DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

CENTERS FOR DISEASE CONTROL AND PREVENTION

Minutes of Meeting

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES
June 28 & 29, 1995

Atlanta, Georgia

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES
Centers for Disease Control and Prevention
June 28-29, 1995 - Auditorium A

JUNE 28

8:30 AM	Introduction	Dr. J. Davis Dr. D. Snider
9:00 AM	The Approach to Developing ACIP Vaccine Recommendations	Dr. S. Schoenbaum Dr. D. Snider Dr. J. Ward
9:45 AM	Hepatitis A Vaccine - Use in High Endemic Populations	Dr. J. Cheek Indian Hlth Service Dr. C. Shapiro Dr. T. Welty Indian Hlth Service
10:45 AM	BREAK	
11:00 AM	Varicella Update	Dr. M. Wharton
11:30 AM	Vaccines for Children Program Hepatitis A Hepatitis B Varicella	Dr. S. Hadler Dr. H. Margolis Dr. C. Shapiro
1:00 PM	LUNCH	
2:00 PM	Polio Vaccine Policy	Dr. S. Hadler Dr. P. Strebel Dr. R. Sutter
3:30 PM	BREAK	
3:45 PM	Polio Vaccine Policy (continued)	
5:30 PM	Adolescent Immunization Visit	Dr. F. Averhoff Dr. W. Williams
6:00 PM	ADJOURN	

JUNE 29

8:15 AM	Polio Wrap-up	
8:45 AM	Vaccine Safety Update Measles Vaccination: a Risk Factor for Inflammatory Bowel Disease Large-Linked DataBase (LLDB) Result: Tape 2 Preference of DTaP over DTP for 4th & 5th Doses	Dr. B. Chen Dr. P. Rhodes Dr. S. Rosenthal Dr. G. Terracciano
9:30 AM	Measles Elimination Update	Dr. S. Redd
10:00 AM	Diphtheria and the New Independent States Update U.S. Contingency Plan	Dr. I. Hardy Dr. P. Strebel
10:30 AM	BREAK	
10:45 AM	Programmatic Strategies to Increase Immunization Coverage	Dr. E. Maes
11:30 AM	Pneumococcal Vaccine	Dr. J. Butler
12:00 PM	Harmonization of Immunization Recommendations	Dr. J. Gindler
12:30 PM	LUNCH	
1:15 PM	National Vaccine Program Update	Dr. R. Breiman
1:45 PM	Acellular Pertussis Vaccine Trials - Status	Dr. P. Strebel
2:00 PM	ACIP Recommendations and Package Inserts	Dr. S. Hadler Dr. M. Wharton
2:15 PM	Electronic Updating of ACIP Recommendations	Dr. S. Hadler Dr. P. O'Carroll
2:45 PM	Injury Compensation Program Update	Dr. G. Evans
3:00 PM	Public Comment	
3:15 PM	ADJOURN	

ATTENDEES:

Committee Members
Dr. Jeffrey Davis (Chair)
Dr. Barbara Ann DeBuono
Dr. Kathryn Edwards
Dr. Marie Griffin
Dr. Fernando Guerra
Dr. Neal Halsey
Dr. Rudolph Jackson
Dr. Steve Schoenbaum
Dr. F. Thompson
Dr. Joel Ward

Ex Officio Members
Dr. Geoffrey Evans, (VICP)
Dr. Carolyn Hardegree (FDA)
Dr. G. Rabinovich (LaMontagne)
Dr. Jerry Zelinger, (HCFA)

Liaison Representatives
Dr. Robert Breiman (NVPO)
Dr. William Butler (DOD)
Dr. Richard Clover (ATPM)
Dr. Thomas Copmann (PhRMA)
Dr. David Fleming (HICPAC)
Dr. Stanley Gall, (ACOG)
Dr. Pierce Gardner (ACP)
Dr. William Glezen (IDSA)
Dr. Randolph Graydon, (HCFA)
Dr. Caroline B. Hall (AAP)
Dr. Edward Mortimer (AMA)
Dr. Kristin Nichol (VA)
Dr. Georges Peter (AAP)
Dr. William Schaffner (AHA)
Dr. David Scheiffle (NACI)
Dr. Richard Zimmerman (AAFP)

Executive Secretary
Dr. Dixie Snider

Officer of the Director
Dr. Alan Hinman

Office of the General Counsel
Mr. Kevin Malone
Mr. Eugene Matthews

Office of Public Affairs
Barbara Reynolds

CDC Clinic
Lindsey Bowman

National Center for Infectious Diseases
Dr. Ruth Berkelman
Dr. Pekka Nuoti
Dr. Gary Sanden

National Center for Prevention Services
Rosamond Dewart

National Immunization Program
Dr. Francisco Averhoff
Dr. Bob Chen
Kim Crumly
Dr. Vance Dietz
Jon Deirer
Dr. Elias Durry
Connie Ferrar
Judy Gantt
Dr. Jacqueline Gindler
Dalya Guris
Dr. Steve Hadler
Dr. Iain Hardy
Edward Hoekstra
Dr. Sonja Hutchins
Hector Izurieta
Dr. Alan Kendal
Hugh Mainzer
Martha Mayfield
Dr. Mark Miller
Dr. Bill Murain
Bill Nichols
Dr. W. Orenstein
Mark Papania
Dr. Steve Redd
Dr. Susan Reef

Linda Schultz
Dr. Robert Snyder
Sonsrere Cobb Sonzo
Dr. Peter Strebel
Dr. Ray Strikas

National Immunization Program Cont.
Dr. Roland Sutter
Carlene Tsai
Dr. Frederik VanLoon
Dr. Joe Williams
Dr. Walter Williams
Dr. Melinda Wharton

National Vaccine Program Office
Mr. Steve Sepe

CDC
J. Christensen
Trent MacKay

Indian Health Service
James E. Cheek

National Institutes of Health
Bruce Gellin

Food and Drug Administration
Miles Braun
Judy Beeler
Nancy Cherry
James Donlon
Carl Ellison
Dr. Elaine Esber
Dr. Karen Goldenthal
Marie Mann
Karen Midthun
Manette Niu
Ann Wion
Bob Wise

Navy Environmental Helath Center
CDR. Gil Potter

Others Present
James P. Altomare, Merck & Co., Inc.
Luis Barreto, Connaught Labs, Ltc.
Linda J. Bell, M.D., SC Department of Health
Florence Berut, Connaught Labs., Inc.
Ann Bostrom, School of Public Policy, Georgia Tech
Lindsey Bowman, CDB Healthcare
Dee Breeden, MD, Bureau Preventive Health Services
Klaus Bro-Jorgensen, M.D., D.Sc., Statens Seruminstitut
Brian Budisak, Wyeth-Lederle Vaccines & Pediatrics
Les Burd, IZ Branch, State of California
Jill Chamberlain, Vaccine Bulletin
Mike Chaney, Georgia Immunization Program
Helen Conner, Georgia Immunization Program
Dack Dalrymple, Bailey Robinson
Paul Darden, M.D., Medical University of South Carolina
Corry Dekker, Chiron
Carmen C. Desden, M.D., Department of Health, Puerto Rico
Gary Dubin, M.D., SmithKline Beccham Pharmaceuticals
Ruth Ann Dunn, M.D., Michigan Department of Public Health
thur Y. Elliott, North American Vaccine
John Forrest, M.D.

Joan Fusco, AMVAX/NAVA
Eugene J. Gangarosa, Private Consultant, EJG Associates
Elizabeth Goss, Fox, Bennett, & Turner
vid E. Gottlieb, Connaught
aristine Grant, Connaught Labs
Jesse Greene, SC Department of Health
Jill G. Hackell, Wyeth Lederle Vaccines & Pediatrics
Mark Hounshell, Chiron Biocine
Barbara J. Howe, SmithKline Beecham
S.G. Humiston, M.D., University of Rochester
Clifton Irby, Christian Science Committee on Publication
Cheryl Jones, Infectious Diseases in Children
Cathy Jordon, NAPNAP
Sam Katz, M.D., Duke University Medical Center
David Krause, M.D., SmithKline Beecham
Barb Kuter, Merck
Bob Laurenzo, Wyeth-Lederle Vaccines & Pediatrics
Lucinda Long, Wyeht-Ayerst
Carlton Meschievitz, Connaught Labs
John Modlin, M.D., Darthmouth Medical School
Victor M. Negron, FLorida Immunization Program
Peter Paradiso, M.D., Wyeth Lederle Vaccines
Steve Perkins, SmithKlein Beecham
Robert Pietrusko, SmithKline Beecham
Stanley Plotkin, Pasteur-Merieux
ce Pope, North Carolina Immunization Section
eoff Porgos, Merck & Co., Inc.
Eileen Provot, Connaught Labs
Jerald C. Sadoff, Merck & Co. Inc.
Bob Scott, Wyeth Ayerst Laboratories
Robert Sharrar, Merck & Co.
Frederic Shaw, M.D., J.D., Health Policy Group
Judith Shindman, Connaught Laboratories Ltd.
Natalie Smith, M.D., California Department of Health Services
Judy Snow, Georgia Immunization Program
Dan Soland, SmithKline Beecham
Michael Speipel, Wyeth-Lederle Vaccines & Pediatrics
Barbara Sweeney, National Association Pediatric Nurse Practioners Association
Helene Tixier, Connaught Labs
Miriam E. Tucker, Pediatric News, Famityl Practice News
Sam Turner, Fox, Bennett & Turner
Margaret Vaillancourt, Immunization Action Coalition
Thomas M. Vernon, M.D., Merck & CO., Inc.
Wanda Warner, SmithKline Beecham
Beth Waters, Cooney/Waters
Deborah Wexler, Immuniztion Action Coalition
Jo White, M.D, Jo White, M.D., P.C.
a Zuberi, M.D., Morehouse School of Medicine

Full Minutes

Dr. Jeffrey P. Davis, Chair, Advisory Committee on Immunization Practices (ACIP), opened the ACIP meeting on June 28 at 8:30 a.m. at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. Dr. Dixie Snider, Acting Executive Secretary, ACIP, began the announcements by informing the Committee that Dr. Robert Breiman accepted the invitation to serve as the Acting Director of the National Vaccine Program Office, which moved to CDC from the Office of the Assistant Secretary of Health. Dr. Phil Lee will remain in charge of the National Vaccine Program, but the office to support the National Vaccine Program efforts, will be located at CDC.

Dr. Snider recognized the three members who are rotating off the committee: Kathy Edwards, Neal Halsey, and Rudolph Jackson. The new members have not been confirmed, and if they are not appointed by the October 1995 meeting, the current members will be asked to continue to serve until the new members are appointed. However, it is anticipated that the nomination package will be approved in Washington prior to that date.

Dr. Davis extended his thanks and appreciation to the retiring members of the committee for their contributions and work. He announced the next ACIP meeting is scheduled for October 18-19, 1995.

Committee members, liaisons, ex-officio members, and meeting participants introduced themselves. Appointed committee members who had to resubmit the SF450 should have already received a signed copy, if they had not, they were instructed to see Gloria Kovach. ACIP members were asked to disclose any potential conflict of interest. Members were reminded that regardless of a potential conflict, they may participate in discussions of all issues provided that full disclosure of potential conflict of interest has occurred. However, the persons with a direct conflict cannot vote on any issue related to the conflict.

Because there have been questions raised concerning what constitutes a direct conflict, Dr. Snider read from the definition which has been used in the past. Direct financial interest includes stock ownership, employment contracts, receipt of grant funds directly or as part of salary when the member also works on the grant from which the funds come, and you do not have to be the principal investor for this to apply.

