DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

CENTER FOR DISEASE CONTROL
Atlanta, Georgia

# SUMMARY MINUTES OF MEETING

July 6-7, 1978

The Immunization Practices Advisory Committee met in Atlanta, Georgia, July 6-7, 1978, in conjunction with the Panel on Review of Viral Vaccines and Rickettsial Vaccines of the Bureau of Biologics, and others. Those participating in the meeting are listed below:

COMMITTEE MEMBERS PRESENT
Dr. E. Russell Alexander
Dr. Edwin D. Kilbourne
Dr. Reuel A. Stallones
Dr. Thomas Vernon, Acting Chairman

Ex-Officio Members Present
Dr. William Jordan
Dr. Harry Meyer, Jr.

Liaison Members Present
Dr. Edward A. Mortimer, AAP
Dr. Asher Finkel, AMA
Dr. Crawford Anglin, Canada
(for Dr. J.M.S. Dixon)

COMMITTEE MEMBERS EXCUSED
Dr. Suzanne E. Dandoy

PROPOSED NEW MEMBERS PRESENT
Dr. Maxine Hayes
Dr. Jay P. Sanford
Dr. Catherine Wilfert
Dr. Kenneth Wilcox

PROPOSED NEW MEMBERS ABSENT
Dr. William J. Curran

BUREAU OF BIOLOGICS (Review Panel)
Dr. John P. Fox
Dr. Saul Krugman
Dr. Kenneth McIntosh
Dr. June Osborn

Biologics Steering Committee
Dr. David Karzon
Dr. Samuel Katz

BUREAU OF BIOLOGICS, Continued
Staff
Dr. Frank Ennis
Dr. Paul Parkman
Mr. Lawrence Fraise
Dr. Gerry Quinnan
Ms. Hope Hopps

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
Contractors and Advisors
Dr. Gordon Mieklejohn

Staff
Dr. George Curlin
Dr. George Galasso
Dr. John LaMontagne
Dr. John Seal
Dr. Jacqueline Smith

CENTER FOR DISEASE CONTROL
Mr. Windell Bradford
Mr. Arthur C. Curtis
Dr. Walter Dowdle
Dr. H. Bruce Dull
Dr. Alan R. Hinman, Acting
Executive Secretary
Dr. Alan Kendal
Ms. Katherine Lord
Dr. Philip Nieburg
Dr. Gary Noble
Dr. Stephen Preblud
Mrs. Kathy Rufo

VACCINE MANUFACTURERS
Robert C. Brackett (Parke Davis)
F. Brandon (Parke Davis)

VACCINE MANUFACTURERS, Continued
Michael J. DuBois (Sandoz)
Dr. Alan Gray (Merck Sharp & Dohme)
Dr. Geoffrey Kalish (Lederle)
Ms. Bonnie Ryan Lynn (Lederle)
Frank McCarthy (Wyeth)
Patricia H. McVery (Connaught)
Dr. Eugene Timm (Parke Davis)
Dr. Howard Tint (Wyeth)
Mr. Bill McIntosh (Merck Sharp & Dohme)

OTHERS
D. W. Boucher
Health and Welfare Canada

A. Boudeault
Institut Armand Frappier

Dr. J. A. Morris
Greenbelt, Maryland

Ms. Frances R. Ogasawara
American Lung Association

Vytoutas Pavilanis
Institut Armand Frappier

Ron Smith
General Accounting Office

Charles Taylor
United Press International

Dr. Peter Wright
Vanderbilt University

The meeting was called to order by the Acting Chairman. The agenda as circulated was followed. Materials handed out to participants formed the primary basis for discussion during the course of the meeting. The entire meeting was devoted to review of information on influenza, the influenza vaccine clinical trials, and development of recommendations on influenza vaccines.

A brief summary of influenza activity at the present time was presented. There has been no influenza activity in the United States since the previous meeting. Both H3N2 and H1N1 strains have been reported from Argentina and Brazil; H1N1 influenza has been recovered from Chile, and H3N2 from Ecuador. There are as yet no reports of significant influenza activity in the southern hemisphere outside of the Americas.

The present status of the proposed influenza immunization program was discussed. A formal proposal has been presented to Congress and hearings have been held before 3 of the 4 affected committees. Final actions were expected by Congress within the next 4-8 weeks.

Review of data regarding the occurrence of Guillain-Barre syndrome and influenza vaccine in Ohio had suggested a significantly higher association with one particular lot of vaccine than with others used in Ohio. National data regarding the occurrence of GBS and particular lots of vaccine were reviewed. The lots varied in size from about 60 thousand doses to over 1 million doses. Of the more than 150 lots of vaccine which were used in the swine influenza program, approximately one-third had no cases of GBS associated. Among other lots there was wide variation in the number and rate of cases reported. However, this variation did not differ significantly from what would have been expected by random chance. That is, there were no obvious "hot lots."

The Committee was presented with findings of a group of outside consultants who had recently been asked to review the CDC's approach to measuring excess mortality and to comment on its utility and validity. The consultants concluded that there was continuing merit in measuring excess mortality associated with influenza and recommended that attempts be made to improve the means of calculating expected mortality and validating the data.

There was then a presentation on the use of micrograms of hemagglutinin protein as a standard measurement of vaccine content compared to previous measurements using chick cell agglutinating units. Because there is not a straight-line correlation between microgram hemagglutinin content and CCA unit strength, it is not possible to make a single statement regarding conversion from one potency measuring system to the other. Data were then presented indicating that the neuraminidase activity of the A/USSR antigen is 4-15 fold lower than that of the A/Texas antigen.

