 18-through-24 age groups about the need for one dose and a possible need for a second dose at a later unspecified time. The under-18 age groups had to be informed that no dosage recommendations had been made for them but that one might be made later. When recommendations were received for essentially

all age groups in September and November, project directors had to develop procedures for informing and educating the under-25 age groups about the recommendations and for administering vaccine doses at least 4 weeks apart.

Because the recommendation for normal children ages 3 to 18 was not made until November 19, 1976, insufficient time was available to protect them before the predicted flu season. Because of the lack of sufficient quantities of vaccine, inherent problems in administering a two-dose regimen, and the fact that normal children generally do not suffer severe complications from flu, HEW did not encourage community-wide programs for this age group.

Fewer than 4 million of the approximately 27 million young adults (both high-risk and normal) in the 18-through-24 age group had been vaccinated by November 19 when the recommendation for a 2-dose regimen 4 weeks apart was made. Assuming that immunization project directors could adjust or develop strategies and schedules to reach this age group in such settings as schools, colleges, and industry, the group still would not have received full protection until late December, or well into the predicted flu season.

LIMITED INITIAL QUANTITIES AND DELAYED DELIVERY OF VACCINE

Project directors could not implement approved plans for achieving a complete readiness status because of the uncertainties concerning vaccine availability. A basic assumption in developing program strategies for immunizing the population before the next flu season was that adequate vaccine supplies would be available to start programs in July 1976. Vaccine was not made available to immunization projects until October 1. From June through late September, delivery dates and quantities of vaccine were uncertain. Both vaccine production estimates and delivery dates were changed several times during this period.

The uncertainties surrounding vaccine availability inhibited the ability of immunization project coordinators to make firm commitments for (1) program strategies, (2) staffing, (3) clinic locations and dates, and (4) promotional publicity.

Project strategies required repeated modification

Delays in delivery dates and subsequent decreases in vaccine quantities (see ch. 6) invalidated many project strategies and timetables. Immunization schedules were shortened, and gradually accelerating programs, planned for July through November 1976, were changed to shorter, high-intensity programs beginning in October 1976. Two-phased strategies planned in many projects were merged into single-phased operations, and some project strategies that called for organized State teams to carry out immunization on a county-by-county basis were changed to county-operated programs.

To immunize the entire population by the end of November, most State and local health agencies planned large-scale, communitywide mass immunization programs. To reach all the population, private medical resources and other health care delivery systems were also considered essential. By June 17, 1976, the projects had developed acceptable plans and received grants totaling about $24.2 million to carry out their immunization programs.

Most project plans called for a two-phased program. The first phase was designed to begin immunizing high-risk groups in mid-July, and the second phase, directed at the remaining population, was scheduled to start in September. Project plans provided for delivering vaccine to high-risk groups through private physicians, nursing homes, retirement homes, special clinics for the aged, and health departments. The second phase included using organized settings, such as clinics, schools, industries, nursing and medical facilities, private physicians' offices, and health departments plus shopping centers and other places where large groups of people could be reached.

Immunization strategies varied significantly among projects. Some projects chose to form central or regional immunization teams to travel from community to community conducting immunization clincs. Other projects either relied on existing health care delivery systems and completely delegated planning, organization, and implementation to local health jurisdications or used a combination or variation of the above strategies.

Officials at some projects reviewed had adopted a "wait and see" attitude in August and September 1976 even though vaccine had been promised for October 1, 1976. The general

feeling among project directors was that the type of program eventually run would depend on when and how much vaccine would become available and who would be recommended for immunization. Some directors pointed out that continually changing the program was counterproductive to the immunization goals.

Of the 63 projects, 48 requested $1.6 million in supplemental grants. Many offered justifications based on program modifications caused by vaccine delivery delays and related uncertainties.

Staffing delayed because of nonavailability of vaccine

Although swine flu vaccine use was scheduled to begin in July 1976, some projects had not recruited and trained staffs as late as August or September because of uncertainties surrounding vaccine availability.

All projects reviewed planned to use existing State and local health department employees for key positions and to supplement them with temporary employees. However, in four of the five projects reviewed, temporary staffing had not been completed.

Each of the four project directors told us that staffing had been delayed pending firm data on vaccine availability. The directors said that if their programs had been staffed early based on initial plans for vaccine deliveries, they would have exhausted existing grant funds before--or shortly after--program implementation. Another director, who had recruited and formed staff in August 1976, stated that staffing funds would be spent by December 1976.

At least 12 project directors ultimately requested supplemental grant funds totaling about $184,000 for local staffing. Also one other project obtained direct personnel assistance from CDC valued at about $2,800. Justification for many of these supplemental assistance requests was based on vaccine delays, decreases in vaccine quantity, and extension of the program.

Clinic locations and dates could not be finalized

County coordinators were primarily responsible for scheduling and publicizing clinic sites and dates. Although some tentative site schedules were established in August and September 1976, coordinators told us that firm schedules could not be made until vaccine quantity and flow had been firmly established.

Some coordinators who scheduled clinics without specific advance information on vaccine availability had to cancel and reschedule them when quantities were found to be less than expected. For example:

--Many counties which planned clinics beginning from mid-September through early October had to cancel and reschedule them as vaccine became available.

--Some projects had to change original plans to use schools as organized settings for mass immunizations because of uncertain vaccine recommendations for the younger age groups.

--A massive "Flu Sunday" scheduled for a metropolitan area in October 1976 had to be delayed until November.

Public awareness activities restricted

Uncertainties and delays in receiving vaccine and vaccine dosage recommendations severely limited promotional activities within most projects. Also, because of concerns about the liability issue, supplemental national publicity was untimely. HEW and the projects published very little positive, timely promotional information to offset negative or conflicting publicity in the news media about the need for the program, adverse reactions, and deaths associated with vaccination.

Project publicity activities restricted

Many project directors did not initiate multimedia publicity campaigns until early October 1976 or later, when vaccine was available to begin mass immunization. Some directors pointed out that it would be counterproductive to promote the program and then have to cancel clinics or be unable to meet demand for vaccine. They chose instead to begin their public awareness efforts slowly so that demand would not outstrip the limited supply. One project, which planned to begin its multimedia campaign in August 1976, spent about $2,600 for advertising clinic locations and dates which later had to be rescheduled.

Recognizing the promotional problems, CDC made additional grant funds available to the projects in November to launch promotional campaigns. Although some States obtained supplemental grants for publicity in November and December 1976, the program was suspended on December 16 because of adverse reactions to the vaccine.

Untimely supplemental national publicity

To achieve public awareness and promote demand for the vaccine, CDC planned to work with the Advertising Council, Incorporated, to develop a motivational theme and informational and promotional material to be used in national, State, and local publicity campaigns. CDC intended to give State and local health agencies this material before immunization began. However, material prepared by the council was not disseminated to the States and media until late November 1976.

The council is a nonprofit advertising organization representing some of the largest advertising agencies across the country. The council assists in publicity campaigns which meet its criteria of public service, including programs of nonprofit and nonpolitical intent.