Committee members were reminded to disclose attendance at scientific meetings, or human resources, travel, or paid honoraria.

Dr. Steve Schoenbaum, Medical Director, Harvard Community Health Plan of New England, reported no personal stock or other interest in pharmaceutical companies, but he said that his wife holds stock in Abbott Laboratories, Amgen, Bristol Meyers Squibb, and Glaxo. Early in June, 1995, she sold her stock in Merck.

Dr. Barbara Ann DeBuono, Commissioner, State of New York Department of Health, reported no conflict of interest.

Dr. Joel Ira Ward, Professor of Pediatrics, UCLA Center for Vaccine Research, reported no financial interests or consulting relationships with any companies; however, the University of California at Los Angeles Center for Vaccine Research, directed by Dr. Ward, receives research grants from Merck Sharpe & Dohme and VRI. He also reported receiving a minimal amount of travel reimbursement by Smith Kline Beecham and Merck Sharpe & Dohme.

Dr. Kathryn Edwards, Professor, Department of Pediatrics, Vanderbilt University School of Medicine, reported laboratory research and clinical research funded by Lederle Praxis, Biocine Sclavo, and Connaught. She is also a consultant for Smith Kline Beecham and Pasteur - Merieux.

Dr. Marie R. Griffin, Associate Professor, Department of Preventive Medicine, Vanderbilt University School of Medicine, reported consulting with Wyeth-Ayerst.

Dr. Fernando A. Guerra, Director of Health, San Antonio Metro Health District, reported that he is presently serving as the principal investigator on a field trial taking place in the Public Health Department in San Antonio, Texas, for a vaccine developed for young infants by North American Vaccine Company.

Dr. Neal A. Halsey, Professor, Department of International Health, Johns Hopkins University School of Hygiene and Public Health, reported no financial interests or stock in any vaccine manufacturer. He is currently conducting a trial on hepatitis B vaccine schedules for Smith Kline Beecham for which he is receiving 5% salary. He reported no other active grants or contracts with any manufacturer at that time. His group has been asked to pull out data from an acellular pertussis trial that was done four years ago, for which he is receiving no salary; however, nurses, statisticians, and others are. He reported receiving travel money from Chiron Biocene and that he will check on any other travel reimbursement from other companies in the last twelve months.

Dr. Jeffrey P. Davis, Chief Medical Officer, Department of Health and Social Services, State of Wisconsin, reported no conflicts of interest.

Dr. Dixie E. Snider, Associate Director for Science, Centers for Disease Control and Prevention, and Executive Secretary for the ACIP, reported no financial conflicts of interest.

The Approach to Developing ACIP Vaccine Recommendations

Dr. Snider discussed the methods by which the ACIP develops recommendations. These methods are constantly under review and are undergoing improvement. In order to provide background for the committee, Dr. Snider provided a review of the charter which outlines the functions of the ACIP. ACIP functions are to provide advice and guidance regarding

appropriate use of vaccines, antisera, and immune globulins, and to establish and periodically review and revise a list of vaccines for routine administration to children including a periodicity, dosage, and contraindications. Some of the specific functions of the ACIP include a review of current recommendations to see if they require updating, a review of labeling and package inserts for each vaccine, and a review of both published and unpublished scientific literature. ACIP reviews morbidity and mortality of disease in the general population and in specific risk groups to determine priories that certain vaccines should receive, and to determine how to target efforts for vaccination of high risk groups. The ACIP considers the feasibility and cost effectiveness of existing vaccine programs.

Dr. Steve Schoenbaum then presented his personal opinions regarding ACIP policies and issues to stimulate discussion regarding where ACIP is today and the direction it is going. Two specific areas of the charter were discussed which state the ACIP should:

1. Advise regarding the most appropriate application of antigens and related agents for effective disease control in the civilian population.

2. Review and report regularly on immunization practices and recommend improvements in the national immunization efforts.

Dr. Schoenbaum specifically cited language of the ACIP charter which is unclear. "Advise" often seems to mean "reconcile" as it pertains to ACIP review of package-insert information and documents of other organizations. The statement, "appropriate application of antigens for effective disease control in the civilian population," as it is used in the charter seems to imply something broader than safe or effective use for individuals, and brings forth issues around policy options and performance goals. The structure for the "review and report" function as set forth in the charter is unclear and does not seem to exist in a formal way. The charter states that the committee is to "recommend improvements in the national immunization efforts," and while it fulfills the function of recommending practices, it fails to recommend improvements in delivery or delivery-system options.

The ACIP meeting process, according to Dr. Schoenbaum, needs improvement. He cited the need to specify the function of each agenda item in order to aid in composing the agenda and allocating appropriate discussion time. He also advocated a standardized approach to developing recommendations using agreed-upon evidence tables, policy-option frameworks, and common goal definitions for all attendees.

Dr. Schoenbaum presented recommendations and suggestions for improving the process functions of the ACIP which included: development of formal processes for the development of recommendations by ACIP; specification of the roles of ACIP members, CDC staff, liaisons, and others in the development/approval process; definition of the services which might be necessary to support the ACIP recommendations process (e.g. policy analysis, meta-analyses);definition of the role of face-to-face group meetings, Delphi surveys, and conference

calls; and consideration of separate recommendation and recommendation-revision processes for emerging, new, and old vaccines.

Dr. Joel Ward stated that the functional role of the ACIP increases as the policy issues ACIP addresses become more important, and more costly. Therefore, it is necessary to understand and solicit input from the private- and public sector constituencies and their various levels before anything is imposed in order to allow formalization of input and information-gathering. In addition, he said, because ACIP's expectations are not always clear, inconsistency in its approach at times has been a problem. Several questions Dr. Ward posed were: Is ACIP at liberty to make recommendations without a definitive date? Should there be options and flexibility if there is relatively equivalent safety and efficacy? He also said that time perspective should be first considered, then monitored sequentially. According to Dr. Ward, a better understanding of whether there are financial or other limitations ensures that ACIP does not step beyond the limit when performing its functions.

Dr. Ward cited several recommendations for dealing with the increasing challenge of improving the way the ACIP functions, including designing a system to track and schedule deliberations throughout the year, which would be useful for anticipating meeting and collecting necessary data improving written recommendations in format, style, and consistency, perhaps with the help of a professional writing consultant and increasing the formalization of stages of evaluating infectious disease prevention. He called for suggestions and ideas that may fit with CDC's contract program for research in post-licensure studies.

Dr. Snider acknowledged that the scope of these issues is broad and suggested that a working group be established to address into some of the issues and present recommendations to the Committee regarding how it might better define its role for members and for other contributors, and more clearly define the process the Committee will use in developing recommendations. Committee members emphasized that:

1. It would be helpful to stipulate for each agenda item the action anticipated and when decisions and actions are required.
2. Bringing the liaison members and the committee members together at the same table would facilitate discussion.
3. Restricting voting because of a perceived conflict of interest with a single vaccine manufacturer who produced multiple vaccines may be too strict; if such restrictions continue, the ACIP's natural tendency may be to select members having less technical expertise because they have not participated early on in the studies with those vaccines.
4. It would be helpful to have received background information, data from trials and other pertinent data prior to listing an item on the agenda so members would be able to make more informed decisions.
5. Developing a regular schedule for each ACIP recommendation to be reviewed periodically would ensure that recommendations are current and up to date.

Summary of Recommendations from the Committee

1. Prioritize items and schedule meeting better.
2. Establish more systematic processes, standardize formats of statements and develop guidelines on quality of data.
3. Consider major changes in the process of the committee, including the composition and number of persons voting, liaisons, the conflict-of-interest issue and dealing with the work load.

Hepatitis A Vaccine Use in Highly Endemic Populations

Dr. Craig Shapiro, Hepatitis Branch, NCID, CDC, introduced the section of the meeting on hepatitis A vaccine. During the ACIP meeting in February 1995, questions were raised about including hepatitis A vaccine into the Vaccines for Children Program. In response to these questions, three presentations were made during the June meeting to provide the background information and rationale for inclusion of hepatitis A vaccine in the Vaccines for Children Program for use in communities with high rates of hepatitis A virus infection and periodic hepatitis A outbreaks. Dr. James Cheek, Indian Health Service, presented an overview of the Indian Health Service and hepatitis A among American Indians and Alaska Natives; Dr. Shapiro reviewed the experience in two high-rate communities in which large-scale hepatitis A vaccination programs were conducted; and Dr. Hal Margolis, Hepatitis Branch, NCID, CDC, presented data from an economic analysis of using hepatitis A vaccine in high-rate communities.

Dr. Cheek provided the committee with an overview of the health of native Americans in the United States, information about the Indian Health Service, and information about the IHS immunization program. Dr. Cheek also reviewed historical data on hepatitis A and provided current information about the impact of hepatitis A in this group.

According to Dr. Cheek, there are over 500 federally recognized tribes in the United States. An important concept which impacts all dealings with these tribes is that each tribe functions essentially as an independent country with its own government, a sovereign nation. The Indian Health Service provides service to 1.2 million American Indians and Alaska Natives, most of whom live on reservations or in Alaska villages. It's a young population; in 1993,-over 20 thousand were under one year of age, almost 500 thousand were under age 15, and almost a third live below the poverty level.

The Indian Health Service has 12 regional offices and is in the process of reorganization. Most IHS facilities are in the western part of the United States, corresponding with the largest Indian populations. The Nashville area office services Indians living in the east. The IHS has 41 hospitals and 114 health centers, most on rural areas or reservations. One of IHS's primary activities is public health home nursing visits. IHS does not purchase vaccines; they are

provided by the states, and with the exception of Alaska, all provisions come through VFC. IHS provides the delivery system for the vaccine. Coverage rates for most vaccines are over 90% in children under 2 years of age.

The epidemiology of hepatitis A in Native Americans is very similar to that in developing countries. They experience periodic outbreaks with a cycle occurring every 7 to 10 years. In many areas with frequent outbreaks, many of the children are seropositive by age 10.

Data suggests that American Indians and Alaska Natives should receive hepatitis A vaccine. Compared to the rest of the country, the rate of hepatitis A in American Indians is almost 10 times the overall total rate, higher than any other racial group in the country.

Dr. Shapiro presented data from Alaska and Monroe, New York regarding experiences using the hepatitis A vaccine during community wide outbreaks. In Alaska, hepatitis A outbreaks occur statewide every 10 - 15 years, with the highest attack rates among children age 10 - 15 years. Control with immune globulin has not been effective, and the Alaska Department of Health has made a recommendation not to use immune globulin aggressively in an attempt to control these outbreaks. In 1993, the Indian Health Service and the Alaska Department of Health offered hepatitis A vaccine to persons less than 30 years of age living in several communities experiencing hepatitis A outbreaks. Depending on the village, between 50% and 70% of the target population was vaccinated. Within several weeks of the vaccination campaign, the number of reported cases in these communities decreased dramatically. In Kiryas Joel, New York, where the original efficacy study with Merck hepatitis A vaccine was conducted, the number of reported hepatitis A cases in the community decreased shortly after initiation of the study. Since termination of the efficacy study, a substantial proportion of young children in the community have continued to receive the vaccine by participation in subsequent immunogenicity studies. Very few cases of hepatitis A have occurred in the community. These data from Alaska and New York suggest rapid vaccination during ongoing outbreaks can help control outbreaks in areas where immune globulin has not been effective. Also, routine childhood vaccination and vaccination of older children can help control outbreaks in progress and actually prevent future outbreaks from occurring.