Attention then turned to the design, conduct, and results of the field trials. Initial design considerations indicated that, in order to make the most detailed analysis of all possible combinations of vaccine type, dosage, manufacturer, and age group, a total of more than 4,000 volunteers in the civilian population would be desired. Since the military was considering even different dosage levels, 450 military volunteers were desired. At the time of the meeting, a total of 2,066 individuals (including 134 in the military) had been enrolled in the clinical studies. The clinical trial protocols involved drawing a pre-vaccination serum, administering vaccine, drawing a second serum 4 weeks later, and administering a second dose of vaccine, and drawing a third serum 2 weeks after the second dose of vaccine. The field trials began in April and were ongoing at the time of the meeting. All sera obtained from patients were tested at CDC. Antibody titers to A/USSR were tested with both whole virus (traditional) and an ether-treated "split" virus. Data were then presented indicating the

antibody response of individuals infected with A/USSR as determined using these techniques. Generally speaking, the levels detected with the split-virus test were approximately 1 dilution higher than those with using the old whole-virus test.

Data from the field trials indicated that, for those 26 years of age and older, a single dose containing 7 micrograms of each of the 3 antigens would give a satisfactory antibody response (70-90%) with systemic reactions to the vaccine at a level not significantly different from that in the placebo group. For the 13-25 age group, the data indicated that 2 doses would be necessary and that 20 micrograms of the A/USSR antigen were superior to 7 micrograms in producing antibodies at a titer of 1:40 or greater. Data presented on children under 13 years of age were quite limited, and the Committee did not feel that the data were adequate to make a final recommendation about dosage.

Presentations were made of data from field trials carried out by Parke Davis company, by the Armand Frappier Institut of Montreal, and in the United Kingdom. In general, these data indicated the need for 2 doses of A/USSR vaccine for those less than 26 years of age and that a single dose at essentially any dosage level in those 26 years of age or older would yield satisfactory antibody levels. In an outbreak of A/USSR in asthmatic children in Denver, the attack rate was quite high (67% in one building), but the character of the illness was relatively mild. At Lowry Air Force Base there was a sharp outbreak of influenza due to A/USSR which appeared only in recruits and not in the permanent staff. Limited data in younger individuals at Lowry indicated that 60 micrograms of A/USSR antigen in a single dose would give a fairly good serologic response. whereas a single dose of 20 micrograms would not.

The question of availability of influenza vaccine was then discussed. Representatives of 2 vaccine manufacturers, without committing themselves officially, indicated that vaccine stock had already been made, and that this stock would be adequate to produce as much vaccine as would reasonably be required at a 7-microgram dosage level, but that there would be substantial problems in providing adequate numbers of doses if everyone required a 20-microgram dosage level.

There was general agreement that a single dose of the trivalent vaccine containing 7 micrograms each of the 3 antigens would be adequate for those 26 years of age and over. For those under 26, it was agreed that the vaccine should contain 20 micrograms of A/USSR and 7 micrograms each of the other 2 vaccines and should be given twice.

Prior to adjournment, Drs. Stallones and Hayes were asked to review information about influenza and influenza vaccine in pregnancy, particularly in view of a letter submitted by Dr. Stephen Schoenbaum on the subject;

Dr. Russell Alexander was asked to chair a small group to review the sections of the Preliminary Recommendations dealing with "Influenza Vaccine for 1978-79" and "Vaccine Usage;" and Dr. Jay Sanford was asked to chair a small group to address the subject of "Side Effects."

The meeting was reconvened at 8:30 a.m. on July 7. The first item of discussion was whether or not data were adequate to make final recommendations for those under the age of 13. It was decided that, since data on a much higher proportion of the 280 children now in the study would be available in approximately 2 weeks, a subcommittee would review the data as soon as they become available. Given these circumstances, it would be necessary to postpone issuance of a final statement until the MMWR issue of August 4, 1978. Drs. Karzon, Mortimer, Wilcox, Vernon, and Kilbourne agreed to serve on a subcommittee to review data on children as soon as they become available.

Discussion then turned to whether whole or split virus vaccine ought to be recommended for those between the ages of 13 and 25. A special printout of results from the clinical trials was obtained and indicated no difference in reaction rates for younger individuals between whole and split virus products. It was, therefore, the consensus that either whole or split virus products could be used for those between 13 and 25 years of age.

General and specific discussion of the draft statements ensued with the result that many proposed revisions were indicated and given to the Acting Executive Secretary and Acting Chairman for circulation to the group.

General discussion then followed as to whether or not the traditional recommendation as to "high risk groups" were appropriate. Dr. John Fox was of the opinion that ultimately we ought to aim at reducing morbidity, not just mortality, and therefore influenza immunization programs ought to aim at annual influenza immunization of virtually the entire population. Dr. Morris stated that he would not recommend that this vaccine be used for anyone. Dr. Vernon stated that the data indicated that the vaccine is safe and effective and that the question is, who should most appropriately receive it. Dr. Osborn pointed out that the Secretary's January 30 conference recommended a priority listing of the entire population with no absolute cut-off of individuals who should or should not receive vaccinations. Dr. Meyer then indicated that repeated conferences had come to the view that influenza vaccine was "acceptably safe" and "acceptably effective."

It was then agreed that a draft "Final Statement" minus the specific recommendations for those under age 13 would be circulated to Committee members within the week; that the aforementioned subcommittee would review

data on those under 13 as soon as they became available; and that every effort would be made to issue a final statement in the August 4 issue of MMWR.

The meeting adjourned at 12:00 noon on July 7, 1978.

I hereby certify that, to the best of my knowledge, the foregoing summary of minutes is accurate and complete.

Alan R. Hinman, MD 31.VII.78

Acting Executive Secretary Date