In March 1976 the council offered to help develop the promotional and informational material required. However, the advertising agency assigned to develop the material was also providing promotional services to one of the vaccine manufacturers. In addition, the council was concerned that it too could be held liable in suits alleging failure of a program participant to provide adequate informed consent.

On July 22, 1976, CDC and the council agreed to terminate their contract because the manufacturers' liability issue had not been resolved. The council had not developed any publicity material when the contract was terminated.

When the liability issue was resolved in August 1976, the council again offered its services to CDC. However, a contract for these services was not finalized until October 4, after States had begun immunization programs. During October the council's publicity effort had to be redirected from promoting the program to responding to adverse and conflicting publicity. Thus, material prepared by the council was not disseminated to the States and media until late November 1976--almost 2 months after immunizations began.

Untimely response to negative publicity associated with adverse reactions

CDC's national publicity objectives were to (1) inform the public of the potential for a swine flu epidemic and (2) motivate the public to be immunized. These objectives would be met through organized generation and release of

information to program participants and the media and through responses to media inquiries. However, between beginning immunizations on October 1, 1976, and late November 1976, when the council's material became available, CDC's publicity was often limited to responding to media inquiries concerning crises that arose, such as publicity associating deaths with the immunization program.

When the council's initial contract was terminated on July 22, 1976, no publicity material had been developed. CDC, with some assistance from two consultants, assumed the added responsibility of developing the material, including television and radio advertisements, posters, newspaper layouts, and slide presentations. This material was disseminated to the States before the immunization phase of the program began on October 1, 1976.

CDC officials stated that publicity efforts were adequate up to the occurrence of deaths during October 1976, which were initially attributed to the program. An HEW official said that CDC knew that some individuals who had been vaccinated would die within a short time due to other causes. However, CDC had not developed the quantity, variety, and quality of material needed to immediately counter the adverse publicity that resulted. Therefore, CDC could not provide the projects facts to respond to initial media inquiries.

Many States did not have the facts to counter the adverse publicity. Some projects responded by closing their clinics, which further fostered suspicions concerning the safety of the vaccine.

LESS-THAN-EXPECTED PARTICIPATION BY PRIVATE MEDICINE, OTHER HEALTH CARE PROVIDERS, AND VOLUNTEERS

In developing the national strategy, HEW noted that involvement by private medicine, other health care providers, and volunteers was essential for reaching all groups of people. Most projects planned for extensive participation by these groups. In general, however, participation by these groups was less than expected.

Limited participation by private medicine

To stimulate interest, support, and participation of private physicians, representatives of medical societies were appointed to project advisory committees, flu facts and other

educational materials were published in physicians' bulletins, and State and county flu coordinators contacted physicians directly. Also CDC contacted national medical associations to obtain their support and participation. However, CDC's medical professional liaison stated that no national medical organization had ever formally endorsed the program. In only two of the five projects reviewed did a State medical society generally endorse the flu program and encourage its members to participate.

CDC coordinators and some immunization project directors reported that cooperation and participation from private medicine was generally less than expected. They said physicians were reluctant to participate because of the many uncertainties and controversies over issues such as liability coverage; rationale for the program; complex dosage recommendations; safety and efficacy of the vaccine; complicated informed consent requirements; and confusing labeling, which did not distinguish between the types of vaccine.

In many projects, active participation in mass immunization clinics was minimal and some physicians even discouraged their patients from being vaccinated. For example:

--One county originally intended to have private physicians conduct the entire program, including the mass immunization clinics. However, private physicians withdrew their support because of their concern over liability coverage. The program was ultimately conducted by county health personnel.

--Only about 400 of the 1,900 physicians expected to participate in 1 city requested vaccine, and 106 of them requested 50 doses or less. In another city about 380 of the estimated 1,000 physicians requested vaccine.

--In 3 counties of 1 State, fewer than 200 of about 1,500 physicians requested vaccine.

Participation by other health care providers was less than expected

HEW anticipated using nursing homes, hospitals, retirement homes, and industries to immunize their patients and employees. These organizations offered a setting in which large groups of people could be reached. Most immunization projects planned to make full use of these organizations.

In some projects participation by these organizations was less than expected. For example, less than 55 percent of one project's industries, nursing homes, and senior citizen centers responded to the initial request to provide vaccinations. Because of the low response, project health department personnel provided vaccinations at many nursing homes and senior citizen centers. CDC officials reported that concern over liability coverage, informed consent, and deaths associated with the vaccine diminished initial commitments. They noted that many industries which were originally willing to vaccinate their own employees decided instead to send them to public clinics.

Vaccine availability lessened the extent of involvement by health care providers. Some projects could not or did not make vaccine available to industries in the quantities requested until mid-October or later. These projects discovered that earlier demands of some industries had waned. For example, as of November 1976, one county had allocated about 98 percent of all the vaccine it had received. The county could not meet requests from private industries for 80,000 doses. One industry originally requested 20,000 doses, but rejected the 6,000 doses offered because this limited amount could not meet anticipated demand. When excess vaccine became available, demand had decreased and the request was retracted.

Volunteer support was less than expected

Most projects developed plans for establishing a corps of volunteers to assist in all phases of the program. CDC coordinators for immunization projects stated that uncertainties concerning vaccine delivery and recommendations had led to a loss of trained volunteers and disenchantment of large volunteer organizations, such as the Red Cross.

Two counties visited did not plan weekend and holiday clinics due to a lack of volunteers. Clinics in these counties were limited to weekdays when enough volunteers were willing to participate. Other clinics had fewer volunteers than originally planned, but enough for the small number of persons desiring immunization. Some clinics visited did not have enough trained volunteers to assist in all phases of operations as planned. Some counties originally planned for 24 to 30 registered nurses and other volunteers at each clinic. Due to the reduced demand for vaccine, original estimates were reduced to 5 to 8 registered nurses and 15 other volunteers. In one county, only three registered nurses and two other volunteers showed up at one clinic

visited. Another two volunteers were pulled from the line of persons waiting to be vaccinated. Because of the reduced number of volunteers, the three jet injectors at the clinic site were not in constant use and vaccinees were required to stand in line for up to 1 hour.

OTHER WEAKNESSES IN PROJECT OPERATIONS

Our review of 5 projects and 26 clinics together with monitoring data available from CDC also identified the following weaknesses:

--Some projects and counties limited clinic operations to local health departments and neighborhood clinics, with disappointing results.

--Some projects, counties, and clinics did not comply with informed consent procedures and could not account for all vaccine used or wasted.

Inaccessible clinic sites reduced public participation

CDC reported that clinic accessibility is a key factor in delivering services. Accessibility is largely a product of clinic location and the hours of operation. Clinics held on weekdays in health departments and neighborhood centers were generally less productive than clinics held on weekends and at night in shopping centers and other natural gathering places.

Clinics conducted on weekends seemed most successful for reaching large numbers of vaccinees in many urban areas. CDC reported that many areas conducted followup weekend clinics which were usually as productive as the initial ones.