Dr. Margolis reviewed the results of an economic analysis examining use of hepatitis A vaccine in high rate communities. Direct and indirect costs of hepatitis A cases were obtained through retrospective analysis of hepatitis A cases occurring in two American Indian communities in South Dakota. These costs were then used in a model evaluating the routine use of hepatitis A vaccine in one-year-old children over a 25 year period. The analysis found this strategy to be cost saving. Sensitivity analysis showed that the program remained cost-saving over a wide range of vaccine prices.

During the ensuing discussion, a committee member commented that it will be important to identify the issues or conditions that might result in a high rate of hepatitis A in selected native populations. The issues of sanitation, clean water, and sewage might be topics for the Indian Health Service to address. Dr. Cheek commented that there are a number of enteric diseases

that are common among residents of the rural remote areas, and he explained that IHS has had an engineering component for a number of years developing water systems and attempting to improving sanitation. However, that engineering task is made difficult on reservations because communities are dispersed across a wide area, households have no running water, and most are not near a town. Nonetheless, it is important to note that hepatitis A virus transmission in these areas occurs not because of contaminated water, but through person-to-person contact. The relatively young population and crowded living conditions facilitate person-to-person transmission.

Dr. Shapiro stated that currently the definitive data are not available to state that the vaccine can protect post-exposure or that it can replace immune globulin. The Committee explored the type of data needed to make a recommendation, possibly a side-by-side efficacy study looking at vaccine versus immune globulin in contacts of persons with hepatitis A.

The use of hepatitis A vaccine in travelers was raised by a committee member. Immune globulin is still suggested for use in people who will be placed at risk within a short time after leaving the United States. A reexamination of this statement was suggested, particularly in light of the evidence of possible post-exposure protection from vaccine observed in the Monroe Study.

Another member pointed out that there are certain populations which are often forgotten when discussing the at-risk, high-endemic populations such as those in the inner city who live in conditions of overcrowding and intense sustained poverty. Many times these individuals work in occupations that place a large number of people at great risk, either as domestic workers, food-service industry workers, or childcare workers.

A committee member noted, because an emphasis of the use of hepatitis A vaccine in high-risk populations is pediatric, the committee should explain why it chooses not to include hepatitis A vaccine in the regular childhood-immunization series; hepatitis A is a serious health problem, causing 100 deaths per year. Dr. Shapiro mentioned the vaccine is currently licensed for persons 2 year of age and above. More data regarding use of the vaccine in children less than 2 years of age are needed. The availability of combination vaccines would also be helpful.

Another member noted the portion of the hepatitis A vaccination recommendation discussing day care centers states that 15% of the reported cases occur among children or employees of day care centers. It then states that the frequency of outbreaks in day care centers is not sufficient to warrant consideration of this group as routinely being at risk and therefore eligible for immunization, which seems paradoxical. Dr. Shapiro responded that in some communities, outbreaks in day care centers are occasionally the source of larger community-wide epidemics, and the ACIP recommendations suggest use of vaccine in day care centers in such communities. He added that overall in the United States, a large percentage of children are in day care; when examined with control groups in areas not experiencing day care center outbreaks, contact with day care centers has not been clearly shown to be a risk factor for hepatitis A, but additional studies are needed.

Dr. Davis asked that the committee members and the liaisons clearly state their concerns regarding review of the current draft of the hepatitis A statement and provide it to the program within one week of the meeting. He state that a revised statement reflecting these comments would likely be provided to the committee within three weeks.

Varicella Update

Dr. Melinda Wharton, National Immunization Program, lead discussion to finalize the varicella statement, which has gone through two revisions since the February meeting. Dr. Wharton asked that the committee review the restructured section related to immunization of adolescents and adults 13 years of age or older and the summary table at the end of the statement, and provide comments.

A committee member stated that a number of institutions are currently doing serological testing for evidence of immunity prior to employment. Some questions posed were: With the two-dose strategy for adults, how long will antibody persist? Would it be advisable to anticipate screening persons moving into new positions of employment? Would screening be advisable for adolescents presently being immunized and moving into the system? The current varicella recommendation does not address the need for institutional guidelines for vaccinated health-care workers who continue to have patient contact after significant exposure to the virus. Should it? The statement was designed to provide overall guidance; however, each institution must address these specific issues to best meet its needs because data are not currently available specifically to address these concerns.

Other questions raised: Should recently vaccinated children visiting in the hospitals be screened for recent vaccination and, if vaccinated, should they be in any way restricted? What is the interval to development of the vaccine-associated rash?

The package insert contains a very strong cautionary statement stating that people who have been immunized should not have contact with immunocompromised individuals. It is apparent that this statement has delayed anticipated hospital immunization programs. The ACIP statement, which is much more permissive, is awaited; some hospitals may proceed with their hospital immunization programs on that basis.

A committee member noted the conflict between the manufacturers and the FDA over the issue of transmissibility of vaccine virus from vaccinees to contacts, which is in conflict with the ACIP recommendations and the American Academy of Pediatrics regarding immunization of household contacts of immunocompromised newborn and pregnant women. Oncologists have long awaited the opportunity to vaccinate the household contacts of the immunocompromised children; however, the package insert states not to do that. This would jeopardize the protection of the immunocompromised children in the household and unnecessarily place some children at increased risk of varicella. FDA commented that inclusion of this statement was based upon limited data suggesting that transmission might occur in the normal child, and that transmission has been shown in individuals who were immunocompromised, given vaccine, and subsequently

transmitted virus. It is not a contraindication, but appears in the precautions section. A committee member stated that it would be helpful for FDA to reconsider the wording of the package insert.

The Group Health Association of America recently sent a letter to its Childhood Immunization Advisory Group asking that their group members offer support, concerns or comments to ACIP regarding varicella vaccine. These have been forwarded to a committee member for distribution to the full ACIP. Concern was expressed that the use of varicella vaccine in children will simply delay occurrence burden of disease into adulthood. An extensive document prepared by the Immunization Subcommittee of the Committee on Prevention of Group Health Cooperative of Puget Sound presents their formal system for recommendations and a grading system. One of the recommendations they are likely to make is to give vaccine to household contacts of immunocompromised patients when the household contact is not immunocompromised but varicella susceptible. They would also like to give varicella vaccine to health care providers and child care workers, nonpregnant women of childbearing age and other varicella-susceptible adults and children and make it discretionary for all other individuals and situations, not recommending it as a performance indicator. Their concern is that the use of the vaccine in children will eventually lead to more disease in adults than currently occurs.

A Committee member noted that the American Academy of Family Physicians, in March, 1995, developed a policy on varicella vaccination recommending routine childhood vaccination.

Following discussion, a motion was made by Dr. Kathryn Edwards, to approve, with minor modifications of wording, the current general varicella statement. The motion was seconded. The vote was in favor 9 (Davis, DeBuono, Edwards, Griffin, Guerra, Halsey, Jackson, Schoenbaum, and Ward), none opposed and 1 was absent (Thompson). The motion carried.

Vaccines for Children Program

Hepatitis B Vaccine

Dr. Harold Margolis addressed hepatitis B vaccine and the VFC Program.

The recommendation regarding vaccination of sexual partners of persons with acute hepatitis B has been modified and now reads: All susceptible sexual partners of persons with acute hepatitis B virus infection should receive a single dose of hepatitis B immune globulin (HBIG) and hepatitis B vaccination should be started. The dose of HBIG to be administered is 0.06 mL/kg and the recommended dosages and schedules for hepatitis B vaccine are contained in tables 1 and 2 which are appended to the recommendation. The recommendation for vote is:

> The ACIP recommends that HBIG and hepatitis B vaccine be given to sexual partners of persons with acute hepatitis B virus infection and be included in the Vaccines for Children Program as described in the above paragraph.

A motion was made by Dr. Jackson and seconded. The vote carried 5 in favor (Jackson, DeBuono, Griffin, Guerra, and Davis), none opposed, 4 abstentions (Schoenbaum, Ward, Edwards, and Halsey), and 1 absent (Thompson).

Hepatitis A Vaccine

The next VFC issue discussed was the use of hepatitis A vaccine in children in communities with high rates of hepatitis A virus infection and periodic hepatitis A outbreaks. The following recommendations were approved by the ACIP in February 1995 and will be included in the statement entitled, "Prevention of Hepatitis A through Active or Passive Immunization":

- Children living in communities with high rates of hepatitis A virus infection and periodic outbreaks of hepatitis A should be routinely vaccinated at or after 2 years of age.

- In addition, catch-up vaccination of previously unvaccinated older children is also recommended to prevent epidemics of hepatitis A. The highest priority should be given to vaccination of children prior to school entry, followed by vaccination of school-aged children. Catch-up vaccination should be accomplished within 5 years of initiation of routine childhood vaccination programs. The upper age for catch-up vaccination should be determined using age-specific rates of hepatitis A or seroprevalence data if available. Vaccination is not warranted in age groups with the lowest rates of disease because the prevalence if immunity is high (e.g., adults).

- Routine vaccination of young children, and accelerated implementation of catch-up vaccinations of older children, should be used to prevent or control ongoing outbreaks in these communities. The following footnotes and tables clarify this recommendation:
  1. Characteristics of communities with high rates of hepatitis A virus infection and periodic hepatitis A outbreaks are shown in Table 1 appended to the recommendation.
  2. The recommended doses and schedules for hepatitis A vaccination are shown in Table 2 appended to the recommendation.

A Committee member asked how "community" would be defined for the purpose of VFC. When entire populations are used this could prove very costly. When specific census tracts or zip code areas are used, much smaller communities are defined which would be more manageable. For the Indian reservation setting, Pacific Islanders, and religious communities living within a larger community this should be accomplished fairly easily. However, in other high rate communities, this will be more difficult and the possibility of forming a working group to discuss how to address the issue was raised.

A Committee member asked what age was being defined for the "catch-up vaccination" year and it was explained that while age 19 years had been used for the calculation, the upper age limit of the data is probably somewhere between 12 and 15 years of age. This would be a local

decision based on both age specific incidence data (disease data) or seroprevalence data where available.

A Committee member stated that it would be advantageous to build flexibility into the votes in light of new information that is likely to become available regarding the dosage schedule. A one dose schedule, if approved for licensure, would be a more cost effective alternative that could then be utilized.

A Committee member noted inconsistencies that already exist in the adolescent dosage schedule and the impact that additional visits to a caregiver might add to the cost of the immunization. Changes in the dosing schedule are anticipated as new formulations or new vaccines are licensed and become available and VFC-related recommendations will be modified as needed. The recommendation for vote was stated as:

> The ACIP recommends that hepatitis A vaccination be included in the Vaccines for Children Program as described in the previous paragraphs.

A motion was made and seconded. The vote carried 6 in favor (Jackson, Schoenbaum, DeBuono, Griffin, Guerra, Davis), none opposed, 3 abstentions (Ward, Edwards, Halsey), and 1 absentee (Thompson).

The second issue regarding hepatitis A vaccine focused on vaccination in outbreak settings. Intermediate rate communities, where an outbreak may be localized and the whole community may not be experiencing a hepatitis A outbreak, are impacted by this VFC recommendation. The proposed wording is very similar to wording used for measles outbreak control and reads:

> It is the intent of the ACIP to provide hepatitis A vaccine for the control of such community-wide outbreaks. The following footnotes and tables clarify this recommendation:
>
> 1. Characteristics of communities with intermediate rates of hepatitis A virus infection and periodic hepatitis A outbreaks are shown in Table 1 (appended).
>
> 2. The recommended doses and schedules for hepatitis A vaccination are shown in Table 2 (appended).