In four metropolitan counties in one State project reviewed, almost half as many persons were vaccinated on one Saturday in November as had been vaccinated during the entire first 6 weeks of the program. However, CDC reported that this metropolitan area had not established consecutive weekend clinics and had lost the momentum generated, which had limited participation. In another major city, over 16,500 persons were vaccinated during 1 weekend. A followup clinic accounted for over 18,200 vaccinations. Combined, the vaccinations given on these two weekends accounted for over 10 percent of all vaccinations given during the city's program.

A suburban county visited held weekend clinics at neighborhood schools with varying degrees of success by geographic area. On a given weekend some school clinics vaccinated 3,000 or more persons while others vaccinated fewer than 200. The only clinic this county held in a shopping center was on a Friday and Saturday in November, when over 4,600 persons were immunized. Also 2 weekday clinics held at a neighborhood center and a school in a metropolitan city averaged fewer than 50 vaccinations a day. Each clinic was staffed with at least eight health department employees who spent most of their time in relative inactivity.

In addition, a CDC official said other factors, such as economic and racial background, had affected vaccine acceptance. However, CDC felt that clinic accessibility could be readily identified and dealt with. CDC reported that some States had adjusted their operational strategies for the swine flu program with great success by establishing more night and weekend clinics in shopping centers and other high traffic areas.

Informed consent procedures not adhered to

HEW developed guidelines for the projects aimed at assuring that persons immunized by other than their private physicians were informed of the swine flu vaccine's benefits and risks. The guidelines set forth eight minimum requirements for informed consent. Every grant application included procedures for securing informed consent before vaccination that were acceptable to HEW. The requirements and procedures then filtered down from the projects through various health jurisdictions to clinics where the vaccinations were given.

Most of the 26 clinics visited met many of the HEW requirements; however, most clinics did not meet all of the requirements. (See next page.) A few clinics visited were so poorly organized that even minimum informed consent requirements could not be assured. For example:

--A clinic run by HEW employees for HEW employees (1) did not have the introduction to the two-page consent form available, (2) permitted some persons to be vaccinated who had not signed a consent form or registered in any way, and (3) did not collect all consent forms that had been signed.

--A county clinic did not maintain adequate crowd control. Thirty to 40 persons were crowded around the vaccination area, and nurses were vaccinating anyone with a consent form. No one verified that the forms had been signed. One operator admitted that he had no idea whom he was vaccinating and subsequently stopped using the jet injector.

Minimum informed consent requirements	Compliance by clinics visited: Yes	No
Gave every person a written statement (registration and introduction forms)	23	3
Documented that the statement had been provided	22	4
Screened to determine if person could read statement provided	8	a/18
Screened to identify high-risk individuals	24	2
Answered questions about vaccine, contra-indications, risks, and benefits	25	1
Maintained translations of written statement	20	6
Displayed posters showing recommendations for age groups under 25	13	13
Directly advised persons under 25 years of age regarding the recommendations	17	9

a/Clinic screeners told us that persons had not been specifically asked if they could read the form, but they assumed those who could not read would so indicate.

HEW's methods to assure compliance with the requirements included (1) periodic site visits to clinics by swine flu officials, (2) additional visits by HEW regional personnel in conjunction with monitoring visits for other health programs, and (3) distribution of a supplemental questionnaire to all grantees concerning their planned policies and procedures to comply with HEW guidelines. A CDC official told us that results of HEW clinic visits had been discussed but not documented. Also the results of the questionnaire were collected but not summarized. Consequently, although changes at some clinics may have resulted from these reviews, the overall effectiveness of HEW's monitoring efforts could not be determined.

State health department officials also made periodic visits to vaccination clinics. Some State officials reported changes in clinic operations as a result of these visits. In addition, State health officials, using HEW guidelines, trained clinic managers and other key program personnel. However, in the absence of monitoring each clinic, States could not assure that consent forms were being handed out, read, understood, signed, and turned in. CDC officials said that the small number of individuals attending clinics and the quality of clinic organization made failures in the consent process unlikely.

As part of a national opinion survey conducted monthly on the swine flu program, CDC questioned a sample of persons vaccinated to measure their awareness of informed consent. According to CDC, the results are useful in assessing the overall implementation of informed consent procedures, although they are based on individual recollections of what occurred and are subject to the limitations of national sampling procedures.

The January 1977 survey showed that 90 percent of people vaccinated recalled having been shown or given a form which told about the benefits and risks of swine flu vaccination. This includes persons vaccinated by private physicians and hospitals, which were not required to use the informed consent form.

As CDC has reported, the informed consent system was obviously not perfect.

Vaccine inventory and accountability requirements not adhered to

On September 1, 1976, HEW issued a flu assessment manual which provided a prototype vaccine inventory and accountability system. Though HEW noted no significant problems in project compliance with the manual, final vaccine accountability and project assessment may not be possible.

The most common problem was obtaining accurate usage information from private physicians. Most projects initially gave physicians a limited amount of vaccine. When reordering, physicians were to report usage by age group and type of vaccine. However, when physicians did not reorder and when the program was halted in December 1976, project staff were faced with the task of contacting each physician that had been provided vaccine to ascertain the necessary data. Examples of resulting problems follow.

--One county asked about 380 physicians who had received vaccine to account for it. Only about half of the physicians responded. According to the county coordinator, physicians who did not respond were not subsequently contacted because (1) there were too many for the project staff to telephone individually and (2) it would be an insult to the physicians' professional status.

--Private physicians who participated in another project's mass immunization clinics occasionally took vaccine from the sites for their own use. At the end of the program, several physicians mailed vaccine back to the State. One physician mailed back 300 doses of bivalent vaccine which, after being unrefrigerated for days, had to be discarded.

Another problem was the failure of some projects to comply with HEW inventory and accountability requirements. Although all the projects could account for vaccine received and shipped out, the system occasionally deteriorated as the vaccine was distributed to health districts, regions, counties, and other jurisdictions.

Neither of two health districts in one State visited could determine the exact quantities of vaccine used or wasted. For example:

--Neither district recorded distributed vaccine when it was returned. When the vaccine was redistributed it was counted again, resulting in an understatement of vaccine inventory. Therefore, the district could not accurately determine either the amount of vaccine distributed or on hand.

--Clinics in both districts could not account for vaccine used or wasted. Neither district required each clinic to submit a daily tally sheet of vaccine administered or to determine the amount of vaccine wasted.

Military participation in the projects was voluntary

In May 1976 a project visited requested the assistance of military personnel and equipment. The project director was informed that all Army bases had been instructed not to commit personnel and equipment to civilian projects. The project actively solicited military participation through June and July 1976. The director felt that the medical expertise

of military personnel, especially those in reserve units who are trained in delivering health services and in using military jet injectors, could have been effectively used.

On July 31, 1976, the project was informed that the Department of Defense was developing a national policy regarding using military personnel and equipment to support civilian immunization programs. Until this policy was issued, commitment of military personnel and equipment, even for planning purposes, was precluded.

The Department of Defense issued its policy on September 22, 1976. Since neither the funds nor the authority had been provided to use military personnel in support of civilian projects, the policy limited military participation to training activities by National Guard and Reserve medical units. Any service performed by these units had to be a byproduct of this training. Medical equipment could be loaned, upon request, but military personnel could participate in civilian programs as volunteers only.

By the time the Department of Defense policy was issued, the projects knew that vaccine would not be available in the quantity needed to begin simultaneous mass immunizations on October 1, 1976. When the projects had sufficient vaccine, demand had decreased to a point where planned clinics were being canceled. As a result, military participation in civilian projects was not pursued.

LACK OF STATE LIABILITY INSURANCE

The inability of some States to secure adequate liability protection for some or all participants nearly prevented their participation in the immunization program. However, the legislative solution arrived at may provide an effective precedent for future immunization programs.

A statement prepared by HEW's General Counsel noted that since States are sovereigns, most State and local governments are immune from tort liability under the doctrine of sovereign immunity. In addition, most local governments are not liable for employee negligence in the administration of vaccine in programs regarded as "government" functions. However, when a State or local government purchases liability insurance, immunity from tort liability is generally waived to the extent of the insurance coverage.

The HEW statement continued that, though most State and local governments are immune from tort liability, State and

local government employees may be liable for negligence in performing routine functions, such as administering vaccine in public clinics. Private physicians and other health professionals who serve either as employees of, or volunteers for, State and local governments are also probably liable for their own negligence.

Private physicians, health professionals, and State and local government employees who administered the swine flu vaccine in publicly run clinics could be sued by the Federal Government for damages and litigation costs resulting from (1) negligent administration of the vaccine, (2) failure to give adequate warning of the benefits and risks of vaccination, or (3) negligence in storing or handling the vaccine before its administration.

Some States required or authorized one or more types of protection for State and local government employees against whom suits are brought for acts of omission within the scope of their official duties. The three most common types of protection required or authorized were (1) the purchase of liability insurance, (2) indemnification of employees for damages and litigation costs, and (3) legal representation for employees sued for acts within the scope of their official duties.

In June 1976 CDC conducted a State-by-State analysis of the liability protection provided for program participants in publicly run immunization clinics. The analysis showed that only 10 States provided adequate liability protection for all participants. Fourteen States provided no liability protection for any participant. The remaining 26 States provided either liability insurance; indemnification; immunity under a tort claims act or other State law; or sovereign immunity to some, but not all, participants.

The solution--an effective method of assuring State participation

The swine flu program legislation was designed to achieve participation by public and private agencies and organizations and by medical and other health personnel by protecting them against liability claims for other than their own negligence. Like the vaccine manufacturers, State and local government employees and professional and nonprofessional volunteers, who administered the vaccine without charge and in compliance with CDC's informed consent procedures, were protected by the Federal Government against the costs associated with nonmeritorious claims. However, the Federal Government has,

notwithstanding any provision of State law, the right to recover damages awarded or paid as well as litigation costs resulting from negligent conduct on the part of any participant.

A CDC official said that only one State had purchased liability protection against the Government's right to recover. This insurance protection cost $90,000 and was limited only to the swine flu program.

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE IMMUNIZATION PROGRAMS

Project readiness and implementation were limited by biological and liability problems beyond the projects' control. For example:

--The lack of vaccine dosage recommendations for the entire population limited the projects' ability to develop strategies for immunizing persons under 25 years of age.

--Uncertainties surrounding vaccine availability inhibited the ability of the projects to make firm commitments for (1) program strategies, (2) staffing, (3) clinic locations and dates, and (4) promotional publicity which normally require specific advance scheduling.

Consequently, we could not determine whether State or local projects could be ready for future mass immunization programs.

Project operations

State and local agencies will have to make consistent firm commitments if any future mass immunization program is to succeed. In addition, they will need better program guidance and assistance from HEW in managing local projects. We recommend that the Secretary, HEW, revise and refine existing guidelines to provide:

--Criteria for establishing clinic locations and hours of operation to assure that sites selected are the most accessible for mass immunization.

--An informed consent procedure checklist, setting forth the minimum requirements established by HEW, to be completed at every clinic and returned through the project to HEW.

--Standardized vaccine inventory and accountability requirements relating to (1) obtaining accurate usage information from private physicians and health districts, regions, counties, and other jurisdictions and (2) obtaining accurate vaccination coverage rates by geographic area so that if vaccine is limited, it can be allocated accordingly.

--Procedures for obtaining the use of military jet injectors and personnel if the current national policy is revised.

Future mass immunization programs may be conducted under more stringent time constraints due to the timing of any detected flu activity and resulting increased demand for vaccine. If a flu outbreak or an epidemic is to be prevented, every component of the Nation's health system must be fully used. However, current national policy does not assure maximum use of military medical expertise in State and local programs. Therefore, the Secretary, HEW, should request the Department of Defense to revise its policy.

State liability insurance

We recommend that the Congress consider the potential impact of inadequate liability protection on State participation in future immunization programs. For future programs, the Federal Government can (1) assume total program liability, (2) assume no liability for participants, or (3) assume limited liability similar to that provided under the swine flu program.

If the Federal Government assumes total program liability, it will be assuming responsibility for functions over which it has no control. HEW cannot assure that the vaccine will be effectively administered, that adequate warning will be given, or that the vaccine will be adequately stored and handled. Although this alternative will effectively relieve the States of the need for liability protection, it could result in a significant increase in program costs to the Federal Government.

If the Federal Government assumes no liability for participants, some States will have to purchase additional liability protection for participants or limit program involvement to individuals already protected. The cost of insuring all participants may be prohibitive, or insurance may be unattainable; therefore, States may have to indemnify against damages and litigation costs, provide State exemptions from liability, or perhaps not participate in the program.

If the Federal Government assumes limited liability similar to that provided under the swine flu program, the cost of liability protection will be more equitably distributed. While the Government will assume the costs associated with nonmeritorious claims, it will retain the option of recovering damages and litigation costs resulting from negligent conduct on the part of participants. The States may then select the type of liability protection they can most effectively provide participants against potential Federal Government suits.

CHAPTER 8

PROGRAM COSTS

Total costs for the swine flu program cannot yet be accurately determined. In some instances, accounting data is too limited to identify precise costs, and in others, not all costs have been incurred or determined. Some costs--such as lost opportunity costs to other health programs--can be estimated only over time. However, total cost attributable to the swine flu program may far exceed the $135 million appropriated.

Total program costs include:

--Expenditures from funds appropriated for the program.

--Expenditures from other Federal funding sources.

--Expenditures from State and local funds to supplement the Federal grants.

--Lost opportunity costs to other health programs.

--Costs incurred for health care and lost earnings by individuals who have adverse reactions to the vaccine.