A Committee member expressed that it may be construed as a misuse of the VFC program to distribute vaccine for this purpose and that this is a state or local responsibility. It was pointed out that this wording is consistent with wording for all of the vaccines in the VFC program which may be used when indicated for controlling outbreaks, consistent with ACIP recommendations.

Another Committee member suggested that prevention should also be considered when dealing with outbreaks in these settings. Large urban communities experience a constant unrelenting number of cases of hepatitis A year after year which cause community members to be at

continual risk. In addition to examining the issue of outbreak control, it may be appropriate to consider additional preventive measures. More data need to be collected and refined on the magnitude of the problem in various communities; a working group could be formed to examine surveillance data and develop recommendations.

A Committee member stated that if prioritization for financial reasons were to become an issue this may need to be considered to decide which groups and communities would receive in vaccine. However, the Committee does not currently anticipate any recommendations that would require members to consider prioritization for financial reasons.

A Committee member stated a fundamental concern that the ACIP understand the reality that VFC is under siege by Congress and that the VFC program could be very different with the states, the CDC, the federal government, or Congress doing the priority setting. A number of vaccines may be added to this program and either the ACIP, the National Vaccine Program or the states will have to do serious prioritization if VFC is made part of the block grant funding.

Dr. Davis provided a perspective from a state health department that each time changes are made regarding how programs must be implemented, state agencies that are charged with developing these programs are affected. Energy that could be put into distributing the vaccine to children is expended to implement a new program. In the end, it is the children that are being hurt by these changes. The best action would be to develop the best delivery system which will provide vaccine to the people that need it while trying not to harm the programs already in place.

The language of the recommendation for vote is as follows:

> During community-wide outbreaks of hepatitis A in communities with intermediate rates of hepatitis A virus infection, the ACIP recommends that state and local health authorities be given flexibility to provide vaccine under the VFC program for VFC eligible children, provided that those outbreak control measures are consistent with existing ACIP recommendations.

A motion was made by Dr. Guerra and seconded by Dr. Griffin. The motion carries with 6 in favor (Jackson, Schoenbaum, DeBuono, Griffin, Guerra, and Davis), none opposed, 3 abstentions (Ward, Edwards, Halsey), and 1 absentee (Thompson).

A Committee member suggested a resolution that a study committee be appointed to continue to examine the additional unresolved issues related to hepatitis A. Dr. Davis suggested that the current hepatitis A committee be retained with the addition of representation from Merck and SKB.

A Committee member asked if there was going to be a discussion about why the ACIP was not making persons with chronic liver disease, adolescent drug users, adolescent homosexual boys eligible for VFC vaccine. It was explained that these groups would be considered individually within the working group and would be brought up in a subsequent vote.

Varicella Vaccine

Dr. Steve Hadler summarized the many issues for consideration in recommendations for varicella vaccine use in the VFC program. This vaccine has not previously been considered for VFC as it was licensed in March 1995 after the last ACIP meeting. The current ACIP recommendations for use of varicella vaccine are as follows:

For children age 12 - 18 months:

All children should be routinely vaccinated between 12 - 18 months of age.

For children age 19 months - 12 years:

Varicella vaccine is recommended for all children aged 19 months to the 13th birthday who have not been immunized previously and who lack a reliable history of varicella infection. Vaccination may occur any time during childhood but before the 13th birthday. Varicella vaccine should be administered to eligible children at the routine adolescent immunization visit at age 11 - 12 years.

For adolescents 13 years of age and older adults:

Assessment of varicella immunity status and vaccination of those who are susceptible is desirable for all adolescents and adults. Specific assessment efforts should be focused on those at highest risk of exposure and transmitting disease to others.

Specific assessment efforts should be focused on those with highest risk of exposure and transmitting VZV to others:

A. Vaccination is recommended for susceptible persons who will have close contact with persons at high risk for serious complications:

   1. Health care workers
   2. Susceptible family contacts of immunocompromised individuals

B. Vaccination should be considered for susceptible persons in the following groups who are at high risk of exposure:

   1. Persons who live or work in environments in which there is a likelihood of transmission of VZV (e.g., teachers of young children, day care workers and residents and staff in institutional settings).
   2. Persons who live or work in environments in which varicella transmission may occur (e.g., college students, inmates and staff of correctional institutions, and military personnel).
   3. Nonpregnant women of childbearing age.
   4. International travelers. Immunization should be considered for international

travelers without evidence of immunity to VZV, especially if the traveler expects to have close personal contact with local populations.

5. Vaccination of other susceptible adolescents and adults is desirable and may be offered at the time of routine health care visits.

A single dose is recommended for children through age 12 years; persons aged 13 years and older should receive two doses of vaccine 4 to 8 weeks apart.

Five options for inclusion of varicella vaccine in the Vaccines for Children (VFC) program were considered as follows: (Categories are not mutually exclusive)

1. Provide universally for children at age 12 - 18 months.

2. Provide for all susceptible children at school entry.

For school enterers, only children with no history of varicella would be vaccinated (estimate 65% of all 5 year old children). This "catch-up" would only be necessary for 3 - 4 years, until children vaccinated at age 12 - 18 months reach 5 years of age.

3. Provide for susceptible children at entry to middle/junior high school (11 - 12 years of age).

Only children with no history of varicella would be vaccinated (estimate 22% of 11 year old children). This "catch-up" would be necessary for about 10 years if no other catch-up vaccination is done.

4. Provide to all susceptible adolescents (age 13 - 18 years) at the time of routine health visits.

This option would permit vaccine to be purchased under the VFC for adolescents who are seen for routine health care visits and are determined to be susceptible. Approximately 78% of this age group make at least one health care visit each year. Two vaccine doses would be required for susceptible persons.

5. Provide to children and adolescents $\leq$ 18 years in high risk groups:

A. Susceptible persons who will have close contact with persons at high risk for serious complications:

   1. Health care workers
   2. Susceptible family contacts of immunocompromised individuals

B. Susceptible persons in the following groups who are at high risk of exposure:

1. Persons who live or work in environments in which there is a high likelihood of VZV transmission (e.g., teachers of young children, day care workers and residents and staff in institutional settings).
2. Persons who live or work in environments in which varicella transmission may occur (e.g., college students, inmates and staff of correctional institutions, and military personnel).
3. Nonpregnant women of childbearing age.
4. International travelers. Immunization should be considered for international travelers without evidence of immunity to VZV, especially if the traveler expects to have close personal contact with local populations.

Cost estimates for varicella vaccine in the VFC program relative to the five options presented were as follows:

Option 1 - Provide universally at age 12 - 18 months with 2.36 million estimated eligible and an estimated cost of $35.4 to $70.8 million per year.

Option 2 - Provide for all susceptible children at school entry with 1.62 million estimated eligible and an estimated cost of $24.3 to $48.6 million per year.

Option 3 - Provide for susceptible children at 11 - 12 years with .35 million estimated eligible and an estimated cost of $5.2 to $10.4 million per year.

Option 4 - Provide to susceptible adolescents (age 13 - 18 years) at the time of routine health visits with 1.02 million estimated eligible and an estimated cost of $30.6 to $61.2 million per year.

Option 5 - Provide to high risk groups of children and adolescents $\leq$ 18 years with the number of potentially eligible persons being unknown.

Assumptions used in making the cost estimates include:

- Varicella vaccine will range in price from $15 to $30 per dose.
- Estimates are based on full implementation of the recommendations in each scenario.
- Estimates are based on the VFC program covering 60% of children $\leq$ 5 years of age, and 45% of children 6 - 18 years of age.
- Cost estimates are based on percent of children with immunity to varicella (therefore having no need for vaccination) taken from the National Health Interview Surveys conducted from 1980 - 1990.
- Cost estimates assume 78% of adolescents age 13 - 18 year have a least one health visit annually.

The items presented to the Committee for consideration are stated individually with the Committee voting on each separately.

The ACIP proposes that varicella virus vaccine should be included in the Vaccines for Children program, using the following schedule, dosages and contraindications:

The first item considered by the Committee related to the age group 12 - 18 months old and the language was as follows:

> All children should receive varicella virus vaccine at 12 - 18 months of age. The recommended dosage is 1 dose for children age 12 months to 12 years. Varicella vaccine may be given simultaneously with all vaccines recommended for use at 12 - 18 months of age. The following conditions are contraindications to administration of varicella vaccine:
>
> 1. Hypersensitivity reaction to component of vaccine (e.g. gelatin) or anaphylactic reaction to neomycin.
>
> 2. Altered immune status due to: malignant condition (blood dyscrasia, leukemia [expect acute lymphocytic leukemia in remission], lymphoma, or other neoplasms affecting the bone marrow or lymphatic system); primary, or acquired immune deficiency, including acquired immunodeficiency syndrome (AIDS) or other clinical manifestations of HIV infection, dysgammaglobulinemia; family history of congenital or hereditary immunodeficiency, unless immune competence of possible vaccine recipient is demonstrated; individuals receiving immunosuppressive therapy.
>
> 3. Receiving high doses of systemic steroids ($\geq$ 2 mg/kg body weight or 20 mg/day prednisone or equivalent).
>
> 4. Pregnancy. The effects of vaccine on the fetus are unknown, and therefore pregnant women should not be vaccinated. Nonpregnant women who are vaccinated should avoid becoming pregnant for 1 month after each injection.
>
> The following condition is a precaution to receipt of varicella virus vaccine:
>
> 1. Varicella virus vaccine should not be given for at least 5 months after receipt of blood (expect washed red blood cells) or plasma transfusions, immune globulin, or varicella zoster immune globulin.

The recommendation to be voted on was stated as follows:

> The ACIP recommends that varicella virus vaccine be included in the Vaccines for Children program, using the dosages, contraindications, and clarifications listed above. It was suggested that removing pregnancy from the statement as not appropriately applying to this age group would be advisable and this was agreed upon.

Following discussion the motion was made and seconded to vote on the proposed recommendation. The motion carried with 7 in favor (Jackson, DeBuono, Edwards, Griffin, Guerra, Halsey, Davis), none opposed; 2 abstentions (Schoenbaum, Ward), and 1 absentee (Thompson).

The second item pertained to older children and was stated as follows:

> The ACIP proposes that varicella virus vaccine should be included in the Vaccines for Children program for certain groups of older children, using the following schedule and dosages, and contraindications accepted in previous votes:
>
> The recommended dosage is 1 dose for children age 12 months to 12 years, and two doses, separated by 4 - 8 weeks, for children and adolescents age 13 - 18 years. Varicella vaccine may be given simultaneously with all vaccines recommended for use at 12 - 18 months of age, or at 11 - 12 years of age.
>
> The following group(s) of children should be considered for inclusion in the VFC program for receipt of varicella virus vaccine, each by individual vote:
>
> 1. Varicella vaccine should be provided for all susceptible children at entry to primary school.
> 2. Varicella vaccine should be provided for susceptible children at 11 - 12 years of age.
> 3. Varicella vaccine should be provided to all susceptible adolescents (age 13 - 18 years) at the time of routine health visits.
> 4. Varicella vaccine should be provided to susceptible persons in the following groups $\leq$ 18 years who are at high risk of exposure:
>   a) Susceptible persons who will have close contact with persons at high risk for serious complications: health care workers; family contacts of immunocompromised persons;
>   b) Persons who live or work in environments in which there is a high likelihood of transmission of VZV (e.g., teachers of young children, day care workers and residents and staff in institutional settings); persons who live or work in environments in which

varicella transmission may occur (e.g., college students, inmates and staff of correctional institutions, and military personnel); nonpregnant women of childbearing age; and international travelers.