Expenditures from the $135 million appropriated for the swine flu program are projected to be about $100.2 million through June 1977. The total charges to the appropriation and other funding sources will not be known until after the program ends on August 1, 1977. Costs yet to be determined include:

--The final cost of the vaccine. Contracts for purchasing vaccine had not been finalized as of June 16, 1977.

--Department of Justice costs of litigation and Federal funds for settlements and awards for claims over $2,500 which are not recoverable from third parties. (HEW will pay settlements of $2,500 or less from the $135 million appropriated.) The total dollar amount of claims and suits filed as of March 31, 1977, exceeded $300 million.

--Personnel costs of full-time HEW employees detailed from other programs.

--State and local program costs in addition to those funded by the Federal grants, such as

-direct appropriations (one State, for example, appropriated $1.4 million for the program),

-personnel costs of full-time employees detailed from other programs, and

-additional costs for swine flu liability insurance.

--Lost opportunity costs to other programs.

--Costs incurred for health care and lost earnings by individuals because of immunization reactions.

BUDGETED COSTS

The $135,064,000 appropriated for the swine flu program was to underwrite the development, production, and distribution of necessary vaccines and to provide financial aid to help States carry out the immunization program. The budget follows.

Activity by agency		Budget amount
CDC:		
Disease control		$127,851,000
Vaccine	$100,000,000	
Project grants	26,000,000	
Direct operations	1,851,000	
FDA:		
Vaccine licensing and monitoring		3,213,000
NIAID (note a):		
Research		4,000,000
Direct operations	$ 3,500,000	
Grants	500,000	
Total appropriation		$135,064,000

a/National Institute of Allergy and Infectious Diseases.

Funds spent by CDC

CDC's final costs had not been determined as of June 16, 1977. Some direct operation costs were still being incurred, and final vaccine costs had not been determined. CDC had

spent or expected to spend all the funds budgeted for project grants and direct operations.

Vaccine costs

As of March 31, 1977, $66 million of the $100 million had been paid to manufacturers for vaccine production on a provisional payment rate (rate per dose shipped). The $100 million set aside for vaccine was based on an estimated 200 million doses to be purchased at an average cost of $0.50 a dose. However, only about 157 million doses were manufactured, and the unit cost per dose will be less than $0.50.

The exact costs of vaccine had not been determined. As of June 16, 1977, none of the manufacturers had signed final contracts. Interim letter contracts had been signed by all four manufacturers by September 22, 1976. Three of the four manufacturers and CDC have agreed to all cost elements of the final contracts. No elements may be added. Contract signing has been delayed since November 1976 pending (1) an Internal Revenue Service ruling on whether to tax as income $2.5 million included in each contract for self-insurance retention funds and (2) a decision by the Secretary of HEW on whether to waive application of the Government's cost accounting standards because of abnormal pricing provisions in the contracts. The Internal Revenue Service ruling was made on April 27, 1977. The decision regarding waiver of the cost accounting standards was still pending as of June 16, 1977.

In addition, one manufacturer and CDC are still in dispute concerning a $1.2 million production cost for Shope vaccine (a vaccine developed for another strain of swine flu) which could not be used in the program. The CDC contracting officer told us that CDC can make a unilateral determination of the price it will pay for this manufacturer's swine flu vaccine. The manufacturer then has the option to agree to this price and sign the contract or refuse to sign and make a claim against the Federal Government for the disputed amount.

Total expenditures for vaccine production are to be determined within 90 days after final vaccine deliveries are made, when final costs will be negotiated. According to Public Law 94-380, the monovalent swine flu vaccine will be provided at actual cost and a "reasonable" profit will be permitted for the manufacture of the Victoria component of the bivalent doses. Final vaccine costs will be determined only after the HEW Audit Agency has completed a postcontract award audit of all cost elements included in the contracts.

In addition to the costs of vaccine, claims for vaccine-associated injuries which do not exceed $2,500 will be paid from funds budgeted for vaccine purchases. As of March 31, 1977, CDC reported that such claims totaled over $33,000. Since additional claims may be filed and some claims might not be found meritorious, the total cost of claims paid from CDC's budget will become known at some future time.

Immunization project grants

As of March 31, 1977, HEW had awarded $25.8 of the $26 million grant funds to help State and local health departments carry out the swine flu program. CDC officials told us that the remaining $200,000 would be awarded.

Program modification and delays resulting from liability problems, delays in vaccine deliveries, decreased quantities of vaccine, adverse reactions, and other problems have increased the total program cost. Initially, 63 grants were awarded for about $24.2 million to carry out the program during July through November. Forty-eight of the 63 projects subsequently requested supplemental grants totaling about $1.6 million ($1.3 million financial assistance and $300,000 direct manpower assistance). Supplemental grants generally were for additional personnel, publicity, and materials costs associated with (1) the delays in vaccine availability, (2) adverse publicity, and (3) adverse reactions. The delays ultimately led to the extension of the program through January 1977.

Immunization projects are not required to account for expenditures from the Federal grants until 60 days after the end of the flu program. Since the program does not end until August 1, 1977, actual expenditures from the Federal grant funds are not known.

Direct operations

As of March 31, 1977, CDC had spent almost the $1.9 million budgeted. Projected CDC costs through June 30, 1977, for direct operations will exceed the $1.9 million budget by about $100,000.

Funds spent by FDA

FDA was allocated $3,213,000 to test vaccine and to conduct clinical trials. As of March 31, 1977, FDA had spent only $1,334,000 and had projected expenditures of an additional $239,000 through the end of fiscal year 1977.

Of the estimated $1,640,000 remaining, about $1 million will be transferred to the National Institute of Allergy and Infectious Diseases, as explained below.

Funds spent by the National Institute of Allergy and Infectious Diseases

The Institute was allocated $4 million for research. As of March 31, 1977, the Institute had expended about $1.3 million and projected to expend $3.4 million more during the next 3 years. Thus, the Institute's costs will probably exceed the $4 million allocated by about $700,000. To pay these additional costs, about $1 million will be transferred to the Institute from the $1,640,000 not spent by FDA.

PROGRAM COSTS PAID BY OTHER FEDERAL SOURCES

Some costs of the swine flu program have been or will be charged to other Federal sources. Principally, these include (1) salaries of full-time CDC employees diverted to the swine flu program from other health programs, (2) Department of Justice costs for litigating claims for vaccine-associated injuries and deaths, and (3) payments for meritorious claims or suits exceeding $2,500. The total amount of these costs will not be known until after the program has ended and all claims have been adjudicated.

Although CDC had primary responsibility for organizing and coordinating the swine flu program, the swine flu budget did not include funding for recruiting and forming a permanent staff within CDC specifically for the swine flu program. Funds were available for 44 temporary employees to assist with clerical and administrative duties. However, from the beginning, existing full-time CDC employees were expected to be diverted to the swine flu program from other health programs. As of March 31, 1977, the costs of CDC personnel and other resources diverted to the flu program totaled almost $1 million. This amount will increase before the flu program ends.

A Department of Justice official said that on January 28, 1977, the Office of Management and Budget approved a Department of Justice supplemental budget of $1,228,000 for swine flu litigation in fiscal year 1977. The budget included 28 new positions (19 additional attorneys and 9 support staff). The Department estimates that at least 28 positions will be needed through fiscal year 1980. Thereafter, the staff will be reduced based on the number of suits still in litigation.

As of March 31, 1977, the budget request had not been approved by the Congress and the Department had only five attorneys and one support staff detailed to the swine flu program.

All claims and suits for injury or death associated with the swine flu program will be litigated in accordance with the Federal Tort Claims Act, as amended. The number and amount of claims and suits which will be found meritorious and the awards or settlements which will be made cannot be predicted. As of March 31, 1977, 282 claims and 14 suits had been filed totaling over $300 million. 1/ In addition, over 3,000 inquiries requesting procedures for filing claims had been received. A Department of Justice official estimated that between 4,000 and 4,500 claims and suits will ultimately be filed, totaling over $1 billion.

PROGRAM COSTS PAID BY STATE AND LOCAL AGENCIES

In addition to the Federal grant funds, State and local resources were used to develop, organize, and carry out the flu program. Total expenditures by State and local agencies were not available as of March 31, 1977. Though projects may estimate total program costs, they will be able to specifically account for only the Federal grant expenditures.

Public Law 94-380 requires HEW to determine the costs incurred by State and local agencies. HEW expanded an existing contract with the Association of State and Territorial Health Officers to estimate State and local agency costs by surveying State and local agencies. The survey began in March 1977, and HEW intended to give the Congress the costs estimates on April 1, 1977. However, because of administrative routing and approval requirements for the survey and difficulties in obtaining cost estimates from some projects, the report has been delayed.

Commitment of resources has varied from project to project, depending on individual strategies for using volunteers and other health care providers. One project estimated that an amount equal to its approximately $500,000 grant would be expended from State revenues. Another project appropriated $1.4 million in State funds to supplement its $900,000 Federal

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1/This includes one suit for $200 million, which a Department of Justice official stated will probably not result in an award or settlement.

grant. Some projects, while not specifying a cost, indicated that State and county employees had been redirected to the flu program.

Because the program was extended, State and local health employees were diverted from their normal duties for longer periods, thereby increasing costs to State and local projects.

LOST OPPORTUNITY COSTS

A formal determination of lost opportunities to other health programs has not been made. HEW and other swine flu program participants knew from the beginning, however, that some penalty costs to other health programs might be incurred because existing health department personnel would be diverted to the swine flu program.

We did not measure the adverse effects of these diversions. A statistical analysis showing either decreases in the number of people receiving other health services or the number of people diverted from other health programs does not necessarily mean an adverse impact. Determining the impact would require identification and analysis over time of the effects on outcomes, such as disease incidence trends.

The diversions of health department employees had in some cases caused delays, modification, or cancellations to other health programs in projects reviewed. For example:

--A major city had to delay its annual school immunization program until the second semester.

--A county discontinued its diabetes screening until the end of the flu program.

--Throughout the swine flu program, one urban county discontinued a Medicaid program designed to provide early and periodic health care screening and treatment for eligible children.

In addition, CDC delayed plans for expanding an experimental strategy for immunizing against measles because of the priority on the swine flu program. The new strategy--referred to as an outbreak containment strategy--was similar to the smallpox vaccination campaign in Africa in which only persons in areas where a disease outbreak had been detected were vaccinated. At the onset of the flu program, CDC had applied this strategy in five States and planned to expand it in another four States. However, expansion of the experimental strategy was limited to two States because of the priority on the swine flu program.

HEALTH CARE COSTS AND LOST EARNINGS OF INDIVIDUALS WHO HAVE ADVERSE REACTIONS TO THE VACCINE

HEW developed guidelines for reporting and investigating adverse reactions related to swine flu immunization. Any illness occurring after flu vaccination in which the patient required (1) hospitalization or (2) bedcare and an outpatient visit to a public or private health facility was to be reported to HEW. Less serious reactions were not to be reported.

Although HEW provided guidance on when and how adverse reactions were to be reported, it did not provide recommendations on how adverse reactions were to be identified. While some projects planned active surveillance systems, most projects relied on individuals vaccinated, private physicians, hospitals, and health departments to take the initiative for reporting adverse reactions.

The total number of adverse reactions and corresponding health care costs and lost earnings cannot be determined because illnesses which did not require either hospitalization or an outpatient visit were not required to be reported and surveillance systems employed by some projects could not assure that all reportable reactions were identified. One project director indicated that an optimistic goal would be to identify 40 percent of the total adverse reactions in the State. He noted that intensified surveillance by the State after the first Guillain-Barre case was reported, identified 25 other severe reactions that had not been reported.

At least 3,888 adverse reactions to the vaccine had been reported to CDC by April 10, 1977. Although HEW plans to determine certain economic losses associated with these reactions, the final estimate will not reflect all costs incurred.

CONSIDERATIONS FOR FUTURE IMMUNIZATION PROGRAMS

The swine flu program has shown that the total cost of such an effort is difficult to predict and may include much more than funds appropriated. Further, the total direct cost may be difficult to identify and certain indirect costs may be incalculable.

CHAPTER 9

SCOPE OF REVIEW

We made our review at CDC in Atlanta; the Bureau of Biologics, Food and Drug Administration; and the National Institute of Allergy and Infectious Diseases, National Institutes of Health in Bethesda, Maryland. We reviewed legislation, examined records and files, interviewed agency officials, and monitored events as they occurred between August 1976 and March 1977.

We also monitored program implementation at five immunization projects--the States of Florida, Georgia, Maryland, and Pennsylvania and the city of Philadelphia. These projects received over $3.2 million in grants for the program. We examined records and files; interviewed State, county, city, regional, and district health officials; and visited 26 mass immunization clinics within these project areas.

These five projects were not selected as a representative sample of program results in other areas. We supplemented information obtained from these projects with (1) a limited number of project self-evaluation reports and (2) information developed by CDC concerning the other projects. We did not contact the drug manufacturers.

We contacted officials of the Department of Justice in Washington, D.C., to determine the status of claims for damages against the Federal Government resulting from the program. We also contacted HEW Region IV Audit Agency officials concerning their reviews of vaccine cost.

APPENDIX I

IMPORTANT INFORMATION ABOUT SWINE INFLUENZA (FLU) VACCINE (MONOVALENT)

July 15, 1976

The Disease

Influenza (flu) is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

It is unlikely that you have adequate natural protection against swine flu, since it has not caused widespread human outbreaks in 45 years.

The Vaccine

The vaccine will not give you flu because it is made from killed viruses. Today's flu vaccines cause fewer side effects than those used in the past. In contrast with some other vaccines, flu vaccine can be taken safely during pregnancy.

One shot will protect most people from swine flu during the next flu season; however, either a second shot or a different dosage may be required for persons under age 25. If you are under 25 and a notice regarding such information is not attached, this information will be provided to you wherever you receive the vaccine.