The following summarizes the individual votes to be taken:

> The ACIP recommends that varicella virus vaccine, given at the dosage and with the clarifications noted above, be included in the Vaccines for Children program for the groups accepted by individual vote previously.

A Committee member suggested it may be helpful to rank the groups to be considered for coverage in the order of highest priority before voting. The groups to be considered were (1) the population 12 - 18 months old for whom the ACIP recommends routine use (2) the susceptible populations 11 - 12 years of age to be consistent with the adolescent vaccination statement and since it is a catch point for children who would then need two doses if not immunized at this time; (3) the susceptible populations at school entry; and (4) those who have close contact with persons at high risk for serious complications, should also be considered, to be of equal importance with the adolescent group (age 13-18 years).

Following Committee discussion the recommendation to rank by importance the individual groups to be considered was adopted by the Committee. The order of priority for voting was determined to be first, adolescents at age 11 - 12 years of age, followed by the susceptible contacts of persons at high risk of complications, and then revisit the other groups as listed individually.

The first proposed recommendation was considered for vote: Varicella vaccine should be provided for susceptible children at 11 - 12 years of age. There was no further discussion with regard to this item and a motion to vote was made and seconded. The motion carried with 7 in favor (Jackson, DeBuono, Edwards, Griffin, Guerra, Halsey and Davis), none opposed, 2 abstentions (Schoenbaum, Ward) and 1 absentee (Thompson).

The next item, varicella vaccine should be provided to susceptible children and adolescents $\leq$ 18 years who will have close contact with persons at high risk for serious complications, was considered by the Committee in preparation for a vote. A Committee member asked if the vaccine for the health care workers would be paid by the health care facility in order to clarify the coverage of health care workers under this group. A member with experience in a hospital infections program related that volunteers such as candy stripers should be considered as the hospital may be responsible for these individuals. A suggestion was made to focus on only the family contacts and exclude the health care workers in this vote. In order to further clarify the proposed recommendation the Committee first decided to vote on an amendment to the language of the proposal to exclude the coverage of health care workers under the proposal.

A motion was made and seconded to vote on the proposed exclusion of health care workers from VFC funding regarding the proposal for varicella coverage for close contacts. The motion to exclude health care workers from the proposal carried by majority with 6 in favor.

The restated proposal to be voted on was amended to read:

> Varicella vaccine should be provided to susceptible children and adolescents $\leq$ 18 years who will have close contact with persons at high risk for serious complications, to include only susceptible family contacts of immunocompromised individuals.

In further discussion a Committee member suggested the revision of the word family to the word household. The amended language of the recommendation for consideration was:

> Varicella vaccine should be provided to susceptible children and adolescents $\leq$ 18 years who will have close contact with persons at high risk for serious complications to include susceptible household contacts of immunocompromised individuals.

The Committee then moved to a vote on the proposal as revised. The motion was made and seconded. The motion carried with 7 in favor (Jackson, DeBuono, Edwards, Griffin, Guerra, Halsey, Davis), none opposed, 2 abstentions (Schoenbaum, Ward), and 1 absentee (Thompson).

The Committee was then asked to suggest priority ranking for the next group. A Committee member asked for clarification of vaccine availability as a possible consideration for votes in subsequent proposals. Concerns about costs regarding a vote in favor of coverage for all susceptible children at school entry, acknowledging the great expense which would be incurred by the VFC program if the vote were in favor of coverage for this group, was expressed and discussed by several Committee members. It was noted that coverage in this group would require only one dose. Another Committee member noted that future inclusion of varicella vaccine in the childhood immunization series and possible vaccination requirements for entry into day care and preschool programs could potentially decrease the burden of varicella in subsequent school age groups. Regarding the number of doses supplied to each state for administration, a Committee member suggested some flexibility be allowed while still establishing priorities of the groups to be covered but then allow the states to make decisions regarding catch-up vaccination on a discretionary basis. This suggestion could prove difficult to implement due to VFC contract considerations when states choose to cover a larger cohort. This could cause a significant fiscal impact and impact on vaccine supply. The Committee then proceeded to vote on the proposed recommendation as follows:

> Varicella vaccine should be provided for all susceptible children at entry to primary school.

A motion was made and seconded. The motion did not carry with 3 in favor (Jackson, Guerra, Halsey); 4 opposed (Davis, DeBuono, Edwards, Griffin); 2 abstentions (Schoenbaum, Ward); and 1 absentee (Thompson).

The next item for the Committee's consideration was stated as follows:

> Varicella vaccine should be provided to all susceptible adolescents (age 13 - 18 years) at the time of routine health visits.

There was not Committee discussion and the issue was moved to a vote. The motion was made and seconded. The motion did not carry with none in favor, 7 opposed (Jackson, DeBuono, Edwards, Griffin, Guerra, Halsey, Davis), 2 abstentions (Schoenbaum, Ward), and 1 absentee (Thompson).

The next item for consideration before the Committee was:

> Varicella vaccine should be provided to susceptible persons in the following groups ≤ 18 years who are at high risk of exposure:
>
> > Persons who live or work in environments in which there is a likelihood of transmission of VZV (e.g., teachers of young children, day care workers and residents and staff in institutional settings).
> >
> > Persons who live or work in environments in which varicella transmission may occur (e.g., college students, inmates and staff of correctional institutions, and military personnel).
> >
> > Nonpregnant women of childbearing age.
> >
> > International travelers.

There was no discussion of the Committee and the issue was moved for vote. A motion was made and seconded. The motion did not carry with none in favor, 6 opposed (Halsey, Guerra, Griffin, Edwards, DeBuono, Davis), 3 abstentions (Jackson, Schoenbaum, Ward), and 1 absentee (Thompson).

The Committee was then asked to formally adopt the language which considers the groups recommended to receive VFC funding vaccine based on previous individual votes. The proposal was stated as:

> The ACIP recommends that varicella virus vaccine given at the dosage and with the clarifications noted above be included in the Vaccines for Children program for the groups accepted by individual vote above.

The motion was made and seconded. The motion carried with 7 in favor (Jackson, DeBuono, Edwards, Griffin, Guerra, Halsey, Davis); none opposed; 2 abstentions (Schoenbaum, Ward); and 1 absentee (Thompson).

Polio Vaccine Policy

Dr. Hadler provided an overview of the polio vaccine policy issue for the Committee. Last fall, precipitated by a recognition of change in the epidemiology of polio globally and the certification of eradication of poliomyelitis in the western hemisphere, discussions were necessitated to consider the possible need to change polio vaccination policies from the current reliance on oral polio vaccine (OPV) due in part to the continued occurrence of vaccine associated paralytic poliomyelitis. A change to an IPV based schedule would reduce or eliminate the risk to vaccines and/or their close contacts. A forum was sponsored jointly by CDC and the Institute of Medicine to review the critical issues. Policy, programmatic and cost issues were discussed from a scientific, provider, program and parental perspective, as were ethical and compensation considerations.

Four options were then outlined for the Committee to consider stated as:

Option 1 - No change in policy from reliance on OPV at present.
Option 2 - ACIP should adopt "Intent to Change Policy" and develop a proposed timetable for change of policy, with appropriate lead time (3-6+ months) for each step and contingencies as needed.
Option 3 - Change to strengthening provider/parental option as soon as possible.
Option 4 - Change to IPV based schedule (either sequential IPV-OPV or IPV only) as soon as feasible.

Option 1 was discussed first. The Committee considered criteria to be met before ACIP would reconsider it's current policy. Status of global elimination, availability of additional data on safety and effectiveness of IPV-OPV sequential schedule, availability of additional data on safety/effectiveness of IPV alone, status of development/licensure of DTaP, status of development/licensure of DTaP-Hib or other combination vaccines were presented as factors for framing the issues critical to the polio policy and ACIP polio recommendation.

Dr. Roland Sutter provided a brief summary of and a handout of the pros and cons of the four options with regard to polio policy presented at the CDC-IOM Forum and also, a summary of the conclusions presented at the forum by Dr. Katz.

With Option 1, OPV reliance, meaning no changes in the current policy of oral polio vaccination, the cons are considered to be the continued occurrence of vaccine-associated disease which results in approximately 8 - 10 cases per year, the perceived risk of OPV as lessening consumer acceptability of vaccination programs, and the potential risk that parents cooperating with the immunization program must bear a very small but avoidable risk of vaccine-related paralytic polio in their children for the benefit of enhancing immunity in the non-vaccinated population. In terms of pros of Option 1, the vaccine is extremely effective in reducing the incidence of polio in the United States and globally. The vaccine produces high rates of seroconversion 96 - 100% following 3 doses. OPV-induced humoral antibody is generally believed to be of long duration, and OPV-induced intestinal immunity minimized poliovirus

replication and the potential for spread of wild virus while also providing pharyngeal immunity preventing oral-oral spread. OPV virus is excreted by recipients and it's excretion and circulation interferes/competes with circulation of wild virus providing indirect immunization of some susceptible contacts and may induce secondary antibody response in some nonsusceptible contacts. The previous belief that the occurrence of vaccine-associated contact cases would approach zero as current well-immunized school cohorts (97% having 3 or more doses) become parents has not been borne out by experience. Other pros of Option 1 are OPV is the vaccine of choice in an epidemic, it is easy to administer and achieve high levels of immunity in the population, it is less costly, and there has been a longer period of experience with OPV than e-IPV in the United States. In the IOM workshop there was significant discussion about the secondary spread of OPV virus and on the cons side the progress toward global eradication lessens some of the benefits of OPV in inducing mucosal immunity and secondary spread and perhaps the risk-benefit balance has changed somewhat.

The pros and cons of the second option, IPV reliance, were presented. On the cons side (1) intestinal immunity is less than following OPV, (2) prevention of intestinal replication of polio viruses is less than that following OPV, allowing greater circulation of any introduced wild polio virus, (3) since e-IPV does not spread to contacts, we would need to achieve and maintain higher levels of direct vaccine-induced immunity to pre- and post-school age populations, (4) possible rare adverse effect risks such as Guillain-Barre syndrome are not well studied, (5) IPV can not be used in epidemic control, (6) IPV would probably cost more than OPV, (7) if not combined with DTP, additional injections and additional visits may be required to complete the immunization schedule, (8) IPV is currently not licensed as a combination vaccine in the United States, (9) while short term quantities of vaccine are adequate for nationwide use, continued availability must still be insured, and (10) there is a limited experience with e-IPV in the United States. On the pros side (1) there have been no vaccine-associated cases, (2) no documentation of significant adverse events, (3) high rates of seroconversions (100%) following 3 doses, (4) immunity induced by IPV appears to be of long duration, (5) in other populations IPV use in 90% of the population appears to have provided a herd protection against wild type polio and e-IPV is expected to do at least as well, and (6) IPV could be combined with DTP or DTaP to overcome issues of additional injections and additional visits to accomplish the immunization schedule.

Additional consideration for the IPV-only option were discussed including the issue of mucosal immunity and secondary spread being less relevant now due to polio elimination in the western hemisphere and substantial progress toward global eradication. Other considerations of the IPV-only option are the perceived "no risk" option for individual persons, the increasing body of experience from countries that have implemented this policy (e.g., France, Canada), the possible adverse impacts on the global eradication effort, parental and provider acceptance of the required 3 - 4 injections per visit, the possible potential decrease in vaccination coverage, limited availability of data on interference of IPV with other vaccines administered at 2 and 4 months of age (e.g., DTP, Hib, hepatitis B), limited safety data on rare neurological events (e.g., frequency in the range of 1:500,000 - 1,000,000 doses), and the possible discontinuation of OPV production and non-availability for epidemic control when preferred in that setting.