Possible Vaccine Side Effects

Most people will have no side effects from the vaccine. However, tenderness at the site of the shot may occur and last for several days. Some people will also have fever, chills, headache, or muscle aches within the first 48 hours.

Special Precautions

As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated with severe or fatal reactions. In some instances people receiving vaccine have had allergic reactions. You should note very carefully the following precautions:

- **Children under a certain age should not routinely receive flu vaccine. Please ask about age limitations if this information is not attached.**
- **People with known allergy to eggs should receive the vaccine only under special medical supervision.**
- **People with fever should delay getting vaccinated until the fever is gone.**
- **People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.**

If you have any questions about flu or flu vaccine, please ask.

REGISTRATION FORM

I have read the above statement about swine flu, the vaccine, and the special precautions. I have had an opportunity to ask questions, including questions regarding vaccination recommendations for persons under age 25, and understand the benefits and risks of flu vaccination. I request that it be given to me or to the person named below of whom I am the parent or guardian.

INFORMATION ON PERSON TO RECEIVE VACCINE

Name (Please Print) _____ Birthdate _____ Age _____

Address _____ County of Residence _____

Signature of person to receive vaccine or Parent or Guardian _____ Date _____

FOR CLINIC USE

Clinic Ident. _____

Date Vaccinated _____

Manufacturer and Lot No. _____

CDC 7.31
7-76

U.S. Department of Health, Education, and Welfare / Public Health Service / Center for Disease Control / Atlanta, Georgia 30333

IMPORTANT INFORMATION ABOUT SWINE AND VICTORIA INFLUENZA (FLU) VACCINE (BIVALENT)

July 15, 1976

The Disease

Influenza (flu) is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

It is unlikely that you have adequate protection against swine flu, since it has not caused widespread human outbreaks in the past 45 years. You may or may not have adequate protection against Victoria flu, although many Americans had this flu last winter. It was responsible for over 12,000 deaths.

The Vaccine

The vaccine will not give you flu because it is made from killed viruses. Today's flu vaccines cause fewer side effects than those used in the past. In contrast with some other vaccines, flu vaccine can be taken safely during pregnancy.

One shot will protect most people from swine and Victoria flu during the next flu season; however, either a second shot or a different dosage may be required for persons under age 25. If you are under 25 and a notice regarding such information is not attached, this information will be provided to you wherever you receive the vaccine.

Possible Vaccine Side Effects

Most people will have no side effects from the vaccine. However, tenderness at the site of the shot may occur and last for several days. Some people will also have fever, chills, headache, or muscle aches within the first 48 hours.

Special Precautions

As with any vaccine or drug, the possibility of severe or potentially fatal reactions exists. However, flu vaccine has rarely been associated with severe or fatal reactions. In some instances people receiving vaccine have had allergic reactions. You should note very carefully the following precautions:

- **Children under a certain age should not routinely receive flu vaccine. Please ask about age limitations if this information is not attached.**
- **People with known allergy to eggs should receive the vaccine only under special medical supervision.**
- **People with fever should delay getting vaccinated until the fever is gone.**
- **People who have received another type of vaccine in the past 14 days should consult a physician before taking the flu vaccine.**

If you have any questions about flu or flu vaccine, please ask.

*USGPO: 1976 – 216-225

REGISTRATION FORM

I have read the above statement about swine and Victoria flu, the vaccine, and the special precautions. I have had an opportunity to ask questions, including questions regarding vaccination recommendations for persons under age 25, and understand the benefits and risks of flu vaccination. I request that it be given to me or to the person named below of whom I am the parent or guardian.

INFORMATION ON PERSON TO RECEIVE VACCINE

Name (Please Print) _____ Birthdate _____ Age _____

Address _____ County of Residence _____

Signature of person to receive vaccine or Parent or Guardian _____ Date _____

FOR CLINIC USE

Clinic Ident. _____

Date Vaccinated _____

Manufacturer and Lot No. _____

CDC 7.32
7-76

U.S. Department of Health, Education, and Welfare / Public Health Service / Center for Disease Control / Atlanta, Georgia 30333

APPENDIX III

Important Information from the U.S. Public Health Service about Swine Flu and Victoria Flu Vaccines

INTRODUCTION

You probably have heard a good deal about swine flu and swine flu vaccine. You may know, for example, that swine flu caused an outbreak of several hundred cases at Ft. Dix, New Jersey, early in 1976- and that before then swine flu had not caused outbreaks among people since the 1920's.

With the vast majority of Americans being susceptible to swine flu, it is possible that there could be an epidemic this winter. No one can say for sure. However, if an epidemic were to break out, millions of people could get sick. Therefore, a special swine flu vaccine has been prepared and tested which should protect most people who receive it.

Certain people, such as those with chronic medical problems and the elderly, need annual protection against flu. Therefore, besides protection against swine flu, they also need protection against another type of flu (Victoria flu) that was around last winter and could occur again this winter. A separate vaccine has been prepared to give them protection against both types of flu.

These vaccines have been field tested and shown to produce very few side effects. Some people who receive the vaccine had fever and soreness during the first day or two after vaccination. These tests and past experience with other flu vaccines indicate that anything more severe than this would be highly unlikely.

Many people ask questions about flu vaccination during pregnancy. An advisory committee of the Public Health Service examined this question and reported that "there are no data specifically to contraindicate vaccination with the available killed virus vaccine in pregnancy. Women who are pregnant should be considered as having essentially the same balance of benefits and risks regarding influenza vaccination and influenza as the general population."

As indicated, some individuals will develop fever and soreness after vaccination. If you have more severe symptoms or if you have fever which lasts longer than a couple of days after vaccination, please consult your doctor or a health worker wherever you receive medical care.

While there is no reason to expect more serious reactions to this flu vaccination, persons who believe that they have been injured by this vaccination may have a claim. The Congress recently passed a law providing that such claims, with certain exceptions, may be filed only against the United States Government. Information regarding the filing of claims may be obtained by writing to the U.S. Public Health Service Claims Office, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20852.

Attached is more information about flu and flu vaccine. Please take the time to read it carefully. You will be asked to sign a form indicating that you understand this information and that you consent to vaccination.

CDC 7.32A 8-76 U.S. Department of Health, Education, and Welfare / Public Health Service / Center for Disease Control / Atlanta, Georgia 30333

APPENDIX IV

VOLUNTARY CONSENT FORM

IMPORTANT INFORMATION ABOUT SWINE AND VICTORIA INFLUENZA (FLU) VACCINE (BIVALENT)

February 1977

A program for voluntary immunization of individuals against both swine and Victoria flu was begun in the fall of 1976 under a special act of Congress. Over 42 million people were vaccinated under the program. In December the Public Health Service received reports that some who had been vaccinated had suffered an illness called Guillain-Barré which is described later in this document. As a result, the program was suspended December 16 to determine whether and to what extent Guillain-Barré was caused by the flu shots.

After review of additional and more detailed information and after further consultation with medical and other experts concerning both the occurrence of a limited number of cases of Victoria flu and the causes of Guillain-Barré, the immunization program has been resumed on a limited basis. The reason for this partial resumption is to give certain American people, particularly the elderly and persons with chronic illnesses who have a high risk of suffering serious adverse consequences from influenza, an opportunity to be vaccinated against Victoria influenza.

THE FLU

Flu is caused by viruses. When people get flu they may have fever, chills, headache, dry cough or muscle aches. Illness may last several days or a week or more, and complete recovery is usual. However, complications may lead to pneumonia or death in some people. For the elderly and people with diabetes or heart, lung, or kidney diseases, flu may be especially serious.

If you are less than fifty years old, you are unlikely to have developed natural immunity to swine flu because no significant number of people have been sick with it for some 45 years. You may or may not have some natural immunity to Victoria flu.

While there was a substantial number of cases of Victoria flu last year, there has been no significant number of reported cases of swine flu since a brief and limited outbreak of the disease at Fort Dix, New Jersey in early 1976.

It is not possible to estimate the risk to an individual of getting the flu this year.

THE VACCINE

This vaccine contains the only available immunization against Victoria flu. It also contains the swine flu vaccine. It will not give you flu because it is made from killed viruses. A single shot will protect approximately three out of four persons age 25 and over from these two types of flu for the rest of the current flu season; the vaccination may not be effective in approximately one out of four persons age 25 and over. For persons under 25 a second shot must be taken at least one month after the first shot to provide the same likelihood of protection.

RISKS AND SIDE EFFECTS

Most people will have no harmful side effects from the vaccine. Some will have tenderness in the area of the shot for a day or so. A few will have fever, chills, headaches, or muscular aches within the first 48 hours. However, as with the administration of any vaccine or drug, there is always the possibility of more severe effects and in rare instances even of death.

GUILLAIN-BARRÉ

As mentioned, there is recent evidence that Guillain-Barré appears in some people after vaccination. When it appears, it generally does so within a few weeks of vaccination. Information collected for the purposes of the flu immunization program to date shows that among persons who have not taken flu vaccine, slightly more than one in a million get Guillain-Barré during any eight week period. However, during the period of eight weeks after vaccination, about ten out of every million persons vaccinated have suffered Guillain-Barré. Thus, while the risk is not high, evidence suggests that persons who are vaccinated are approximately ten times more likely to get Guillain-Barré than those who are not vaccinated.

Guillain-Barré can be relatively mild to very severe. It causes a paralysis, usually of the legs and arms. In most cases the paralysis disappears and the recovery is complete. Recent statistics indicate, however, that in about five percent of the cases the patient dies, and in about ten percent of the cases some muscles will be weak for a long time or permanently. Thus, the risk of death from Guillain-Barré for persons of all age groups who are vaccinated is approximately one out of two million. For elderly and chronically ill persons the risk of death from Guillain-Barré is approximately one out of every one million persons vaccinated.

PREGNANCY

Many people ask about the risks of flu vaccination during pregnancy. There is not now any specific data on whether the risks are the same or different from what they are for the general population. For this reason a pregnant woman should be advised by a doctor on the benefits and risks for her or her offspring.

SPECIAL PRECAUTIONS

Some people should not take flu vaccine. You should note very carefully the following precautions.

- A child under 3 years of age in good health should not ordinarily receive flu vaccine. If the child has a serious chronic illness, the vaccine may be recommended but you should see a doctor first.
- People allergic to eggs should be vaccinated only on the advice and under the supervision of a doctor.
- People with fever should not be vaccinated until the fever is gone.
- People who have received another type of vaccine in the past 14 days should see a doctor before taking the vaccine.

If after vaccination you have any symptoms more severe than a moderate fever, chill, headache or mild muscular ache within the first 48 hours or any symptoms continue longer than 48 hours, you should see a doctor.

INJURY CLAIMS

While the risk of harm from flu vaccine is small, those who believe they have been injured by this vaccination may have a claim. The law provides that a claim may normally be filed against the United States Government. Information on how to file a claim may be obtained by writing to the U.S. Public Health Service Claims Office, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857.

IF YOU HAVE ANY QUESTIONS ABOUT FLU OR FLU VACCINE, PLEASE ASK

CONSENT

I have read the above information about Victoria and swine flu, the vaccine, and the special precautions. I have had an opportunity to ask questions, and I understand the benefits and risks of flu vaccination as described in this document. I request that it be given to me or to the person named below for whom I am authorized to consent.

INFORMATION ON PERSON TO RECEIVE VACCINE

Name (Please Print) _____ Birthdate _____ Age _____

Address _____ County of Residence _____

Signature of person to receive vaccine or Parent or Guardian _____ Date _____

FOR CLINIC USE

Clinic Ident. _____

Date Vaccinated _____

Manufacturer and Lot No. _____

U.S. Department of Health, Education, and Welfare / Public Health Service / Center for Disease Control / Atlanta, Georgia 30333

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COMPARISON OF CLINICAL TRIAL POTENCY TEST RESULTS ON MONOVALENT AND BIVALENT SWINE FLU VACCINE

Lot	Designated value (CCAs)	Manufacturer test results	FDA test results
A	200	228	132
B	200	300	180
C	200	208	180
D	200	216	192
E	200	312	194
F	200	252	204
G	200	252	228
H	400	480	300
I	400	396	312
J	400	470	324
K	400	636	348
L	400	420	360
M	400	600	392
N	800	984	660
O	800	861	684
P	800	1,008	696
Q	800	1,224	720
R	800	880	732
S	800	948	768

PRINCIPAL HEW OFFICIALS RESPONSIBLE FOR ACTIVITIES DISCUSSED IN THIS REPORT

	Tenure of Office From	To
SECRETARY OF HEALTH, EDUCATION, AND WELFARE:		
Joseph A. Califano, Jr.	Jan. 1977	Present
David Mathews	Aug. 1975	Jan. 1977
ASSISTANT SECRETARY FOR HEALTH:		
James F. Dickson III (acting)	Jan. 1977	Present
Theodore Cooper	May 1975	Jan. 1977
DIRECTOR, NATIONAL INFLUENZA IMMUNIZATION PROGRAM:		
W. Delano Meriwether	Apr. 1976	Present
DIRECTOR, CENTER FOR DISEASE CONTROL:		
William H. Foege	May 1977	Present
David J. Sencer	Feb. 1966	May 1977
COMMISSIONER, FOOD AND DRUG ADMINISTRATION:		
Donald Kennedy	Apr. 1977	Present
Sherwin Gardner (acting)	Dec. 1976	Apr. 1977
Alexander M. Schmidt	July 1973	Dec. 1976
DIRECTOR, BUREAU OF BIOLOGICS:		
Harry M. Meyer	July 1972	Present
DIRECTOR, NATIONAL INSTITUTES OF HEALTH		
Donald S. Fredrickson	July 1975	Present
DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES:		
Richard M. Krause	Nov. 1975	Present