The pros and cons of the third option, sequential use of IPV and OPV were then presented. The cons are considered to be (1) the likelihood that some vaccine-associated cases, particularly in contacts, will continue to occur; (2) the increased number of required doses of childhood vaccines potentially resulting in a higher cost until combination vaccines are available; (3) the feasibility of delivering the combined vaccine schedule is uncertain; (4) less experience and data are available on which to base the recommendation for a sequential schedule; (5) uncertainty regarding the complexities of implementation, and (6) the vaccination of contacts without their knowledge and consent with regard to the OPV dose. Pros are considered to be (1) elimination of vaccine-associated cases in recipients; (2) decreases of vaccine-associated disease in susceptible contacts by reducing spread of virus and providing e-IPV for contacts; (3) the provision of indirect immunization of some susceptible contacts by possibly inducing secondary antibody response in some nonsusceptible contacts through excretion of the OPV virus; (4) provision of long duration humoral, intestinal and pharyngeal immunity; (5) the possibility of interruption of the spread of wild virus; (6) high degree of herd immunity; (7) the opportunity to gain experience with e-IPV while still capitalizing on the benefits of OPV, and (8) still allows OPV to be available for use in epidemic control.

Additional considerations for a sequential schedule presented to the Committee were reversion of OPV virus when OPV is given after 1 or 2 doses of IPV, the labeling of vaccines for use in the sequential schedule needs clarification, unknown immunogenicity of the sequential schedule, optimal schedule still needs to be determined, the possibility of increase in susceptibility due to less secondary spread of OPV virus, and the programmatic issues of additional injections.

The pros of Option 4, no stated preference in recommendation (parental choice) were expanding the range of available choices to the informed individual and three doses of either OPV or IPV are acceptable for school entry in almost every state and provide high levels of immunity. The cons of Option 4 were the highly technical issues and potential difficulty for the general public to comprehend the advantages and disadvantages of OPV and IPV for the individual and the community when the decision of choice is left entirely up to the provider and recipient, combination vaccines are not licensed in the United States, the uncertainty of OPV and IPV demands, it may be difficult to predict a necessary supply, tracking of immunization status may be difficult because of possible mixture of the vaccines used and mobility of the U.S. population, herd immunity may decrease if vaccine coverage drops because of implementation difficulties, predominant use of IPV could possibly allow transmission of wild virus if introduced, costs of the program would be uncertain, and the issue of who would be responsible for contact cases if OPV is chosen by the consumer. Additional considerations included the shifting of the responsibility from the society to the individual parent, predominant selection of IPV possibly leading to nonavailability of OPV for epidemic control, and programmatic issues which would require further discussion such as stocking of multiple vaccines, wastage, and informed consent.

After presenting the pros and cons of the various options being considered regarding polio vaccine policy, Dr. Sutter summarized the IOM workshop which took place on June 7 - 8, 1995 in Washington, DC, particularly the presentation of Dr. Samuel Katz, who provided the concluding remarks in the workshop.

During the IOM workshop, Dr. Katz stated that a change in polio vaccination policy is warranted, the continued exclusive reliance on OPV was unacceptable, a no vaccine option was also unacceptable, and it may be too early to implement an IPV-only option and lose the advantages of OPV. He believed the sequential IPV-OPV option would offer the best balance of risks and benefits. Dr. Katz sent a clear message to FDA to give priority to licensure of combination products to make them available as quickly as possible. Factors which contributed to the conclusions presented at the IOM workshop include: vaccine-associated polio is the only form of paralytic polio detected in the U.S. since 1979, elimination of polio in the western hemisphere greatly decreased the risk of wild poliovirus importation in the U.S., IPV is a safer alternative to OPV and consumer awareness has created a desire for informed decision making. The WHO expressed concerns and cited obstacles to changing current policy which include the potential for rising levels of susceptibility, programmatic considerations, ethical considerations, and supply and cost implications. Each option was discussed at the IOM workshop and the concerns regarding each option mirrored those presented earlier by Dr. Sutter. Conclusions from the IOM workshop were that policy change appears to be warranted and a deliberate approach is desirable. Policy change in Canada occurred because of the availability of a combination vaccine (DTP-IPV-Hib) and the change was determined to be cost-neutral. Finally, the effect on the global eradication program should be minimized and any change in policy in the United States should not impede or delay global eradication efforts.

Following Dr. Sutter's presentation, Dr. Katz noted the workshop attendees were very moved by the statements of parents and of persons with vaccine-associated paralytic polio. Regarding consideration of the sequential dose option, the manufacturers will be looking to ACIP for leadership in the development of schedules and dosing information. Unless ACIP makes a very firm recommendation the manufacturers will not invest in developing the necessary vaccines.

Regarding global eradication, a Committee member asked which countries would possibly switch, following the example of the United States, and discontinue using an OPV only schedule. Dr. Sutter could not specifically answer; however, he believed the concern was in sending the wrong message to polio-endemic countries. Further discussion among Committee members suggested that perhaps the following two concerns were unfounded: that the United States policy will influence what is done globally and the fear that a decision to move from a predominantly OPV only policy in the United States would effect global eradication.

Dr. Sutter then presented data from two studies related to the secondary spread of OPV virus, which was also a topic of concern among the IOM workshop participants. Data and studies related to secondary spread are limited. Secondary spread of OPV virus occurs frequently in families and somewhat less frequently in communities. Therefore, it can be concluded that secondary spread will induce immunity in some susceptible contacts, it will boost humoral antibody in some nonsusceptible contacts, and may reinforce mucosal immunity which is generally believed to be short lived.

Dr. Sutter then discussed the risk of poliovirus importation into the United States and presented information regarding risk factors for potential importation. Arrival data into the United States

was examined regarding the possible entry of persons arriving from areas still considered to be polio endemic. A summary of these data led the workshop participants to conclude the risk is clearly very low and should be even lower with the dramatic drop in the polio cases worldwide. However, for every one paralytic case there are probably 200 - 1000 infections and it is unknown how many inapparent infections are imported into the United States each year.

A Committee member asked if data related to exposure risk was available regarding the age of persons traveling in and out of the country. Dr. Sutter stated the data for immigrants would be available, but data for U.S. travelers to polio endemic areas may not be because these data are obtained from the Department of Commerce and are not broken down by age. With regard to immigrants, usually those traveling are middle to upper class and better vaccinated as compared to someone of lower income from the same country. Another committee member suggested that ensuring immigrant immunization would have a great potential impact on the risk associated with poliovirus importation.

Dr. Gindler discussed the impact of integration of IPV vaccination into the recommended childhood immunization schedule. Issues to be considered when developing IPV containing schedules include the total number of injections that need to be given for the particular immunization series, the number of injections at each visit, the number of visits required to complete the series, availability of combination vaccine products, and the anticipated licensure of DTaP for infants which will result in another injection until combination products become available.

Dr. Mark Miller presented information regarding cost effectiveness considerations of IPV using the Prevention Effectiveness Model depicting incorporation of IPV into the immunization schedule as a 4 dose IPV schedule and also with the sequential 2+2 schedule. Assumptions of the model included: no wild-type poliomyelitis infections with either vaccine, annual doses administered were based on the 1991 National Health Interview Survey, vaccine cost based on current public and private sector catalogue prices with volume discounts applied, VAPP compensation based on awarded settlements, and all costs and benefits discounted by 3%. The model assumed that IPV could be administered as a combined product with other injectable vaccines however, the current formulation of IPV requires an additional injection and there is the possibility of additional visits to accomplish immunization and reluctance of the provider to administer or client to receive an additional injection. Conclusions were for the base case, at proposed prices it would cost $30.3 million more annually to use an IPV only program and $16.1 million more annually to use a sequential schedule program. It would cost $2.4 million/VAPP case prevented with an IPV only program and $2.6 million/VAPP case prevented for a sequential schedule. The price of IPV is a sensitive issue with the break even price for IPV at $6.85 assuming a combines vaccine product which would require no additional visits. However, even if IPV were to cost the same as OPV, if an additional visit were required the cost of the additional visits would outweigh the benefit of the VAPP prevented.

Dr. Mark Grabowsky discussed the integration of IPV into the recommended childhood immunization schedule. Information presented included the total number of injections (using all

OPV, 9-13 injections are needed through age 18 months depending upon whether DTP-Hib is used and 11-16 injections needed if IPV is added) the number of injections required at each visit, the number of visits required to complete the series, the availability of combination vaccine products, and the anticipated licensure of DTaP for infants. Dr. Grabowsky presented prospective schedules and contrasted them with the existing schedules. In the first 2 years of life the AAP recommends 10 well child visits and the AAFP recommends 6. Compliance with the number of recommended well child visits is poor, particularly among inner city minority populations. Data from surveys of providers and parents reflecting the attitudes regarding the acceptability of multiple injections suggest that one third of family physicians and one third of pediatricians would not give 4 vaccines simultaneously (including OPV), 60% of pediatricians and family physicians were concerned about giving 3 injections and 80% were concerned about giving 4 injections. Reasons cited were parental acceptance, vaccine efficacy, side effects, immune response, cost, and pain. Sixty-four percent of parents preferred 1 visit for 3 injections and 58% preferred 1 visit for 4 injections. An interesting finding regarding the accuracy of nurse assessment of immunization status was when a computer determination of immunization status was contrasted with information charted by the nurses, nurse assessment was found to be accurate only 27% of the time. Conclusions from those data were the addition of IPV adds extra injections to the schedule; incorporating sequential IPV-OPV vaccination into the current schedule requires 3 injections at 2 months, or an additional visit at 1 month for the 2nd dose of Hep B (if DTP-Hib is used); the use of IPV alone would require splitting the 12 - 15 month doses into 2 visits to avoid 5 injections at one visit; and when DTaP is licensed for use in infants an additional injection will be required until DTaP-Hib other combination vaccines become available.

Dr. Spann, representing the American Academy of Family Physicians, spoke on the acceptability of third and fourth injections and parental choices. During the past three years the AAFP has invested much effort in prevention, specifically on age appropriate immunization. The AAFP advocates the continuation of the current OPV schedule until a cost effective vaccine with IPV becomes available. Factored into this position were concerns about the increased number of injections required by adding IPV (IPV-only or sequential IPV-OPV), potential decrease in compliance, and subsequent or consequent decrease in herd immunity against polio and other vaccine preventable diseases as well. Given the reality of infant and health care needs which compete for finite health care resources, cost effectiveness must remain an issue. Also, some managed health care plans which cover a significant number of people are limiting specific vaccine reimbursement forcing physicians to pay associated costs of additional and more expensive vaccines out of preexisting capitation payments or to pass the costs along to their patients. A change in polio immunization, which could be more costly, could lead to a decrease in compliance with the recommended schedule. In conclusion the AAFP advocates continuation of the current schedule until such time as a cost-effective combined injectable vaccine containing IPV becomes available in the United States.

Presentations were made from the manufacturers perspective, Dr.Carleton Meschevitz, Connaught discussed availability of IPV, cost, and supply issues. Connaught currently has the license for 2 injectable inactivated polio vaccine, IPOL and Poliovax, and application for

licensure of an oral polio vaccine product. Data was presented from a randomized control trial on immunogenicity comparing the IPV from Connaught Labs in Canada, the IPV from Pasteur-Merieux in France, and the Lederle OPV. Immunizations were given at 2, 4, and 18 months of age and serology tests obtained at 2,4,6, 18 and 20 months; the study population included over 1000 infants. The data confirms immunogenicity of all the vaccines. At 6 months after the second dose, each vaccine produced a neutralizing antibody seroconversion in greater than 90% of individuals. Relative to safety, the authors concluded DTP with IPV does not increase the rate of either local or systemic reactions compared to DTP and OPV. Regarding future combination vaccines, Connaught intends by year end to file data for the two products currently under trial, Biken acellular pertussis and Biken DTaP with PRPT. Current work with Merck is underway for multi-component vaccines that contain IPV, estimated date of completion of trials and anticipated application will be in 1998. Regarding supply, discussions have taken place with CDC staff and it is anticipated that supply needs for IPV can be met within the time frame necessary to conclude the contracts and implement the change. The current price with quantity discounts and promotional activities would allow for a private sector price of $11.55 per dose and a public sector price of $4.99 per dose.

Dr. Peter Paradiso, representing Wyeth-Lederle, discussed data on simultaneous vaccination. He expressed concerns about the IPV-OPV schedule in terms of lack of available data, implementation of an IPV schedule, schedules, and possible impact on the global eradication program. Wyeth-Lederle is producing an acellular pertussis vaccine for which review and submission should be complete by year end. Combinations containing acellular pertussis and Hib will follow shortly. Work has been underway for the past 2 years on an IPV product and testing of the product demonstrates an immunogenicity profile equivalent to that for enhanced IPV currently made and sold in the United States. Regarding labeling of Orimune, difficulties due to lack of a sufficient database present problems in accommodating a combined schedule with IPV. From Wyeth's perspective the IPV alone or the OPV alone are the regimens for which there are sufficient data required for decision making while the combined schedule needs considerably more work.

Barbara Howe, Smith-Kline Beecham, discussed timetables for the development of combination vaccines. Smith-Kline has an enhanced inactivated polio vaccine manufactured by Smith-Kline Beecham Biologicals. In 1989 safety studies commenced in adults followed by immunogenicity studies in infants. Due to the advent of combination vaccines it is not anticipated this will be developed as a stand-alone project. Smith-Kline Beecham has 3 DTaP vaccines with several combinations with one additional antigen, either hepatitis B, Hib, or IPV under clinical development. Development of combinations are in the early phases with clinical trials ongoing inside and outside of the U.S. The DTaP-hepB-IPV combination has not yet entered clinical trials but will shortly.

The last manufacturer presentation was from Amvax, the operations arm for North American Vaccine, also regarding the issue of timetables for development of combination vaccines. An acellular pertussis vaccine, sponsored by the NIAID in phase 1, phase 2, and phase 3 clinical trials in the United States and Sweden, is licensed exclusively to Amvax and formulated into a

DTaP vaccine with all components purified prior to detoxification and is a triple toxoid. Amvax believes because of its purity, it is important in the future combination with other vaccines. In trials the vaccine was well tolerated, immunogenic and effective with no serious vaccine related adverse reactions. The DTaP was then used to start formulation studies in preclinical and clinical for combination vaccines. Combinations employ both DTaP-IPV and DTaP-IPV-Hib. Clinical studies have shown the DTaP-IPV combination vaccine to be well tolerated and immunogenic with no serious vaccine related reactions. Other findings included high antibody levels to all six vaccine antigens and no apparent immunological interference.

A Committee member asked about the status of bridging studies with DTaP alone and DTaP-IVP in the United States. Amvax reports they have done both safety and immunogenicity studies with DTaP in the United States using the same vaccine lots used in their Sweden study. Amvax plans to start DTaP clinical trials in the United States next year and has made application for the DTaP licensure this year.

Following the presentations from the manufacturers the meeting was adjourned for the day to recommence at 8:15 a.m. on June 29, 1995. An announcement was made that the pneumococcal working group would be meeting at 7:00 a.m. in the cafeteria on June 29.

The second day of the Advisory Committee on Immunization Practices meeting convened June 29, 1995 at 8:30 a.m. The discussion continued on polio with Dr. Hadler reviewing the options which had been outlined previously. The options were:

Option 1 - No change in policy from reliance on OPV
Option 2 - ACIP should adopt "Intent to Change Policy" and develop a proposed timetable for the policy change with appropriate lead time (3 - 6 + months) for each step and contingencies as needed.
Option 3 - Change to provider/parent choice as soon as feasible
Option 4 - Change to an IPV based schedule as soon as feasible

Consideration of the potential impact on global elimination, the need for more data on the safety and effectiveness of a sequential schedule and of IPV alone, and the factoring-in of combination vaccines and DTaP with potential impact on selection of options are considerations and concerns common to discussion of all options. Regarding Option 1, an effort to address those who believe parent choice needs to be strengthened now could be to reaffirm that OPV is the option of choice, but parents and physicians should be informed of the availability of each of several options.

In Option 2, developing a timetable for an "Intent to Change" policy with contingencies, the plan should address: when to implement changes, what the changes will be (the possibility of parental/provider choice versus a sequential OPV-IPV or IPV alone), the sequence of changes to be made, availability of sufficient quantities of vaccine, availability of combination vaccines, data needed to make each change, and the contingencies, data, and research needed to implement

the change. Considerations of cost, global eradication and global polio trends need to also be addressed if this option is selected. An advantage of option 2 is that it does allow for manufacturers to anticipate the change and prepare. This could be accomplished by strengthening the parent/provider choice option in 1996, and assuring availability of IPV and supplies of appropriate materials available to educate parents and providers. Subsequently in 1997 a recommendation could be made for a primary reliance on a sequential schedule contingent upon Committee satisfaction of the response to IPV-OPV and that it can be integrated into the harmonized schedule with possible clarification of the situation regarding DTaP and combination vaccines. In the third year a move to IPV only could be considered contingent upon the development and availability of a combination vaccine.

Option 3, a change to provider/parent choice as soon as feasible, would require: an adequate supply of IPV as demand increases, assurance that a policy to administer OPV only remained an acceptable standard of practice, revision of the vaccine information sheet, development of appropriate educational material on risks and benefits and some schedule options, a decision to provide choice of the sequential schedule as an accepted option, research and data to aid implementation, practical implementation at a clinical level, acceptability to providers, staff, and parents, consideration of the impact on programs and the length of time needed to inform and obtain consent, stocking of sufficient quantities of each vaccine, and assessment of the impact on vaccine wastage.

Option 4 was divided into two possibilities. One to change to a sequential schedule as soon as feasible with consideration of negotiating a federal contract and adequate supplies and with consideration of adequate data to recommend this option which includes determination of an appropriate regimen, data on simultaneous immunization with the remainder of the schedule, safety, and vaccine labeling. The acceptability to parents and providers of additional injections necessary to initiate this option, acceptability of the number of injections scheduled per visit, additional visits needed, and if multiple injections are not acceptable how to prioritize vaccines for administration at the earliest age are difficult issues that would need to be addressed by the Committee. The potential impact of DTaP licensure for use in infants on Option 4 would also need to be addressed.

The options as framed were then brought before the Committee for further discussion. A Committee member expressed that there will likely be confusion regarding the options because any change will be immediate and the question of what happens in the interim will become the greater issue. A Committee member stated that Option 1 would need to be addressed before it would be appropriate to consider other options, does the Committee want to change from it's current recommendation, change or no change?

A suggestion was made to vote on Option 1 to ascertain whether further deliberation on the other options would be necessary. The Committee was asked for any further discussion prior to voting on Option 1. The Committee voted agreeing that change was needed and further discussion of the other options commenced.

Regarding Option 2, a Committee member suggested not setting a specific date because of variables, particularly on the implementation side. With "Intent to Change", an option could be provided acknowledging three relatively equivalent options, OPV only, IPV only or a combination. In other recommendations relatively equivalent options have been stated without stating that one is absolutely preferred and this approach may make sense until the Committee is in a position to recommend IPV only as a preferred choice. Another suggestion from a Committee member was to clearly state why the change is being made and make a decision now regarding further direction of the recommendation. This was echoed by another Committee member who added that providers and public health agencies may become confused when confronted with options. Also, purchasing decisions by health departments and others need to be made. A Committee member pointed out the impracticality of not issuing a specific date for change as none of the options considered could possibly be immediately implemented, with possible the exception of parent/provider choice. Another member noted that once the decision is made to provide "intent" then you have to give choice for a licensed IPV vaccine. The issue of liability was raised in discussion and it was stated that the program views this as not affecting practitioner or manufacturer and the products are covered by the National Vaccine Injury Compensation Program with the only possible issue being the labeling aspects. Elimination of VAPP as a motivator for changes in the recommendation should weigh heavily in the decision and the direction of the change. Interim measures should be geared toward this eventual goal and issues to be resolved should be clearly identified. A provider from the public health sector presented the public health program perspective noting choice and flexibility may result in confusion and more time is needed to prepare.

Following Committee discussion a motion was made and seconded. Those with potential conflicts of interest with Wyeth, Lederle and Connaught were asked to abstain. The issue to be voted on was:

> The ACIP recommends a sequential dose schedule of polio vaccines of 2 doses of IPV followed by 2 doses of OPV with the intent of moving toward an IPV only schedule and a preference for the use of combination antigens to reduce the number of injections.

The motion carried with 3 in favor (Davis, Guerra, DeBuono); 2 opposed (Schoenbaum, Ward); 4 abstentions (Jackson, Halsey, Edwards, Griffin); and 1 absentee (Thompson).

Following the vote the Committee attempted to address issues of concern for those members not in favor of the proposed recommendation. Those concerns included failure to address VAPP issues directly in the language, unresolved issues of multiple injections and increased cost, time frame issues, and number of doses given in each sequence. Issues of implementation need to be considered which include consideration of the preparation of educational materials, supply issues and a suggested date. A concern of many of the members was the necessity to alert the manufacturers by sending a clear message regarding the future direction of polio vaccination. A suggestion was made to form a working group to work on the issues of implementation and language of the polio vaccine recommendations. A proposal was made to suggest an implementation date and express that in the language as "not before" a particular stated date to

alleviate possible concerns that the ACIP expects this recommendation to be implemented immediately. Following Committee discussion it was summarized that the intent of the Committee was to make a change; however, many important issues remain to be addressed. Dr. Davis instructed that a working group on the short term issues to be addressed meet during the noon hour. Persons name to the working group were Dr. Schoenbaum, Dr. Griffin, Dr. Halsey, Dr. DeBuono, Dr. Ward, Dr. Davis, Dr. Hardegree, Dr. Zimmerman, and Dr. Fleming, a representative of Connaught and a representative of Wyeth-Lederle.

Vaccine Safety Update

An update on vaccine safety issues was presented by the Vaccine Safety and Development Activity (VSDA), NIP. Despite the large number of VAERS reports, when scientific experts examined these data, it was inconclusive as to whether the VAERS events were truly caused by the respective vaccines. There is a need for more research.

Dr. Phil Rhodes updated the Committee on the Large-Linked Data Base Project (LLDB). He reported the Large-Linked Data Base study is conducted in 4 HMO's. The second year tape from the study includes approximately 12-31 months of data on vaccines and outcomes from the 4 HMO's, about 676,000 children under 7 years of age. The eight vaccines of primary interest are DTP, Hib, OPV, MMR, hepatitis B, DT, DTaP, and influenza. VAE's are considered in 34 broad categories of outcomes. Automated data from hospitalizations, ER encounters and some clinical visits are screened. Routine chart reviews are conducted (approximately 1-2% of all charts) to validate vaccine exposure and case status. Specific chart reviews are conducted during specific studies on outcomes such as seizures. Other sources of information come from pharmacy and lab files, medical procedure files, and birth certificate records. One goal of the study is determining the extent to which the vaccine adverse event associations can be studied using only automated data. Combinations of vaccines are currently being evaluated, including MMR.

A Committee member asked if there were any data available on anaphylactic reactions and Dr. Rhodes responded that there are very few such instances in the data set and it is included in a category called allergic reactions.

Dr. Steve Rosenthal discussed the post-marketing surveillance data on the safety of DTaP and DTP for 4th and 5th doses, and summarized the experience of adverse event reporting after pertussis vaccination since licensure of DTaP in December, 1991. From 1991 - 1993 approximately 27 million doses of DTP and 5 million doses of DTaP were administered to children 15 months to 7 years of age, respectively. The rate of adverse events reporting in this age group for each of the outcomes after DTaP were 1/3 and 1/4 those occurring after DTP. Compared to 1991, the reporting to VAERS of all adverse events after any pertussis vaccine dropped significantly in 1993. Data are being analyzed from other ongoing studies examining specific outcomes by age group. The results confirm that minor adverse events are less frequent following administration of DTaP vaccine. Rare serious adverse events associated with pertussis vaccination also seen to be less frequent following administration of DTaP in age groups for

whom it is recommended. Confirmation of these findings will require controlled studies; however, whether the current recommendation language that DTaP may be preferred for the 4th and 5th dose should be strengthened could be accomplished by replacing the "may be preferred" with "is preferred" or "is recommended". The Committee agreed to defer decision until results of the NIAID trials are available.

Information related to measles vaccination as a risk factor in inflammatory bowel disease was mailed to Committee members.

Adolescent Immunization Visit

The status of the current version of the draft ACIP document on adolescent immunization was reviewed by the Committee. Additions and language revisions to several sections of the revised draft were noted including establishing an immunization visit for all adolescents age 11 - 12 years to assess vaccine needs and administer indicated vaccines including hepatitis B vaccine, MMR 2nd dose, varicella vaccine, a tetanus-diphtheria booster, and immunizing those with indications for influenza vaccine, pneumococcal vaccine, and hepatitis A vaccine. In addition the statement encourages simultaneous administration of indicated vaccines, documentation of prior vaccination, state immunization requirements, and the provision of other preventive services. Current related activities include review for joint publication by the AAP, AAFT, NMA, and the AMA, seeking national endorsement for adolescent immunization, and the inclusion of questions on adolescent immunizations in the National Health Interview Survey. Publication of this document is pending concurrence of the Committee with the suggestion that the Committee provide final comments soon to facilitate timely publication and allow distribution of a final draft to those organizations seeking joint publication.

A Committee member pointed out it may be worthy to seek input from the Immigration and Naturalization Service. Dr. Davis asked that comments be made by July 21, 1995.

Pneumococcal Polysaccharide Vaccine

Dr. Schoenbaum presented the Committee with issues considered when formulating the draft of the revised pneumococcal recommendation. They include: the rationale for the vaccine itself, more clear documentation of vaccine efficacy and cost effectiveness and whether issues related to bacteremia and invasive disease can be separated from issues of pneumonia, drug resistant Streptococcus pneumoniae, increased risk of disease in day care centers, and issues concerning earlier vaccination and revaccination. Data were presented to the Committee on efficacy, cost effectiveness, DRSP, and revaccination. A plan for measurement of performance/evaluating the effectiveness of recommendations will be undertaken and reported to the Committee. It is anticipated that a recommendation can be brought to the full ACIP by early October.

Programmatic Strategies to Increase Immunization Coverage: Practice Assessment, Reminder and Recall

Dr. Maes explained that his group would like to ask ACIP to review strategies to increase immunization levels and draft a statement. Reminder and recall, a message to a parent or guardian before a visit is due (reminder) or after the visit is missed (recall). The evaluation of effective ways to accomplish reminder and recall, the type of message, when the message should be delivered, and how many times to deliver the messages have been considered. Information from several studies depicting various approaches was presented all showing reminder and recall to be an effective means to increase rates of immunization. Additional information related to cost effectiveness is forthcoming.

Following Committee discussion, Dr. Davis asked if enough information was currently available to necessitate formation of a working group. Dr. Maes indicated the data does exist and is ready for consideration.

Harmonization of Immunization Recommendations

Following the lunch break, Dr. Jacqueline Gindler, NIP, presented information regarding immunization recommendations. Updates included the need to develop an interim version of the schedule (titled, "Recommended age for Administration of Currently Licensed Childhood Vaccine - July 1995"), reflecting recommendations for varicella and adolescent hepatitis B vaccination pending official publication in January 1996, timetable for the publication of the January 1996 schedule, and a review of the parent version and issues related to the accelerated schedule. A clarification of the hepatitis B footnote was published in the MMWR after publication of the January schedule because of confusion in the wording related to a dosage volume which could have potentially resulted in children born of hepatitis B surface antigen positive mothers receiving an inadequate dose. In the last ACIP meeting it had been agreed that the schedule would be published once a year; however, changes in recommendations since that time may require consideration of the distribution of a schedule prior to that time reflecting these changes. Agreement on the revisions incorporating the changes is sought from ACIP, AAP and AAFP to allow a timely distribution of the updates.

Committee consensus was that publishing a schedule reflecting the changes could be postponed until January 1996 and could be formatted to highlight the changes that have taken place. It was suggested that it could be further enhanced by the inclusion of language from the adolescent statement as appropriate and consideration could be given to minor revisions in language. A suggestion was made to educate nurses on current immunization practices and the correct application of the current immunization schedule as a way to reduce the potential for missed opportunities and increase immunization levels. A conference call will be held this summer among the working group to review issues related to footnotes and to develop a schedule for accelerated immunization of children who are not up-to-date, for approval at the October ACIP meeting and publication in January 1996.

National Vaccine Program Update

Dr. Breiman, acting director, National Vaccine Program Office (NVPO), stated that as a result of reorganization and of government at the HHS level, the location of the NVPO has been shifted to CDC; however, the director will still report to the Assistant Secretary of Health, Dr. Phil Lee. The purpose of the NVP is to provide coordination and direction for a wide range of immunization activities including vaccine research and development, safety and efficacy, testing of vaccines, licensing of vaccine manufacturers and vaccines, production, procurement, and the distribution of vaccines and to fund federal agencies where gaps exist in research in these areas. NVPO also provides support to the National Vaccine Advisory Committee (NVAC) and opportunities for a symbiotic relationship with ACIP; developing this relationship should be explored.

Return to Polio Discussion

Dr. DeBuono motioned to rescind the resolution formally voted on regarding specifying a sequential schedule prior to the ultimate use of an IPV only schedule. The motion was seconded and then carried with 4 in favor (Davis, Ward, Schoenbaum, DeBuono), none opposed; 1 abstention (Halsey), and 5 absentee (Edwards, Griffin, Guerra, Jackson,Thompson).

Following the vote Dr. Davis read the following statement formulated by the working group:

> Dramatic progress toward global eradication of poliomyelitis through the use of oral polio vaccine (OPV) has led to the elimination of this disease in the western hemisphere and has greatly decreased the incidence of polio worldwide. There has been no circulation of wild-type polio in the United States since 1979. However, OPV rarely can cause paralytic disease; there are 8 - 10 cases of vaccine-associated poliomyelitis (VAPP) each year in the United States.
>
> To decrease the occurrence of VAPP in the United States, the ACIP is currently developing a new polio vaccination policy that will include a greatly enhanced role for inactivated polio vaccine (IPV). An ACIP working group has been formed to explore policy options and to develop a proposed plan for implementation which will be presented to the entire committee at its October meeting. Combination vaccines that include IPV will enhance implementation by minimizing the number of injections needed. Until a new policy is developed and implemented, the ACIP reaffirms its current polio vaccination policy of primary reliance on OPV.

The proposed statement was then discussed the Committee and the consensus was that it was acceptable. A proposal was made to include public education, availability of alternative vaccine, and the development of a schedule allowing the increased use of IPV as concerns to be further discussed prior to making any change in the current recommendation. With further clarification of those issues it is anticipated that the proposal will again come before the full Committee at

the October ACIP meeting. Committee discussion explored an amendment to delete the last five words of the proposal. The revised statement is as follows:

> Dramatic progress toward global eradication of poliomyelitis through the use of oral polio vaccine (OPV) has led to the elimination of this disease in the western hemisphere and has greatly decreased the incidence of polio worldwide. There has been no circulation of wild-type polio in the United States since 1979. However, OPV rarely can cause paralytic disease; there are 8 - 10 cases of vaccine-associated poliomyelitis (VAPP) each year in the United States.
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> To decrease the occurrence of VAPP in the United States, the ACIP is currently developing a new polio vaccination policy that will include a greatly enhanced role for inactivated polio vaccine (IPV). An ACIP working group has been formed to explore policy options and to develop a proposed plan for implementation which will be presented to the entire committee at its October meeting. Combination vaccines that include IPV will enhance implementation by minimizing the number of injections needed. Until a new policy is developed and implemented, the ACIP reaffirms its current polio vaccination policy.

A motion was made to vote on the revised proposal and this was seconded. The motion carried with 4 in favor (Davis, Schoenbaum, DeBuono, Ward); none opposed; 1 abstention (Halsey); and 5 absent.

Injury Compensation Program Update

Dr. Evans updated the Committee on the status of the National Vaccine Injury Compensation Program. Currently the program has a total of 4800 claims, 15% of the claims involve vaccines given after October 1, 1988 and 145 of these being received this fiscal year. Fiscal 1995 reflects an increase possibly attributable to finalization of changes to the vaccine injury table which caused people to file claims prior to implementation of the revised table. Approximately half of the claims filed have been adjudicated with the awards totaling over $550 million overall, with $850 million in reserves in the Compensation Trust Fund. Changes are being proposed in the vaccine excise tax, which is creating an over funding of the trust fund with a proposal of moving to a .50 per antigen cost. Legal issues currently include a suit filed in Boston against the Secretary which alleges the Secretary has exceeded her authority by revising definitions in the aids to interpretation section of the vaccine injury table as well as adopting the final rule without properly consulting the Advisory Commission on Childhood Vaccines, and by giving retroactive application to this rule. This should be heard in court in the fall and the final outcome will be reported to the Committee. Work is in progress on the vaccine injury table which includes changes in the conditions and adding new vaccines. Other activities of the program include working with public health agencies developing vaccine safety information and the coordination link ups with the VAERS program, and with the large-linked database (LLDB).

Dr. Robert Chen, NIP, made an important point regarding the lack of adequate funding in the areas of vaccine safety and suggested the vaccine excise tax should set aside $0.05 per antigen to increase work done in this area.

ACIP Recommendations and Package Inserts

Dr. Hadler stated that a table of differences between vaccine package inserts and ACIP recommendations was presented to the Committee. These were also to be sent to the manufacturers for review and comment; however, due to time constraints this has not occurred, but will during the coming summer. The FDA sent a letter in early May to the manufacturers with their list asking them to review package inserts and address differences that have been identified with ACIP recommendations, review their labeling, and determine whether data is available to support a change in labeling and return their comments to the FDA. Responses of both FDA and CDC requests should be available for the next meeting.

Public Comment

Dr. Davis then opened the meeting for public comment. There were none present who indicated they wished to make public comment.

Dr. Davis thanked the Committee and others present for their participation and adjourned the meeting at 3:30 p.m.

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

Jeffrey P. Davis, M.D.
Chairman, Advisory Committee on Immunization Practices

DATE: March 7, 1996